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Calculation of Physiologic Deadspace: Comparison of Ventilator Volumetric Capnography to Measurements by Metabolic Analyzer and Volumetric CO_2 Monitor.

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Abstract

Background: Calculation of physiologic deadspace (V_D/V_T) using the Enghoff modification of the Bohr equation requires measurement of the partial pressure of mean expired CO_2 ($PeCO_2$) by exhaled gas collection and analysis, use of a metabolic analyzer, or use of a volumetric CO_2 monitor. The Drager XL ventilator is equipped with integrated volumetric CO_2 monitoring and calculates minute CO_2 production (VCO_2). We calculated $PeCO_2$ and V_D/V_T from ventilator derived volumetric CO_2 measurements of VCO_2 and compared it to metabolic analyzer and volumetric CO_2 monitor measurements.

Methods: A total of 67 measurements in 36 in patients recovering from acute lung injury or acute respiratory distress syndrome were compared. Thirty-one ventilator derived measurements were compared to measurements using 3 different metabolic analyzers and 36 ventilator derived measurements were compared to measurements from a volumetric CO_2 monitor.

Results: There was a strong agreement between ventilator derived measurements and metabolic analyzer or volumetric CO_2 monitor measurements of $PeCO_2$ and V_D/V_T. Correlation, bias, and precision between ventilator and metabolic analyzer measurements for $PeCO_2$ were $r = 0.97$, $r^2 = 0.93$ ($p < 0.0001$), bias –1.04 and precision ± 1.47 mm Hg and for V_D/V_T $r = 0.95$, $r^2 = 0.91$ ($p < 0.0001$), bias 0.024 and precision ± 0.034. Correlation between ventilator and volumetric CO_2 monitor for $PeCO_2$ were $r = 0.96$, $r^2 = 0.92$ ($p < 0.0001$), bias –0.19 and precision ± 1.58 mm Hg and for V_D/V_T $r = 0.97$, $r^2 = 0.95$ ($p < 0.0001$), bias 0.006 and precision ± 0.033.

Conclusion: $PeCO_2$ and therefore $V_D/V_{T\ can}$ be accurately calculated directly from the Drager XL ventilator volumetric capnography measurements without use of a metabolic analyzer or volumetric CO_2 monitor.

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Introduction

Deadspace ventilation, the portion of a tidal volume that does not contribute to gas exchange, was first described and calculated by the Bohr equation in 1891[1], and later by the Enghoff modification of the Bohr equation in 1938.[2] Physiologic deadspace fraction (V_D/V_T) as defined by Bohr and Enghoff, is the sum of anatomic or airway deadspace (VD_{anat}) and alveolar deadspace (VD_{alv}) divided by the tidal volume (Vt). The definition of pure deadspace is ventilation without perfusion whereby alveolar gases do not contact blood flowing through the pulmonary capillaries. All conducting airways (anatomical and mechanical deadspace), areas of pure shunt (pulmonary capillary perfusion with no ventilation), areas of pure deadspace, and the presence of gas exchange units with any degree of inequality of ventilation in relation to perfusion, can contribute to the calculated deadspace ventilation.

Assessing V_D/V_T in critically ill patients during mechanical ventilation is important for several reasons.[3] The prognostic value of V_D/V_T has been linked to mortality risk in acute respiratory distress syndrome (ARDS) [4-7] and to other important clinical indices. V_D/V_T is known to correlate with the severity of lung injury, [8-12] can be useful as an indicator of lung recruitment versus overdistention in patients with acute lung injury (ALI) and ARDS,[13-17] may be helpful as a predictor of successful extubation in pediatric [18] and adult patients,[19] and may be useful in diagnosing and assessing the severity of pulmonary embolism.[20, 21]

Simplified bedside calculation of V_D/V_T requires a measurement of the partial pressure of mean expired CO_2 ($PeCO_2$) and use of the Enghoff modification of the Bohr equation.[2] The Enghoff equation differs from the original Bohr equation by the substitution of $PaCO_2$ for the partial pressure of mixed alveolar CO_2 ($PACO_2$). The Enghoff equation became the standard in clinical practice for calculation of V_D/V_T because $PACO_2$ has been difficult to accurately

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measure or estimate at the bedside. The traditional technique of measuring $PeCO_2$ used the Douglas bag method of exhaled gas collection and analysis.[22] Technological advancements allow the use of a metabolic analyzer,[23, 24] and more recently, use of volumetric capnography and a volumetric CO_2 monitor.[25]

The Drager XL ventilator (Drager Medical, Telford, PA) is equipped with integrated CO_2 and volume measurement capabilities (volumetric CO_2). We calculated $PeCO_2$ and V_D/V_T directly from the Drager XL ventilator volumetric CO_2 measurements of VCO_2 and compared it to metabolic analyzer and volumetric CO_2 monitor measurements of $PeCO_2$ and V_D/V_T.

