Fluid Dynamics in Applied Physiology: Instrumentation and Validation of a Venturi Airflow Sensor for Expired Gas Analysis Indirect Calorimetry

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Praneel Titheradge

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School of Exercise Science, Sport & Health

Faculty of Science
Charles Sturt University
Bathurst NSW 2795
Australia
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Declaration of Authorship

I, Praneel Titheradge, hereby declare that this submission is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which to substantial extent has been accepted for the award of any other degree or diploma at Charles Sturt University or other educational institution, except where due acknowledgement is made in the thesis “Fluid Dynamics in Applied Physiology: Instrumentation and Validation of a Venturi Airflow Sensor for Expired Gas Analysis Indirect Calorimetry”. Any contribution made to the research by colleagues with whom I have worked at Charles Sturt University or elsewhere during my candidature is fully acknowledged. I agree that this thesis be accessible for the purpose of study and research in accordance with the normal conditions established by the Executive Director, Library Services or nominee, for the care, loan and reproduction of theses.

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Publications


Conference Presentations

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List of Abbreviations

- fT → Turbine gas flow meter
- fV → Venturi Tube
- fP → Pneumotachograph
- Pa → Pascals (Unit of pressure)
- ID → Inside Diameter of a pipe (mm)
- V → Voltage unit
- VDC → Volts Direct Current
- volts:L → Ratio of volts per Litre
- Hz → Hertz (Frequency)
- s → Time (seconds)

\[ \dot{V} = A_1 \frac{2(P_1 - P_2)}{\rho \left( \frac{A_1}{A_2} \right)^2 - 1} \rightarrow \text{Theoretical Flow} \]

- \( \dot{V} \) → Volumetric Flow Rate (L·s⁻¹)
- \( A_1 \) → Area of original pipe diameter (m²)
- \( A_2 \) → Area of constricted pipe diameter (Throat section) (m²)
- \( (P_1 - P_2) \) → Differential pressure (Pa)
- \( \rho \) → Fluid density (kg·m⁻³)

\[ \left( \frac{\dot{V}_{\text{Theoretical}}}{\dot{V}_{\text{Actual}}} \right) = C_D \rightarrow \text{Discharge Coefficient} \]

- \( S_{YX} \) → standard error of the estimate
- r → correlation coefficient

- \( L_{\text{ATPS}} \) → Litres of air at Atmospheric Temperature Pressure Saturated conditions
- \( L_{\text{BTPS}} \) → Litres of air at Body Temperature Pressure Saturated conditions
- KE → Kinetic Energy
- PE → Potential Energy
- W → Work
- F → Force
- L → Distance or Length
- V → Volume
- P → Pressure
- m → Mass
- $g \rightarrow$ Gravity (9.81 m·s$^{-2}$)
- $Z \rightarrow$ Height
- $C \rightarrow$ Velocity
- $hp + y \rightarrow$ pressure head
- $L\cdot s^{-1}$
- $L \rightarrow$ Litre
- $L\cdot \text{min}^{-1} \rightarrow$ Volume per minute
- $ml\cdot kg^{-1}\cdot \text{min}^{-2} \rightarrow$ volume relative to body weight per minute
- $P_1 - P_2 \rightarrow$ differential pressure
- $\dot{V}O_2 \rightarrow$ Rate of oxygen consumption
- $\dot{V}CO_2 \rightarrow$ Rate of carbon dioxide production
- $\dot{V}O_2\text{max} \rightarrow$ Maximal rate of oxygen consumption
- $\dot{V}O_2\text{peak} \rightarrow$ Peak rate of oxygen consumption
- $VT \rightarrow$ Ventilation Threshold
- $\text{RER} \rightarrow$ Respiratory Exchange Ratio
- $\text{EGAIC} \rightarrow$ Expired Gas Analysis Indirect Calorimetry
- $\dot{V}_A \rightarrow$ volume of alveolar ventilation per minute
- $\dot{V}_A/\dot{Q} \rightarrow$ Ventilation/perfusion ratio
- $\text{UL} \rightarrow$ Upper limit of agreement
- $\text{LL} \rightarrow$ Lower limit of agreement
- $VT \rightarrow$ Tidal Volume

- $Re = \frac{\rho v D_H}{\mu} = \frac{v D_H}{v_A} = \frac{\dot{V}D_H}{v A} \rightarrow$ Reynolds Number

- $D_H \rightarrow$ Hydraulic diameter of the pipe, where $D_H = \frac{4(\pi D^2/4)}{\pi D} = D, L, (m)$
- $\dot{V} \rightarrow$ Volumetric flow rate (m$^3$·s)
- $A \rightarrow$ Pipe cross-sectional area (m$^2$)
- $v \rightarrow$ Mean velocity of the fluid (SI units: m·s)
- $\mu \rightarrow$ Dynamic viscosity of the fluid (Pa·s/m= kg/(m·s))
- $v \rightarrow$ Kinematic viscosity $(v = \frac{\mu}{\rho})$ (m$^2$·s)
- $V_D \rightarrow$ physiological dead-space
- $\dot{Q}_{PS} \rightarrow$ Physiological shunt of blood flow Litres per minute
- $\dot{Q}_T \rightarrow$ Measured cardiac output litres per minute
• \( C_iO_2 \rightarrow \) Oxygen concentration in arterial blood if \( V_A/\dot{Q} \) ratio is “ideal”
• \( CaO_2 \rightarrow \) Measured concentration of oxygen in arterial blood
• \( CvO_2 \rightarrow \) Measured concentration of oxygen in venous blood
• \( V_{dphys} \rightarrow \) Physiological dead space
• \( P_aCO_2 \rightarrow \) Partial pressure of carbon dioxide in arterial blood
• \( P_{eCO_2} \rightarrow \) Average partial pressure of carbon dioxide in the entire expired air
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Abstract

This thesis covers three studies that investigated the design, instrumentation, and application of a novel pulmonary ventilation measurement device, based on the Venturi effect, a fluid dynamic principle theorised in the 1700’s. The device is called a Venturi airflow sensor (fV), which uses a Venturi tube and differential pressure transducer that quantifies fluid flow based on the differential pressure that occurs between two sections of pipe that are of different diameters. This method of fluid flow measurement has never been validated for use in pulmonary ventilation applications. Collectively, the aim of this thesis was to provide a thorough investigation that would lead to acquisition of the scientific evidence needed to validate the application of fV technology to measurements of human pulmonary ventilation during exercise.

Study 1 looked at the instrumentation processes involved in designing a fV device suitable for human pulmonary ventilation conditions during exercise, that is, measurement of pulmonary ventilation with airflow rates between 0.1 L·s⁻¹ to 10 L·s⁻¹. Therefore, the main features that were focused on, were the effects of fV throat radius and differential pressure input/output specifications on measurement range and sensitivity. This was investigated via the application of the Bernoulli Principle for theoretical computations of airflow based on a fV configuration and transducer specification, which were then compared to actual measurements taken from a fV airflow sensor manufactured to the same specifications. The results indicate that the theoretical airflow measurements were in close agreement with actual airflow measurements. Thus, a technician can use this computational method to design a fV to suit their application.

Study 2 looked at components of airflow sensor performance, which included signal quality, response time and frequency response, and accuracy and reliability of volume measurements. The aim of this study was to see if the fV device had similar performance to two industry accepted criterion devices, the Turbine, and Pneumotachograph. Results indicate the fV device has close agreement with both criterions for their respective advantages. The findings conclude the fV device has adequate signal quality, dynamic response, and acceptable error in volume measurement following calibration, which allow for reliable measurements of pulmonary ventilation from rest to exercise conditions.

Study 3 looked at a clinical application of the fV device, where it was used to quantify pulmonary ventilation during expired gas analysis indirect calorimetry. The aim of the study was to compare differences in simultaneous pulmonary ventilation measurements between the fV and 2 criterion methods, during exercise to volitional exhaustion on a stationary cycle ergometer. Results indicate all three devices had close agreement, which had minimal effect on subsequent computations in indirect calorimetry, such as the rate of oxygen consumption. Additionally, this study is the first of its kind that shows in-vivo results for different types of airflow sensor method contribution to technical error in measurements within EGAIC.
Chapter One

Introduction
Fluid flow measurement in manufacturing and specific transportation vehicles (e.g. aircraft velocity) is based on application of the Venturi effect, named after Giovanni Battista Venturi (1746 – 1822), an Italian physicist who first discovered and reported this phenomenon in 1791 (Venturi, 1797). Venturi (1797) observed that when fluid flows through a larger to a smaller diameter pipe, there is an increase in fluid velocity and a decrease in fluid pressure. Fluid velocity must increase to maintain the principle of continuity, and fluid pressure must decrease based on the principle of conservation of mechanical energy. While Venturi (1797) documented this effect for fluid flow in pipes of different diameter, Daniel Bernoulli had reported the relationship between fluid velocity and pressure decades earlier in 1738 (Bernoulli, 1738). It was known at the time that an object exchanges its kinetic energy for potential energy, and Bernoulli (1738) reported that fluid, like objects, acts in a similar nature in that fluid exchanges its kinetic energy for fluid pressure. Thus, Venturi recognised and applied the Bernoulli principle to fluid flow through pipes of different diameter. Tubes or pipes that have different diameters are referred to as Venturi tubes (fV), and are used to quantify fluid flow by the measurement of the differential pressure that occurs between the two pipe diameters. Based on the Bernoulli principle, the pressure differential between the two pipe diameters is proportional to fluid flow.

The convergent angles of a fV, as well as the smoothness of internal pipe wall and diameter ratio ($\beta$), greatly affect the amount of friction encountered between the fluid and the fV wall during turbulent flow (LaNasa & Upp, 2014). There is ample literature investigating the ideal configurations for fluid measurement, with most agreeing a classical Venturi meter has configurations of a 21˚ convergent angle, 7˚ divergent angle and $\beta$ of 0.5 to 0.75 (LaNasa & Upp, 2014). These features allow for a coefficient ($C_D$) close to 1 for liquid-based fluids. It has been suggested however that these configurations, especially the convergent angle, are not ideal for gas flow measurement with a convergent angle of 10.5˚ providing much smoother data, that is, less variability or scatter of data during repeated gas flow measurements (Reader-Harris, Brunton, Gibson, Hodges, & Nicholson, 2001). The relevance of these findings to the development of the fV are unknown, as data presented by Reader-Harris et al., (2001), were for high-pressure gas measurement, and so the gas properties are substantially different to that of human pulmonary ventilation.

Despite the development and application of the fV in manufacturing and transportation, measurement of pulmonary ventilation using a fV has not occurred in human basic and applied physiology, such as for expired gas analysis indirect calorimetry (EGAIC). Continued reading and pilot testing of different fV configurations since unpublished findings, has further reinforced this interest.

A feasibility study was conducted (Titheradge & Robergs, 2018. In Press) that revealed similar performances in volume measurement between a criterion Turbine airflow sensor (fT) and a fV made of PVC piping and a commercial differential pressure transducer sensitive from 0-1000 Pa, with a certified calibration error of 0.38 % FS. Comparisons via group analysis during volumetric air flow measurements (Figure 1) referenced to a calibrated 3 L syringe, revealed the fV and fT attained a mean estimate of $2.972 \pm 0.02017$ L; Error = 0.9% Vs. $3.066 \pm 0.02211$ L; Error = 2.2 %, respectively.
Figure 1. Comparison of fV and fT 3 L volume measurements across different peak airflow conditions 1 – 9 L·s⁻¹. Each data point = average of 5 samples.

Furthermore, the data revealed that there is merit for the incorporation of fluid dynamics measurement into the measurement of airflow used in quantifying human ventilation. More specifically, the use of the Bernoulli Principle that underpins the fluid behaviour within an fV, has demonstrated its usefulness and potential in quantifying human ventilation as indicated by the mean estimate and acceptable error within Figure 1. The comparison to the fT that is made within Figure 1, further exemplifies the potential of the fV. The fT is one of the widely accepted criterions used within spirometry and EGAIC, for the purpose of quantifying pulmonary ventilation (Frayne et al., 1994; Howson, Khamnei, OConnor, & Robbins, 1987). Apart from fragility, and lack of responsiveness in high frequency breathing oscillation applications, the fT has very little complications from changes in gas composition that can affect other airflow sensor technologies, especially during anaesthesia (Ilsley, Hart, Withers, & Roberts, 1993). Thus, the fT requires simplistic calibration, which subsequently leads to ease of technician operation. Acknowledging the findings within Figure 1, that reveal the fV produced statistically similar volume measurements to the fT, whilst considering the criterion status of the fT, highlights the potential for the fV in human pulmonary ventilation.

A review of the scientific literature reveals that Venturi technology for measuring pulmonary ventilation is scarce. In regard to human applications, Venturi technology is commonly used as a mixing device of gaseous mixtures, such as administration of medications like anti-histamines and decongestants via nebuliser delivery (Flickinger, 1999), and oxygen therapy through the use of a Venturi mask (Campbell, 1960; Jones, 2004). Interestingly, the only past evidence of a fV used for pulmonary ventilation was seen in equine exercise stress testing (Seeherman & Morris, 1990). The fV was manufactured by a large scale, industrial venturi manufacturer (BIF, Akron, Ohio, USA), and used in an open-flow indirect calorimetry model, whereby the horse wore a loose-fitting facemask and continuous flow was created through a centrifugal exhaust. The researchers employed
this method to alleviate increased work of breathing that occurs for horses during a fully-sealed face-mask model. (Seeherman & Morris, 1990). The centrifugal volumetric flow rates seen within testing of these horses were between 10,000 and 14,000 L·min. Interestingly, equine minute ventilation was not reported, with only the rate of oxygen uptake ($\dot{V}O_2$) and the rate carbon dioxide production ($\dot{V}CO_2$) via 30 s averaging reported, which raises concerns as to how they managed to correct for the high frequency intermittent changes in gas composition, and the effects this would have on fV L·min estimation. Additionally, the study did not outline detailed methodology for volumetric airflow measurement, only that a calibration curve provided by the manufacturer was used. Furthermore, the study does not demonstrate any validation of the methodology by comparison to criterion references, that is, no validation of accurate airflow estimation under intermittent changes in gas composition, or gas sampling under high volumetric flow rates that may affect the expired gas mixing (Seeherman & Morris, 1990). An overview that discussed the various methods for quantifying gas volume and gas flow, provided a modest theoretical overview of the Venturi principle used as a fluid flow meter (West & Theron, 2015). Although they mention the Venturi is widely used, it remains unclear as to whether they are referring to the delivery of medications such as volatile anaesthetics, anti-histamines, decongestants and oxygen therapy, which refers to Venturi principle used as a mixing/pump device, and not a volumetric/mass fluid flow-rate sensor. Additionally, there was no mention of a fV device in the abstract, unlike every other airflow measurement technology described in the article (West & Theron, 2015).

In conclusion, although Venturi fluid dynamics are employed in certain respiratory care methods, empirical evidence does not exist for the validation of a fV to human pulmonary ventilation. However, there is past evidence of an fV used in equine science (Seeherman & Morris, 1990), although the validity of the methodology for its use remains inconclusive, due to the unaccounted changes in gas composition to Venturi air flow measurement, which highlights the need for further scientific scrutiny of the Venturi method."

Therefore, this thesis focuses on the investigation of validating fV technology for human ventilation measurement. This thesis presents a series of studies that provide evidence supporting the use of fV devices to accurately and reliably measure airflow and breath-by-breath tidal volume during rest and exercise for expired gas analysis research.

**Statement of the Problem**

Despite the theoretical utility of a fV to the measurement of pulmonary ventilation across the human physiological range, no empirical evidence exists to validate the utilisation of the fV for such applications. Evidence of fV use for pulmonary ventilation in equine science, provides some insight for potential use in human pulmonary ventilation. However, this evidence is lacking in validation, thus prompting thorough investigation. The Titheradge & Robergs (2018) findings in conjunction with the lacking validation evidence of pulmonary ventilation measured by fV, form the basis of the research studies presented in this thesis.
The fV device was limited by the design with multiple PVC connectors used as reducers that formed the convergent and divergent angles (see Figure 2) that likely caused excessive friction, which distorts differential pressure readings and can result in over-estimation of airflow. Minimal resistance to airflow as it travels through two pipe diameters is achieved through smooth transitions via conical convergent and divergent angles that connect each section of pipe. A suitable design for a fV device used in human ventilation measurements has not been evaluated.

**Figure 2. Illustrated diagram of fV and fT setup for data collection within the 2014 feasibility study.**

The fV data in figure 3 is higher than the fT data. This can be explained by the absence of airflow correction applied to the data as indicated by $C_D = 1$. Therefore, the fV data is considered theoretical, and does not account for frictional forces occurring between fluid and surface walls of the fV. Additionally, the fV voltage signal was converted to differential pressure, using a predetermined regression based on a manufacturer calibration certificate. This can ultimately change the slope of the fV data.

**Figure 3. fV Airflow measurements before airflow correction.**
In Figure 4a fV data is plotted on the X-axis because it is the fV in need of calibration. This subsequently left fT data to be plotted on the Y-axis. This allowed for a linear regression analysis presented in Fig. 4a. Through applying the linear regression equation from Fig. 4a to the data of Fig. 3, allowed for a fV calibration that resulted in high correlation between fT and fV flow, with low standard error (S_{xy}), presented in Fig. 4b. This method of fV data correction was appropriate, as it allows for future fV measurements independent of a criterion.

Figure 4. a) transformed data to express fV data on x-axis with resulting linear regression b) application of regression equation from transformed data to fV airflow data c) Bland-Altman analysis for bias and agreement of fV corrected data and criterion airflow data.
Lack of sensitivity at the low-end of airflow measurement (≤ 0.5 L·s⁻¹), was originally thought to be the result of the throat diameter developed with too large of an area to allow for sensitivity below 0.5 L·s⁻¹. However, Titheradge & Robergs latest understanding of the sensitivity of a fV device depends not only on the throat diameter, but also the signal quality of the transducer and the resolution capability of the data acquisition device. This understanding regarding sensitivity of fV devices is yet to be demonstrated. The reason for a change of understanding stems from the use of volts:pressure calibration equation provided by the transducer manufacturer, that was used to convert voltage output to differential pressure units, then subsequently used in airflow computations, which was the method used in the Titheradge & Robergs, (2018) study. Through retrospective experimentation, it was discovered that this ultimately changed the slope of the pressure:flow relationship and resulted in signal outputs during ≤ 0.5 L·s⁻¹ conditions to equal zero when computed for pressure and volumetric airflow.

For example: the Volts:Pa conversion factor is shown in equation 1.

\[
\Delta P_a = 99.73 \text{ (volts)} - 5.122
\]

Equation 1

Therefore, a differential pressure reading below 5.122 Pa would return a zero reading. Removal of the manufacturer volts:pressure factor may allow for sampling of airflow rates less than 0.5 L·s⁻¹. This method of fV data processing has not been tested, and may need to consider the signal quality at such low amplitudes to validate its use. Additionally, the fV device was limited by the 0-1000 Pa range, restricting airflow measurement to approximately 9 L·s⁻¹. For example, if 4.684 L·s⁻¹ was reached at 1000 Pa, using a fV with an ID and throat specification of 38 mm & 6 mm, respectively, then 6.625 L·s⁻¹ would be reached if the transducer input was increased to 2000 Pa, using the Venturi-optimised Bernoulli equation 2.

\[
\dot{V} = A_1 \frac{2(P_1 - P_2)}{\rho \left(\frac{A_1}{A_2}\right)^2 - 1}
\]

Equation 2

Collectively, the inability to sample very low amplitude differential pressure readings due to conversion factor, the irregular transition sections of the fV causing excessive friction, and input capacity of 1000 Pa allowed for airflow measurement of 0.5 L·s⁻¹ to 9 L·s⁻¹, which does not cover the entire physiological range of human pulmonary ventilation. Appropriate transducer fV configurations suitable for pulmonary ventilation measurements must be evaluated.

In summary, the fV device has significant potential as a valid ventilation measurement device, yet the instrumentation of such a device for human ventilation has yet to be evaluated. Based on previous findings, questions regarding the applicability of the fV device for human physiology include, what configurations of a fV would be suitable for such an application? What electronic hardware requirements would be needed to match these configurations? Once established, will this instrumentation design have
the accuracy and dynamic performance capacity to monitor pulsatile volumetric airflow conditions? Given there is no empirical research evidence of fV devices used in human practice, how will the fV perform in a practical setting measuring human pulmonary ventilation?

**Venturi Project Aims and Hypotheses**

This thesis consists of three research studies that aim to demonstrate the validity of a fV for measuring airflow during human pulmonary ventilation. The recommended standards for spirometers stipulated by the American Thoracic Society, that this thesis will focus on, are sensitivity, measurement range, and static and dynamic performance. These standards form the instrumentation processes that can be used as the main parameters for basic science validation. Subsequent demonstration of a prototype fV used in a clinical setting, will provide an applied approach to validation. This research thereby proposes the following aims and hypotheses:

**Study 1**

**Aim:** to examine the changes in transducer voltage output due to changes in throat diameter area of a fV device, under the same airflow conditions. This evidence will reveal the theoretical understanding of the Bernoulli and Continuity Laws of fluid dynamics whereby an inverse relationship exists between fluid pressure and fluid velocity. Data from this study will provide insight as to how one can computationally derive the appropriate dimensions required for a particular airflow range and sensitivity.

**Hypothesis:** fV devices of identical configurations (38mm inlet & outlet ID; 7° convergent and divergent angle), that differ only by throat area, will produce higher voltage outputs for a given airflow rate, for those fV’s with a relatively smaller throat area, that is, the smaller the throat area, the higher the voltage output for a given airflow rate. The larger changes in voltage output for smaller throat area will indicate increased differential pressure. Based on the Venturi and Bernoulli Principle, the increased differential pressure will be attributed to higher airflow velocity within the throat section, relative to the inlet section of the fV. Consequently, this higher voltage output per volumetric airflow will decrease the overall range for fV’s with relatively narrower throat sections for a given differential pressure range.

**Study 2**

**Static Component**

**Aim:** to evaluate the accuracy and reliability of fV airflow measurements compared to a criterion method, for airflow conditions within the human exercise pulmonary ventilation range.
**Hypothesis:** The fV device will not be statistically different to the criterion method for airflow measurements between 0.1 - 10 L·s\(^{-1}\) and produce similar results in signal quality for reliable measurements.

*Dynamic Component*

**Aim:** to evaluate the dynamic performance of fV device by comparing it to a criterion method well known for its dynamic performance, the Pneumotachograph. A comparison of response times in both devices will subsequently demonstrate the acceptable performance of the fV.

**Hypothesis:** The temporal differences in measurements of volumetric airflow, between a fV and Pneumotachograph, will not be statistically different, thus revealing suitable dynamic performance for the fV, that is, adequate response time, and frequency response.

**Study 3**

**Aim:** to demonstrate the performance of three different airflow sensor technologies for measurements of air flow (L·s\(^{-1}\)), tidal volume (V\(_T\)), ventilation (L·min\(^{-1}\)) and subsequent measurements of whole body \(\dot{V}O_2\) (L·min\(^{-1}\)), \(\dot{V}CO_2\) (L·min\(^{-1}\)) and the product of \(\dot{V}CO_2/\dot{V}O_2\) presented as the respiratory exchange ratio (RER), during EGAIC exercise testing.

**Hypothesis:** The fV device will not be statistically different to other established methods for quantifying volumetric airflow and subsequent derived variables within EGAIC. However, the fV will have better agreement with the Pneumotachometer, compared to the Turbine. This will be attributed to the physical parameter by which these three devices quantify volumetric airflow. The fV and Pneumotachometer measure changes in fluid differential-pressure. Whereas, the Turbine’s dependency on impeller revolutions will cause the agreement between itself and the fV to be comparatively wider due the difference in method.
Chapter Two

Review of Literature
Overview

Indirect calorimetry and basic human spirometry use airflow devices that quantify flow rate and volume in real-time, which is an essential part of determining pulmonary function, cardiorespiratory fitness, energy expenditure, as well as use in clinical settings for assessment and patient monitoring. The purpose of this thesis is to assess the Venturi methodology for measurement of fluid in motion, and its validity for a novel application in the form of human pulmonary ventilation. Since this investigation has a particular focus on the development of and subsequent measurement of the accuracy and reliability of an electronic device, this literature review begins with an overview of the fundamental knowledge for understanding electronics, instrumentation and measurement concepts. Thereafter, a discussion on pulmonary ventilation and its role in respiratory gas exchange is presented, then proceeded by an outline of airflow sensor technology used in expired gas analysis indirect calorimetry. A justification of each airflow measurement device’s strengths and weaknesses will be stated, leading into the discussion of the Venturi airflow physics, including the law of Continuity and the Bernoulli Principle, and how fluid measurement is derived from an understanding of fluid dynamics. Finally, the Overview will cover the rationale for a Venturi airflow sensor to quantify airflow during expired gas analysis indirect calorimetry.

Electronics Fundamentals and Measurement Concepts

A Brief History

In the years 1814 to 1879, Heinrich Geissler experimented with removing the air from within vacuum tubes and found that when current would flow through the vacuumed space, the tube would glow (Reif-Acherman, 2015; Susskind, 1970). Soon after these observations, Sir William Crookes reported that the current flowing through the tubes were made up of particles (DeKosky, 1973). Others who experimented with electricity such as Thomas Edison (Kettering, 1947) and Sir Joseph Thomson (Thomson, 1912) measured the physical properties of these particles, which were later classified as electrons. Electronics was essentially a 20th century invention that began with the development of the vacuum tube amplifier. John A. Fleming was responsible for constructing a vacuum tube in 1904 that allowed a current move in only one direction, and this tube was rightly called the Fleming Valve (Brittain, 2007). This vacuum tube was the precursor to the vacuum tube diode. In 1907, a grid was added to the vacuum tube by Lee deForest, allowing for amplified signals, for which he named the audiotron (Nebeker, 2001). The next step involved the addition of a control element, and by doing so, deForest revolutionised and essentially ushered in the beginning of the electronics age, as it allowed for transcontinental telephone and radio technology to thrive. The 1920’s saw the very first inventions of the television picture tube (Magoun, 2007). In the 1930’s, many developments in radio technology, such as directional antennas were commercially available and the rise of the electronic computer. A man by the name of John Atanasoff at Iowa State University, envisioned a binary machine concept that could solve complicated mathematical problems. By 1939, a graduate student Clifford Berry and Atanasoff invented a binary machine called ABC, which stood for Atanasoff-Berry Computer (Bairstow, 2011; Mackintosh, 1987; Smiley, 2010). The inventors used vacuum tubes for logic and capacitors for memory. During World War II, technology such as radar and very high-frequency communication were made possible by
the magnetron and klystron microwave oscillators that were invented in earlier years (Barton, 1984). The 1940’s saw the first commercially available computer, as well as one of the most important electronic components ever, the transistor (Brinkman, Haggan, & Troutman, 1997). Solid-State electronics first arrived on the scene with use of crystal detectors in early radios. However, the invention of the transistor during 1947 in Bell Labs, began the era of solid-state electronics (Brinkman et al., 1997). Printed circuit boards (PCB) also appeared in 1947, as well as the commercialisation of the transistor in 1951. Moving forward to the 1950’s, another revolutionary piece of electronic hardware arrived: the integrated circuit. The electronic circuit developed by Jack Kilby in 1958 (Bhat, 2012), created the modern computer era, which led to accelerated advancements in medicine, manufacturing, the entertainment industry, and the communication network.

The following driving force for electronics evolution encapsulated the entire world: the space race during the 1960’s. Perhaps the most notable invention during this time was the operational amplifier (Op-Amp): A special type of amplifier exhibiting very high open-loop gain, very high input impedance, very low output impedance, and good rejection of common-mode signals. The most influential version of this device developed at Fairchild Semiconductor, the 741, was taking shape in this decade due to the revolutionary work of Bob Widlar and Dave Fullagar (Lawes, 2010). By 1971, a newly formed company derived from Fairchild, going by the name of Intel, produced the very first microprocessor: the 4004 chip (Betker, Fernando, & Whalen, 1997). This 4004 chip was said to have the same processing power as the Eniac computer (Aspray, 1997). The Eniac, which stood for Electronic, Numerical, Integrator and Computer, was first developed in 1946 at the University of Pennsylvania (Haigh, Priestley, & Rope, 2014; McCartney, 1999). The Eniac was herald as the “Giant Brain” by many, and had speeds one thousand times faster than that of early electro-mechanical machines, such as the Bell Model V computer. Thus, a comparison of the 4004 chip, to the eniac computer placed Intel’s achievement into perspective, as one of great magnitude.

Better yet, the 4004 chip released in 1971, was later that year eclipsed by Intel’s first 8-bit processor: the 8008 chip (Aspray, 1997). By the 1980’s, most of homes had cable telecommunications hook-ups instead of antennas, and the reliability, speed and miniaturisation of electronics continued throughout this decade. This allowed for automated testing and calibration of PCB’s, which led to the use of computers for instrumentation and hence the creation of the virtual instrument. The 1990’s saw the spread of the world wide web, which has undoubtedly changed the way human society exist, providing access to knowledge, services, and enhanced methods in science and medicine, the world over. Also in this decade, the Federal Communications Commission of the United States, allocated spectrum space for the Digital Audio Radio Service. Digital television standards were adopted in 1996 in the United States of America, with Australia following suit in the year 2000, with fully phased out analogue signals by late 2013.

A thorough understanding of electronic instruments that utilise direct current (dc) and alternating current (ac) circuit technology, begins with an understanding of the chemistry of voltage, current, and resistance, followed by a preview of the different types of components that make up electronic devices. Knowledge of these components used in integrated circuits to function as an
instrument provides the fundamental background for understanding the technology used today in measuring differential pressure. The strain-gauge pressure sensor is a common method for quantifying differential pressure in pressure-based airflow sensors such the Pneumotachometer, Orifice Tube, and Pitot-Static Tube, as well as the airflow sensor of interest: The Venturi airflow sensor. The following discussion is a detailed overview of the aforementioned content, beginning with the atom, and concluding with the measurement of fluid pressure.

**Atoms**

The discovery of the atom first takes shape through philosophical and geological concepts to explain the existence of matter, such as Atomism from the works of Democritus and Leucippus (Nicholson, 2010). However, it wasn’t until John Dalton in the early 1800’s, and a string of scientists that subsequently tested the concepts of Dalton’s Law, that atomic theory was experimentally validated (Clarke, 1903; Viana & Porto, 2010). The atom is the smallest particle of an element, which is uniquely characterised of having a planetary type of structure that consists of a central nucleus surrounded by orbiting electrons. The nucleus is described as having positively charged particles called protons, and particles with no charge, called neutrons. Elements are distinguished by the number of protons, neutrons, and electrons. For example, hydrogen is considered the simplest atom with only having one proton and one orbiting electron. Whereas helium is characterised with a nucleus made of two neutrons, two protons, and two orbiting electrons. The atomic number of an atom arranges the elements in numerical order in the periodic table/chart by the number of protons located in the nucleus. When there are equal amounts of protons and electrons in an atom (considered a neutral or normal state), the positive charge of protons and the negative charge of electrons cancel each other out, resulting in an atom that is electrically balanced. The orbiting electrons of an atom are assorted in layers of shells. The orbit refers to the distance of the electron to the nucleus and the shell refers to energy level, with further distance from the nucleus resulting in higher energy levels. Additionally, the successive layers have greater capacity to hold more electrons and follow a predictable pattern with the number of electrons equated to $2N^2$, where $N$ is the order of the shell. The first shell can hold up to two electrons, meaning by the third shell an atom can potentially hold up to eighteen electrons. The electrons located on the outermost shell attain the largest distance from the nucleus, thus the negative and positive charge attraction is decreased, and as a result are loosely bound to the atom and hold higher levels of charge. The outermost shell is called the valence shell, and the electrons located here are called valence electrons. By having the highest energy levels and loosely bound, these valence electrons are responsible for the chemical reactions and bonding within a material, and determine the material’s electrical properties.

**Ionisation**

The process of gaining and losing electrons to form ions is called ionisation. The comprehension of this phenomenon was established by the revolutionary work of English Physicist and Chemist, Michael Faraday, who found the then-unknown species
that goes from one electrode to the other through an aqueous medium (Faraday, 1832). The energy levels of an electron can be raised, for example, when an electron encounters a heat source or light. When external energy is absorbed into an atom, the loosely bound valence electrons readily shift to higher orbits within the valence shell. If enough energy is absorbed by the atom, the valence electrons can escape the outer shell and the atom’s influence, resulting in the loss of negative charge and a gain of positive charge. For example, a neutral hydrogen atom is symbolised as H. When the valence electron escapes the outer shell, the hydrogen atom now has more protons than electrons, and called a positive ion, which is expressed as H⁺. Likewise, if a neutral hydrogen atom gains a free electron, resulting in more electrons than protons, a negative charge is achieved and subsequently called a negative ion; this is symbolised as H⁻. If the element, copper, were to be viewed down to its atomic structure within a material, one would see that copper has 29 electrons that orbit the nucleus in four shells, with only one valence electron. With adequate thermal energy present, a sea of free electrons unbound to any particular atom occurs, making copper an excellent conductor of electrical current.

**Electrical Charge, Voltage, Current, and Resistance**

Electrical charge is a fundamental characteristic for understanding electronics, and is symbolised by \( Q \). There are two types of charge: negative and positive charge. A negative charge is achieved when an excess of electrons is present relative to protons. A positive charge is achieved when an excess of protons is present relative to electrons. Negative and positive charges cause a force of attraction between them. In contrast, materials of the same charge cause a force that repel or pushes the particles away from each other. These forces occur in what is known as the electric field, where increases of electrons or protons increases the electrical charge. The unit of charge is defined as Coulombs and symbolised by C. The unit of charge is named after Charles Augustin Coulomb (1736-1806), who is best known for his work on electricity and magnetism due to his development on electrostatic attraction and repulsion described by the inverse square law for the force between two charges (de Coulomb, 1785). One coulomb is the total charge possessed by 6.25×10¹⁸ electrons. Equation (3) describes the computation of \( Q \). Thus, a single electron has a charge of 1.6×10⁻¹⁹C.

\[
Q = \frac{\text{number of electrons}}{6.25 \times 10^{18} \text{electrons/C}}
\]

Equation 3

Electrons and protons maintain a certain distance from each other within atoms and between atoms. Due to the attractive forces of electrons and protons, a source of energy must exist to keep these particles apart. This force and the magnitude of this force dictating the potential difference in space between particles, is known as Voltage. Named after Alessandro Volta (1745-1827) for his investigations into reactions between dissimilar metals, who also developed the first battery in 1800 (Haas, 1997). Voltage or volt (V) is defined as energy (W) per unit of charge (\( Q \)) and is given by equation 4, where \( W \) is expressed in joules (J) and \( Q \) is in coulombs (C).
Voltage provides the energy to electrons that allows them to move from lower orbiting shells to higher orbiting shells, and from atom to atom, which provides a flow of electrons within a circuit, known as current. The unit of current is the Ampere, named after André Marie Ampère (1775-1836), who was the first to measure the rate of electron movement per unit time, symbolised as \( I \) (Ampere, 1826). Current is found by equation 5, where \( I \) is current in amperes, \( Q \) is the charge in coulombs, and \( t \) is the time in seconds.

\[
I = \frac{Q}{t} \quad \text{Equation 5}
\]

As discussed earlier, highly conductive material such as copper naturally consist of free electrons drifting from atom to atom in no particular direction. When a voltage force is applied over the copper material, one end becomes negatively charged and the other end becomes positively charged. The negative charge at one end drives the free electrons across the copper material, whilst the positive charge at the other end pulls and attracts the free electrons. The result is a net movement of free electrons from the negative to positive end of the copper material. As electrons flow through a material, they inevitably collide into atoms, which essentially cause a loss of energy. The more collisions that occur, the greater the resistance to flow of electrons. Resistance \((R)\) to current is measured in units of ohms and is symbolised by the Greek letter omega \((\Omega)\). Quantifying resistance is fulfilled by equation 6.

\[
R = \frac{V}{I} \quad \text{Equation 6}
\]

The unit for resistance is named after Georg Simon Ohm, who started his research with the battery cell (Gupta, 1980). Using instrumentation devices, he created, Ohm had found that a direct proportionality existed between the resultant electric current and the initial voltage (potential difference) when applied across a conductor. This relationship is known as Ohm's law and is essentially described by equations 4, 5, 6, and summarised in equation 7.

\[
\text{Ohm's Law} = (V = IR) = \left( I = \frac{V}{R} \right) = \left( R = \frac{V}{I} \right) \quad \text{Equation 7}
\]
Categories of Materials and Components

There are three categories of materials used in electronics, which include conductors, semiconductors, and insulators. Conductors are materials that readily allow current, with large numbers of free electrons, and one to three valence electrons in their structure. The elements, silver and copper are considered very good conductor materials. However, copper is the most cost-effective, thus, copper wiring is the most common conductor material in electronic circuits. Semiconductor material such as silicon and germanium, have fewer free electrons than conductor material, and so have less capacity to support the transmission of current. These unique properties have allowed for the development of many different components within electronics such as the diode, transistor, and the integrated circuit. Insulating materials do the opposite of conductors, in that current does not readily transmit through these types of material because of the lack of free electrons present. This allows for the utilisation of insulating material to stop or prevent current where it is not wanted; which can be handy for controlling the flow of electrical power within a circuit.

Some common types of components used in electronic circuits include resistors, capacitors, inductors, transformers, and semiconductor devices. The resistor is a component that simply resists, or limits, electrical current in a circuit; a method used for controlling the flow of current. Capacitors store electrical charge and are used to block dc and pass ac. They consist of two conductive plates separated by an insulating material that allows for capacitance: the ability of a material to store electric charge. Inductors, often referred to as coils, are used to store energy in an electromagnetic field, which is underpinned by Faraday’s law of induction (Faraday, 1832), and Oestred’s Law on electric current and magnetic fields (Dibner, 1962). This electrical device is formed by a wire wound in a coil around a core having the property of inductance: a property by which a change in current through it induces an electromotive force. This in-turn allows for the capability to store energy in its electromagnetic field, as well as nearby conductors. Transformers are used to couple ac voltages from one point in a circuit to another, or from circuit to circuit, as well as to increase or decrease ac voltage. This is achieved through electromagnetic induction properties of the transformer, which essentially transfer electrical energy via the electromagnetic field.

As previously mentioned, semiconductor material such as silicon and germanium, have unique properties in that they do not consist of enough electrons to be considered a good conducting material. Nor do they lack in electrons to be considered good insulating material. Silicon, atomically, has less shells than germanium, which means the valence electrons orbiting a silicon atom are more stable at higher temperatures than germanium. For this reason, silicon is more widely utilised for electronic components in integrated circuits. When silicon atoms bond with each other forming silicon material, they do so in a fixed pattern, called a crystal. In its pure form, silicon atoms share their valence electrons creating a covalent bond between atoms, and subsequently attaining a chemically stable environment. Manufacturers of electronics components incorporate a chemical bonding method developed by John Robert Woodyard (Woodyard, 1950), and later works by Bell Labs (Kopf, Kuo, Luftman,
called doping, which allows the mixing of the original silicon or other semi-conductive material with impurities. By introducing a pentavalent atom to the silicon crystal, such as arsenic, phosphorus, or antimony (which have five valence electrons), a net gain in electrons is achieved in the silicon material. This essentially creates a new material with a negative potential. The same process is done to achieve a positive potential material by adding trivalent atoms with three valence electrons to the silicon material, such as aluminium, boron, and gallium. These elements essentially consume a valence electron from a silicon atom within their atomic bond. This leaves a ‘hole’ in the valence shell of the silicon crystal, resulting in more protons than electrons. When constructing a component out of the negative and positively doped material at either end, a directional bias of current flow is created with a barrier potential in the middle. The barrier potential provides a junction of resistance to current, where conduction will only occur with enough force to cause electrons to cross this junction. When a voltage source is applied across the component, it provides the resulting force for the electrons to cross the barrier potential, and the additional electrons for continual flow. The amount of voltage required for conduction to occur through the device is dictated by the constructed material. Manipulation of the semi-conductive material with doping impurities, combined with the fundamentals of Ohm’s Law for testing the voltage, current, and resistance or conductance of a component, has allowed manufacturers the flexibility to design and develop a vast range of different components to suit their application needs.

The Electric Circuit
A basic electric circuit consists of a voltage source, usually provided by a battery for dc, or a power point for ac; conductor material in the form of wires, creating a path for the voltage source to travel through; and a load device that is acted upon by the current travelling to it. For example, a lamp connected to a battery represents a basic circuit, with the battery providing the voltage source, the lamp is the load source drawing current from the battery, and the wires connecting the battery to the lamp and back to the battery provides the conductive path for the current. The circuit is considered a closed circuit whilst current is flowing through it, and subsequently classed as an open circuit when the current path is broken. This is achieved for example, with a light switch that opens and closes a moveable arm, termed a pole. The switch maintains a connected circuit whilst closed resulting in the lamp to emit light, and breaks the circuit whilst left open, turning the lamp off.

Other methods of manipulating the current path include more complex switches that affect multiple contacts that essentially turn off one path and redirect current flow down another path. Buttons are another method for controlling current path connections, and vary based on their physical characteristics, such as normally open push-buttons (NOPB), normally closed push-buttons (NCPB), and rotary buttons that connect one contact and any one of several other contact paths. Additionally, variable resistors such as rheostats that provide a variable resistance to current, and potentiometers that divide the voltage applied through the current path can be used to manipulate the amplitude of the current.
Excessive current within the circuit can lead to damage of vital components by generating enough heat that causes the chemical bonds of the material to permanently change, leading to subsequent component degradation (Ye, Basaran, & Hopkins, 2006). To avoid this, fuses and circuit breakers are utilised in the electronic circuit to provide a protective feature, where the components deliberately break the current path when a specified current amplitude is reached, resulting in an open circuit. Fuses differentiate from circuit breakers in that they must be replaced after they serve their function, whereas circuit breakers can be simply switched back to the closed position.

The electric circuit would not be completed without an understanding of the ground function, especially when multiple loads draw upon the same voltage source. The term, ground, refers to a method used to provide directionality for current paths within a circuit. This reference point of contact has a voltage of 0 V relative to other points in the circuit, and do not differ between other ground points, hence the term common points, or common ground. By having a ground point, the current has a path with zero resistance that provides a return connection to the voltage source and allows for multiple loads to connect to the same voltage source in a circuit.

**Strain-Gauge Pressure Sensor: The Basis of Airflow measurement via Differential Pressure**

Strain is defined by the deformation of an object, where the object may undergo expansion or compression due to a force acting upon it (Mase, Smelser, & Mase, 2009). If a component’s material is exposed to such forces, whilst a current is conducted through it in an electronic circuit, a proportional change in resistance is created that can be detected (Gassmann, 2014). As indicated by equation 5, an increase in resistance will result in an increase in voltage if the current is maintained. Therefore, if a voltmeter is applied across the circuitry, a proportional voltage signal can be acquired. A strain gauge pressure transducer or sensor, is basically a drum-shaped cavity with a very thin filament adhered to a pliable diaphragm. The strain gauge pressure sensor integrated into an electronic circuit with current conducting through it, undergoes the following during measurement. One end of a sample tube is placed in situ of a fluid of interest, and the other end of the sample tube attaches to the pressure sensor. Changes in pressure within the sample fluid creates a force against the diaphragm, which subsequently deforms both the diaphragm and the strain gauge filament, producing a proportional change in resistance, and subsequent voltage output. All differential-pressure-based airflow sensors are underpinned by this fundamental measurement concept, even though the methods employed to create a differential pressure are individually unique.

**Pulmonary Ventilation and its Role in Respiratory Gas Exchange**

The four main components of cellular respiration include pulmonary ventilation, diffusion of oxygen and carbon dioxide from the alveoli air to pulmonary capillary blood, transport of the oxygen and carbon dioxide in the blood to and from the body’s tissues, and the multifaceted regulation of pulmonary ventilation. For this thesis, a brief focus on pulmonary ventilation and the
role it plays in gas exchange across the respiratory membrane will be discussed. This knowledge is fundamental to understanding the importance of quantifying pulmonary ventilation via electronic airflow sensors, in combination with expired gas analysis.

The mechanics and fluid dynamics of pulmonary ventilation can be summarised by the muscular actions of the respiratory muscles, osteokinematics of the thorax, and the corresponding pulmonary pressure changes created. The lungs can be expanded and contracted via two methods: (1) by downward and upward movement of the diaphragm via contraction and relaxation (recoil), which lengthens and shortens the chest cavity, and (2) by depression and elevation of the ribs to decrease and increase the anteroposterior diameter of the chest cavity (Aliverti et al., 1997). When breathing in a rested state, pulmonary ventilation is almost exclusively attributed to the first method. During shallow breathing, approximately 500ml of air is drawn into the lungs and expired out by contraction and relaxation of the diaphragm, and the elastic recoil of the lungs (Kenyon et al., 1997). However, during physical exertion where rapid inspiration and expiration is required, the powerful abdominal muscles, external and internal intercostal muscles, as well as the sternocleidomastoid, anterior serrati, and the scalene muscles, all work synergistically to provide the change in chest cavity area (Aliverti et al., 1997). The lungs adhere to the chest cavity wall via a thin wall of fluid space called the pleural cavity, which naturally has a relative negative pressure creating a suction effect that keeps the lungs inflated and prevent the lungs from collapse during changes in chest cavity area (Agostoni, 1972; Lai-Fook, 2004). For air to move from one compartment to another, a pressure gradient must be created that disrupts its hydrostatic equilibrium. Thus, when inspiration occurs from contraction of inspiratory muscles increasing the chest cavity area, a vacuum effect is created inside the lung. This causes atmospheric air pressure to become temporarily greater than intrapulmonary pressure, which subsequently creates an influx of air into the lung. When airflow is ceased, a tidal volume (a given volume of air inside the lungs) is reached and the pressure gradient becomes zero. Conversely, during forced expiration the expiratory muscles contract synergistically to compress and decrease the chest cavity, creating a positive intrapulmonary pressure, which creates the pressure gradient needed for the air to be expelled into the atmosphere.

Earth’s atmospheric air is made up of approximately 20.95 % oxygen, 78.08 % nitrogen, and 0.04 % carbon dioxide (Williams, 2016) (and some quantitatively minor gases), with each gas exerting its own partial pressure, and subsequently contributing to the total pressure of atmospheric air. The detailed composition of atmospheric air is presented in table 1. To some various extent, water vapour is present within atmospheric air and exerts its own pressure, which is of importance when considering alveolar partial pressure of different gases, and alveolar-capillary gas exchange. On a cool clear day, water vapour can approximate to a value of 0.5 %. As atmospheric air is inspired, it travels through the nasal cavity, pharynx, trachea, main bronchus, lobar bronchus, segmental bronchus, bronchiole, then terminal bronchiole, which summates to the conductive division of the lungs. The air continues deep within the lung through the respiratory bronchiole, alveolar ducts, atrium, then alveolus, which is summated to the divisional region where the only gas exchange occurs, called the respiratory region.
### Table 1. Composition of atmospheric air.

<table>
<thead>
<tr>
<th>Gas</th>
<th>Symbol</th>
<th>% by Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrogen</td>
<td>N₂</td>
<td>78.08</td>
</tr>
<tr>
<td>Oxygen</td>
<td>O₂</td>
<td>20.95</td>
</tr>
<tr>
<td>Argon</td>
<td>Ar</td>
<td>0.93</td>
</tr>
<tr>
<td>Carbon dioxide</td>
<td>CO₂</td>
<td>0.04</td>
</tr>
<tr>
<td>Neon</td>
<td>Ne</td>
<td>0.0018</td>
</tr>
<tr>
<td>Helium</td>
<td>He</td>
<td>0.00052</td>
</tr>
<tr>
<td>Methane</td>
<td>CH₄</td>
<td>0.0002</td>
</tr>
<tr>
<td>Krypton</td>
<td>Kr</td>
<td>0.00011</td>
</tr>
<tr>
<td>Nitrous oxide</td>
<td>N₂O</td>
<td>0.00005</td>
</tr>
<tr>
<td>Hydrogen</td>
<td>H₂</td>
<td>0.00005</td>
</tr>
<tr>
<td>Xenon</td>
<td>Xe</td>
<td>0.000008</td>
</tr>
<tr>
<td>Ozone</td>
<td>O₃</td>
<td>0.000002</td>
</tr>
<tr>
<td>Radon</td>
<td>Rn</td>
<td>trace</td>
</tr>
<tr>
<td>Other</td>
<td>----</td>
<td>0.00426</td>
</tr>
</tbody>
</table>

The respiratory membrane is the physical location of where gas exchange occurs. This barrier separates alveolar gas and liquid blood within the capillary region. Therefore, for gas exchange to occur, a force must be exerted to cause gas to diffuse through this respiratory membrane. This is where the partial pressure of gases and the pressure gradient that occurs between alveolar gas, and pulmonary capillary blood is of significance. At sea level, atmospheric air has a total pressure of 760 mmHg, thus at concentrations of 20.95 %, 78.62 %, 0.04 %, and 0.5 % for oxygen, nitrogen, carbon dioxide and water vapour, the corresponding partial pressure for each gas equates to 159 mmHg, 597 mmHg, 0.3 mmHg, and 3.7 mmHg respectively. As the atmospheric air enters the lungs, it becomes almost completely saturated with water vapour as it comes in contact with the fluids that cover the respiratory surfaces, resulting in water vapour pressure to increase to 47 mmHg at a normal body temperature of 37˚C (Ingelstedt, 1956; Keck, Leiacker, Heinrich, Kühnemann, & Rettinger, 2000). This increase in water vapour partial pressure dilutes the partial pressure of all other gases, resulting in oxygen and nitrogen partial pressures of humidified alveolar air to average 104 mmHg and 569 mmHg, respectively. The two gases of physiological relevance for their role in cellular metabolism are oxygen and carbon dioxide. The partial pressure of these gases dissolved in venous blood returning from body tissues averages 40 mmHg and 46 mmHg for oxygen and carbon dioxide, respectively (Otis, 1964). Thus, a pressure gradient exists between pulmonary capillary blood and alveolar gas, with the direction of diffusion dictated by the area of less pressure, that is, gas molecules will move to areas of less pressure until equilibrium is achieved. This pressure gradient provides the force required for oxygen molecules to become bound to haemoglobin loaded on the red blood cells (RBC) passing through the capillaries, and carbon dioxide to unload off the RBC’s, from within plasma, and bound to blood proteins to the alveolar air.
The rate of this gas exchange is influenced by several factors, including the thickness of the membrane, the surface area of the membrane, the diffusion coefficient of the gas (effected by its solubility in liquid and molecular weight), and the partial pressure difference (or pressure gradient) of the gas between the two sides of the membrane (Rahn & Farhi, 1964). The air that reaches the respiratory region and its rate of replenishment is considered alveolar ventilation. It is equal to the respiratory rate multiplied by the amount of new air that enters the respiratory region with each breath (equation 8); where $\dot{V}_A$ is the volume of alveolar ventilation per minute, frequency refers to breaths per minute, $V_T$ is the tidal volume, and $V_D$ is the physiological dead-space or conductive region of the lung.

$$\dot{V}_A = Frequency \times (V_T - V_D)$$

Equation 8

Oxygen and carbon dioxide are continuously absorbing and unloading through the respiratory membrane, thus decreasing their respective partial pressures. New oxygen and carbon dioxide from atmospheric air are continually entering the respiratory region through pulmonary ventilation, thus exerting their concentration and corresponding partial pressures. Therefore, the concentration and subsequent partial pressure of alveolar air is influenced by (1) the rate of gas diffusion across the respiratory membrane, and (2) the rate of new air in the respiratory region, that is, the rate of alveolar ventilation entering the lungs via the ventilatory process.