Methods

A total of 67 measurements were performed in 36 patients who met the American-European Consensus Conference criteria for ALI or ARDS.[26] Measurement were done at varying time periods after ALI or ARDS criteria were met (Table 1). Phase 1 of the study compared 31 ventilator derived measurements in 25 patients to measurements from three different metabolic analyzers, Metascope (Cybermedic, Louisville, CO) n = 9, Deltatrac (Sensor Medics, Yorba Linda, CA) n = 4, and Vmax Encore (Viasys, Yorba Linda, CA) n = 18. Use of the various metabolic analyzers was based on functional availability. All metabolic analyzers used were maintained by annual biomedical engineering preventative maintenance and performance verification. In phase 2 of the study, 36 ventilator derived measurements in 11 patients were compared to the $NICO_2$ Respiratory Profile Monitor (Philips Healthcare, Andover, MA).

V_D/V_T measurements were performed when requested by the ICU team. Arterial blood gas samples for $PaCO_2$ determination and V_D/V_T calculation were obtained from arterial catheters. Prior to all measurements, ventilator, metabolic analyzer, and $NICO_2$ monitor CO_2 and flow sensors were calibrated using manufacturers specifications. Following all ventilator circuit disconnections, approximately 30 minutes was allowed for patient stabilization. Ventilator

measurements were done simultaneously during metabolic analyzer and $NICO_2$ monitor measurements for comparison. The ventilator circuit was checked for leaks and patients with active pulmonary air leaks were excluded from the study. The study was approved by the Committee on Human Research at the University of California, San Francisco.

Ventilator Volumetric CO2 Measurements

The Drager XL ventilator (Drager Medical, Telford, PA) mainstream CO_2 sensor was placed between the ventilator circuit and the patient connection. The ventilator expiratory flow sensor positioned at the distal side of the expiratory valve measured exhaled tidal volume (Vt) and exhaled minute ventilation (VE). Ventilator volumetric CO_2 measurements were initiated and displayed on the ventilator trend data screen. After measured values stabilized and reached a steady state, ventilator trend data for minute CO_2 production (VCO_2) and VE were averaged over 5 minutes. All measurements were reported at body temperature, pressure, and saturated (BTPS).

The fraction of exhaled CO_2 ($FeCO_2$) was calculated manually by dividing the ventilator derived VCO_2 by the VE whereby:

(1) $FeCO_2 = VCO_2 / VE$

$PeCO_2$ was then calculated by multiplying $FeCO_2$ by the barometric pressure minus water vapor pressure:

(2) $PeCO_2 = FeCO_2 \times (760 - 47)$

PeCO2 was then used to calculate V_D/V_T by the Enghoff modification of the Bohr equation:

(3) $V_D/V_T = (PaCO_2 - PeCO_2) / PaCO_2$

The automated ventilator correction for delivered and measured Vt was used by performing a circuit compliance test at device start up. The automated ventilator correction adjusts the delivered and measured Vt and therefore the ventilator calculated values for VCO_2

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and VE reflect the adjusted values and eliminated the need for a manual circuit compression volume correction.

Metabolic Analyzer Measurements

The metabolic analyzers were warmed-up for 20-minutes and calibrated per manufacturers recommendations. The fraction of inspired gases were sampled from the ventilator inspiratory limb and the fraction of exhaled gases and volumes were measured by directing expiratory gas flow into the metabolic analyzer (Metascope and Deltatrac) or by placement of the metabolic analyzer flow sensor and expired gas sampling line at the ventilator expired gas outlet (Vmax Encore). After a stable10-minute measurement period, $FeCO_2$ averaged over a 5 minute period from the metabolic analyzer was used to calculate $PeCO_2$ using Equation 2 above.