Once equilibrium is achieved across the respiratory membrane, the deoxygenated blood from venous capillaries becomes oxygenated with a partial pressure of 104 mmHg. After arteriovenous blood mixing due to anastomosis, the arterial partial pressure of oxygen averages about 95 mmHg when leaving the lungs via the pulmonary veins. Simultaneous unloading of carbon dioxide molecules into the alveolar air occurs, with a subsequent change in partial pressure from 46 mmHg in venous blood, to 40 mmHg in arterial blood. Therefore, a net diffusion of gas molecules occurs. Due to cellular metabolism and the need for oxygen replenishment and carbon dioxide removal, the function of pulmonary ventilation and resultant alveolar ventilation, plays a crucial role in providing the driving force for the gas partial pressure renewal in alveolar air, and subsequent pressure gradient maintenance across the respiratory membrane. Without pulmonary ventilation, net diffusion of gas molecules will not occur. Therefore, the measurement of pulmonary ventilation is important for studying and interpreting the various inferences that can be made. These include the assessment of respiratory disease diagnosis and severity, monitoring progression and regression of the disease, as well as rate of oxygen consumption and the subsequent analyses of cellular metabolism.

In addition to alveolar ventilation, an added complexity of respiratory gas exchange is realised when also considering pulmonary capillary perfusion dynamics. A simplistic assumption made in many pulmonary respiratory models is that all alveoli are ventilated equally, and that all alveoli capillaries receive equal cardiac perfusion for each alveolus. However, even in normal functioning lungs to some extent, and certainly in many lung diseases, areas of the lung can receive adequate alveolar ventilation,
with no pulmonary capillary perfusion, whereas, other areas of the lung may receive adequate pulmonary capillary perfusion and limited alveolar ventilation (West, 1977). In either of these conditions, respiratory gas exchange is severely impaired. These abnormalities may occur, even though total pulmonary ventilation and total pulmonary blood flow are normal (West, 1977). Thus, a unique method for quantifying imbalances in alveolar ventilation and alveolar perfusion is used, called the ventilation-perfusion ratio ($\dot{V}_A/\dot{Q}$). In the normal healthy lung, regional gas exchange is greatest at the apex, that is, an ideal $\dot{V}_A/\dot{Q}$, and decreases approximately linearly towards to the base of the lung (West, 1962; West & Dolley, 1960).

In cases where inadequate blood flow prevails, a concept called the ‘physiological dead space’ is used to describe the wasted ventilation of the anatomical dead space, and the abundant alveoli oxygen, coupled with the inability of its removal across the respiratory membrane via pulmonary capillary blood flow (Asmussen & Nielsen, 1957). This ‘space’ is measured via appropriate laboratory blood and expiratory gas measurements and using the Bohr equation:

$$\frac{\dot{V}_{Dphys}}{\dot{V}_T} = \frac{Pa_{CO_2} - P\dot{e}_{CO_2}}{Pa_{CO_2}}$$

Equation 9

Where

- $\dot{V}_{Dphys}$ = Physiological dead space
- $\dot{V}_T$ = Tidal volume
- $Pa_{CO_2}$ = Partial pressure of carbon dioxide in arterial blood
- $P\dot{e}_{CO_2}$ = Average partial pressure of carbon dioxide in the entire expired air

Whenever the physiological dead space is large, the majority of the pulmonary ventilation work is said to be wasted effort, as most alveolar ventilation never interacts with pulmonary capillary blood.

Likewise, cases where inadequate alveolar ventilation occurs, a concept called the ‘physiological shunt’ is used to describe the abundant pulmonary capillary blood flow, and the inability to sufficiently oxygenate all of the available blood in the alveolus. A fraction of the blood that returns to the heart for circulation, remains deoxygenated because of this oxygenation deficiency. This fraction of blood is considered shunted blood. In addition, normal bronchial vessel perfusion occurs, and this blood also remains deoxygenated, which usually equates to 2% of pulmonary cardiac output. The volumetric rate per minute of the combined bronchial shunted blood, and alveolar shunted blood, is called the ‘physiological shunt’, and is calculated via equation 10

$$\frac{\dot{Q}_{PS}}{\dot{Q}_T} = \frac{CiO_2 - CaO_2}{CiO_2 - CvO_2}$$

Equation 10
Where:

- \( \dot{Q}_{PS} \) = Physiological shunt of blood flow per minute
- \( \dot{Q}_T \) = Measured cardiac output per minute
- \( C_{iO_2} \) = Oxygen concentration in arterial blood if \( V_A / \dot{Q} \) ratio is “ideal”
- \( C_{aO_2} \) = Measured concentration of oxygen in arterial blood
- \( C_{vO_2} \) = Measured concentration of oxygen in venous blood

Therefore, as the physiological shunt becomes larger, a greater proportion of pulmonary capillary blood remains deoxygenated.

**Evolution of Human Ventilation Methods used in Metabolic Gas Analysis Systems**

Before the 1970s, methods involving a Douglas bag and Tissot-tank spirometer were used in order to acquire measurements of metabolic and respiratory variables such as the volume of expired air and to allow subsequent analysis of expired gas fractions, (Consolazio, Johnson, & Pecora, 1963). In order to provide the fractional concentrations of oxygen (FEO\(_2\)) and carbon dioxide (FECO\(_2\)), methods such as the Lloyd-Haldane (Lloyd, Jukes, & Cunningham, 1958) and the Scholander apparatus (Scholander, 1947) were used, which involved chemical absorption of small portions of expired gas. These early methods have been used in succeeding studies conducted in the decades following, as the criterion method to which other methods are compared, because they are considered very accurate (Jensen, Jørgensen, & Johansen, 2002; Poole & Maskell, 1975; Shephard, 1955). However, they remain a tedious and timely operation and are highly dependent on operator knowledge and consistency, as well as lacking data signals and control over gas diffusion through fabric/rubber Douglas bags used in earlier methods (Rahaman & Durnin, 1964; Shephard, 1955). Furthermore, the douglas bag method for indirect calorimetry is limited by decreased sampling frequency, and inability to measure breathing patterns i.e. breathing frequency, and tidal volume, as seen in breath-by-breath methods (Astorino, Robergs, Ghiasvand, Marks, & Burns, 2000). A need for improved data signals, control of gas diffusion and overall improvement in ease of use, led to technology developments since the 1970s. This gave rise to subsequent developments of a variety of mechanical and electronic devices such as rapid response gas analysers, and volume and flow-sensing devices integrated with a computer to produce data for metabolic analysis and automated data recording.

**Gas-Volume Meters**

In the 1960s, the mechanical gas volume meter, which was electronically integrated to a potentiometer to record circular displacement and therefore, used to measure the tidal volume during breathing. However, these devices are quite large and heavy and are known to have reliability problems due to inertia, especially at low flow rates and rapid breathing frequencies. For instance, a study conducted on the performance of two pre-calibrated DTM-325 dry gas meters (American Meter Co., Philadelphia, PA, USA) compared to a criterion 350 L Collins chain-compensated gasometer (Warren E. Collins Inc., Braintree,
MA, USA) and reported that the devices under-estimated continuous airflow during low velocities (<60 L·min⁻¹) (Hart, Withers, & Ilsley, 1992). The researchers concluded dry gas meters are unsuitable for measuring small volumes (25% alinearity of 1 L = 250 ml absolute error, 250 ml/25 L = 1% relative error (Hart et al., 1992; Hart & Withers, 1996). Though historically, volume-based meters have been considered more accurate than flow-based meters (Gardner, Hankinson, & West, 1980; Gerald, Smith, & Gaensler, 1974; Wever, Britton, Hughes, Van der Plas, & Wever-Hess, 1981). In addition to these accuracy claims, it should be noted, the main findings of (Hart et al., 1992), were that the pre-calibrated dry gas meters were valid volume measuring devices for continuous flow between 60 and 150 L·min⁻¹ at <1% error, and sinusoidal volumes between 8 and 100 L·min⁻¹ at <2% error, provided that at least 25 L was passed through devices to alleviate the alinearity of the meter diaphragm.

**Flow-Rate Meters**

Volumetric flow-rate meters work based on an electronic voltage signal produced in response to air flowing within the device, that is considered proportional to the airflow being measured. This signal is then integrated over time to give estimates of both gas-flow rate and volume. Metabolic analysis systems have predominantly used four main types of electronic flow-sensing devices: airflow turbine, pneumotachometer, pitot-static tube, and hot-wire anemometer.

**Turbine device**

Impeller turbine airflow devices consist of a rotating vane situated inside a tube-like housing that rotates as air flows through the device (See figure 5 and 6). A light beam is shone across the vane to a photocell and as the vane rotates, it breaks the light source whilst the photocell counts each impulse and integrates the signal into flow and volume. fT meters are considered quite effective, as they are not affected by gas composition, temperature or humidity. However, fT meters can be quite expensive and sensitive to damage and are known to experience linearity problems at low flow caused by friction, also known as ‘lag-before-start’ (Yeh, Adams, Gardner, & Yanowitz, 1987). Attempts to compensate for this lag effect have been made through interventions in both hardware and software (Wilmore, Davis, & Norton, 1976). fT meters also experience problems with inertia at high flow rates, described as ‘spin-after-stop’, causing over-estimations of flow duration that are difficult to counteract (Yeh et al., 1987). The study at question compared a Fleisch pneumotachometer system (fP) producing 5% accuracy for \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) at rest and exercise, to a fT that produced up to 20% error for \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) at rest, (Yeh et al., 1987). At the end of inspiration or expiration, the turbine signal continued after the fP signal had returned to zero. The authors claimed the “lag-before-start” and “spin-after-stop” effects of the fT caused larger than acceptable error for the \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) measurements at low flow rates (Yeh et al., 1987). When a fT signal is being used to determine the beginning and end of each breath, then substantial timing errors may occur due to its inherent friction and inertia problems. This issue has encouraged researchers to use a fT in conjunction with a fP, allowing higher precision in flow rates and volumes from the turbine and reliable determination of respiratory tidal volume durations from the fP (Howson et al., 1987).
Another study that examined the performance of 62 different spirometers, of which three were fT’s, through 3 L calibrated syringe manoeuvres, as well as dynamic waveform methods, produced startling results (Nelson, Gardner, Crapo, & Jensen, 1990). The study based their level of acceptable performance on the 1987 American Thoracic Society standards (Gardner & Hankinson, 1988), which require attaining $\pm 3\%$ error measurement. Results showed that all three fT-based flow meters encountered difficulty with determining end-of-test during forced vital capacity (FVC) test, as well as excessive errors between 3 L syringe testing and dynamic waveform testing to the extent that their data was not used, hence producing 100% unacceptable performance (Nelson et al., 1990). In summary, apart from being limited by fragility and inadequacy for high frequency oscillatory airflow measurements, the fT, is insensitive to changes in gas composition, which leads to ease of use for the technician due to simple calibration, and allows for measurement of pulmonary ventilation at the mouth.

![Vacumed Turbine airflow sensor](image)

**Figure 5. Image of the Vacumed Turbine airflow sensor. Topical view.**
Figure 6. Image of the Vacumed Turbine airflow sensor used in the experimental studies. The rotating vane sits inside the housing unit and can be disassembled for servicing.

Pneumotachometer

fP airflow meters use a small resistive mesh screen or fleisch (series of capillaries) that creates a pressure drop as air flows through the device (See figure 7 and 8). The pressure differential created is then used to estimate the airflow rate. The estimations of airflow only remain accurate if the airflow is laminar. Laminar flow is characterised as streamline flow, without lateral mixing, which usually is seen in lower flow rates. Thus, during high flow rates, turbulence may occur and the pressure drop becomes disproportional to the airflow being measured, leading to inaccurate estimations. For example, earlier investigations that tested 62 spirometers, of which 17 were fP-based flow meters, resulted in only 8 fP meeting acceptable performance according to American Thoracic Society standards (±3 % error = ≤90 ml for 3 L syringe manoeuvres) (Nelson et al., 1990). More specifically, one pneumotach attained 94 mL mean difference during fast flow 3 L syringe trials, however remained within the ±3 % error margin during slow flow (mean difference = 48 mL) (Nelson, et al, 1990). These findings support the notion of disproportional effects of turbulent flow on fP during higher flow conditions.

Other limitations to consider are the resistive element itself, which may be compromised due to a build-up of debris from condensation, contaminants and mucus, particularly during expired gas measurement. The resistive element is a known constant resistance, so when an accumulation of debris occurs, it can alter the characteristics of the element, thus creating an unknown resistance. One strategy to counteract the effects of condensation is to electronically heat the resistive element, however, this creates an additional expensive cost and threat to the validity of the device’s ability to maintain accurate measurements during high airflow rates. Furthermore, measurements can become compromised if the heating element causes fluctuations in the temperature of the mesh screen (Wasserman, Hansen, Sue, Casaburi, & Whipp, 1994). Nevertheless, it has been suggested that
fPs are considered to be quite proficient in response time (Allan, 2010; Courtney et al., 1990; Zock, 1981), robust in design and provide linear outputs across the human physiological breathing range (Finucane, Egan, & Dawson, 1972). In addition, further calibration procedures have been developed that negate alinearity issues in fP devices (Strömberg & Grönkvist, 1999; Tang, Turner, Yem, & Baker, 2003; Yeh, Gardner, Adams, & Yanowitz, 1982).

Figure 7. Image of the Hans Rudolph Pneumotachometer used in the experimental studies. Topical view.
**Figure 8.** Image of the Hans Rudolph Pneumotachometer used in the experimental studies. Internal view; note the resistive screen that allows for differential pressure contions.

*Pitot-static Tube*

A pitot-static tube is a fluid measurement device, commonly known for their commercial application in determining air speed in aviation or fluid measurement inside ducts. This device consists of a static tube and pitot tube connected to each other creating, a U-tube manometer. As air flows through the device, the difference in pressure of the static tube (measuring static pressure) and pitot tube (measuring total pressure) allows for a determination of a pressure differential that is considered proportional to the airflow going through the pipe. The Pitot-static tube’s differential pressure signal is a function of the square of airflow rate, and is mathematically like the fV device as they both incorporate the Bernoulli equation to describe the fluid dynamic behaviour. The Pitot-static tube is considered a durable, cheap and very light device with evidence supporting its suitability for human ventilation (Ruppel, 2003) via recommendations by the American Thoracic Society in accuracy and precision (Miller et al., 2005). The unfavourable issue with the pitot-static tube is the non-linear signal and the sensitivity to variations in gas composition (density, viscosity) during changes in inspired and expired ventilation, as well as temperature, which requires complex equations in order to linearise and correct any errors in the signal (Hart & Withers, 1996). For example, an earlier investigation reported a $27.4 \pm 5.3\%$ mean difference in tidal volume measurements when compared to a plethysmograph, thus signalling the need for complex logarithmic adjustments for Pitot-static tube calibration (Hager et al., 2006).
**Hot-wire Anemometer**

Hot-wire anemometers (HWA) consist of a tube-shaped housing with two platinum wires electronically heated to a constant temperature. As air flows through the device, a cooling of the wires occurs. The additional voltage required to maintain the constant temperature is considered proportional to the airflow going through the device. Two wires are needed to determine the direction of flow, creating additional costs, as well as decreasing its sturdiness due to the platinum wires being prone to damage. Also, this type of flow meter encounters problems with changes in gas composition and temperature, limiting its flow measurement range and requiring correction methods to account for the misinterpretation of a velocity change due to temperature (Benjamin & Roberts, 2002). Furthermore, the wires increase in their inherent resistance with age, therefore, causing potential for inaccurate communication between the wire and processing unit given excessive voltage input, which has led to calibration techniques to counteract these issues (Talluru, Kulandaivelu, Hutchins, & Marusic, 2014).

**The Importance of Flow-Rate Meters for the Validity of Expired Gas Analysis.**

Advancements in technology have led to the commercial production of automated systems of analysis for determining metabolic function during exercise. This has led to a presumed understanding that expired gas analysis via an automated system will facilitate an increase in accuracy, reliability and objectivity (Wilmore et al., 1976). This understanding however, needs to be reinforced by sufficient evidence in support of the validity and reliability of these systems.

The accuracy of the airflow device used during expired gas analysis indirect calorimetry is important for validity of the calculation of the physiological variables that can be attained during such tests (Howley, Bassett, & Welch, 1995). The importance of this accuracy exists because the initial measurement of ventilation determined by the airflow sensor is one of the variables from which all other computations are calculated. Therefore, any error in ventilation measurement will create inaccurate calculations of other variables, such as air flow (L·s⁻¹), tidal volume (Vₜ: L), ventilation (L·min⁻¹), \(\dot{V}O_2\) (L·min⁻¹), \(\dot{V}CO_2\) (L·min⁻¹) and RER (respiratory exchange ratio).

**Bernoulli Principle and its application to Venturi Fluid Measurement**

Bernoulli’s law indicates that if an inviscid (not viscous) fluid is flowing along a pipe consisting of different internal diameters, the pressure (P) is relatively low at constricted section where the velocity is high and conversely, is relatively high where the pipe opens out and the fluid velocity stagnates. This phenomenon is often referred to as the Venturi effect, because Venturi was the first to report it (Venturi, 1797).
When Bernoulli was laying the foundations of hydrodynamics, he assumed that the fluid was incompressible (not affected by changes in density); that the shear stresses associated with viscosity were zero, and that the P was isotropic. He arrived at a simple law relating the change of P along a streamline to the change of velocity (C), which serves to explain many of the phenomena exhibited by real fluids in steady motion (Bernoulli, 1738).

Bernoulli’s theorem indicates that if a fluid flows horizontally so that gravitational potential energy remains negligible, then a change in the fluid’s pressure is directly proportional to its velocity. Venturi used Bernoulli’s knowledge to demonstrate this relationship between a fluid’s pressure and velocity by designing a pipe consisting of a convergent section, leading into a narrow throat section, followed by a divergent section where the pipe then returns into its original diameter. The combination of these features is known as a Venturi Tube (fV), which can be used as a vacuum pump or a fluid measuring device (Figure 9).

Consider a small element of fluid of mass (m), which is acted on only by P and not subject to the forces of gravity. The fluid is regarded as isotropic and may differ from point to point in space, but does not differ with time. It is a well-known effect of Newton’s laws of motion that when a particle of m moves under the influence of its weight (mg) (where g is the gravitational acceleration, -9.8 m·s⁻²) and an additional force (F), from a point (1) where its velocity is C₁ and its height is Z₁, to another point (2) where its velocity is C₂ and its height is Z₂, the work done by the additional force is equal to the change in kinetic and potential energy of the particle. (refer to Figure 10)

To understand Bernoulli’s principle, one must first understand the different types of energy within a fluid:

Kinetic Energy: refers to the energy of a fluid related to its velocity and the force it exerts on another object. Mathematically, kinetic energy is expressed as;

\[ KE = \left(\frac{1}{2} C^2\right) \]  

Equation 11

Potential Energy: refers to the energy due to the effects of height and is mathematically represented by equation 12, where m is the mass, g is the effects of gravity and Z is the height.
Flow Work Energy: refers to the energy required to displace the fluid and is mathematically represented by equation 13 where the pressure is $P$, and $V$ is the volume.

$$FW = PV$$  \hspace{1cm} \text{Equation 13}

Internal Energy: refers to the energy due to the temperature of the fluid and is mathematically represented by equation 14. However, at this point, internal energy will not be considered in this thesis.

$$IE = U$$  \hspace{1cm} \text{Equation 14}

Force in this scenario refers to pressure applied over the cross-sectional area of a pipe, as seen in equation 15. The force is moving and thus producing work, which is a product of energy.

$$F = PA$$  \hspace{1cm} \text{Equation 15}

The work done is equal to the force applied over a distance shown in equation 16, where $L$ stands for distance, $P$ for pressure and $A$ for area.

$$W = PAL$$  \hspace{1cm} \text{Equation 16}

Volume is the area by length shown in equation 17 and so Flow Work is represented in equation 18.

$$AL = V$$  \hspace{1cm} \text{Equation 17}

$$PV = \text{Flow Work}$$  \hspace{1cm} \text{Equation 18}

Bernoulli’s work was derived from the law of conservation of energy, which implies that the energy at one section of a pipe is equal to the energy at another section of the pipe:

$$\text{Energy at 1} = \text{Energy at 2.}$$  \hspace{1cm} \text{Equation 19}

To determine the total energy at each point of the pipe (1 & 2), an understanding of the different types of energy within a fluid must be known:

$$\left(\frac{1}{2}C_i^2\right) = \text{Kinetic} = \left(\frac{1}{2}C_f^2\right)$$  \hspace{1cm} \text{Equation 20}

$$(mgZ_1) = \text{Potential} = (mgZ_2)$$  \hspace{1cm} \text{Equation 21}

$$(P_1V_1) = \text{Flow Work} = (P_2V_2)$$  \hspace{1cm} \text{Equation 22}

From here, the equation can be represented as:

$$(P_1V_1) + \left(\frac{1}{2}C_i^2\right) + (mgZ_1) = (P_2V_2) + \left(\frac{1}{2}C_f^2\right) + (mgZ_2).$$  \hspace{1cm} \text{Equation 23}
Bernoulli assumed the fluid to be incompressible, allowing volume to be considered a constant

\[ V_1 = V_2 = V. \]  \hspace{1cm} \text{Equation 24}

After dividing both sides of the Bernoulli equation by \( V \), the equation is represented as:

\[ P_1 + \frac{1}{2} \rho C_1^2 + \frac{mgz_1}{v} = P_2 + \frac{1}{2} \rho C_2^2 + \frac{mgz_2}{v} = \text{Constant}. \]  \hspace{1cm} \text{Equation 25}

Density refers to the mass divided by its volume and is mathematically represented as equation 26, where \( \rho \) stands for density.

\[ \rho = \frac{m}{v} \]  \hspace{1cm} \text{Equation 26}

From here it is now possible to work in terms of pressure rather than energy. For example, \( \rho g Z \) is the same as \( \rho gh \), (hydrostatic pressure). Thus, the Bernoulli equation can be expressed as equation 27, where:

\[ P \] Refers to a fluid’s static pressure
\[ \frac{1}{2} \rho C^2 \] Refers to a fluid’s dynamic pressure
\( \rho g Z \) Refers to a fluid’s hydrostatic pressure.

\[ P + \frac{1}{2} \rho C^2 + \rho g Z = \text{Total Pressure} \]  \hspace{1cm} \text{Equation 27}

Hydrostatic pressure refers to the fluid’s potential energy determined by height. Dynamic pressure represents the energy that the fluid exerts on another object affected by its velocity. Static pressure refers to the pressure within a fluid that is measurable upon any point of its element, sometimes referred to as gauge pressure. Thus, as expressed in equation 27, total pressure is the sum of the static, dynamic and hydrostatic pressures.

The total pressure must remain a constant. Thus, if there is an increase in a fluid’s velocity/kinetic energy/dynamic pressure, and height/potential energy/hydrostatic pressure remains the same, then \( P \) will decrease. Likewise, if the fluid must travel upwards through an elevated section of a pipe and all other variables remain the same, then a decrease in \( P \) will occur:

\[ P_1 + \frac{1}{2} \rho C_1^2 + \frac{mgz_1}{v} = P_2 + \frac{1}{2} \rho C_2^2 + \frac{mgz_2}{v} = \text{constant}. \]  \hspace{1cm} \text{Equation 28}

For this derivation of the Bernoulli equation to remain effective, certain conditions must apply:

- No heat transfer (adiabatic)
- No work done (no pumps or turbines that take away the energy of the fluid)
- Flow is frictionless (no temperature change or interaction with pipe walls)
- Flow is incompressible ($\rho = constant$) where flow rate is less than $100 \, m/s$ for gases.

**Flow Rate Measurement with a Venturi Meter**

When considering flow rate measurement, the continuity law indicates that a decrease in area leads to an increase in velocity as fluid flows through a pipe of different diameters.

$$\dot{V} = AC$$

Equation 29

Where $\dot{V}$ indicates volumetric flow rate.

The Bernoulli equation implies that an increase in fluid velocity results in a decrease in fluid pressure.

$$P + \frac{1}{2}C^2 + \rho g Z = Total\ Pressure$$

Equation 30

Thus, when used in conjunction with the continuity equation, a differential pressure and velocity can be determined, which will allow $\dot{V}$ to be estimated.

Consider this diagram of a fV device with a U-tube mercury manometer:

Figure 10. Venturi meter with a U-tube manometer. P1 and P2 = location of differential pressure measurement; A and B = location of effect of pressure difference on manometer fluid. $hp + y = pressure\ head.$
Total pressure at A is equal to that of B inside the U-tube manometer. To determine the pressure differential of the fluid at the original pipe diameter \( P_1 \) and throat diameter \( P_2 \), the Bernoulli equation can be expressed in a way to find the pressure at \( P_A = P_B \). For the original pipe diameter, the pressure is expressed as:

\[
P_A = P_1 + \rho g (hp + y)
\]

Equation 31

Where \( hp + y \) refers to the fluid head, which is equal to its energy per unit weight. Thus, total pressure is that of the static pressure of the fluid at point 1 and the weight of the fluid from the centre of the water column to the distance of A. Likewise, \( P_B \) is expressed in a similar order, except that the element of mercury \( \rho_m ghp \) must be added:

\[
P_B = P_2 + \rho g y + \rho_m ghp.
\]

Equation 32

As total pressure is the same at A and B of the U-tube manometer, they can be equated together as:

\[
P_1 + \rho g (hp + y) = P_2 + \rho g y + \rho_m ghp.
\]

Equation 33

From here, manipulation of the equation can be done to find differential pressure:

\[
P_1 - P_2 = \rho g y + \rho_m ghp - \rho g y.
\]

Equation 34

A duplicate of \( \rho g y \) leads to an elimination of this variable, resulting in:

\[
P_1 - P_2 = \rho_m ghp - \rho ghp.
\]

Equation 35

From here, the effects of \( ghp \) will act upon both densities and so the equation can be simplified to:

\[
P_1 - P_2 = (\rho_m - \rho) ghp = \text{Differential Pressure}.
\]

Equation 36

When the fluid that is being measured through the fV device is in a liquid state, it can be assumed that \( \rho_m \) and \( \rho \) are of similar magnitude. However, when dealing with gas flow measurement, the density of a gas such as air will be relatively smaller in comparison to the density of the mercury fluid within the U-tube manometer. Thus, the effects of the density of air on the calculations will be minimal and quite often are regarded as negligible. Thus,

\[
P_1 - P_2 = \rho_m ghp.
\]

Equation 37

However, during applications where operating pressure is very high, gas can become dense, thus treated as a homogeneous material and calculated via continuum flow mechanics (Jitschin, 2004).

Instead of observing a height difference in a U-tube manometer, an electronic pressure transducer that simply samples the pressure in the two sections of pipe (original diameter section preceding constriction and the throat section) may also be used to quantify differential pressure \( (P_1 - P_2) \) in a modern fV system.
So far, the calculations have arrived at the differential pressure, however, the fV device is a flow rate meter and to determine the flow rate, the fluid velocity must be determined, as seen in equation 38.

\[
\dot{V} = AC.
\]  

Equation 38

Since there is no height variable associated with a fluid going through a fV, the term \(Z\) can be neglected:

\[
Horizontal \ Z_1 = Z_2
\]  

Equation 39

Thus, leaving the static pressure and dynamic pressure:

\[
P_1 + \frac{1}{2} \rho C_1^2 = P_2 + \frac{1}{2} \rho C_2^2
\]  

Equation 40

To determine velocity, all the velocity terms are moved to one side of the equation and all other terms to the other side:

\[
\frac{1}{2} \rho C_2^2 - \frac{1}{2} \rho C_1^2 = P_1 - P_2.
\]  

Equation 41

With a duplicate of \(\frac{1}{2} \rho\) cancelling each other out, the equation can be simplified to:

\[
C_2^2 - C_1^2 = \frac{2(P_1 - P_2)}{\rho}.
\]  

Equation 42

\(C_2^2\) & \(C_1^2\) (Velocities), however, are still unknown.

This is where the continuity equation is used to show the relationship of the area and fluid velocity, as the continuity law indicates:

\[
A_1 C_1 = A_2 C_2 \rightarrow C^2 = \left(\frac{A_1}{A_2}\right)^2 C_1
\]  

Equation 43

As kinetic energy is expressed in terms of \(\frac{1}{2} mC^2\), the continuity equation can be shown as equation 44, as \(C_2\) is related to \(C_1\) by the ratio of areas.

\[
C_2^2 = \left(\frac{A_1}{A_2}\right)^2 C_1^2
\]  

Equation 44

Once adding the continuity equation to the Bernoulli equation, it can be represented as equation 45

\[
C_2^2 - C_1^2 = \frac{2(P_1 - P_2)}{\rho}.
\]  

Equation 45

\(C_1^2\) can be removed from the left side of the equation, displaying equation 46.

\[
C_1^2 = \left[\left(\frac{A_1}{A_2}\right)^2 - 1\right] = \frac{2(P_1 - P_2)}{\rho}.
\]  

Equation 46

The ratio of area squared can be moved to the other side by dividing both sides of the equation, resulting in equation 47.
\[ C_1^2 = \frac{2(P_1 - P_2)}{\rho \left( \left(\frac{A_1}{A_2}\right)^2 - 1 \right)} \]  

Equation 47

To get the fluid velocity of \( C_1^2 \), the square-root (\( \sqrt{\cdot} \)) function is used on both sides of the equation:

\[ C_1 = \sqrt{\frac{2(P_1 - P_2)}{\rho \left( \left(\frac{A_1}{A_2}\right)^2 - 1 \right)}} = \text{Theoretical Velocity}. \]  

Equation 48

Now it is possible to determine the volumetric flow rate \( \dot{V} \), by simply multiplying the area of the original pipe diameter \( A_1 \) by the theoretical velocity:

\[ \dot{V} = A_1 C_1 \text{ or } \dot{V} = A_1 \sqrt{\frac{2(P_1 - P_2)}{\rho \left( \left(\frac{A_1}{A_2}\right)^2 - 1 \right)}}. \]  

Equation 49

At low velocities, differential pressure \( (P_1 - P_2) \) is greatly affected by viscosity and therefore flow rate estimation is unreliable, as Bernoulli assumed that the fluid is limited to only inviscid flow fluid-states.

During laminar flow, viscosity of a fluid during motion refers to the shear stresses that occur between laminae as one stream moves faster over another stream, causing an equal and opposite reaction, as stated by Newton. As the top lamina slips over the lamina below it, a frictional force in the forward direction is created and therefore the top lamina is bound to experience a frictional force in the opposite direction. Therefore, with higher viscosity fluids, the shear interactions during laminar flow between laminae are higher, ultimately affecting the flow mechanics of the fluid (LaNasa & Upp, 2014).

So far, the equations discussed result in the calculation of what is known as a theoretical flow and therefore one must account for the important factor of drag force experienced as fluid flows through a fV device. A fluid stream will create a drag force on any obstacle it encounters as it remains in motion. As fluid interacts with the walls of a fV device, particularly its convergent cone section, a frictional force is created. The theoretical flow calculated by the Bernoulli equation is then corrected by the dimensionless figure, the discharge coefficient \( (C_D) \). The discharge coefficient accounts for the friction caused by the interaction of the fluid with the wall of the fV device. In regard to flow in fV pipes, the \( C_D \) is dependent on the ratio of pipe diameters, the angles of convergence and divergence, as well as the characteristics of the fluid, along with the velocity at which it is being measured (Lipták, 2005).

\( C_D \) is simply the theoretical flow rate divided by the actual flow rate:

\[ \left( \frac{\dot{V}}{\dot{V}_{\text{Actual}}} \right) = C_D. \]  

Equation 50
However, the actual flow rate is unknown and thus what the fV device is estimating is unknown. This is where dimensional analysis of fluids is of importance, as it is called upon to show that the $C_D$ must be a function of another dimensionless quantity called the Reynolds number, which is depicted here as:

$$Re = \frac{\rho v D_H}{\mu} = \frac{v D_H}{\nu} = \frac{\dot{V} D_H}{v A}$$  \hspace{1cm} \text{Equation 51}$$

where:

- $D_H$ → Hydraulic diameter of the pipe, where $D_H = \frac{4(D^2/4)}{\pi D} = D, L, (m)$
- $\dot{V}$ → Volumetric flow rate (m$^3$·s)
- $A$ → Pipe cross-sectional area (m$^2$)
- $v$ → Mean velocity of the fluid (SI units: m·s)
- $\mu$ → Dynamic viscosity of the fluid (Pa·s·m= kg/(m·s))
- $\nu$ → Kinematic viscosity ($\nu = \frac{\mu}{\rho}$) (m$^2$·s)
- $\rho$ → Density of the fluid (kg/m$^3$).

To find the Reynolds number, a series of experiments must be conducted. Fortunately, this function is universal and thus once $C_D$ is plotted against the Reynolds number, one can predict the $C_D$ for a particular fluid undergoing interaction with a fV device of similar characteristics (Jitschin, 2004).

The fV device is normally used, except for when the velocity is large enough for the flow to be turbulent (Reynolds number $\geq 100,000$). In such a circumstance, the derived Bernoulli and continuity equation predicts values for $\dot{V}$ that agree with values measured by more direct means to within a fraction of a percent (%). The precision remains reliable for a fV device even though the flow pattern is not steady. However, a fV device will experience a limitation described as choked flow, where the velocity of the fluid exceeds the critical ratio value of differential pressure for a fluid. Thus, any increase in velocity during choked flow will not cause an increase in differential pressure that is proportional to the fluid’s velocity. Consequently, a fV device cannot determine an increase in volumetric flow rate during conditions of choked flow, even though an increase in fluid velocity may be occurring due to an upstream force.

**Rationale for Application to Human Ventilation**

The instrumentation design of any airflow sensor for EGAIC needs to consider the rudimentary respiratory flows at rest and exercise. Figure 11 presents data collected from one female subject performing a graded exercise test on a stationary bicycle. During this exercise test, the subject was asked to remain stationary in a rested state for two minutes, followed by two minutes of cycling at 50 W and a cadence of 70 Rev·min$^{-1}$. After this time, a ramp function of 30 W·min$^{-1}$ ensued
until the subject reached a limit of volitional tolerance. Group analysis of the initial 120 s representing no cycling, revealed mean ± 95% CI for $f_B$: 17.8 Breath·min$^{-1}$ ± 16.5 – 19.1; $V_T$: 0.897 L ± 0.821 – 0.974; $V_E$: 16.67 L·min$^{-1}$ ± 14.55 – 18.79. The average $V_T$ of 0.5 to 1 L by the subject is reflective of common values reported for rested conditions (McArdle, Katch & Katch, 2010). As $V_E$ increases during progressive exercise, the initial increase is achieved by increases in $V_T$, and to a lesser extent, $f_B$ (Hey, Lloyd, Cunningham, Jukes, & Bolton, 1966; Whipp & Pardy, 1986; Younes & Kivinen, 1984). At heavier intensities of exercise, the increase in $V_E$ is met primarily by increasing $f_B$, while the rise in $V_T$ is attenuated, and reaches a plateau (at approximately 50-60 % of the vital capacity: (Clark, Hagerman, & Gelfand, 1983; Hey et al., 1966; Martin & Weil, 1979). The factors determining the $V_E$-$V_T$-$f_B$ association in intense physical exertion depends on the integration of the depth and frequency required to attain a given ventilatory demand, which appears to be independent of known respiratory stimuli and may reflect a pattern of breathing that results in a minimal amount of work or force generation, (Hey et al., 1966).

Figure 11. Rudimentary respiratory air flow measurements of breathing frequency ($f_B$ Breath·min$^{-1}$), tidal volume ($V_T$), and the integration of both tidal volume and breathing frequency over one minute ($V_E$ - L·min$^{-1}$) for one subject performing a graded exercise test.

Airflow sensors can be assessed based on their performances in terms of both dynamic (i.e., short response time and adequate frequency response) and static (i.e., signal quality, resolution, and accuracy across its measurement range) characteristics. Due to the inherent non-linear output that creates limitations such as reduced measurement range, and low sensitivity at low airflow rates described for fixed orifice-meters (Schena, Massaroni, Saccomandi, & Cecchini, 2015),
gives reason to assess the fV airflow sensor during very low airflow measurements (< 0.5 L·s⁻¹), as it also produces a non-linear signal output. Additionally, the complication of accounting for fluid-state transitions between laminar and turbulent flow needs to be investigated for the fV method for volume measurements. This becomes apparent when considering a given tidal volume of breath, is produced in an oscillating sinusoidal pattern, consisting of various airflow velocities due to the pulmonary mechanics of the lungs.

One important variable, is the ventilation threshold, whereby increases in ventilation rate exceed increases in the rate of oxygen consumption. The ventilation threshold correlates with blood lactate accumulation, which are indicators for the onset of metabolic acidosis. Another important variable is maximum oxygen consumption (VO₂max). To attain a high level of oxygen consumption, requires a diverse interaction of the human body’s physiological systems. Therefore, VO₂max provides a quantitative measure for exercise performance and cardiovascular health. The fV device would be suitable for determining both these important variables, as they occur at moderate to high ventilation rates, where high airflow rates prevail. However, pulmonary mechanics of the human lung inherently produce sinusoidal tidal volumes at all ventilation rates. This means, for any given tidal volume of human breath, the initial and end components of the flow curve, will consist of airflow rates less than 0.5 L·s⁻¹ (see Figure 12). Thus, the use of a fV device for measuring human pulmonary ventilation, must account for differential pressure distortion caused by fluid friction during laminar flow.

![Figure 12. The fV air flow sensor measuring tidal volume of inspired air. Each curve represents the measurement of one inspired breath. Note the small area at the base of the flow-volume curve, where the signal is below 0.5 L·s⁻¹ at the beginning of each inspiration.](image-url)
fV devices can be used for measuring flow rate of dry gases such as air and wet gases such as steam (He & Bai, 2012). However, they are usually used for the measurement of liquids at high velocities as they have the advantage of measuring clean liquids, slurries and dirty liquids with predictable performance, whilst maintaining its inherent stability over a long period of time (Liptak, 2005).

Interestingly, there is evidence of fV devices being used to quantify gas flow through ducts, such as applications in vacuum science (Jitschin, 2004). It has been suggested that a fV device can be used with modest accuracy, suitable for testing pumps (Jitschin, 2004). Regarding the science of measurement, where certain applications demand high validity, it is possible to calibrate a Venturi meter in order to meet these standards (Jitschin, 2004). A classical fV device has configurations of a 21° convergent angle, 7° divergent angle and diameter ratio of (β) 0.5 to 0.75. It has been suggested however that these configurations, in particular the convergent angle, are not ideal for gas flow measurement (Reader-Harris et al., 2001), with a convergent angle of 10.5° providing much smoother data in high-pressure applications.

Yet, no prior research has validated the use of fV devices in the measurement of animal or human ventilation. However, there is past evidence of an fV device used during equine exercise stress testing (Seeherman & Morris, 1990). The lack of comparison to a criterion reference, and lack of airflow measurement methodology in this study creates a strong argument against the validity of the fV to be used in this way. They have not measured respiratory ventilation here. There is controlled flow through a loosely fit mask which caused contamination to room air based on the expired air. Based on this alteration of gas fractions, the investigators can calculate total CO₂ production and O₂ consumption, and hence then calculate ventilation. There is a great deal of complications present in the methodology. There is atmospheric temperature, pressure, saturated (ATPS) air condition for most of the air flow, which is then altered by body temperature, pressure, saturated (BTPS) expired air, causing sinusoidal alterations of air moisture and density, which of course is not ideal for a method requiring application of the Bernoulli equation. The Venturi-optimised Bernoulli equation (equation 49) accounts for changes in gas volumes due the changes in gas composition through the incorporation of a fluid density variable. There has been no mention of how they account for the high frequency intermittent changes of BTPS and ATPS air conditions during measurements of minute ventilation, which can subsequently cause variation in fluid density (Seeherman & Morris, 1990). This is evidence for the need of more scientific scrutiny regarding validation and use of the Venturi method.

Consequently, there is basic science and an applied science rationale for conducting this research. From a basic science perspective, there is a need for research that verifies the suitability of fV devices for measurement of low to high airflow rates relative to human ventilation conditions (0.1 to 10 L·s⁻¹). Based on this preliminary work, added research can then be performed to ascertain the suitability of Venturi meter airflow measurement to human indirect calorimetry. For this research initiative, a comparison of fV device airflow measurements to fT and fP technology as criterion methods can be accomplished.
to verify validity and reliability. Titheradge & Robergs (2018), have conducted research identifying the suitability of a Venturi application to human indirect calorimetry. This project aimed to demonstrate the feasibility of the fV as a valid alternative to more expensive, yet valid methods such as fP and fT devices.

**Figure 13 Model for Venturi and Turbine (Titheradge & Robergs, 2018)**

A pressure transducer sensitive from 0 to 1,000 Pa combined with fV made from retail PVC tubing (50 mm Inside Diameter (ID) at inlet, 17.5 mm ID throat section) allowed for airflow measurement of 0.5 to 8 L·s⁻¹. To create the constriction between the original and throat diameter, a series of right angle sections were glued together (see figure 13). A fT was used as the criterion method. Variable airflow was produced through manual 3 LATS manoeuvres of a calibration syringe and constant air flow was induced using a commercial air compressor. The fV produced valid volumetric airflow (\( \dot{V} \)) estimates across non-steady state pulsatile flow conditions (±0.22 L·s⁻¹ 95% confidence limits with zero bias for Bland-Altman) (Figure 14).
Figure 14. a) Data and subsequent linear regression results for fV vs. fT air flow. b) The improved regression after the fV data were re-processed to compute an adjusted fV flow based on the regression equation of a). c) Results for the Bland-Altman plot of agreement between the regression adjusted fV flow data and fT flow.
The fV also made valid $\dot{V}$ measurements for steady-state continuous flow ($\pm 0.065 \, \text{L} \cdot \text{s}^{-1}$ 95% confidence limits with zero bias for Bland-Altman). (see Figure 15).

Figure 15. (a) Raw output signals (Volts) from the fT and fV resulting from two separate trials for constant flow from an air compressor. (b) Result from linear regression correction of the fV data as for the data of figure 14b (c) Bland-Altman plot of the data from graph (b).
Figure 16. Comparison of the 3 L syringe data for fT and fV after optimal calibration data processing as explained in Methods.

An unpaired t-test based on Figure 16 revealed fV volume estimation at different flow rates (0.5 to 8 L·s⁻¹) to be similar to the criterion fT volume measurements (2.972 ± 0.02017 vs. 3.066 ± 0.02211 L (No difference F = 1.202; df = 13,13; p = 0.7455) for fV and fT, respectively), though with less than half the percentage error (0.9 vs. 2.2 %, respectively). Both the fT and fV met the < ± 3 % minimum error of the airflow and integrated volume reading required by American Thoracic Society standards (Miller et. al., 2005). The results indicate that flow measured by this fV is suitable for valid measurements in human ventilation, such as airflow (L·s⁻¹), tidal volume (Vₜ: L) and minute ventilation (L·min⁻¹) within an airflow range of 0.5 - 8 L·s⁻¹.

The fV device was limited by the use of a differential pressure transducer with a range from 0 – 1000 Pa, which limited the fV to a peak flow rate measurement of 8 L·s⁻¹. Along with this, it was found that the fV device was unable to accurately measure airflow below 0.5 L·s⁻¹. During resting measures of human ventilation, this could become a considerable problem, as typical Vₜ values of an average-sized person breathing are approximately 500 ml per breath. Preliminary experimentations have revealed the throat diameter of the fV dictates the sensitivity at the lower end of ventilation measurement, and thus the beginning of airflow measurement. To elaborate further on this issue, there is a need to identify at what airflow velocity (and thus throat diameter) becomes meaningful to capture an entire inspired or expired human breath at rest and transition into exercise, whilst considering restriction to airflow in the development of a fV tube design. The ATS standard for spirometer sensitivity is set at
Due to the laws of continuity and conservation of energy in fluid motion, a fluid travelling through a constricted section of a pipe must increase in velocity. The velocity of the fluid is proportional to the quadratic function of the differential pressure in a fV device. By narrowing the throat section, the velocity will subsequently increase; thus, creating a larger change in static pressure earlier for a given volumetric airflow rate in the pipe stream. This not only lowers the discrimination threshold, but also improves the resolution of the signal output. Through theoretical experimentation of the Bernoulli principle as it applies to fV devices (see equation 49), we have found that in order create a fV device with a discrimination threshold of approximately 0.1 L·s⁻¹, a throat diameter of 10 to 12 mm is required (See figure 17. For improved Venturi design using 3D printing of throat ID 9 to 12 mm for experimental testing). The two-millimetre discrepancy is suggested due to the unknown coefficient of friction affecting the sensitivity, which can be revealed through experimentation of theoretical readings compared to actual readings in application. Additionally, the resolution of the acquisition device dictates the discrimination threshold. The signal quality of any reading will validate the reliability of the signal by indicating more signal than noise.

\[
\dot{V} = A_1C_1 \text{ or } \dot{V} = A_1 \sqrt{\frac{2(P_1-P_2)}{\rho \left[ \left( \frac{A_1}{A_2} \right)^{2-1} \right]}}.
\text{ Equation 49}
\]

Theoretical experimentation of the Bernoulli principle has shown that expanding the differential pressure range (e.g. from 0-1000 to 0-7000 Pa) will allow for an increase in range of ventilation measurement. These preliminary results are promising for the future of a fV ventilation system suitable for human expired ventilation across the entire physiological range during exercise. Therefore, further investigation must be conducted to establish the fV device’s validity for the entire human physiological range during exercise. The use of Venturi meters in human physiology research and clinical measurement will provide an alternative and potentially valid method of measurement, which in turn will lower cost and improve ease of use.
Figure 17. Image of 3D-printed Venturi sensor prototypes 1) a bi-directional version with symmetrical conical inlet and outlet sections with a throat ID: 12mm; the following three venturi designs listed as 2, 3, 4 are uni-directional (one way airflow direction) versions with a 23° conical inlet, and 8° conical outlet, with throat ID: 10 mm, 11 mm, & 12 mm, respectively. 5) The venturi design enabled the dismembering of the tube into two sections, which allowed for ease of sanitisation and maintenance. The specification of the dismembered model included a throat ID of 9 mm, and a 23° conical inlet (not shown), and 8° conical outlet.
Chapter Three

Validation of computational methods for designing a Venturi Airflow Sensor
Title: Validation of Computational Methods for Designing a Venturi Airflow Sensor

Abbreviated title: Designing a Venturi Airflow Sensor

Authors: Praneel Titheradge¹, Robert Robergs²

Institutions:
1 School of Exercise Science, Sport and Health, Charles Sturt University, Bathurst NSW, Australia
2 School of Exercise & Nutrition Sciences, Faculty of Health, Queensland University of Technology, Brisbane, QLD, Australia

Corresponding author:
Praneel Titheradge
Charles Sturt University
Panorama Avenue,
Bathurst, 2795, NSW Australia
ptitheradge@csu.edu.au

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Abstract

The Venturi principle of fluid dynamics has received minimal application to spirometry, yet provides a suitable alternative to current methods. Furthermore, no empirical evidence exists that establishes suitable Venturi airflow sensor (fV) instrumentation for human pulmonary ventilation measurement during exercise testing. This study determined a suitable fV configuration needed for measuring 0.1 to 10 L·s⁻¹ airflow conditions. Four Venturi tube configurations manufactured via 3D printing, matched with two transducer configurations (1 kPa vs. 7 kPa input, per 10 VDC), were compared to a criterion (Pneumotachograph; fP) during constant stable airflow. Bland-Altman results indicate close agreement and minimal bias for differential pressure data. Bland-Altman results indicate close agreement and minimal bias for airflow data. The findings suggest that a throat ID of at least 11mm to 12mm, matched to a 7 kPa transducer provides adequate peak airflow range to capture pulmonary ventilation during high intensity exercise, and that peak airflow can be confidently identified to be within < ±0.2 L·s⁻¹ without further calibration. We conclude that fV throat diameter and transducer specification needs for output resolution cannot be reliably determined until signal quality analysis during 0.1 L·s⁻¹ is conducted on the transducer.

Key Terms
Pulmonary Ventilation, Venturi Meter, Spirometer, Fluid Dynamics, Pneumotachometer.
Introduction

The method of measuring fluid using a Venturi tube commonly used in manufacturing, aviation and industrial applications, has yet to be evaluated for human pulmonary ventilation measurement. Recently, a study was conducted that confirmed the feasibility of using a Venturi airflow sensor (fV) to quantify airflow and volume, similar to human ventilation (Titheradge & Robergs, 2018). Recommendations were made for further research on improving the design and instrumentation process of developing an fV. Airflow sensor specifications such as airflow resolution output, and peak airflow range need to be considered when designing the fV for an application, whether that be for spirometry (Miller et al., 2005), exercise testing (Macfarlane, 2001), paediatrics (Khemani & Newth, 2010) or continuous monitoring for critically ill patients, such as for mechanical ventilation (Schena et al., 2015). Our interests in developing the fV device, are specifically for the application of pulmonary ventilation measurement during exercise testing. The underpinning fluid dynamics of the fV is the Bernoulli Principle, which there are two main variables that can be manipulated during instrumentation to accommodate the airflow resolution output and peak airflow range specifications. These include the throat diameter of the Venturi tube, and the differential pressure input to signal output ratio of the transducer, which will hereon in, be referred to as transducer specification. For the measurement of pulmonary ventilation, resolution output and peak airflow range are important, as the airflow device must have adequate sensitivity and range to capture enough of the human breath that is regarded physiologically relevant. The American Thoracic Society (ATS) standards for spirometers for graphical output resolution is recommended to be 0.1 L·s⁻¹ for human ventilation measurement (Miller et al., 2005). The ideal throat diameter, matched with an appropriate transducer specification for an fV, is yet to be empirically determined for 0.1 L·s⁻¹ resolution specifications. The differential pressure signal output at any airflow velocity for fV's of different throat diameters and transducer specifications, can be determined computationally via the Bernoulli Principle, which will be detailed further in this study. However, comparison of this computational method to measured signal outputs for an fV device, when subjected to airflow conditions similar to pulmonary ventilation, do not exist. Thus, establishing the instrumentation of an fV device for exercise testing cannot be reliably determined until such testing is conducted. The validation of this method will allow for determining the signal output at a resolution specification of 0.1 L·s⁻¹, which will subsequently identify appropriate transducer specifications matched with an appropriate Venturi tube throat diameter. The instrumentation of an fV must also consider the peak airflow range, and the implications this has on determining suitable throat diameter and transducer specifications. The ATS stipulate the capability to measure up to 14 L·s⁻¹ for spirometry devices used for spirometry testing (Miller et al., 2005), yet no standards exist for airflow sensors used for exercise testing. The ATS discusses the use of 14 L·s⁻¹ for maximal voluntary ventilation (MVV), a specific spirometry test, which could be argued as most applicable to exercise testing. However, humans rarely demonstrate peak expiratory/inspiratory airflow of 14 L·s⁻¹ during exercise due to the mechanical inefficiency caused by added work of breathing (Dempsey, Harms, & Ainsworth, 1996). Furthermore, peak airflow
measurement of 10 – 12 L·s⁻¹ are commonly seen in airflow sensors used in exercise testing, such as the Turbine airflow sensor (Universal Ventilation Meter; VacuMed, Ventura, CA, USA), and the Pneumotachograph (fP; model 3813; Hans Rudolph, Inc. Shawnee, Kansas, USA). Therefore, we conclude the fV peak airflow capacity should at least measure up to 10 L·s⁻¹.

The purpose of this study was to demonstrate the instrumentation process of multiple fV’s, designed computationally via the Bernoulli principle, to determine a suitable fV configuration needed for measuring 0.1 to 10 L·s⁻¹ airflow conditions. The fV configurations were manufactured and tested during various airflow conditions, for the purpose of comparing criterion values to measured values of differential pressure output, to reveal bias and agreement. The differential pressure output was then used to compute volumetric airflow for the purpose of revealing the clinical relevance of the measured differential pressure readings. Minimal bias and close agreement between criterion and measured differential pressure data would then conclude that resolution output, and peak airflow range can be reliably determined.