All metabolic analyzer measurements of $PeCO_2$ were corrected for circuit compression volume as previously described [23-25, 27-29] whereby the $PeCO_2$ was multiplied by the ratio of the observed Vt divided by the observed Vt minus the calculated compression volume using the following equations:

(4) Compression Volume = (Peak Inspiratory Pressure – PEEP) x Circuit Compliance

(5) Corrected $PeCO_2$ = $PeCO_2$ x (Vt / [Vt – compression volume])

Ventilator circuit compliance factors of 2.5 and 2.0 mL / cm H_20 were used pre and post a ventilator circuit configuration change that was implemented during the study period. The circuit compliance factor of 2.5 mL / cm H_2O was used for the Metascope and Deltatrac, and 2.0 mL /cm H2O was used for the Vmax Encore. Circuit compression volume was determined by laboratory testing and confirmed by the ventilator circuit compliance test mentioned above. Vt was derived by dividing the VE by the respiratory rate measured by the metabolic analyzer. The Drager XL ventilator uses a non bias flow triggering method and therefore additional correction for potential measurement error caused by bias flow was unnecessary.

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$NICO_2$ Monitor Measurements

The $NICO_2$ monitor combined CO_2 / flow sensor was allowed to warm-up for 5 minutes until stable measurements for $PeCO_2$ were obtained. Both the $NICO_2$ combined sensor and the ventilator mainstream CO_2 sensor were placed between the ventilator circuit and the patient. The position of the $NICO_2$ sensor and the ventilator CO_2 sensor were placed distal and proximal to each other in random order. In a previous bench study, the distal or proximal position of either sensor did not result in position related bias.[30] $PeCO_2$ derived from the ventilator measurements was rounded to the nearest whole number for comparison to the $NICO_2$ monitor display of $PeCO_2$.

Since the $NICO_2$ combine CO_2 / flow sensor measures distal to the ventilator "Y" adapter, the effects of ventilator circuit compression volume and the utilization of a correction factor are unnecessary.

Statistical Analysis

Ventilator derived measurements of VCO_2, $FeCO_2$, $PeCO_2$ and V_D/V_T were compared to metabolic analyzer measurements. $PeCO_2$ and V_D/V_T derived from ventilator measurements were compared to $NICO_2$ monitor measurements. The data was compared and analyzed by correlation measured by Pearson product-moment correlation coefficient (r) and coefficient of determination (r^2). Bias and precision was assessed by Bland-Altman analysis. Statistical analysis was done using commercially-available software (Microsoft Office Excel 2011, version 14.2.2, Redmond, WA). Correlation results were considered to be significant when $p < 0.05$.

Results

There was a strong correlation, agreement and accuracy between ventilator derived measurements and metabolic analyzer or volumetric CO_2 monitor measurements of VCO_2, $FeCO_2$, $PeCO_2$ and V_D/V_T .

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In phase 1 of the study, correlation between ventilator derived measurements compared to metabolic analyzer measurements for VCO_2 and $FeCO_2$ were $r = 0.92$, $r^2 = 0.85$ ($p < 0.0001$) and $r = 0.95$, $r^2 = 0.91$ ($p < 0.0001$). Bias and precision for VCO_2 and $FeCO_2$ was 24 ± 31 mL / min and 0.07 ± 0.23 percent respectively. Correlation for $PeCO_2$ was $r = 0.97$, $r^2 = 0.93$ ($p < 0.0001$) (Figure 1), and bias and precision were –1.04 and ± 1.47 mm Hg (Figure 2). Correlation for V_D/V_T was $r = 0.95$, $r^2 = 0.91$ ($p < 0.0001$) (Figure 1), and bias and precision was 0.02 ± 0.04 (Figure 3). The p value of two tailed probability Pearson correlation coefficient reached statistical significance for each metabolic analyzer for both $PeCO_2$ and V_D/V_T except for one where the sample size was very small (DeltaTrac, $n = 4$, V_D/V_T, $p = 0.09$). Similarly, bias and precision remained within clinically acceptable ranges when individual measurements between the three metabolic analyzers were compared to the combined data from all three analyzers (Table 2).