**Materials and Methods**

To conduct this study, conceptual principles of the fV device must prevail to understand its application. A venturi tube consists of an original pipe area known as the inlet, followed by a constricted area (throat section), which subsequently returns to its original diameter known as the outlet, as shown in figure 18.
The Venturi tube is situated in series for measurements of fluid flow through pipes by quantifying the fluid's differential pressure that occurs as it flows through the device. This differential pressure occurs due to the fluid dynamic principles that describe its behaviour, otherwise known as the Bernoulli principle of fluid dynamics (Bernoulli, 1738), and the Law of Continuity (Leibniz, 1710; Leibniz, 1701). As fluid travels from a larger to smaller area within a pipe, its velocity must increase, maintaining the Law of Continuity, whilst its static pressure simultaneously decreases, maintaining the principle of mechanical energy, as described by Daniel Bernoulli (Bernoulli, 1738). This inverse relationship between a fluid’s pressure and velocity was applied to pipes of different diameter by an Italian Physicist, Giovanni Venturi, who discovered the volumetric flow rate of a fluid within a pipe can be solved through observing this phenomenon when the area of the pipe diameter is known (Venturi, 1797).

The Bernoulli principle applied to a fV is given by equation 49 and used to estimate volumetric fluid flow rate ($\dot{V}$), whether that be for liquid or gas fluids.

$$\dot{V} = A_1 \sqrt{\frac{2(p_1 - p_2)}{\rho}} = \text{Theoretical Flow}$$  \hspace{1cm} \text{Equation 49}

$\dot{V} = \text{Volumetric Flow Rate}$

$A_1 = \text{Area of original pipe diameter}$

$A_2 = \text{Area of constricted pipe diameter (Throat section)}$

$(p_1 - p_2) = \text{Differential pressure}$

$\rho = \text{Fluid Density}$

However, if $\dot{V}$ is known, and the variable of interest is $p_1 - p_2$, as would be needed for this study, then the equation can be expressed as:

$$p_1 - p_2 = \left(\frac{\dot{V}^2}{A_1} \cdot \rho \cdot \left(\frac{A_1}{A_2}\right)^2 - 1\right)^{\frac{1}{2}}$$  \hspace{1cm} \text{Equation 52}

By developing multiple fV's with various throat diameters, and utilisation of equation 52, the testing allowed for determining the effect of throat diameter, and transducer specification on differential pressure readings and subsequent signal output. The airflow condition was determined by the use of a criterion device to establish $\dot{V}$ in equation 52, to reveal criterion $p_1 - p_2$. This allowed for measured fV $p_1 - p_2$ signal output to be compared to a criterion, to determine if the observed effects from Venturi tube throat diameter, and transducer specification on fV $p_1 - p_2$ signal output, resulted in close agreement with criterion values. Close agreement would then conclude that resolution output, and peak airflow range can be reliably determined.
**Instrumentation**

Four fV's were designed using drafting software (SolidWorks, Waltham, MA, USA), with an inlet and outlet internal diameter (ID) of 38 mm, and a 23° conical confusor section for diameter transition. The fV's differed only by throat ID, with diameters of 9 mm, 10 mm, 11 mm and 12 mm, creating an area ratio ($\beta$) of 0.24 $\beta$, 0.26 $\beta$, 0.29 $\beta$, 0.32 $\beta$, respectively. Prototypes were then manufactured using a 3-D printer (Airwolf3D, Fountain Valley, CA, USA), and acrylonitrile butadiene styrene (ABS) thermoplastic, with approximately 4 hours printing time for each tube. Holes (4mm) were drilled into each inlet and throat diameter section for static pressure sampling with luer connectors inserted and glued into place, then connected via pliable tubing to a differential pressure transducer. Two differential pressure transducers (Setra Systems, Inc, Boxborough, MA, USA, Model 267), were utilised with specifications of 0-1 KPa and 0-7 KPa inputs per 0-10 VDC output, respectively. Collectively, the fV connected to a differential pressure transducer resulted in the final product.

**Experimental Procedure**

A testing model (figure 19) was constructed with low resistance tracheal tubing (VacuMed, Ventura, CA, USA), connected to an industrial vacuum (WorkHero, International Cleaning Solutions Pty Ltd, Victoria, Australia), and ball-valve for control of airflow conditions. The criterion airflow device; a Pneumotachograph (fP; model 3813; Hans Rudolph, Inc. Shawnee, Kansas, USA), was situated in series with two fV devices, and 1m tracheal tubing separating each device. The airflow devices were then subjected to a constant and stable airflow condition, with signals acquired at 50 Hz using a data acquisition device: 16 channel analogue/digital input; 16-bit resolution; sensitivity = 153 $\mu$V for 10 V range (National Instruments, Austin, TX), integrated to a user interface. The condition lasted 10 s, with the last 5 s of signal acquired to capture stable airflow. Thus, 251 data points were averaged to determine the signal for each condition. With the fV devices in-situ, the transducers were swapped, then all devices subjected to the same airflow condition. The fV devices were then removed from the model, and replaced with remaining fV devices, which were tested for the same airflow condition. This procedure was done for all fV devices and subsequent transducer configurations for each airflow condition.
Post-acquisition data processing

The $\dot{V}$ for each airflow condition was detected by the fP, and subsequently used for computation within equation 2. Relative humidity, room temperature and atmospheric pressure were recorded via weather station (Model: WS5029, Holman Industries, Osborne Park, Western Australia) for each condition and used for determining the air density (equation 3) for utilisation in equation 2.

$$\rho = \rho_{da}(1 + x)/(1 + 1.609x)$$  \hspace{1cm} \text{Equation 3}$$

Where

$\rho = \text{density of moist air (kg}\cdot\text{m}^{-3})$

$\rho_{da} = \text{density of dry air (kg}\cdot\text{m}^{-3})$

$x = \text{humidity ratio by mass (kg}\cdot\text{kg})$

$1.609 = \text{gas constant ratio between water vapour and air}$

The criterion derived $P_1 - P_2$ for each airflow condition was then compared to the measured $P_1 - P_2$ for each fV configuration, which was conducted via the following sequence of events. The raw voltage output data was saved as text files, and imported into a data analysis software program (Prism, Graphpad Software Inc., La Jolla, CA, USA). The data were baseline-corrected for removal of zero-span differences between device signals. The fP signal was corrected via a volts:Litre calibration factor as recommended by manufacturer operational procedures, in order to reveal $\dot{V}$. The $\dot{V}$ was then used within equation 2, along with the measured environmental parameters influencing air density, resulting in a criterion derived $P_1 - P_2$. Additionally, the fV signal was converted to Pascals via the transducer input/output regression.
of either 100Pa/V or 700 Pa/V, thus revealing the physically measured $P_1 - P_2$ for each fV configuration for each condition, allowing for a comparison of methods.

**Statistical Analyses**

Criterion $P_1 - P_2$ was compared to measured $P_1 - P_2$ via Bland-Altman analysis for bias and agreement with 95% confidence intervals reported. Further clinical evaluation of $P_1 - P_2$ for the two methods were carried out via computed airflow measurements with subsequent Bland-Altman analysis for bias and agreement with 95% confidence intervals reported.

**Results**

All data presented are considered relative, as environmental conditions affecting gas composition, and subsequent differential pressure reading, were measured and factored into the results to account for variations between data collections. Measurement of environmental conditions must be considered when developing the fV for resolution and range, to maintain valid results.

The Bland-Altman analysis of the measured versus criterion $P_1 - P_2$ for the 1 kPa transducer matched to all fV configurations (figure 20) revealed an average discrepancy of 8 Pa. Applying this discrepancy to airflow as it would be used in a clinical setting, reveals the bias is not large enough to be important, with a subsequent bias of just 14 ml·s⁻¹ revealed in figure 22. The Bland-Altman analysis of the measured versus criterion $P_1 - P_2$ for the 7 kPa transducer matched to all fV configurations (figure 21), revealed an average discrepancy of 0.1 Pa, with zero bias between methods. The results of this data computed for airflow reveals a bias of 5 ml·s⁻¹ as shown in figure 23. All Bland-Altman analyses of the data reveal there are no deviating trends from the average. The variability of the data points initially spread very close to the bias line, then rapidly increase, then remain consistent throughout the 95% confidence limits of agreement.

Theoretical differential pressure signal output at any airflow velocity for fV’s of different throat diameters and transducer specifications, can be determined computationally via equation 2. Therefore, fV diameter configurations of inlet ID: 38 mm, throat ID: 9 mm, 10 mm, 11 mm and 12 mm, measuring airflow at 0.1 L·s⁻¹ will produce differential pressure inputs of approximately 1.45 Pa, 0.95 Pa, 0.65 Pa, and 0.46 Pa, respectively. The corresponding approximate voltage output at 0.1 L·s⁻¹ for both 1 kPa and 7 kPa transducers would be 14488 μV and 2070 μV for 9 mm ID, 9492 μV and 1356 μV for 10 mm ID, 6471 μV and 924 μV for 11 mm ID, and 4557 μV and 651 μV for 12 mm ID throat sections. With environmental conditions at 20 °C, 44 % relative humidity and atmospheric pressure at 742 mmHg, the ultimate airflow range at 10 V maximum output for the fV devices matched to the 1 kPa and 7 kPa transducers are approximately
2.627 L·s⁻¹ and 6.951 L·s⁻¹ for 9 mm ID, 3.246 L·s⁻¹ and 8.588 L·s⁻¹ for 10 mm ID, 3.931 L·s⁻¹ and 10.401 L·s⁻¹ for 11 mm ID, and 4.684 L·s⁻¹ and 12.393 L·s⁻¹ for a 12 mm ID throat diameter.

Figure 20. Bland-Altman analysis of \( P_1 - P_2 \) bias and agreement for all four fV configurations matched to a 1kpa transducer, across various outputs, induced by airflow. The difference represents the measured \( P_1 - P_2 \) minus estimated \( P_1 - P_2 \), plotted against the average of the two methods. Each data point on the graph represents the average of 251 data samples from a stable signal acquired in response to constant airflow conditions.
Figure 21. Bland-Altman analysis of $P_1 - P_2$ bias and agreement for all four fV configurations matched to a 7 kPa transducer, across various outputs, induced by airflow. The difference represents the measured $P_1 - P_2$ minus estimated $P_1 - P_2$, plotted against the average of the two methods. Each data point on the graph represents the average of 251 data samples from a stable signal acquired in response to constant airflow conditions.
Figure 22. Bland-Altman analysis of $\dot{V}$ for all fV and 1 kPa transducer configurations (expressed in L·s$^{-1}$, with reported bias and agreement), calculated from the two methods of $P_1 - P_2$ results. The difference represents the measured method minus the estimated method, plotted against average airflow. Each data point on the graph represents the average of 251 data samples from a stable signal acquired in response to constant airflow conditions.
Figure 23. Bland-Altman analysis of $\dot{V}$ for all fV and 7 kPa transducer configurations (expressed in L·s$^{-1}$, with reported bias and agreement), calculated from the two methods of $P_1 - P_2$ results. The difference represents the measured method minus the estimated method, plotted against average airflow. Each data point on the graph represents the average of 251 data samples from a stable signal acquired in response to constant airflow conditions.
Discussion

The purpose of this investigation was to determine $P_1 - P_2$, which occurs as air flows through fV's of various throat diameters and transducer input ranges, can be predicted computationally with reasonable validity when compared to a criterion $P_1 - P_2$. Furthermore, by using a valid airflow sensor to determine the airflow, minimal bias and close agreement between criterion and measured differential pressure data would then conclude that resolution output, and peak airflow range can be reliably determined. A comparison of 95 % confidence limits of agreement between the 1 kPa (figures 20 and 22) and 7 kPa (figures 21 and 23) transducers matched to all fV configurations reveals that the 1 kPa 95 % confidence limits are less wide than 7 kPa results, with almost half the width. However, the 7 kPa transducer’s measured $P_1 - P_2$ and $\dot{V}$ results compared to the criterion method derived from the fP, produced zero bias. This may suggest the larger 95 % confidence limit for 7 kPa is simply a product of the significantly larger differential pressure input range (7-fold), allowing for higher flows, and subsequent loss of precision in sampling this may have caused, yet revealing equivalent variability to the fP.

The close agreement, and bias close to zero presented in all figures, indicate the two methods for determining the $P_1 - P_2$ and subsequent $\dot{V}$, systematically produce similar results overall. However, the limits of agreement for very low average values of differential pressure and subsequent volumetric airflow measurements, are potentially narrower if only these data samples were considered. The interpretation of this finding can be seen from the scatter of the data points initially spread very close to the bias line, then rapidly increase, then remain consistent throughout the 95 % confidence limits of agreement, in all figures. Thus, the confidence limits within these analyses should only be applied to peak airflow range. Our findings suggest that a throat diameter of at least 11mm to 12mm diameter, matched to a 7 kPa transducer provides adequate peak airflow range to capture pulmonary ventilation during high intensity exercise, and that peak airflow can be confidently known to be within < ±0.2 L·s$^{-1}$ without further calibration. The implications of this finding is that the instrumentation should allow for < ±0.2 L·s$^{-1}$ limits of agreement when establishing the transducer specification, and throat diameter for a specific peak airflow range. If the aforementioned fV specifications are used, then fV diameter configurations of inlet ID: 38 mm, throat ID: 11 mm and 12 mm, measuring airflow at 0.1 L·s$^{-1}$, will produce differential pressure inputs of approximately 0.65 Pa, and 0.46 Pa, respectively. The corresponding approximate voltage output at 0.1 L·s$^{-1}$ for 7 kPa transducer would be 924 μV for 11 mm ID, and 651 μV for 12 mm ID throat sections. These findings call for the need to investigate the signal quality of the transducer at such low amplitudes in order to validate the fV capability to measure 0.1 L·s$^{-1}$. We conclude that fV throat diameter and transducer specification needs for output resolution cannot be reliably determined until such testing is conducted.
These results also support that differential pressure input to subsequent signal output ratio dictates the resolution capability of an fV, and therefore the overall sensitivity of the instrumentation design. The range capability of an fV design depends on both resolution and the differential pressure input specifications of the transducer used. This will allow the technician to determine fV configuration and transducer specification needed for their application.

**Study Design Limitations**

*Manufacturing Anomalies*

There are additional factors that need to be accounted for that can potentially improve the accuracy of \( \dot{V} \) estimation. Anomalies in 3-D printing of the fV may have led to the area of the pipe diameters to be slightly different to its specification, that is, a specification of 12 mm throat diameter might be slightly larger or smaller than 12 mm. These discrepancies, however, can be detected through further calibration if the airflow is known.

**Air Composition**

To improve the accuracy when determining \( P_1 - P_2 \) and \( \dot{V} \) with a fV, environmental factors affecting air density must be corrected. These variables were solved for through independent measurement before each trial and recorded for post-acquisition data processing. This involved measurement of the differences in room temperature, relative humidity, and atmospheric pressure between data acquisition trials, and utilised within equation 3.

**Fluid Friction**

Another factor that affects the \( P_1 - P_2 \) and \( \dot{V} \) reading is the effect of fluid friction. A fluid stream will create a drag force on any obstacle it encounters as it remains in motion (LaNasa & Upp, 2014). As fluid interacts with the walls of a fV device, particularly its convergent cone section, a frictional force is created. The theoretical flow calculated by the Bernoulli equation (equation 1) is then corrected by the dimensionless figure, the discharge coefficient \((C_D)\) (Reader-Harris et al., 2001). The discharge coefficient accounts for the friction caused by the interaction of the fluid with the wall of the fV device.

**Laminar-Turbulence Transition**

Another factor affecting the \( C_D \) is the transition from laminar to turbulent airflow. The relative friction within these fluid states is larger during laminar flow, due to the viscosity and subsequent friction this causes between laminae (Hoffman & Johnson, 2007). Ultimately, laminar flow distorts the differential pressure reading, which leads to over-estimation of \( \dot{V} \) if it is not accounted for. The function of the \( C_D \) during this transition is found through experimentation and
subsequent calibration, which is beyond the scope of this study. The cause of variation between fV devices in $P_1 - P_2$ and subsequent $\dot{V}$ measurement can be argued to be the result of differences in frictional properties between devices, such as the throat diameter & anomalies in internal wall surfaces. These findings suggest that although close agreement, and minimal bias presented is sufficient for instrumentation purposes, when it comes to precise measurement of $\dot{V}$, further calibration via $C_D$ correction for $P_1 - P_2$ distortion is needed for improved validity of fV devices.

In conclusion, airflow sensors are used in a range of different applications, and so their specification needs can vary. These include sensitivity and range, which are dependent upon the transducer specifications and airflow method configuration. The purpose of this study was to provide empirical evidence for the instrumentation of an airflow sensor based on the Venturi principle of fluid measurement. This included establishing a suitable fV configuration needed for measuring 0.1 to 10 L·s$^{-1}$ airflow conditions, such as pulmonary ventilation measurement during exercise testing. Our findings suggest that a throat ID of at least 11mm to 12mm, matched to a 7 kPa transducer provides adequate peak airflow range to capture pulmonary ventilation during high intensity exercise, and that peak airflow can be confidently known to be within $< \pm0.2$ L·s$^{-1}$ without further calibration. We conclude that fV throat diameter and transducer specification needs for output resolution cannot be reliably determined until signal quality during 0.1 L·s$^{-1}$ is conducted on the transducer. Additional calibration is required for precise airflow and volume measurement, for use in clinical setting.
Chapter Four

Static and Dynamic Performance of a Venturi Airflow Sensor
Title: Static and Dynamic Performance of a Venturi Airflow Sensor

Abbreviated title: Airflow Sensor Evaluation

Authors: Praneel Titheradge¹, Robert Robergs²

Institutions:
¹ School of Exercise Science, Sport and Health, Charles Sturt University, Bathurst NSW, Australia
² School of Exercise & Nutrition Sciences, Faculty of Health, Queensland University of Technology, Brisbane, QLD, Australia

Corresponding author:
Praneel Titheradge
Charles Sturt University
Panorama Avenue,
Bathurst, 2795, NSW Australia
ptitheradge@csu.edu.au

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Abstract

Venturi-meters have received limited application to the measurement of human air flow. A 3-D printed Venturi airflow sensor (fV) was integrated to a differential pressure sensor for the purpose to document signal quality, dynamic performance during instantaneous flow, and airflow analysis, with subsequent calibration for volume measurement. In addition, we assessed these results for potential use in measurement of human pulmonary ventilation. The fV was developed via drafting software program and 3-D printer (38 mm ID inlet, 12 mm ID constriction, and 23° conical transition sections). The fV was matched to a differential pressure transducer (0-7 kPa input per 0-10 VDC output). The fV was connected in series with a Pneumotachometer (fP) and Turbine airflow sensor (fT), with 1 m length tracheal tubing (ID: 35 mm), separating the devices. Airflow conditions were controlled by an industrial vacuum for constant flow with a manual-operated ball valve connected in series, and a criterion 3 L calibrated syringe for instantaneous flow. Repeated baseline data were collected for signal stability, and to identify the signal-to-noise ratio for signal quality. Airflow estimates and signal quality analysis were performed on repeated constant airflow conditions that spanned the transducer 0-10 VDC output. Repeated syringe manoeuvres that spanned the transducer 0-10 VDC output were used to determine the dynamic performance of the fV. Paired t-test revealed no statistical difference between fV and fP for signal quality across all airflow conditions (p = 0.2028). A paired t-test of dynamic performance data revealed no statistical significance between response times for the fV Vs fP. A calibration method was tested for validation in volume measurements, which resulted in a mean estimate = 3.032 L; CV = 1.14 %; n = 83. The fV is easily manufactured with a durable and simple design, making its potential use for ventilation measurement an affordable and reliable technology. These findings provide a reasonable basis to pursue fV technology in applied validation studies, such as inspired and expired ventilation measurement.

Key words
Ventilation, Venturi Meter, Airflow sensor, Airflow meter, Pneumotachometer.

Introduction

Measurement of human ventilation requires the use of an electronic device that can quantify volumetric airflow, integrated to a transducer and user interface, which is otherwise known as an airflow sensor or spirometer. The utilisation of the spirometer in many fields has arguably advanced the effectiveness and outcomes of those fields, with common application in mechanical ventilation, spirometry, indirect calorimetry and patient monitoring. There are many validated spirometry devices, including the pneumotachometer (fP) (Blumenfeld, Turney, & Cowley, 1973; Finucane et al., 1972; Kreit & Sciarba, 1996; Ross & Kao,
Tubes or pipes that have sections in series consisting of different diameters are referred to as fV’s, named after Giovanni Venturi (Venturi, 1797), which are used to quantify fluid flow by the measurement of the differential pressure that occurs between two sections of pipe of different diameter. As fluid moves from a larger to smaller diameter, fluid velocity increases based on the laws of continuity, whilst pressure decreases simultaneously to maintain the conservation of fluid energy. The pressure differential between the two pipe diameters is considered proportional to the fluid flow according to the Bernoulli principle (Bernoulli, 1738). Despite the development and application of the fV in manufacturing and transportation, measurement of ventilation using a fV has not occurred in human basic and applied physiology, such as spirometry and open-circuit indirect calorimetry. This may be due to the need for high sensitivity during low velocity ventilation measurements, such as resting ventilation (< 0.5 L·breath⁻¹), and the inherent non-linear output in differential pressure for a given change in airflow measured by a fV. The non-linear output and the use of initial transducer technology with inadequate amplification, may have been a discouraging method of airflow measurement for these applications. However, with advancements in transducers, amplifiers, and acquisition technology, differential pressure transducers and acquisition devices now exist that allow improved signal quality for very low differential pressure change conditions. This provides an opportunity to investigate the design and application of a fV for airflow measurement with potential use in human ventilation applications.

The combination of the construct validity of the Bernoulli principle and applications to a fV, combined with the deficient empirical research evidence validating (nor invalidating) the use of fV technology for airflow measurement, supports the need for experimental research. The fV has great potential as the device has a simple design, can be easily maintained and sanitized with no moving parts or sensitive electronics located inside the apparatus like some common airflow sensors, and is relatively inexpensive to manufacture.

Airflow sensors can be assessed based on their performances in terms of both dynamic (i.e., short response time and adequate frequency response) and static (i.e., signal quality, resolution, and accuracy across its measurement range) characteristics. Due to the inherent non-linear output that creates limitations such as reduced measurement range, and low sensitivity at low airflow rates described for fixed orifice-meters (Schena et al., 2015), gives reason to assess the fV airflow sensor during very low airflow measurements (<0.5 L·s⁻¹), as it also produces a non-linear signal output. Additionally, the complication of accounting for fluid-state transitions between laminar and turbulent flow needs to be investigated for the fV method for volume measurements. This
becomes apparent when considering a given tidal volume of breath, is produced in an oscillating sinusoidal pattern, consisting of various airflow velocities due to the pulmonary mechanics of the lungs.

The aim of the study was to conduct simultaneous airflow measurements from a new 3D-printed fV, an fT (Universal Ventilation Meter; VacuMed, Ventura, CA, USA), and fP (model 3813; Hans Rudolph, Inc. Shawnee, Kansas, USA) during airflow velocity rates commonly observed in human pulmonary ventilation. The fV was compared for its accuracy in airflow measurement, signal quality, and dynamic performance, to each criterion device for their respective advantages. Comparison of fV signal output to the criterion fT, provided fV airflow analysis that revealed the fluid-state transition characteristics and subsequent calibration of the fV for volume measurements. The decision to compare the fV with this criterion, was based on the reported error of +/- 0.5 % by the manufacturer for stable airflow conditions. This decision is further reinforced, as it is known the fP is not entirely linear throughout its conductance (Tang et al., 2003; Yeh et al., 1982).

The need for a stable and reliable signal for steady flow becomes apparent when deriving the fV coefficient response to airflow. A fluid stream will create a drag force on any obstacle it encounters, as it remains in motion. As fluid interacts with the walls of a fV device, particularly its convergent cone section, a frictional force is created. The theoretical flow calculated by the Venturi equation (eq. 49) is then corrected by the dimensionless figure, the discharge coefficient (C_D) (eq. 50), which essentially calibrates the fV for fluid-state transitions between laminar and turbulent flow. Incorporating the C_D for fV volume measurements, improves its validity, as the accuracy of the device relies on a non-linear signal output, where turbulent flow prevails. Thus, the C_D accounts for the initial linear signal output caused by laminar airflow, and subsequent transition.

\[ \dot{V} = A_1 \sqrt{\frac{2(P_1-P_2)}{\rho \left(\left(\frac{A_1}{A_2}\right)^2-1\right)}} = \text{Theoretical Flow} \]  

Equation 49

Where

\( \dot{V} = \text{Volumetric Flow Rate} \)

\( A_1 = \text{Area of original pipe diameter} \)

\( A_2 = \text{Area of constricted pipe diameter (Throat section)} \)

\( (P_1-P_2) = \text{Differential pressure} \)

\( \rho = \text{Fluid Density} \)

\[ C_D = \frac{\dot{fTV}}{\dot{fV}} \]  

Equation 50

Where

\( \dot{fT}\dot{V} = \text{fT volumetric flow rate} \)

\( \dot{fV}\dot{V} = \text{fV volumetric flow rate} \)
A calibration method for the fV device is discussed and tested, using repeated volume measurements of a criterion volume reference. The fV signal quality was compared to the criterion fP, as both devices quantify airflow and integrated volume, based on differential pressure readings. Therefore, both fV and fP devices utilise the strain-gauge method for sensor output, making a valid comparison of signal quality. Additionally, by establishing the signal quality of the fV for low airflow rates, evaluates the reliability of the signal for low airflow and volume conditions. The fP device is also widely accepted as having a very good signal response time, and so a comparison of dynamic performance was performed using this device during instantaneous flow. We have identified the signal quality, volume measurement accuracy, and dynamic performance as fundamental parameters for an airflow sensor that need to be established for its application, where continuous monitoring of pulsatile airflow is required.

Methods

Instrumentation

For a fV with configurations of a 34 mm ID inlet and 12 mm ID throat section, theoretical calculations of the Venturi airflow equation (equation 49) were conducted, revealing the required differential pressure suitable for monitoring an airflow range of 0-12 L·s⁻¹. This resulted in the purchase of 0-7 kPa input per 0-10 V output differential pressure transducer (Setra Systems, Inc, Boxborough, MA, USA, Model 267).

A Venturi tube was designed in an open-source drafting software (SolidWorks, Waltham, Massachusetts, USA), with an inlet ID of 38 mm, 12 mm ID constricted throat section, 23° conical sections for diameter transitions, followed by an outlet ID of 34 mm; total length 150 mm (Figure 16). A prototype design was then manufactured using a 3-D printer (Airwolf3D, Fountain Valley, CA, USA), and constructed of acrylonitrile butadiene styrene (ABS) thermoplastic, with approximately 4 hrs printing time. Holes (2 mm) were drilled into each diameter section and luer connectors were inserted and glued into place to allow connection to the two ports of the differential pressure transducer using pliable tubing (Figure 24).

Figure 24. Schematic of testing set-up for all data collection trials. 3 Airflow sensors connected in series.


**Experimental Procedure**

The criterion sensors and fV were connected in series via 1 m length tracheal tubing (38 mm ID). An industrial vacuum and ball-valve were used to create and control airflow conditions, respectively. A 16 channel analogue input data acquisition device, integrated to a user interface, allowed for signal collection of the criterion sensors and fV at 50 Hz (LabVIEW, National Instruments, Austin, TX). Signal quality was determined by the signal-to-noise ratio (SNR), with the following sequence of experimental procedures performed. Firstly, four hours of fV baseline data were acquired and repeated over 4 days, to identify any signal drift and warm-up time. Once a warm-up time was established, the three airflow methods were then subjected to repeated constant airflow conditions, spanning the 0-10 VDC output capacity of the differential pressure transducer.

**Testing procedure for airflow measurement and signal quality**

The first condition identified as ‘baseline-after-use’ involved all airflow sensor devices turned on, and exposed to moderate airflow, with subsequent cessation after 25 s of exposure. Baseline data were then acquired from the sensors for a total of 25 s during zero-flow, and repeated 30 times over an approximate 30 min period. The baseline-after-use condition was developed so that characteristics of the baseline noise of the transducers during pulsatile flows were revealed. The lowest airflow condition that could be controlled for was repeated 30 times with an initial 2 s baseline, proceeded by 25 s of condition exposure. Data acquired between 5 and 20 s were used for analysis to ensure a steady signal capture and avoid the lag in airflow rise created by the vacuum. These experimental procedures were then repeated for the subsequent increased airflow conditions that spanned the transducer 0-10 VDC output capacity. Simultaneous data collection of the criterion airflow sensors allowed for identification of airflow rates for all conditions. This established the airflow rate for the lowest reliable signal, the signal quality throughout, and airflow analysis for fV calibration.

**Testing procedure for dynamic performance**

A 3 L calibrated syringe (Hans Rudolph, Inc. Shawnee, Kansas, USA), connected to a one-way T-shaped valve, was used to draw air through the criterion sensor and fV connected in series via tracheal tubing. Data acquisition procedures mentioned in experimental procedure, were also used for this analysis. Repeated 3 L syringe manoeuvres were collected for instantaneous airflow conditions, manually produced to span the fV transducer output capacity of 0-10 VDC. The experiment was conducted twice with airflow produced in both directions. This changed the order of the airflow sensor relative to the 3 L calibrated syringe, without dissembling the airflow sensor and connected tubing. The change of airflow direction enabled us to identify if the order of sensor in series had an influence on dynamic performance, by producing two sets of data for comparison.
**Testing procedure for volume measurement**

The fV device was connected to tracheal tubing (1 m) and a one-way T-shaped valve for controlling airflow direction. Data collection involved acquisition methods mentioned in experimental procedure, with repeated volume measurements based on manual operation of a calibrated 3 L syringe (Hans Rudolph, Inc. Shawnee, Kansas, USA), produced at various ventilation rates.

**Post-Acquisition Data Processing and Analysis**

For all data collections, data was saved as a text file, and imported into a data analysis software program (Prism, Graphpad Software Inc., La Jolla, CA, USA), where the following post-acquisition procedures were conducted. For the baseline-after-use condition, a condition-specific baseline-correction using an average deduction method was used. For repeated constant airflow conditions, the data was baseline-corrected using a trial-specific average deduction method, acquired from the initial 2 s baseline collection. For repeated instantaneous airflow, and repeated volume data, the data was baseline-corrected using a trial-specific average deduction method, acquired from the baseline before and after each 3 L syringe manoeuvre. Subsequent analyses were then performed.

**Statistical Analyses**

**Signal quality**

The SNR data were used to give estimates of signal quality for each device under measuring air flow. The root-mean-square (RMS) voltage amplitude using peak voltage ($V_P$), for the lowest airflow condition was compared to the RMS voltage of the baseline noise via ratio computations, conducted through the following procedures. Both $V_P$ and RMS voltage condition’s 30 trial data were compiled via row means, then computed for RMS voltage (equation 54). These results were then converted to SNR decibel units via equation 55. Acceptance of a reliable signal was determined by the SNR ratio exceeding 1 (0 dB), thereby indicating that signal magnitude to be more than baseline noise (Placko, 2013).

\[
V_{RMS} = \frac{1}{\sqrt{2}} * V_P = 0.707 * V_P \quad \text{Equation 54}
\]

\[
dB_{SNR} = 20 \log 10 \left( \frac{RMS_{signal}}{RMS_{noise}} \right) \quad \text{Equation 55}
\]

For condition-specific signal quality throughout the 0-10 VDC output, comparisons of signal amplitude to signal noise took place via the following series of procedures. For each condition, the 30-trial data were compiled via row means, then baseline-corrected using the condition signal amplitude between 5 and 20 s. Equation 54 was then utilised to process the data, revealing the within-signal RMS voltage noise of each airflow condition. SNR values were then computed by comparison of the within-
signal RMS voltage noise to the baseline-corrected RMS voltage signal for each airflow condition, then converted to SNR decibel units (equation 55).

**Dynamic performance**

The response time for both devices when measuring pulsatile airflow were identified by area under the curve analysis, with the peak curve measured and matched to the time it occurred (peak X). The difference in peak X values for the criterion and fV were reported for each manoeuvre and plotted against the corresponding volumetric airflow for that manoeuvre (See figure 25). Finally, the data set were compared via an un-paired t-test for statistical differences between group means, establishing the dynamic performance of the two methods across different pulsatile airflow conditions.

![Figure 25](image)

*Figure 25. Visual representation of dynamic performance analysis. The comparison is between the differences in time where the peak of the curve takes place for each airflow sensor measuring inspired pulmonary ventilation.*

**Airflow analysis and calibration method**

The fV airflow was identified by comparing signal output of the fV transducer and subsequent computations using equation 49, to the airflow rate measured by the criterion fT device for each airflow condition, with the following procedures conducted. For the fT device, a calibration constant was derived by repeated 3 L syringe manoeuvres revealing a volts:litre calibration factor
that was acquired before each condition, and subsequently used to correct airflow measurements. For the fV, voltage output was converted to pressure via slope-intercept correction (700 Pa:1 Volt), then computed for volumetric airflow using equation 49. Relative humidity, room temperature and atmospheric pressure were recorded using a weather station (Model: WS5029, Holman Industries, Osborne Park, Western Australia), for each condition and used for determining the air density (equation 53) for utilisation in equation 49.

\[ \rho = \rho_{da} (1 + x)/(1 + 1.609x) \]  
Equation 53

Where
\( \rho \) = density of moist air (kg·m\(^{-3}\))
\( \rho_{da} \) = density of dry air (kg·m\(^{-3}\))
\( x \) = humidity ratio by mass (kg/kg)
1.609 = gas constant ratio between water vapour and air

Calibration of the fV involved using the fT to determine the reference \( \dot{V} \) for the 30 repeated trials of each airflow condition, up to 10 L·s\(^{-1}\). The \( C_D \) (eq. 50) was found by dividing the fT \( \dot{V} \) estimate, by the fV \( \dot{V} \) estimate for each condition, then plotting the \( C_D \) against fV \( \dot{V} \). This revealed the \( C_D \) function for the fV, which was best fitted with a One-phase Association exponential model, shown in equation 56.

\[ Y = Y_0 + (Plateau - Y_0) \times (1 - EXP(-K \times \dot{V})) \]  
Equation 56

The fV signal acquired during the volume measurement procedure, were computed via equation 49 and 53, with the addition of equation 56.

**Statistical Analyses**

A paired t-test was used to compare the signal quality, and response time of fP and fV data, with reported mean of differences, SD, two-tailed P value, t, df, and the summary of statistical significance. Statistical significance accepted at \( P = \leq 0.05 \).

The calibration method for fV volume data was analysed for minimum error requirements via area under the curve (AUC) analysis, with additional mean 3 L estimates and coefficient of variation (CV), and subsequently compared to fV volume data without the calibration method.
Results

A paired t-test comparing the signal quality of fP Vs. fV for the data presented in figure 25, revealed no significant difference (mean of differences = 5.07, SD = 11.67; two-tailed p value = 0.2028; t = 1.374, df = 9: significance accepted p = ≤0.05; Summary = ns). The lowest airflow condition that could be controlled for, resulted in a signal quality of 6.2 dB Vs. 24.8 dB at 0.043 L·s⁻¹ for fV and fP, respectively. The highest airflow condition that could be controlled, resulted in 54.3 dB Vs. 52 dB at 12.366 L·s⁻¹ for fV and fP, respectively. The highest signal quality was reported for the 2nd highest airflow condition with 55.7 dB Vs. 53.1 dB at 12.080 L·s⁻¹ for fV and fP, respectively.

A paired t-test comparing the response time of the fP Vs. fV for the data presented in figure 26, revealed no significant difference (mean of differences = 0.0067 s; SD = ±0.027; two-tailed P value = 0.08; t = 1.783, df = 53: significance accepted p = ≤0.05; Summary = ns). Airflow direction: From Right to Left (in reference to Figure 24).

A paired t-test comparing the response time of the criterion Vs. fV for the data presented in figure 27, revealed no significant difference (mean of differences = -0.0044 s, SD = ±0.063; two-tailed P value = 0.469; t = 0.7267, df = 109: significance accepted p = ≤0.05; Summary = ns). Airflow direction: From Left to Right (in reference to figure 24).

The effect of applying the calibration (equation 6) derived from figure 21, to the volume computations of repeated syringe manoeuvres at peak flow rates between 0 – 10.5 L·s⁻¹, was revealed via AUC analysis and column statistics, with data presented in figure 29. The results show that without the calibration (fV Vol), the mean estimate was 3.094 L ±0.042, CV = 1.34%; and with the calibration (fV One-phase Association) the mean estimate was 3.025 L ±0.034, CV = 1.14%.
Figure 25. Signal quality reported as decibels (dB) for fP and fV, plotted against volumetric airflow in litres per second (L·s\(^{-1}\)).
Figure 26. Difference in response time (seconds) between the fP and fV, for identifying the peak curve of a syringe manoeuvre, plotted against volumetric airflow in litres per second (L·s⁻¹). Airflow direction: From Right to Left (in reference to Figure 24).
Figure 27. Difference in response time (seconds) between the fP and fV, for identifying the peak curve of a 3 L syringe manoeuvre, plotted against volumetric airflow in litres per second (L·s⁻¹). Airflow direction: From Left to Right (in reference to figure 24).
Figure 28. The $C_D$ response to changes in fluid-state transition between laminar and turbulent flow. The data was best fitted with a one-phase association exponential model. Best fit values and goodness of fit reported.
Figure 29. 3 L data collection acquired from the fV device, at different airflow conditions.
Discussion

The data presented in figure 25 reveals the comparison of signal quality for the fP and fV methods of airflow measurement. Whilst a paired t-test revealed no statistical significance between the differences for the entire data set, the fP produced higher signal quality during airflow conditions less than 0.5 L·s⁻¹. However, the signal quality for the fV for these conditions were still acceptable, with the ratio of signal to noise greater than one, indicated by a response more than 0 dB. As airflow increased, it is evident that signal quality markedly increased for the fV, matching the fP at approximately 1.8 L·s⁻¹, and throughout increasing airflow. The American Thoracic Society which are responsible for outlining universal spirometry standards, stipulate that a spirometer should be able to quantify airflow as low as 0.1 L·s⁻¹ (Miller et al., 2005). The lowest airflow condition was measured at 0.079 L·s⁻¹ for the fV. The use of a data acquisition device with 16-bit resolution (National Instruments, Austin, TX, USA), infers changes of 153 µV can be resolved for a 10 V output. The 0.043 L·s⁻¹ was measured at 413 µV, which equates to an amplitude 270 % more than the lowest precision of measurement capable of this device. The signal quality measured at 0.043 L·s⁻¹ was 6.2 dB for the fV, indicating more signal than noise, resulting in a reliable measurement, which satisfies the expected 0.1 L·s⁻¹ graphical output threshold required for a spirometer.

The data in figure 26 and 27, reveal the dynamic performance of both devices during a comparison of peak tidal volume measurements during pulsatile airflow manoeuvres. Paired t-tests on both data-sets reveal that both airflow sensor technologies have systematically similar response times and frequency response characteristics, when compared during airflow velocity conditions observed in normal human pulmonary ventilation. The direction of airflow relative to airflow sensor position in series, had a quantifiably negligent effect on response time, indicated by the positive and negative mean of differences result (0.0067 s Figure 26 vs -0.0044 s Figure 27).

Figure 28 reveals the laminar-turbulent transition of fluid state within the fV device during increasing airflow velocities. The data shows how fluid friction during laminar flow, causes distortion in differential pressure readings, and subsequent overestimation of airflow at low velocities. This is indicated by the low coefficients during the initial airflow estimations. As the airflow rate increases, the fluid transitions into turbulent flow, reaching full turbulence at approximately 0.5 L·s⁻¹. Unlike linear output airflow sensors, such as the fT and fP, turbulent airflow for the fV means stable and reliable airflow measurements. This feature is advantageous for exercise stress testing, where expired gas analysis indirect calorimetry methods are employed. Airflow sensors with better accuracy and reliability at moderate to high ventilation rates, should improve the validity of determining some standard physiological variables.

One important variable, is the ventilatory threshold, whereby increases in ventilation rate exceed increases in the rate of oxygen consumption. The ventilation threshold correlates with blood lactate accumulation, which are indicators for the onset
of metabolic acidosis. Another important variable is maximum oxygen consumption ($\dot{V}O_{2\text{max}}$). To attain a high level of oxygen consumption, requires a diverse interaction of the human body’s physiological systems. Therefore, $\dot{V}O_{2\text{max}}$ provides a quantitative measure for exercise performance and cardiovascular health. The fV device would be suitable for determining both these important variables, as they occur at moderate to high ventilation rates, where high airflow rates prevail. However, pulmonary mechanics of the human lung inherently produce sinusoidal tidal volumes at all ventilation rates. This means, for any given tidal volume of human breath, the initial and end components of the flow curve, will consist of airflow rates less than 0.5 L·s$^{-1}$. Thus, the use of a fV device for measuring human pulmonary ventilation, must account for differential pressure distortion caused by fluid friction during laminar flow. The fV Vol data in Figure 29, reveals the increased error in volume measurements that occur during peak flows less than 2 L·s$^{-1}$. This evidence indicates, ventilation rates such as rested breathing, would be over-estimated if measured by an fV device without further calibration. However, by computing the fV signal with the addition of the one-phase association model (equation 56), the volume measurements during low velocities are corrected, and all data points remain within the minimum error margin. The CV was also reduced from 1.38 % to 1.14 %, which concludes the calibration method corrected over-estimations in volume, as well as reducing the relative variability.

**Conclusion**

This study has presented the findings on a performance analysis of a new 3D-printed airflow sensor: the fV. These include both static and dynamic features of the device compared to two industry-accepted criterion devices for their respective advantages: the fP, and fT airflow sensor. The results for signal quality, especially during very low airflow rate measurements, as might be seen during resting pulmonary ventilation, indicate the fV signal is of a reliable and accurate standard. The experiments conducted in this study also reveal that both fV and fP produce systematically similar results in response times, revealing the fV to be suitable for high frequency oscillatory airflow conditions. Calibration methods have been detailed, which were tested for measurements of volume manoeuvres, based on a 3 L calibrated syringe. The results revealed high precision, with adequate measurement range to detect normal human pulmonary ventilation observed during rest to volitional exhaustion. The fV has great potential as the device has a simple design, can be easily maintained and sanitized with no moving parts, or sensitive electronics located inside the apparatus like some common airflow sensors, and is relatively inexpensive to manufacture.
Chapter Five

Pulmonary Ventilation Measurement via Venturi Airflow Sensor: Application to Expired Gas Analysis Indirect Calorimetry
Title: Pulmonary Ventilation Measurement via Venturi Airflow Sensor: Application to Expired Gas Analysis Indirect Calorimetry

Abbreviated title: Venturi Applied in Indirect Calorimetry

Authors: Praneel Titheradge¹, Robert Robergs², Alexander MacQuarrie¹

Institutions:
¹ School of Exercise Science, Sport and Health, Charles Sturt University, Bathurst NSW, Australia
² School of Exercise & Nutrition Sciences, Faculty of Health, Queensland University of Technology, Brisbane, QLD, Australia

 Corresponding author:
Praneel Titheradge
Charles Sturt University
Panorama Avenue,
Bathurst, 2795, NSW Australia
ptitheradge@csu.edu.au

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Abstract

This study discusses the clinically applied validation of a Venturi airflow sensor (fV) manufactured via 3D printing. Simultaneous measurements of pulmonary ventilation were taken with the fV, and two well-established airflow sensor technologies (Turbine (fT); Pneumotachograph (fP)), on participants during a cycling ramp test and subsequent steady-state cycling bout, combined with oxygen (O₂) and carbon dioxide (CO₂) gas analysis of expired air. The purpose of the simultaneous pulmonary ventilation measurement was to assess the minute ventilation ($\dot{V}_E$: L·min⁻¹) differences between devices, and subsequent influence these differences had on expired gas analysis indirect calorimetry (EGAIC) computations. Linear regression of fV $\dot{V}O_2$ measurements for all subjects, plotted against fT $\dot{V}O_2$ measurements are: $y = 0.7536 + 0.9657 \times X; r^2 = 0.99; Sy.x = 1.2$ mlO₂·kg·min⁻¹. Linear regression of fV $\dot{V}O_2$ measurements for all subjects, plotted against fP $\dot{V}O_2$ measurements, for linear regression analysis are: $y = 0.1981 + 1.004 \times X; r^2 = 0.98; Sy.x = 2.326$ mlO₂·kg⁻¹·min⁻¹. Results for a mixed ANOVA experimental design, with testing of main effects: Exercise Intensity, Airflow sensor method, and interaction effect, influencing $\dot{V}O_2$ measurements resulted in P = <0.0001; P = 0.96; P = 0.95, respectively. Bland-Altman analysis comparison between fV and fT are: Bias = 0.16 mlO₂·kg⁻¹·min⁻¹; 95 % CI = 2.6 to -2.8 mlO₂·kg⁻¹·min⁻¹. The main effects: Exercise Intensity, Airflow sensor method, and interaction effect were also assessed for $\dot{V}_E$: P = <0.0001; P = 0.99; P = 0.98, respectively. Bland-Altman analysis comparison between fV and fP for $\dot{V}O_2$ are: Bias = 0.15 mlO₂·kg⁻¹·min⁻¹; 95 % CI = 4.4 to -4.7 mlO₂·kg⁻¹·min⁻¹. The $\dot{V}_E$ Bland-Altman comparison for low flow: Bias = 0.011 L·min⁻¹ and +4.436 L·min⁻¹ to -4.414 L·min⁻¹ 95 % CI for fV and fT; Bias = 0.196 L·min⁻¹ and +3.196 L·min⁻¹ to -3.524 L·min⁻¹ 95 % CI for fV and fP. The results indicate the pulmonary ventilation measurement taken by a fV, reveals both statistical and practical validity for use in EGAIC from rest to peak exercise intensities for healthy populations. Additionally, this study is the first of its kind that shows in-vivo results for different types of airflow sensor method contribution to technical error in measurements within EGAIC.

Key words

Indirect Calorimetry, Pulmonary Ventilation, Venturi, Pneumotachograph, Turbine.
Introduction

Changes in heat production in a biologic system provides a useful technique to monitor the energy dynamics of any process of energy transfer. As demonstrated with combustible compounds in bomb calorimetry, the human body metabolises food sources for energy production (mainly carbohydrates and fats, and to a less extent, proteins), which results in heat (Kcal) liberated from the chemical reactions based on the balance of free energy release and chemical capture in the form of adenosine-triphosphate (ATP) (Lehninger, Nelson, & Cox, 2013). Because oxygen drives the respiratory chain, providing the cellular work needed for complete combustion of food substrates, the total energy exchanged during this catabolic feature of metabolism can be inferred readily from oxygen consumption measurement (Ferrannini, 1988).

The measurement of oxygen consumption via expired gas analysis indirect calorimetry (EGAIC), represents a fundamental tool in exercise physiology. Expired gas analysis indirect calorimetry involves a subject inhaling ambient air, made up of a mixture of gases, which currently measure at 20.95%, 0.04% & 78.08% for oxygen, carbon dioxide, and nitrogen, respectively (Williams, 2016). An airflow sensor is used to quantify the inhaled or exhaled volume of air. Rapid gas analysers are used to sample the changes in oxygen and carbon dioxide within the expired air relative to ambient air inhaled. This methodology assumes that no nitrogen is consumed or produced by the human body, which is given by equation 57, known as the Haldane transformation (Wilmore & Costill, 1973):

\[ V_I = V_E \times F_{EN_2} + F_{IN_2} \]  
Equation 57

Where \( V_I \) is the volume of inspired air, \( V_E \) is the volume of expired air, \( F_{EN_2} \) is the expired gas fraction of nitrogen, and \( F_{IN_2} \) is the inspired gas fraction of nitrogen. Because ambient air concentrations of nitrogen, carbon dioxide and oxygen are known, and with nitrogen assumed physiologically inert, only \( V_I \) (or \( V_E \)) and the gas concentrations of the expired carbon dioxide \( F_{ECO_2} \) and oxygen \( F_{EO_2} \) are needed to calculate the rate of oxygen consumed \( \dot{V}O_2 \), (Bassett et al., 2001; Croonen & Binkhorst, 1974; Wilmore & Costill, 1973).

The computation for \( \dot{V}O_2 \) is given by equation 58:

\[ (\dot{V}O_2) = \left( \dot{V}E \times \frac{F_{EN_2}}{F_{IN_2}} \right) \times F_{IO_2} - (\dot{V}E \times F_{EO_2}) \]  
Equation 58

Where

\[ F_{EN_2} = 0.99063 - (F_{EO_2} + F_{ECO_2}). \]
The airflow sensor, gas analysers, data acquisition and user interface are all assembled together on a trolley called the metabolic cart. Many automated metabolic cart systems that are currently available on the market utilise validated airflow sensors such as those based on differential pressure, that is, pneumotachometer (Blumenfeld et al., 1973; Ross & Kao, 1961; Turney & Blumenfeld, 1973; Yeh et al., 1987; Yeh et al., 1982; Zock, 1981), pitot-static tube (Kirkness et al., 2010; Meriläinen, Hänninen, & Tuomaala, 1993; Porszasz et al., 1994; Wolf & Volgyesi, 1987), and fixed or variable orifice tubes (Fortuna & Gurd, 1999; Osborn, 1978). Other airflow sensors used include those based on the conversion of fluid energy to mechanical work like the turbine (Frayne et al., 1994; Howson et al., 1987; Isley et al., 1993), or those that depend on thermodynamics of wind speed, such as the hot-wire Anemometer (Bruner, 1947; Caruso, 1973; Lundsgaard et al., 1979; Plakk et al., 1998). However, some clinicians maintain the use of early methods of gas volume measurement via direct volume displacement spirometers such as the Tissot-tank (Allingstrup et al., 2016). The measurement of ventilation needed for the quantification of $\dot{V}O_2$ is a relatively simple measurement compared to that of determining changes in gas concentration. Yet, without valid measurements of ventilation, the quantification of $\dot{V}O_2$ is flawed with large error, as this decisive variable essentially drives all subsequent computations of $\dot{V}O_2$. Thus, emphasis should be placed on the use of valid, practical, and durable ventilation technology for determining $\dot{V}O_2$.

Despite the abundant range of methods to measure pulmonary ventilation in EGAIC, the use of the Venturi principle; a method of fluid measurement that has existed since the 1700’s (Venturi, 1797), and readily used in many applications (He & Bai, 2012; Huang, Li, Liu, Wang, & Li, 2007; Jitschin, 2004; Miller, 1974; Reader-Harris et al., 2001), has yet to be applied and validated for the measurement of human pulmonary ventilation. However, evidence does exist of a Venturi used in equine exercise stress testing (Seeherman & Morris, 1990), although detailed methodology of minute ventilation calculation is limited. The testing model allows for intermittent air contamination, causing fluctuations in air humidity, temperature and density, which of course are not ideal for an airflow method that involves the Bernoulli Principle. Consequently, there is basic and applied science rationale for conducting validation research. From an applied science perspective, research verifying the suitability of the Venturi principle for valid measurements in human pulmonary ventilation is essential based on the lack of scientific scrutiny of its use. This fundamental measurement is influential in the science of indirect calorimetry and subsequent measurements of whole body $\dot{V}O_2$ (L·min⁻¹), $\dot{V}CO_2$ (L·min⁻¹), RER, and energy expenditure (Kcal·min⁻¹).