In phase 2 of the study, correlation, bias, and precision between ventilator and volumetric CO_2 monitor measurements for $PeCO_2$ were $r = 0.96$, $r^2 = 0.92$ ($p < 0.0001$) (Figure 4), bias –0.19 and precision ± 1.58 mm Hg (Figure 5), and for V_D/V_T $r = 0.97$, $r^2 = 0.95$ ($p < 0.0001$) (Figure 4), bias 0.01 and precision ± 0.03 (Figure 6).

Discussion

The results of this study confirm that $PeCO_2$ and therefore V_D/V_T using the Enghoff equation can be accurately calculated directly from the Drager XL ventilator volumetric capnography measurements without use of a metabolic analyzer or volumetric CO_2 monitor. In a recent study, use of volumetric capnography calculations of V_D/V_T from the Drager XL ventilator were shown to be a predictor of extubation success.[19] However, to our knowledge the results of our study are the first to validate the accuracy of the Drager XL measurements of V_D/V_T against previously accepted methods.

These findings have several important implications. This simplified approach to V_D/V_T measurement will improve availability, allow early and repeated measurements, and will increase the utilization of V_D/V_T for prognostic, diagnostic, and disease severity monitoring in the critical care setting. V_D/V_T has been shown to be predictive of the mortality risk in patients with ARDS in both the early and intermediate phases of the disease progression in single center or small cohort studies.[4-8] Patients with $V_D/V_T \geq 0.57$ where found to have higher mortality with a 45 percent increase in the odds of dying for every 0.05 increase in deadspace fraction.[5] V_D/V_T is also known to be a marker of the severity of lung injury.[9-13] Serial monitoring of V_D/V_T over the duration and course of ALI/ARDS can be useful as a means to assess the need and effects of supportive therapeutic strategies and interventions.[12, 13] V_D/V_T measurements in patients with ALI/ARDS have been found to be useful for titrating positive end expiratory pressure and optimizing cardio-pulmonary function,[14 -16] and may be useful as a tool to monitor lung recruitment versus overdistension.[17] Assessment of V_D/V_T may also be used to predict successful of extubation in pediatric[18] and adult patients.[19] $V_D/V_T \leq 0.50$ and ≥ 0.65 in infants and children were found to be predictive of extubation success or failure[18] where as in adult patients the V_D/V_T cut off value which offered the best sensitivity and specificity of predicting extubation failure was 0.58.[19] The use of V_D/V_T measurements in addition to other clinical assessments and diagnostics test has also been used in diagnosing and assessing the severity of pulmonary embolism.[20,21] The culmination of the broad clinical value of V_D/V_T assessments in the critical care setting support the integration of this measurement into routine clinical practice.

Additionally, use of a separate stand alone device for V_D/V_T measurements with the associated acquisition and supply costs, and staff utilization time may become unnecessary. Elimination of a metabolic analyzer or volumetric CO_2 monitor simplifies the determination of V_D/V_T. Use of ventilator derived volumetric CO_2 makes the potential to evaluate physiologic

deadspace fraction more accessible for use in clinical practice as ventilator manufacturers incorporate volumetric CO_2 monitoring capabilities into newer ventilator platforms.[31] The calculations performed for his study where done manually using ventilator derived measurements but could easily be incorporated as an automated feature by ventilator software modification. Methods for estimating V_D/V_T by predictive equations have been described using the arterial to end tidal CO_2 gradient[32, 33] and estimation of VCO_2.[34] The increasing availability of volumetric capnography make the use of predictive equations unnecessary.

The results of this study are consistent with prior data which confirm the accuracy of different methods of calculating V_D/V_T (Table 3). Similar correlation and accuracy of the exhaled gas collection method using a Douglas bag to the metabolic analyzer,[23, 24] metabolic analyzer to the volumetric CO_2 monitor,[25] and ventilator based volumetric capnography to both metabolic analyzer and volumetric CO_2 monitor are now demonstrated.

Limitations of this study include a relatively small sample size in each study phase and the use of three different metabolic analyzers in phase 1. Also the ventilator circuit configuration and therefore the circuit compression volume were changed during the study. Despite these factors, the resiliency of the ventilator derived data in relation to the correlation, bias, and precision between measurements remained consistent. Although number of individual measurements between the three metabolic analyzers used varied markedly, the agreement of correlation, bias, and precision remained consistent between individual metabolic analyzers when compared to the combined data from all three analyzers (Table 2). Additionally, the change in ventilator circuit configuration and compression volume did not significantly alter the correlation and agreement of the measurements (Table 2).

V_D/V_T calculated by the original Bohr equation has been recognized as "true deadspace" or the balance between effective and ineffective ventilation. The Bohr deadspace equation relies

on the calculation or estimation of $PACO_2$ from mixed alveolar gas. $PACO_2$ is affected by the dilution of CO_2 from the alveolar side of the alveolar-capillary membrane before the affects of shunt and venous admixture on $PaCO_2$. Bohr deadspace is affected by areas of high ventilation to perfusion matching such as alveolar overdistension by excessive PEEP and or Vt, pulmonary vascular occlusion, and pulmonary hypoperfusion secondary to hypovolemia.[35] The Enghoff equation on the other hand relies on the $PaCO_2$ of arterial blood and is thus an index of "true deadspace" plus the effects elevated $PaCO_2$ from global gas exchange inefficiency and shunt (Figure 7). Elevated $PaCO_2$ can result from all causes of low ventilation to perfusion matching and shunt such as atelectasis, pneumonia, COPD, and asthma. Furthermore, $PaCO_2$ can rise when an increase in metabolic rate and CO_2 production are not accompanied by an increase in CO_2 excretion. Changes in $PaCO_2$ are determined by the relationship between VCO_2 and minute alveolar ventilation (V_A) whereby $PaCO_2 = VCO_2 / V_A$. If VCO_2 increases without a proportional rise in V_A, CO_2 production exceeds CO_2 excretion and $PaCO_2$ increases. Therefore the Enghoff deadspace equation can overestimate V_D/V_T in the presence of shunt and regions of low ventilation to perfusion ratios (Figure 8).

Use of volumetric capnography to determin $PACO_2$ for Bohr deadspace calcuation has been demonstrated[39] and validated in an animal model of lung injury.[40] $PACO_2$ measured at the mid point of phase III of the expired volume capnogram was compared to the $PACO_2$ mathematically derived using the multiple inert gas elimination technique (MIGET). There was a close linear correlations between the two methods for calculating $PACO_2$ ($r = 0.99$, $p < 0.001$) and Bohr deadspace ($r = 0.96$, $p < 0.001$). The mean $PACO_2$ and Bohr deadspace from volumetric caonography was similar to the calulation obtained by MIGET with a mean bias of -0.10 mmHg, 95% Confidence Interval -2.18 to 1.98 mmHg and 10 mL, 95% Confidence Interval -44 to 64 mL respectively. Given these findings, it has been suggested that simultaneous

assessment of Bohr and Enghoff deadspace using volumetric capnography may provide useful complimentary information in regards to recognizing the effects of shunt and ventilation to perfusion inequality versus "true deadspace" or wasted ventilation in critically ill patients with elevated V_D/V_T.[35] Furthermore, using volumetric capnography to determin Bohr deadspace could be monitored continuously and would not require periodic arterial blood sampling to measure $PaCO_2$.[35]

Conclusion

This study confirms that $PeCO_2$ and V_D/V_T using the Enghoff equation can be accurately calculated directly from the Drager XL ventilator volumetric capnography measurements without use of a metabolic analyzer or volumetric CO_2 monitor.

Future study of the use and development of ventilator based techniques for volumetric capnography measurements of V_D/V_T should continue to confirm and validate measurement correlation and accuracy. Investigation of the meaningful use of continuous Bohr V_D/V_T monitoring and simultaneous measurement of Bohr and Enghoff V_D/V_T using volumetric capnography should also be pursued.

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Figure Legends

Figure 1

Correlation of $PeCO_2$ and V_D/V_T between the Drager XL ventilator and three different metabolic analyzers plotted against the line of identity. $PeCO_2$, $r = 0.97$, $r^2 = 0.93$ ($p < 0.0001$), V_D/V_T, $r = 0.95$, $r^2 = 0.91$ ($p < 0.0001$).

Figure 2

Bland – Altman plot comparing $PeCO_2$ calculated by measurements from the Drager XL ventilator and three different metabolic analyzers. Bias and precision = -1.04 ± 1.47 mm Hg, 95 percent confidence interval limits of agreement -3.91 to 1.84 mm Hg.