This study discusses the clinically applied validation of a Venturi airflow sensor (fV) constructed via three-dimensional (3D) printing. Simultaneous measurements of pulmonary ventilation were taken with the fV, and two well-established airflow sensor technologies, on participants during a $\dot{V}O_2$ cycling ramp test and subsequent steady-state cycling bout. The purpose of the simultaneous measurement was to assess the L·min⁻¹ differences between devices, and subsequent influence these differences had on EGAIC computations.
Methods

Participants
A priori sample size estimation was performed using software (GPower version 3.1.2; Universitat Kiel, Germany), revealing the need for 9 subjects based on an effect size of 0.5, p < 0.05, statistical power = 0.8, 1 group, and 2 trials. As we were unclear of the possible differences between the methods of ventilation, and given the sensitivity of the EGAIC method to small errors in ventilation, we more than doubled this sample size to ensure adequate statistical power, minimal risk of type II errors, and a wider range of physiological capacities between subjects to improve the ecological validity of the results.

Six males (Age: 38 ± 8 yr; Height: 178.8 ± 4.2 cm; Mass: 86.8 ± 9.9 kg) and fourteen females (Age = 44.6 ± 9.6 yr; Height = 164.6 ± 6.9 cm; Weight = 64.9 ± 7.7 kg) were recruited for the study. All participants completed an Adult Pre-Screening System tool to determine that they were in good physical health with no musculoskeletal disorders or risk factors towards an adverse event during intense physical activity. Each participant was recruited on a basis of self-reported physical fitness (minimum requirements: endurance exercise training for at least 3 times/week). An aerobically trained population were recruited on the basis that high pulmonary ventilation rates were desired for testing the airflow sensor range. Written informed consent was obtained from each participant prior to data collection and all methods were approved by the Institution’s Human Research Ethics Committee.

Familiarisation and baseline testing
During the familiarisation session, the participant’s height and mass were recorded, and the cycle ergometer was manually adjusted (seat height, handlebar height and reach etc.) for proficient movement efficiency. Before exercising, the participant remained seated for 5 min to ascertain a resting seated heart rate (HR). The subject cycled at 100 W load for 3-5 min until they had established a comfortable, and constant pedalling cadence between 70-80 revolutions per minute (rev·min⁻¹). This cadence was then used throughout each exercise protocol. Participants were then instructed to perform these exercise bouts after the following equipment setup: subjects fitted with a multiple one-way T-shaped valve and mouthpiece system, supported by an acrylic head unit (Hans Rudolph, Inc. Shawnee, Kansas, USA). A compliant and elastic latex mixing chamber was attached to the expired side of the valve/mouthpiece, which had a gas sampling line inserted for measurements of O₂ and CO₂ gas concentrations (Kim & Robergs, 2012). Electrocardiography (ECG) was also applied to the participant to acquire HR using a 5-lead ECG configuration (CASE, GE Healthcare, Waukesha, USA).

Exercise Protocol
Subjects performed physical exertion on a stationary cycle-ergometer (Lode B.V. Groningen, Netherlands), for measurements of pulmonary ventilation and EGAIC computations. Exercise protocols and subsequent conditions involved seated rested state, incremental exercise to exhaustion (\(\dot{V}O_2\) ramp test), and a steady-state exercise bout induced by a constant Watt load. For the
\( \dot{V}O_2 \) ramp test, each subject was instructed to cycle at a cadence 70 - 80 rev/min, and maintain that cadence for the entirety of the exercise bout. The ramp function for each subject was based on their self-reported cycling fitness and the need to constrain test duration between 8 and 12 min (Astorino et al., 2000; Yoon, Kravitz, & Robergs, 2007). Consequently, the ramp function varied between subjects from 25 to 40 Watts/min. The ramp protocol consisted of two min of rested breathing, followed by two min at double the ramp function Watts for that subject, followed by the near continuous ramp function. The participant was instructed to continue cycling until volitional tolerance (Astorino et al., 2000; Yoon et al., 2007). The test ended when the subject could no longer maintain a pedalling cadence > 40 rev/min. The subject then laid supine for a 60 min recovery period before setup of the following exercise trial.

Using the breath-by-breath \( \dot{V}O_2 \) data collected from the ramp test, the ventilatory threshold (VT) of each subject was determined visually by the excess carbon dioxide method (Gaskill et al., 2001), using a custom designed computer program (LabVIEW™, National Instruments, Austin, TX, USA). The VT was used to determine the power output required for the following steady-state cycling bout. The steady-state exercise bout was limited to 80 % VT, to avoid onset of metabolic acidosis, and subsequent increase in pulmonary ventilation and \( \dot{V}O_2 \) (Gaskill et al., 2001). This exercise bout began with two min of rested breathing, followed by two min of unloaded cycling at 70 to 80 rev/min cadence. Finally, the subject was required to maintain their cadence whilst subjected to 80% VT for eight minutes.

**Instrumentation Model**

A pneumotachograph (IP; model 3813; Hans Rudolph, Inc. Shawnee, Kansas, USA), turbine (fT; Universal Ventilation Meter; VacuMed, Ventura, CA, USA), and fV were connected in series via tracheal tubing with at least one metre length separation (See Figure. 30). The one-way T-shaped valve and mouthpiece system was attached to the tracheal tubing with airflow sensors in situ for measurement of inspired pulmonary ventilation (See Figure. 30). A custom-built metabolic cart using rapid responding gas-analysers (AEI Technologies Inc. Pittsburgh, PA, USA) was used to sample the expired pulmonary breath gas concentrations. Voltage signals from the gas-analysers and airflow sensor devices were simultaneously acquired at 50 Hz using a data acquisition device: 16 channel analogue/digital input; 16-bit resolution; sensitivity = 153 \( \mu \)V for 10 V range, (National Instruments, Austin, TX), integrated to a user interface, using custom-designed virtual acquisition software (LabVIEW™, National Instruments, Austin, TX, USA). The testing model was designed with open-ended entrance and exit of air, allowing for no compression or vacuum effects of air during measurement over time.

Based on the law of continuity, and principles of conservation of mechanical energy, volumetric airflow must be the same at any point along a streamline in a pipe-like structure (Bernoulli, 1738). Therefore, all flow rate devices were exposed to the same volumetric airflow condition, at the same time. The measurements of inspired pulmonary ventilation (L·min\(^{-1}\)), were combined
with sampled gas concentrations to compute subsequent measurements of whole body $\dot{V}O_2$ (ml·kg$^{-1}$·min$^{-1}$), $\dot{V}CO_2$ (ml·kg$^{-1}$·min$^{-1}$) and RER, using the Haldane method for inspired to expired $\dot{V}E$ conversion (see equation 58).

Figure 30. Testing model for indirect calorimetry protocol and instrumentation: Turbine (fT), Pneumotachograph (fP) and Venturi (fV) connected in series via tracheal tubing, with participant connected for inspired ventilation, and mixing chamber for expired gas sampling.

**Airflow Sensor Calibration**

The Pneumotachograph (fP) and Turbine (fT) devices are both linear response airflow sensors. This means that for a given increase in airflow, a proportional voltage increase occurs that can be described by a linear straight line. Therefore, a calibration constant was derived by repeated volume manoeuvres, using a calibrated 3L syringe (Hans Rudolph, Inc. Shawnee, Kansas, USA). This procedure revealed a volts:litre calibration factor that was acquired before each subject trial, and subsequently used to correct pulmonary ventilation measurements. The fV is an inherently non-linear device, producing a signal output that can be described by a non-linear or quadratic function. Therefore, a different series of calibration was employed. This entailed converting the voltage output to pressure (Pascals: Pa) via a slope-intercept correction based on transducer input/output specifications. The Pa signal was then computed for volumetric airflow via equation 49. Relative humidity, room temperature and atmospheric pressure were recorded for each condition via a weather station (Model: WS5029, Holman Industries, Osborne Park, Western Australia), for determining the air density (equation 53) for utilisation in equation 49. Mean ± SD for relative humidity (%), room temperature (degrees Celsius [°C]), and atmospheric pressure (mmHg) during testing were: 47% ± 11; 22°C ± 5; 768 mmHg ± 2, respectively.

$$\dot{V} = A_1 \sqrt{\frac{2(P_1-P_2)}{\rho \left(\frac{A_1}{A_2}\right)^2 - 1}} = \text{Theoretical Flow}$$  
Equation 49
\[ \dot{V} = Volumetric \ Flow \ Rate \]

\[ A_1 = Area \ of \ original \ pipe \ diameter \]

\[ A_2 = Area \ of \ constricted \ pipe \ diameter \ (Throat \ section) \]

\[ (P_1 - P_2) = Differential \ pressure \]

\[ \rho = Fluid \ Density \]

\[ \rho = \rho_{da}(1 + x)/(1 + 1.609x) \]  
Equation 53

Where

\[ \rho = \text{density of moist air (kg·m}^{-3}) \]

\[ \rho_{da} = \text{density of dry air (kg·m}^{-3}) \]

\[ x = \text{humidity ratio by mass (kg/kg)} \]

\[ 1.609 = \text{gas constant ratio between water vapour and air} \]

Further calibration of the fV involved accounting for differential pressure distortion caused from friction loss. The method for determining the drag coefficient (\( C_D \)) function for the fV has been previously detailed in chapter 3, which was best fitted with a One-phase Association exponential model, shown in equation 56.

\[ Y = Y_0 + (Plateau - Y_0) \times \left( 1 - EXP\left(-K \times \dot{V}\right) \right) \]  
Equation 56

All airflow sensor inspired pulmonary ventilation measurements were converted from atmospheric, temperature, pressure, saturated conditions (L·min\(^{-1}\)ATPS), to standard, temperature, pressure, dry conditions (L·min\(^{-1}\)STPD), using equation 59. The standardisation pulmonary ventilation measurements to constant conditions allows for comparison of tests with varying gas temperature, pressure and water vapour content between data collections.

\[ VI_{STPD} = VI_{ATPS} \times \left( \frac{273}{273 + T_{room}} \right) \times \left( \frac{P_B - P_{H_2O}}{760} \right) \]  
Equation 59

Where

\( VI = \text{Volume of Inspired Air (pulmonary ventilation)} \]

\[ 273 = \text{Standard Temperature (0°C = 273°K)} \]

\[ T_{room} = \text{Room Temperature} \]

\[ 760 = \text{Standard Atmospheric Pressure (1 Atmosphere (Atm) = 760mmHg)} \]
\( P_{H2O} \) = Water Vapour Pressure (mmHg)
\( BP \) = Barometric Pressure

**Post-Acquisition Data Processing and Analysis**

For all data collection, data was saved as a text file, and imported into a custom data processing program (LabVIEW™, National Instruments, Austin, TX, USA), where the following procedures occurred. A device signal was selected, where a scroll-bar tool allowed for visual scanning of breath data for 1 min sample of the exercise condition. The signal was initially baseline-corrected using an average deduction method, using the trial-specific baseline signal to remove zero-span differences between devices. For the fP and fT, the voltage integral was then corrected via the Volts:Litre correction factor discussed earlier, resulting in the volume integral. For the fV, the processing program was coded to first employ the calibration parameters discussed earlier, then compute the volume integral with adjustment based on environmental conditions.

**Statistical Analyses**

A mixed ANOVA experimental design was completed to determine the influence of the differences between pulmonary ventilation methods used for computations within EGAIC, when exposed to various exercise intensities. Statistical significance accepted at \( p < 0.05 \). Linear regression analysis of the entire data-set was used for the relationship and variance between methods across the measurement range, with reported correlation coefficient and standard error of the estimate (Sy.x). Finally, Bland-Altman analysis was performed on the entire data set comparing the difference between two methods, against the average of the methods, for average bias and 95% confidence limits of agreement.

**Results**

Figure 31 presents the \( V_E \) (Y-axis) results for a mixed ANOVA experimental design, with data grouped by intensity and labelled by airflow sensor method. Null hypothesis testing for factors: intensity, airflow sensor method, and interaction of these two factors, reveal their influence on \( V_E \) measurements. There was a significant main effect (\( P = <0.0001 \)) difference in \( V_E \) measurements between rest, 80 % VT steady state exercise, and exercise at high intensity. In addition, there was an insignificant main effect (\( P = 0.99 \)) between airflow sensors, as well as an insignificant interaction (\( P = 0.98 \)) difference in \( V_E \) measurements between intensity and airflow sensor.

Figure 32 presents the \( \dot{V}O_2 \) (Y-axis) results for a mixed ANOVA experimental design, with data grouped by intensity and labelled by airflow sensor method. Null hypothesis testing for factors: intensity, airflow sensor method, and interaction of these two factors, reveal their influence on \( \dot{V}O_2 \) measurements. There was a significant main effect (\( P = <0.0001 \)) difference in \( \dot{V}O_2 \) measurements, between rest, 80 % VT steady state exercise, and exercise at \( \dot{V}O_{2max} \). In addition, there was an insignificant
main effect (P = 0.96) between airflow sensors, as well as an insignificant interaction (P = 0.95) difference in \( \dot{V}O_2 \) measurements between intensity and airflow sensor. The average VO\(_2\) rate during the resting condition was 6.699 ml·kg\(^{-1}\)·min\(^{-1}\) ± 2.456.

Figure 31. Mixed ANOVA of device/method mean ± 95% CI, minute ventilation differences across rest, 80% VT steady state exercise, and at high intensity for 20 participants. Main effects are for airflow sensor method, and exercise intensity; interaction effect is for Sensor*Intensity.
Figure 32. Mixed ANOVA of device/method mean, SD differences across rest, 80 % VT steady state exercise, and at $VO_2 \text{max}$ for 20 participants.
Figure 33 presents graph a) fV and fP $\dot{V}O_2$ measurements for all subjects, plotted against fT $\dot{V}O_2$ measurements, for linear regression analysis, with $r^2 = 0.99$ Vs. $r^2 = 0.98$; Sy.x = 1.2 mlO$_2$-kg$^{-1}$-min$^{-1}$ Vs. 2.4 mlO$_2$-kg$^{-1}$-min$^{-1}$ for fV and fP, respectively. Graph b) presents fV and fT $\dot{V}O_2$ measurements for all subjects, plotted against fP $\dot{V}O_2$ measurements, for linear regression analysis, with $r^2 = 0.98$ Vs. $r^2 = 0.98$; Sy.x = 2.326 mlO$_2$-kg$^{-1}$-min$^{-1}$Vs. 2.437 mlO$_2$-kg$^{-1}$-min$^{-1}$ for fV and fT, respectively.

Figure 33. Linear regression analysis with reported $r^2$ and Sy.x for a) fV and fP $\dot{V}O_2$ data, plotted against fT $\dot{V}O_2$ data. b) fV and fT $\dot{V}O_2$ data, plotted against fP $\dot{V}O_2$ data. All units expressed as mlO$_2$-kg-min.

Figure 34 presents the results of a Bland-Altman analysis using the difference between methods (Y-axis), plotted against the average of the two methods (X-axis). For graph a) the comparison is between fV and fT, with Bias = 0.16 mlO$_2$-kg$^{-1}$-min$^{-1}$ and 2.6 mlO$_2$-kg$^{-1}$-min$^{-1}$ to -2.8 mlO$_2$-kg$^{-1}$-min$^{-1}$ for upper limit and lower limit lines of identity, which represent the 95% confidence intervals of agreement. For graph b) the comparison is between fV and fP, with Bias = 0.15 mlO$_2$-kg$^{-1}$-min$^{-1}$ and 4.4 mlO$_2$-kg$^{-1}$-min$^{-1}$ to -4.7 mlO$_2$-kg$^{-1}$-min$^{-1}$ for upper limit and lower limit lines of identity, which represent the 95% confidence intervals of agreement.
Figure 34. Bland-Altman analysis of pulmonary ventilation and $\dot{V}O_2$ data with reported average bias and upper limit (UL) and lower limit (LL) 95% confidence intervals of agreement. Comparisons are for fP and fV, (a and c) and for fT and fV (b and d). Note the difference in units of L·min$^{-1}$ and mlO$_2$·kg$^{-1}$·min$^{-1}$. 
Figure 35 and Figure 36 present the results of a Bland-Altman analysis using the difference between methods (Y-axis), plotted against the average of the two methods (X-axis). For figure 35, the comparison is between $f_V$ and $f_T$, with Bias = 0.011 L·min$^{-1}$ and +4.436 L·min$^{-1}$ to -4.414 L·min$^{-1}$ for upper limit and lower limit lines of identity, which represent the 95% confidence intervals of agreement. For figure 36, the comparison is between $f_V$ and $f_P$, with Bias = 0.196 L·min$^{-1}$ and +3.196 L·min$^{-1}$ to -3.524 L·min$^{-1}$ for upper limit and lower limit lines of identity, which represent the 95% confidence intervals of agreement.

Figure 35. Bland-Altman analysis of low flow pulmonary ventilation with reported average bias and 95% confidence limits of agreement. Comparisons are for $f_V$ and $f_T$. 
Figure 36. Bland-Altman analysis of low flow pulmonary ventilation with reported average bias and 95% confidence limits of agreement. Comparisons are for \( f_V \) and \( f_P \).
Table 2. Results compilation of fV compared to fP and fT, for pulmonary ventilation, $\dot{V}O_2$, $\dot{V}CO_2$, RER for Mixed ANOVA, Linear regression, Bland-Altman analyses.

<table>
<thead>
<tr>
<th>Type of Analysis</th>
<th>Pulmonary Ventilation (L·min$^{-1}$)</th>
<th>$\dot{V}O_2$ (L·min$^{-1}$)</th>
<th>$\dot{V}O_2$ (mlO$_2$·kg$^{-1}$·min$^{-1}$)</th>
<th>$\dot{V}CO_2$ (mlO$_2$·kg$^{-1}$·min$^{-1}$)</th>
<th>RER</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixed ANOVA: Interaction P value</td>
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<td>P = 0.94</td>
<td>P = 0.95</td>
<td>P = 0.95</td>
<td>P = 1</td>
</tr>
<tr>
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<td>$r^2 = 0.9814$</td>
<td>$r^2 = 0.9781$</td>
<td>$r^2 = 0.9843$</td>
<td>$r^2 = 0.9997$</td>
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<td>Sy.x = 4.243</td>
<td>Sy.x = 0.155</td>
<td>Sy.x = 2.326</td>
<td>Sy.x = 2.532</td>
<td>Sy.x = 0.004</td>
<td></td>
</tr>
<tr>
<td>X = fT Linear Regression: r$^2$; Sy.x</td>
<td>$r^2 = 0.9956$</td>
<td>$r^2 = 0.9932$</td>
<td>$r^2 = 0.9932$</td>
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</tr>
<tr>
<td>Sy.x = 2.478</td>
<td>Sy.x = 0.094</td>
<td>Sy.x = 1.293</td>
<td>Sy.x = 1.314</td>
<td>Sy.x = 0.004</td>
<td></td>
</tr>
<tr>
<td>fP Bland-Altman: Bias; UL:LL 95% limits</td>
<td>Bias = 0.236 UL:LL 9.4 to -8.9</td>
<td>Bias = -0.002 UL:LL 0.312 to -0.317</td>
<td>Bias = 0.15 UL:LL 4.4 to -4.7</td>
<td>Bias = 0.27 UL:LL 4.8 to -5.3</td>
<td>Bias = 0.007 UL:LL 0.017 to -0.016</td>
</tr>
<tr>
<td>fT Bland-Altman: Bias; UL:LL 95% limits</td>
<td>Bias = 0.454 UL:LL 5.7 to -4.8</td>
<td>Bias = 0.013 UL:LL 0.210 to -0.183</td>
<td>Bias = 0.15 UL:LL 2.6 to -2.8</td>
<td>Bias = 0.004 UL:LL 2.7 to -2.7</td>
<td>Bias = 0.007 UL:LL 0.017 to -0.016</td>
</tr>
</tbody>
</table>
Discussion

The mixed ANOVA (Figure 32) presented how the pulmonary ventilation variable used in $\dot{V}O_2$ measurements for 20 subjects, were effected by two factors: 1) the type of airflow sensor used 2) the various exercise intensities. As exercise intensity increased, pulmonary ventilation rate was expected to increase across a normal human physiological range (Wasserman, Whipp, & Casaburi, 2011). The airflow sensor main effect ignores the intensity factor and determines whether the $\dot{V}O_2$ measurements are different between airflow devices. The airflow sensors’ insignificant main effect ($P = 0.96$) indicates the $\dot{V}O_2$ mean differences are not statistically significant. If there are indeed differences across various exercise intensities (main effect $P = \leq 0.0001$) then, are these differences the same between airflow sensor devices? The interaction effect ($P = 0.95$) indicates that $\dot{V}O_2$ mean differences between all three airflow devices, across various exercise intensities, are not statistically significant, and that there is $>5\%$ chance that the differences observed were due to random error. The descriptive data for the rested breathing condition reveals slightly elevated metabolic rate above basal metabolic rate. The elevated metabolic state can be explained by the warm-up trial before data collection.

The linear regression analysis results shown in Fig. 33 of $fV$ plotted against $fT$ (a), and $fV$ plotted against $fP$ (b), presents $r^2$ results, to reveal the $fV$ best-fit regression. This value indicates that if $X$ is known, how well $Y$ can be predicted using the linear regression equation. Based on the results, 98% to 99% of the variance in the $fV$ is explained by criterions’ $fV$ and $fP$, respectively. The standard error of the estimate ($Sy.x$) presented in Figure 32, essentially quantifies the goodness of fit for the $fV$ best-fit line to the criterion devices by reporting the error of the residuals in $fV \dot{V}O_2$ units. For Figure 33 a) the $fV$ varies by just 1.2 mLO2·kg·min when compared to $fT$, and b) by only 2.3 mLO2·kg·min when compared to $fP$. This small error is arguably negligible, as normal within-subject biological coefficient variations in energy expenditure during exercise can be as large as 2% and up to 8% for RMR (Donahoo, Levine, & Melanson, 2004).

Bland-Altman analysis results presented in Figure 34, need to be applied in a practical sense, to identify whether the bias and agreement results are ambiguous or definitive. For the $fV$ compared to both methods a) and b), the data is spread evenly above and below the average, resulting an average bias very close to zero for both data-sets. Both a) and b) data-sets reveal a trend of increasing variance as the average increases in magnitude, with a reasonably stable difference beyond 10 mLO2·kg·min. Regardless of the increasing variation, the magnitude of differences for both comparisons are acceptable, due to the very high sensitivity of the EGAIC methodology to small errors in pulmonary ventilation. In summary, the Bland-Altman results reveal that both $fV$ and criterion methods are systematically producing similar results.

The mixed ANOVA (Figure 31) presented how the $V_e$ measurements for 20 subjects, were effected by two factors: 1) the type of airflow sensor used 2) the various exercise intensities. As exercise intensity increased, pulmonary ventilation rate was expected to increase across a normal human physiological range (Wasserman et al., 2011). The airflow sensor
main effect ignores the intensity factor and determines whether the $V_E$ measurements are different between airflow devices. The airflow sensors’ insignificant main effect ($P = 0.99$) indicates the $V_E$ mean differences are not statistically significant. If there are indeed differences across various exercise intensities (main effect $P = <0.0001$) then, are these differences the same between airflow sensor devices? The interaction effect ($P = 0.98$) indicates that $V_E$ mean differences between all three airflow devices, across various exercise intensities, are not statistically significant, and that there is $<2\%$ chance that the differences observed were due to random error.

Bland-Altman analysis results presented in Figures’ 35 and 36, indicate the data is spread evenly above and below the average, resulting an average bias very close to zero for both data-sets. Both Figures’ 35 and 36 data-sets reveal close scatter of data around the central line, with only two examples of data falling outside the limits of agreement. The magnitude of differences for both comparisons are acceptable for EGAIC methodology. In summary, the Bland-Altman results reveal that both fV and criterion methods are systematically producing similar results, which support the use of fV technology to capture resting low flow pulmonary ventilation.

The EGAIC method is not only used for $\dot{V}O_2$ measurements, but a range of physiological variables that can be monitored. For informative purposes, the same statistical analyses performed on $\dot{V}O_2$ data, have been carried out on variables $\dot{V}CO_2$ and RER, the ratio between $\dot{V}CO_2$ and $\dot{V}O_2$ presence in expired breath. A summary of the results is presented in Table 2. Given that both $\dot{V}O_2$ and $\dot{V}CO_2$ are both derived from the same pulmonary ventilation measurement, the linear regression and 95% confidence intervals for both variables are essentially identical. However, the average bias for $\dot{V}CO_2$ is wider for the fV/fP comparison, than fV/fT. The RER is used to calculate the contribution of fat and carbohydrate catabolism during exercise (Gaskill et al., 2001). This in turn, allows one to understand the connections between EGAIC, energy expenditure and heat production. The results for RER analyses conclude that it would not matter which airflow sensor method was used, as the RER values would be categorically identical, based on the non-protein Respiratory Quotient (RQ) Table (Table 3) (Lusk, 1924, 1928; Peronnet & Massicotte, 1991). Thus, the caloric equivalent for $O_2$ used for calculating energy expenditure, would be the same value, regardless of airflow sensor method.
A great deal of research literature exists that examines the extent of energy expenditure variability (Donahoo et al., 2004; Garland et al., 2011; Owen, Healy, Matthews, & Dunstan, 2010). Contribution to energy expenditure variability includes biological variability, that is, within-subject, day-to-day variability. Other components of energy expenditure variability include equipment error and investigator error, which should all be considered. Indeed, statistical methods have been developed to quantify technical error within in vivo test-retest studies (Tenan, 2016). Most validation studies regarding the equipment, mainly focus on the metabolic cart as an entire unit within their experimental procedures (Cooper et al., 2009; Crouter, Antczak, Hudak, DellaValle, & Haas, 2006; Phang, Rich, & Ronco, 1990; Rosdahl, Lindberg, Edin, & Nilsson, 2013; Sundström, Tjäder, Rooyackers, & Wernerman, 2013; Welch, Strath, & Swartz, 2015; Wells & Fuller, 1998), without much consideration to individual components, such as the type of airflow sensor method used. If the airflow sensor method was considered individually within these studies (Crouter et al., 2006; Rosdahl et al., 2013), it was not tested simultaneously. Those studies that compared ventilation measurement to the Douglas Bag technique (Crouter et al., 2006; Rosdahl et al., 2013), still requires some form of ventilation measurement by either a volume displacement or airflow sensor device, after the initial measurements are taken. This method of validation is problematic, as it allows for added variability due to changes in air temperature and condensation.