Figure 3

Bland – Altman plot comparing V_D/V_T calculated by measurements from the Drager XL ventilator and three different metabolic analyzers. Bias and precision = 0.024 ± 0.034, 95 percent confidence interval limits of agreement -0.05 to 0.09.

Figure 4

Correlation of $PeCO_2$ and V_D/V_T between the Drager XL ventilator and the NICO2 volumetric CO_2 monitor plotted against the line of identity. $PeCO_2$, $r = 0.96$, $r^2 = 0.92$ ($p < 0.0001$), V_D/V_T, 0.97, $r^2 = 0.95$ ($p < 0.0001$).

Figure 5

Bland – Altman plot comparing $PeCO_2$ calculated by measurements from the Drager XL ventilator and the NICO2 volumetric CO_2 monitor. Bias and precision = -0.19 ± 1.58 mm Hg, 95 percent confidence interval limits of agreement -3.30 to 2.91 mm Hg.

Figure 6

Bland – Altman plot comparing V_D/V_T calculated by measurements from the Drager XL ventilator and the NICO2 volumetric CO_2 monitor.. Bias and precision = 0.024 ± 0.034, 95 percent confidence interval limits of agreement 0.006 to 0.033.

Figure 7

The three compartment lung model described by Riley[36, 37] represents gas exchange in the lung in regards to the matching of alveolar ventilation (V_A) and perfusion (Q_T), shunt (Q_S), and deadspace (VD). Ideal Compartment represents areas of perfect V_A to Q_T matching. Pure Shunt Compartment represents areas of perfusion without ventilation. Pure Deadspace Compartment represents areas of ventilation with no perfusion. The sum of the regions of alveolar deadspace (VD_{alv}) and anatomic deadspace (VD_{anat}) equal the physiologic deadspace (VD_{phys}). Deadspace fraction is equal to tidal volume (V_T) divided by VD_{phys}. The partial pressure of arterial and venous carbon dioxide ($PaCO_2$, $PvCO_2$), The relationship between $PaCO_2$ to minute CO2 production (VCO_2) and V_A, the partial pressure of mixed alveolar carbon dioxide ($PACO_2$), the

partial pressure of end tidal carbon dioxide ($PETCO_2$), and the partial pressure of mean expired carbon dioxide ($PECO_2$) in relation to the model and the volumetric capnogram are also shown. Modified from references 35 and 38.

Figure 8

Graphical representation of physiologic deadspace fraction determined by volumetric capnography using the approaches of Bohr and Enghoff which shows how use of the Enghoff equation can over estimate alveolar deadspace (VD_{alv}) (shaded areas) by substitution the partial pressure of arterial carbon dioxide ($PaCO_2$) for partial pressure of mixed alveolar carbon dioxide ($PACO_2$) determined by identifying the mid point of phase III of the expired volumetric capnogram.[39, 40] Airway or anatomical dead space (VD_{aw}) determined by the Fowler method identified at the mid point of phase II of the expired volumetric capnogram[41], the partial pressure of end tidal carbon dioxide ($PETCO_2$), and the partial pressure of mean expired carbon dioxide ($PECO_2$) in relation to the volumetric capnogram are also shown. Modified from reference 35.

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Table 1

Female / Male	8 / 28
Age (mean +/- STDV)	49.4 +/- 14.5
ALI / ARDS Day (mean +/- STDV)	7.9 +/- 3.8
ALI / ARDS Etiology	
Pneumonia	8
Trauma	17
Burns	3
Sepsis	5
Pancreatitis	3

Patient characteristics. ALI = acute lung injury. ARDS = acute respiratory distress syndrome. ALI / ARDS Day = number of days after ARDS protocol initiated and study data collected.

Table 2

		Correlation	R squared	p value	Bias	Precision
Combined Data (n = 31)	**V_D/V_T**	0.95	0.91	<0.0001	0.02	0.04
	$PECO_2$	0.97	0.93	<0.0001	-1.04	1.47
Metascope (n = 9)	**V_D/V_T**	0.98	0.96	<0.0001	0.002	0.02
	$PECO_2$	0.98	0.97	<0.0001	-1.39	0.91
DeltaTrac (n = 4)	**V_D/V_T**	0.91	0.82	0.09	0.01	0.03
	$PECO_2$	0.96	0.93	0.04	-0.84	1.69
Vmax (n = 18)	**V_D/V_T**	0.97	0.94	<0.0001	0.04	0.04
	$PECO_2$	0.98	0.95	<0.0001	-1.50	1.49

Correlation, bias, and precision between individual metabolic analyzers compared to the combined data from all three analyzers.