### Table 3. The non-protein RER table from the work of Max Rubner and Graham Lusk.

<table>
<thead>
<tr>
<th>RER</th>
<th>Kcals/L</th>
<th>%CHO</th>
<th>CHO (Kcals)</th>
<th>%Fat</th>
<th>Fat (Kcals)</th>
</tr>
</thead>
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<td>1.00</td>
<td>5.047</td>
<td>100</td>
<td>5.047</td>
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<td>0.99</td>
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<td>4.874</td>
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<td>35.8</td>
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which ultimately affect air volume. Additionally, some studies are generally conducted in-vitro with strict control of influencing variables, such as limited ventilation rates only seen in rested breathing. This may be appropriate for resting metabolic rate conditions and diet-induced thermogenesis (Cooper et al., 2009; Phang et al., 1990; Wells & Fuller, 1998), and perhaps non-exercise activity thermogenesis (Sundström et al., 2013). However, it is hard to extend these findings to measurements taken during intense exercise, where pulmonary ventilation rates can be as high as 250 L·min. In fact, only one study exists that experimentally evaluates simultaneous EGAIC measurements in vivo (Macfarlane & Wu, 2013).

It is important to acknowledge that there are some limitations present within the aforementioned study, 1) EGAIC measurements were only taken within resting and steady-state exercise conditions 2) $\dot{V}O_2$ data are presented in absolute terms, without additional $\dot{V}O_2$ data relative to body mass. To the best of our knowledge, this is the first in-vivo study that elucidates the contribution of airflow sensor method error to variables attained within EGAIC during exercise, from rest to maximal physical exertion. The minimal error and close agreement displayed between airflow sensor methods can largely be attributed to the strict and thorough calibration of each device before every data collection. Great care was taken in ensuring the testing model had no leakages that could have potentially exposed different conditions to the devices during testing. Changes in environmental conditions were closely monitored throughout all tests and recorded for subsequent analysis. However, when comparing pulmonary ventilation (L·min) Bland-Altman data presented in Macfarlane and Wu (2013), in particular, the 95% confidence lines, the results indicate they achieved better agreement for two fP devices vs. our comparison of three different airflow methods. Interestingly, our $\dot{V}O_2$ L·min data also reveals less agreement, than Macfarlane and Wu (2013). This highlights the error contribution of different types of airflow methods. However, it would be informative to reveal the unaccounted error contribution from the four individual gas analysers, within the two Parvo Medics True One 2400 systems via Bland-Altman analysis. To account for technical variability, there is a need for individual analysis of all electronic components that contribute to quantifying EGAIC variables during simultaneous measurement.

Furthermore, it is important to note, our study identified that ventilation method agreement decreases, as pulmonary ventilation increases in response to increasing physical exertion. This finding also explains the wider limits of agreement for our data compared to Macfarlane and Wu (2013), where exercise intensity was limited to steady-state. This is important, as $\dot{V}O_2max$ or $\dot{V}O_2peak$ in ml·kg$^{-1}$·min$^{-1}$, is routinely used as the test-retest variable in exercise and sports science research for changes in cardiorespiratory status, as well as between-subject differences. Yet, our research shows that the largest variability attributed to technical error, occurs at high intensity exercise. The importance of this finding becomes apparent when considering the $\dot{V}O_2$ normative data provided by American College of Sports Medicine (Medicine, 2013). The normative data presents the categorical fitness levels in ml·kg·min units, which differ by a minimum magnitude of 5 units for classification. Thus, future validation studies on exercise-based metabolic cart systems should 1) focus on raw data of simultaneous measurements, retrieved from individual components 2) test the full condition range, from rest to maximal physical exertion, and 3) express data relative to
body mass, as it is used in scientific literature and clinical settings, to further elucidate the true contributions and effects of error within the system. Along with previous literature recommendations, we thoroughly recommend recalibration of the airflow sensor before use at all times, to ensure greater accuracy, precision, and repeatability of the EGAIC method.

**Conclusion**

This study discussed the applied validation of a fV constructed via 3D-printing. The fV device has no sensitive electronic or moving components located inside the housing unit, thus allowing for easy maintenance and sanitization between users without affecting validity. The fV has a simple design, which makes this device highly accessible via 3D printing. A comparison of the fV with two established airflow sensor technologies during testing of the fundamental measurement, pulmonary ventilation, was carried out on 20 participants during a cycle-ergometry-based \( \dot{V}O_2 \) ramp test, and steady-state exercise. The differences in pulmonary ventilation measurement between devices, were assessed for their influence on computations in EGAIC, such as \( \dot{V}O_2, \dot{V}CO_2 \), and subsequent variables, RER, and energy expenditure (Kcal·min\(^{-1}\)). The results indicate the pulmonary ventilation measurement taken by a fV, reveals both statistical and practical validity for use in EGAIC. Additionally, this study is the first of its kind that shows in-vivo results for different types of airflow sensor method contribution to technical error in measurements within EGAIC.
Chapter Six

Overview of Findings
The purpose of study 1 was to document the agreement between estimated Vs. measured differential pressure and volumetric airflow measurements. A criterion airflow sensor was used to determine airflow. Based on airflow being known, the matching of a fV configuration and transducer input/output specification, a computational differential pressure was determined. This variable was compared to the actual measurement of differential pressure by the fV transducer. Findings in this study revealed that computationally designed venturi tubes with different throat and transducer configurations, prototyped through 3D-printing, have close agreement and minimal bias with actual measurements taken under controlled conditions. Consequently, Venturi tubes can be designed computationally for specified range and sensitivity with reasonable validity. This will allow a technician to determine the fV design and transducer specification needed for their application.

Study 2 looked at the static and dynamic features of an fV device compared to two industry-accepted criterion devices for their respective advantages: the fP, and fT airflow sensor. The results for signal quality indicated that the fV signal was of a reliable and accurate standard. The experiments conducted in this study also revealed that both fV and fP produced systematically similar results in response times, revealing the fV to be suitable for high frequency oscillatory airflow conditions. Calibration methods revealed high precision, with adequate measurement range to detect normal human pulmonary ventilation observed during rest to volitional exhaustion.

Study 3 discussed the applied validation of a fV constructed via 3D-printing. A comparison of the fV with two established airflow sensor technologies during testing of the fundamental measurement, pulmonary ventilation. Differences in pulmonary ventilation measurement between devices, were assessed for their influence on computations in EGAIC, such as $\dot{V}O_2$, $\dot{V}CO_2$, and subsequent variables, RER, and energy expenditure (Kcal·min). The results indicated the pulmonary ventilation measurement taken by a fV, reveals both statistical and practical validity for use in EGAIC. Additionally, this study is the first of its kind that showed in-vivo results for different types of airflow sensor method contributions to technical error in measurements within EGAIC.
Chapter Seven

Summary and Conclusions
Thesis Summary

Computational methods involving the Venturi-optimised Bernoulli Principle, have been shown to predict fluid behaviour in actual measurements of differential pressure and volumetric airflow. Assessment of fV dynamic performance revealed the fV is suitable for pulmonary ventilation measurement during exercise to volitional tolerance. Assessment of signal quality indicates fV meets requirements for determining very low amplitude signals with good signal to noise ratio, thus making it suitable for rested breathing measurements. Assessment of a calibration method reveals the fV can accurately determine tidal volumes from rested breathing to high intensity exercise conditions. This calibration method was used within a comparison of in-vivo pulmonary ventilation measurements to criterion methods, which provided statistical and clinical validation of fV use in expired gas analysis indirect calorimetry.

Practical Applications

The fV has great potential as the device has a simple design, can be easily maintained and sanitized with no moving parts, or sensitive electronics located inside the apparatus like some common airflow sensors, and is relatively inexpensive to manufacture. The fV has a unique advantage over some common airflow sensor technology for high velocity airflow measurements. The fV’s precision increases as the $C_D$ stabilises during high airflow velocities, where full turbulence prevails. This is an advantage for determining ventilatory threshold and $\dot{V}O_{2peak}/\dot{V}O_{2max}$, which are two key variables used in EGAIC.

The fV was manufactured with less than AUS $50 of material, with most of the cost coming from the purchase of a AUS $400 differential pressure transducer. Knowledge of electronic circuitry fundamentals could see the cost of construction come down to a total of AUS $100, with included features, such as telemetry-based data acquisition, DC powered, hands-free measurement of pulmonary ventilation at the mouth, thus alleviating the complication of AC noise interference, unwanted respiratory dead space, and improved ease of use. Additionally, measurement at the mouth and subsequent lack of need for tracheal tubing, could result in fV used for field-based measurements.

Although the current version of the Venturi sensor has not been demonstrated on clinical populations i.e. COPD patients, the research findings from Chapter 4, and in vivo findings from Chapter 5 confirm it has the capacity to monitor flow from 0.043 L·s⁻¹ to 12.366 L·s⁻¹. Logically, it makes sense that even though populations who do not possess the capacity to produce high pulmonary minute ventilation rates, they still fall within the range of 0.1 L·s⁻¹ to 12 L·s⁻¹. Therefore, the current version of the Venturi sensor would be suitably capable of cardiopulmonary exercise testing for clinical populations.
Future Research Direction

Currently, the main limitation of the fV would have to be the unknown influence of pressure resistance, and how the fV design could be improved to allow for minimal added work of breathing. This research could involve improved manufacturing settings of 3D printing, such as higher resolution, that is, for example, print settings of 50 microns vs. 100 microns to reduce wall roughness. Acetone bathing is another method to improve internal wall smoothness to address wall friction. Further research on throat radius and throat length should be investigated for these features effects on pressure resistance. In addition to this, validation research should continue for expired human pulmonary ventilation measurement, so that use of the fV can be extended for Spirometry measurements and closed circuit mechanical ventilation. The capability of valid inspired and expired air measurement will improve the fV’s marketability. Further fV calibration and validation, as well as comparison to existing airflow sensor methods should be carried out using a gold standard criterion, such as the flow and volume simulator (Hans Rudolph, Inc. Shawnee, Kansas, USA). Revisiting equine exercise stress testing with thorough scrutiny of fV methodology on horses will allow for valid measurements in equine EGAIC. The fV has the capacity to quantify high volumetric airflow, with inherently reliable measurement over time, thus highly suited to equine pulmonary ventilation. Given that research in this discipline is limited in Australia, application of fV technology to a large animal cardiopulmonary and metabolic measurement system, could potentially improve the methodology, thus leading to ongoing research and teaching with high impact realised nationally and internationally.

Experimental Limitations and Delimitations

Before data collection of voltage signals from the airflow sensors, precautionary steps were taken by acquiring baseline signals for assessing the occurrence of signal drift. In short, signal drift affects the zero-span range of the device, that is, 0.1 to 10.1 V may shift upwards 0.2 to 10.2 V as the device warms up. This can be partially explained by the improved conductance of heated circuitry, as well as interference of electromagnetic noise. For this reason, repeated baseline testing was conducted on all airflow sensor methods to assess signal drift and allow adequate warm-up times. Interestingly, the only device that required further investigating was the fP due to the heating elements utilised within its housing unit. We noticed that every time the heating element cycled ‘on’ it would affect the baseline signal. We addressed this issue by simply turning the heating component off, as it was not needed for measuring inspired air. Another interesting finding was the effect of two wall-mounted reverse-cycle air conditioners on the baseline signal. The cycling on-off of the air-conditioners actually caused the baseline signal to drift for all three devices. Through trial and error, we discovered these effects were being elicited through the AC-circuitry of the room, from which all the electronics were being powered. A subsequent change of power supply from a nearby power outlet alleviated the issue.
Chapter Eight

Reference List


Medicine, A. C. o. S. (2013). ACSM's guidelines for exercise testing and prescription: Lippincott Williams & Wilkins.


Appendix
INFORMED CONSENT

Validation of a Venturi tube for airflow and volume: Suitability for physiological applications

Praneel Titheradge (Principal Investigator)
Ph.D Student
School of Exercise, Sport and Health Sciences
Allen House, N1
Charles Sturt University
Panorama Ave
Bathurst, NSW 2795

Tel: 0411397761
Email: ptitheradge@csu.edu.au

Robert Robergs (Supervisor)
School of Exercise, Sport and Health Studies
Allen House, N1
Charles Sturt University
Panorama Ave
Bathurst, NSW 2795

Tel: (02) 6338 4579
Email: rrobergs@csu.edu.au

I, ________________________ (print name) consent to participating in the research study titled
‘Validation of a Venturi tube for airflow and volume: Suitability for physiological applications’

By consenting to participate in this study, I acknowledge that I have read and understand the following terms:

1. The purpose of the study has been explained to me and I understand all risks and discomforts that may be involved.
2. I have thoroughly read and retained a copy of the information sheet given to me and understand details of the study.

3. I have had an opportunity to ask questions relating to the study and have been given adequate responses to all questions.

4. I understand all that will be required of me through the duration of the study.

5. I understand that my confidentiality is taken very seriously in this study and that by participating, I have been guaranteed that neither my name nor any other identifying information will be used or published.
6. I understand that I can withdraw my consent and cease participation in the study at any time before, during, or after testing, without any penalty.

7. I nominate the person listed below as an emergency contact in an event one is needed:

   Name: ________________________________
   Address: ______________________________
   Phone: ________________________________

8. I understand that I may contact the following should I have any complaints or concerns about this study:

   Executive Officer
   Ethics in Human Research Committee
   Office of Academic Governance
   Charles Sturt University
   Panorama Ave
   Bathurst NSW 2795

   Phone: (02) 6338 4628
   Fax: (02) 6338 4194

Participant Signature ________________________________

Date: ________________________________
Information Sheet

Validation of a Venturi tube for airflow and volume: Suitability for physiological applications

Thanks in advance for your interest in this research project. Please read and understand the information on this page and retain it for your records. If you have questions or concerns regarding this study, please feel free to contact:

**Praneel Titheradge** (Chief investigator)
Ph.D Student
School of Exercise Science, Sport & Health
Allen House, N1
Charles Sturt University
Panorama Ave
Bathurst, NSW
2795

Tel: 0411397761
Email: ptitheradge@csu.edu.au

**Robert Robergs** (Supervisor)
School of Exercise Science, Sport & Health
Allen House, N1
Charles Sturt University
Panorama Ave
Bathurst, NSW
2795

Tel: 6338 4579
Email: rrobergs@csu.edu.au

Background Information

Fluid flow measurement in manufacturing and specific transportation vehicles (e.g. aircraft velocity) is based on application of the Venturi effect, named after Giovanni Battista Venturi (1746 – 1822), an Italian physicist who first discovered and reported this phenomenon in 1791. Basically, Venturi observed that when fluid flows through a larger to a smaller diameter pipe, there is an increase in fluid velocity and a decrease in fluid pressure. Fluid velocity has to increase to maintain the principle of continuity, and fluid pressure must decrease based on the principle of conservation of mechanical energy.

The two main methods of measurement of ventilatory airflow in human physiology are a) a pneumotach or b) an impeller driven turbine. Both methods have sensitive moving parts, and are especially prone to damage caused by moisture or accidental impact, leading to significant...
delays in ongoing research. These units are expensive, costing between $2,000-5,000. Despite its application in manufacturing and transportation, measurement of ventilation using Venturi tubes in human basic and applied physiology, such as for expired gas analysis indirect calorimetry (EGAIC), has not occurred. This project aims to demonstrate the feasibility of such an application.

Purpose
The purpose of this research is to record the pressure differential readings obtained from a Venturi tube to compute airflow and make a direct comparison to an impeller turbine (Vacumed, Ventura, USA), Pneumotachometer (Hans Rudolph, Kansas, USA) and Hexoskin Biometric Shirt and Accessory Kit (Carre Technologies, Montreal, PQ, Canada), measuring the same airflow to establish efficacy. In addition, the Venturi tube will be compared to all the above mentioned airflow sensor technology for ventilation measurement by human subjects in exercise indirect calorimetry.

Participant Requirements
Participants must meet the following requirements for inclusion into this study:
- You already participate in regular exercise (30 min moderate exercise 3 times/week).
- You are Male <45yrs of age
- You are Female<55yrs of age.
- You must complete the AHA/ASCM Pre-participation Screening Questionnaire.
- Participants should not have any symptoms or risk factors for sedentary lifestyle diseases, and no current musculoskeletal condition that would constrain the ability to perform intense cycle ergometry exercise.
- Professionally qualified exercise staff will assess the questionnaire for inclusion into this study.

**Upon Inclusion You Are Required To:**
Adhere to one testing session, consisting of two cycle-ergometer exercise protocols. Exercise sessions will take no longer than 2 hours, including set-up, familiarization and completing the cycling bouts.

Initially, you will complete a VO\textsubscript{2max} test (Bout 1), where you will cycle at a consistent pace, whilst the resistance of pedaling will increase incrementally. The following bout of exercise will be completed following 30 minutes of rest, and the intensity of this exercise bout will be dictated upon your performance during your VO\textsubscript{2max} testing.

We are simply using your ability to produce airflow in order to test our new airflow-measuring device, the Venturi system. However, of benefit to you, VO2max testing is the gold standard for determining aerobic fitness and will allow us to provide you with an accurate determination of your own cardiovascular fitness level.

**On the day of the trial, participants must report to the lab wearing workout clothes and closed running shoes.**

Study design
All testing will be completed at the Exercise and Sport Science Laboratories on the campus at Charles Sturt University, Bathurst (Building S21).
During the familiarization session, participants will be fitted on the saddle of the bicycle, and the appropriate seat height will be determined. The saddle will be fitted so that it allows a slight bend in the knee at the bottom of the pedal stroke. The same shoes should be worn for every trial. At this session, the participants will be required to sign consent forms and fill out a Par Q and Health History form in order to assure inclusion criteria is met.

The familiarization session will also be used to determine the participant’s transition from moderate to more difficult exercise. As previously mentioned, a ramp cycle ergometer protocol (VO2max Test) will be used to determine the participant’s peak power. The participants will be fitted to a 5 Lead ECG, indirect calorimetry equipment and Hexoskin shirt for collection of breath by breath data and heart rate. From this data the participant’s transition to more difficult exercise will be defined based on changes in ventilation during exercise (ventilation threshold, VT). Following 30 minutes of rest, you will be required to cycle for 10 minutes at 85% of your VT watts established in the VO2max test. This session will require approximately 2 hrs.

Participants will be instructed to keep seated on the saddle for the duration of the test. The test will be initiated from a stationary start in both trials, with the appropriate load already applied to the cycle ergometer. The participants will be required to continue cycling for the duration of the trial. Once the trial is completed they have the indirect calorimetry equipment removed. They will then be asked to lie down for 30 minutes of recovery before the next trial. Indirect calorimetry, Venturi Tube airflow & Impeller Turbine airflow and Hexoskin data will be collected on all trials.

Risks and Considerations
Study participants should not experience excessive risks while doing this study. There is always a risk associated with physical activity, including but not limited to, soft tissue damage such as muscle or tendon strains. Participation in this particular study, however, will not significantly increase the risk of injury above normal physical activity levels. All testing will be completed at the Exercise and Sport Science Laboratories, Building 1295, under the supervision of the Chief Investigator and Study Supervisor with appropriate first aid training, should there be an issue.

Data Usage
The data collected will be used for the completion of a Ph.D manuscript by the chief investigator and the Ph.D supervisor. It is expected that the data collected regarding this research study will be used to publish a scholarly research article which discusses the validation of a venturi tube for airflow and volume: suitability for physiological applications.

Confidentiality
The confidentiality of all participants is guaranteed. All data will be kept secure and only the Chief Investigator will have access to the participant’s identities.

Fax: +61 2 63384065
Email: rrobergs@csu.edu.au
It is completely voluntary to participate in this study. All participants have the right to withdraw from the study at any time.

Institutional Review Board
The Human Research Ethics Committee has reviewed and approved this project. Should you have any inquiries or complaints about the ethical conduct of the study, you may contact the Executive Officer:

NOTE: Charles Sturt University’s Human Research Ethics Committee has approved this project. If you have any complaints or reservations about the ethical conduct of this project, you may contact the Committee through the Executive Officer:

The Executive Officer  
Human Research Ethics Committee  
Office of Academic Governance  
Charles Sturt University  
Panorama Avenue  
Bathurst NSW 2795

Tel: (02) 6338 4628  
Fax: (02) 6338 4194

Any issues you raise will be treated in confidence and investigated fully and you will be informed of the outcome.

Thank you for your interest in this research study. If you have decided to agree to participate in the project, please read and sign the consent form attached. Please also keep this information sheet for your records should you have any questions. Thank you!
### ADULT PRE-EXERCISE SCREENING TOOL

This screening tool does not provide advice on a particular matter; it does not substitute for advice from an appropriately qualified medical professional. The wearer of this tool must resort to the advice of a medical professional. Any action taken by the wearer based on the advice contained in the tool is done so at his or her own risk. You may need to consider your own medical history and physical condition before starting any exercise program. This tool is not administered and self–evaluated.

<table>
<thead>
<tr>
<th>Name:</th>
<th>Date of Birth: ___________________</th>
<th>Male □</th>
<th>Female □</th>
<th>Date: ___________________</th>
</tr>
</thead>
</table>

#### STAGE 1 (COMPULSORY)

To identify those individuals with a known disease, or signs or symptoms of disease, who may be at a higher risk of an adverse event during physical activity/exercise. This stage is self–administered and self–evaluated.

1. **Has your doctor ever told you that you have a heart condition or have you ever suffered a stroke?**
   - Yes □
   - No □

2. **Do you ever experience unexplained/pains in your chest at rest or during physical activity/exercise?**
   - Yes □
   - No □

3. **Do you experience faint or have spells of dizziness during physical activity/exercise that causes you to lose balance?**
   - Yes □
   - No □

4. **Have you had an asthma attack requiring immediate medical attention at any time over the last 12 months?**
   - Yes □
   - No □

5. **If you have diabetes Type I or Type II, have you had trouble controlling your blood glucose in the last 3 months?**
   - Yes □
   - No □

6. **Do you have any diagnosed muscle, bone or joint problems that you have been told could make you more prone to participating in physical activity/exercise?**
   - Yes □
   - No □

7. **Do you have any other medical conditions that may make it dangerous for you to participate in physical activity/exercise?**
   - Yes □
   - No □

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**IF YOU ANSWERED YES TO ANY OF THE 7 QUESTIONS, PLEASE SEEK GUIDANCE FROM YOUR GP OR APPROPRIATE HEALTHCARE PROFESSIONAL PRIOR TO UNDERTAKING PHYSICAL ACTIVITY/EXERCISE**

**IF YOU ANSWERED NO TO ALL OF THE 7 QUESTIONS, AND YOU HAVE NO OTHER CONCERNS ABOUT YOUR HEALTH, YOU MAY PROCEED TO EXERCISE LIGHT TO MODERATE INTENSITY PHYSICAL ACTIVITY/EXERCISE**

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I believe that to the best of my knowledge, all of the information I have supplied within this tool is correct.

Signature: ___________________

Date: ___________________
# Calibration Certificate

**Technician:** NX  
**Part No.:** 267110CL2E09ED  
**Model:** 247  
**Serial No.:** 564979  
**Work Order:** 24112495  
**Date:** 09/05/2013  
**Range:** 0 to 1000 PASCAL  
**Nom. Output:** 10.05 to 10.65 VDC  
**Supply:** 24 VDC

## Calibration Data

<table>
<thead>
<tr>
<th>Applied Pressure (Pascal)</th>
<th>Transducer Output (VDC)</th>
<th>Nonlinearity Errors (% FS)</th>
<th>Extrapolated Errors (% FS)</th>
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</thead>
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<td>0.1561</td>
<td>0.064</td>
<td>Zero</td>
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<tr>
<td>1029.8016</td>
<td>10.1632</td>
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<td></td>
</tr>
</tbody>
</table>

## Specifications

1. Nonlinearity: +/- 0.38% FS, BEST FIT STRAIGHT LINE method, ISA.45-37.1
2. Zero pressure output: 0.05 VDC +/- 0.5% FS
3. Full Scale output: 10 VDC +/- 0.5% FS
4. This unit meets the specifications defined above.

## Notes

1. All errors are expressed as: Percent Full-Scale output.
2. Consult specification sheet for additional specifications.
3. This calibration is certified per N.I.S.T. Traceable primary standards.
   NIST# Ppt#1500144638
4. Transfer standard: 239C010656.6, Location of cal.: FCE062
5. This certificate cannot be reproduced except in full, without the written approval of Setra Systems, Inc.

## Comments

159 Swanson Road, Boxborough, MA 01719/Telephone 1-800-257-3872, (978) 263-1400

SS2013-2 Rev. 199
# Calibration Certificate

**Part No:** 267170CLP22A1FP  
**Serial No:** 6776568  
**Tech.:** ST  
**Model:** 267  
**Work Order:** 24223428  
**Date:** 09/10/2015  
**Supply:** 24 VDC

## Calibration Data

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<tr>
<th>APPLIED PRESSURE (PASCAL)</th>
<th>TRANSDUCER OUTPUT (VDC)</th>
<th>NONLINEARITY ERRORS (% FS)</th>
<th>EXTRAPOLATED ERRORS (% FS)</th>
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</table>

\[
y = 399.52x - 32.158
\]

## Specifications

1. Nonlinearity: +/- 0.25 %FS, REST FIT STRAIGHT LINE method; ISA.#8-37.
2. Zero pressure output: 0.65 VDC +/- 0.5 %FS
3. Full Scale output: 10 VDC +/- 0.5 %FS
4. This unit meets the specifications defined above.

## Notes

1. All errors are expressed as Percent Full-Scale output.
2. Consult specification sheet for additional specifications.
3. This calibration is certified per N.I.S.T. traceable primary standards.
   NIST # FlukeRept#1500172044  
   Transfer standard: 2398 FW07.2, Location of cal: PC2002
4. This part uses spec. record number: 267170CLP22A1FP.1
5. This certificate cannot be reproduced except in full, without the written approval of Setra Systems, Inc.

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**159 Swanson Road, Boxborough, MA 01719/Telephone 1-800-257-3672, (978) 263-1400**

S30513-RV 1/99