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Table 3

	Correlation	Bias	Precision	Reference
Metabolic Analyzer vs Drager XL	0.95	0.024	0.035	-
NICO Monitor vs Drager XL	0.97	0.006	0.033	-
Douglas Bag vs Metabolic Analzer	0.92	0.004	0.034	MacKinnon [23]
Douglas Bag vs Metabolic Analzer	0.99	-0.017	0.014	Lum [24]
Metabolic Analzer vs NICO Monitor	0.94	0.02	0.05	Kallet [25]

Correlation, bias, and precision from four studies that compared different methods for calculating V_D/V_T using the Enghoff equation.

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Figure 1

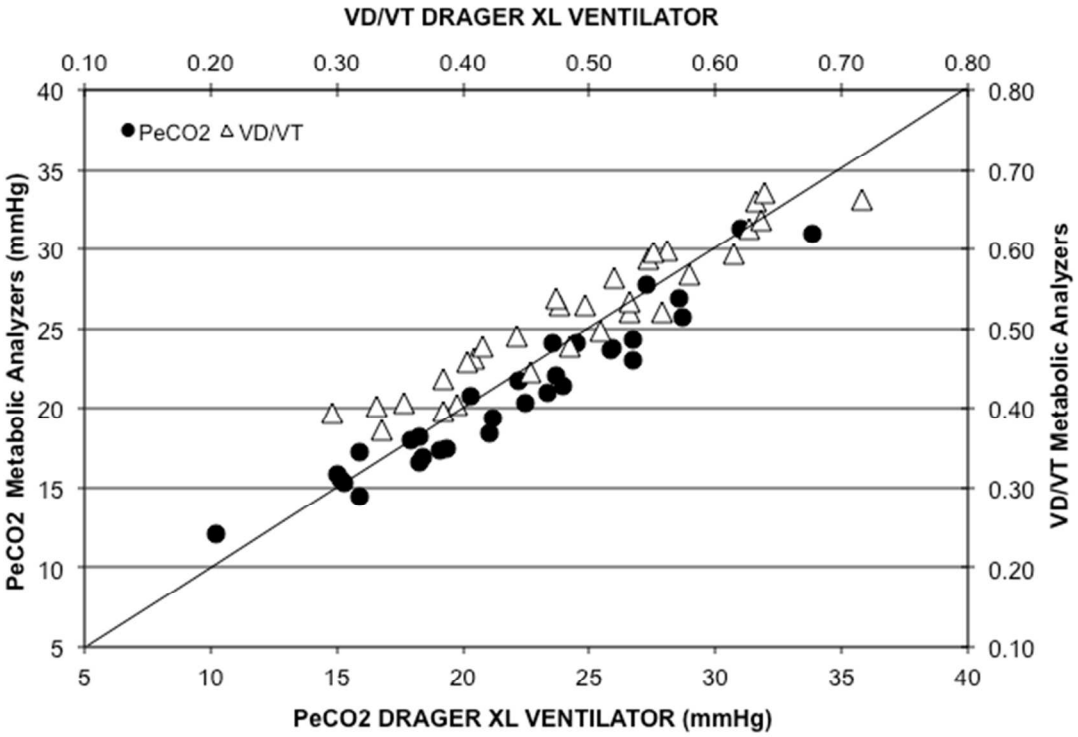

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Figure 2

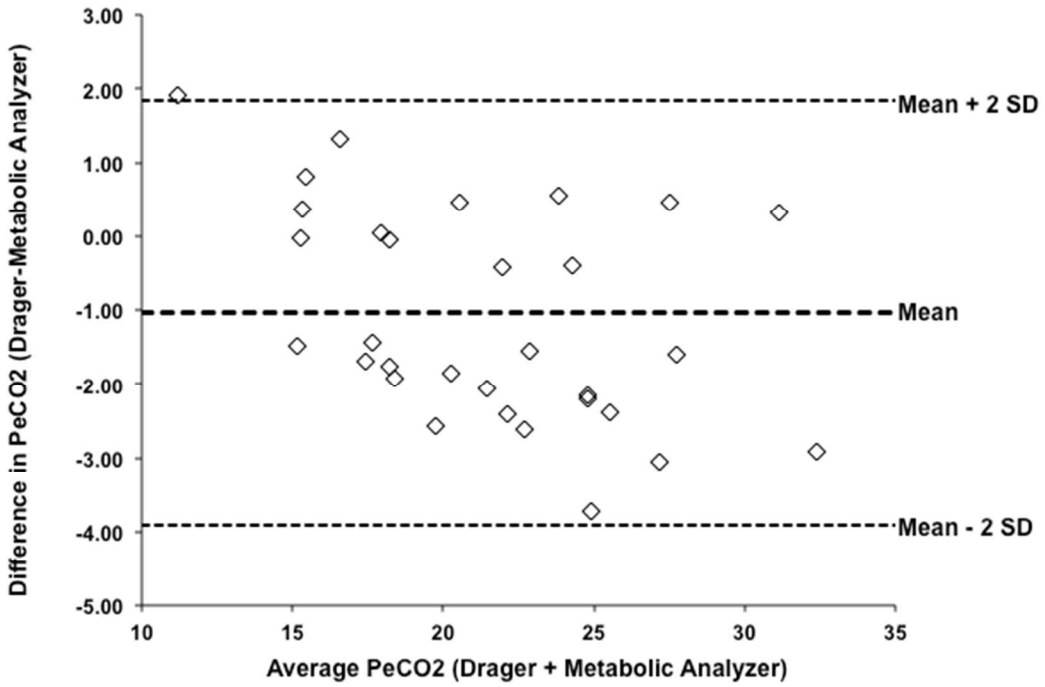

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Figure 3

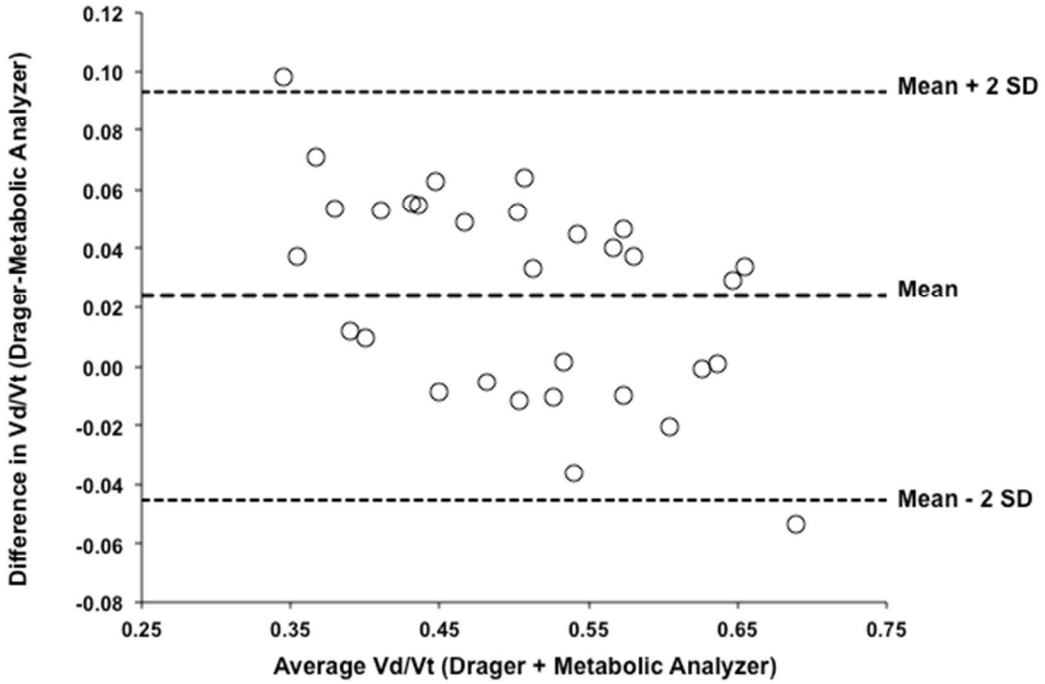

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Figure 4

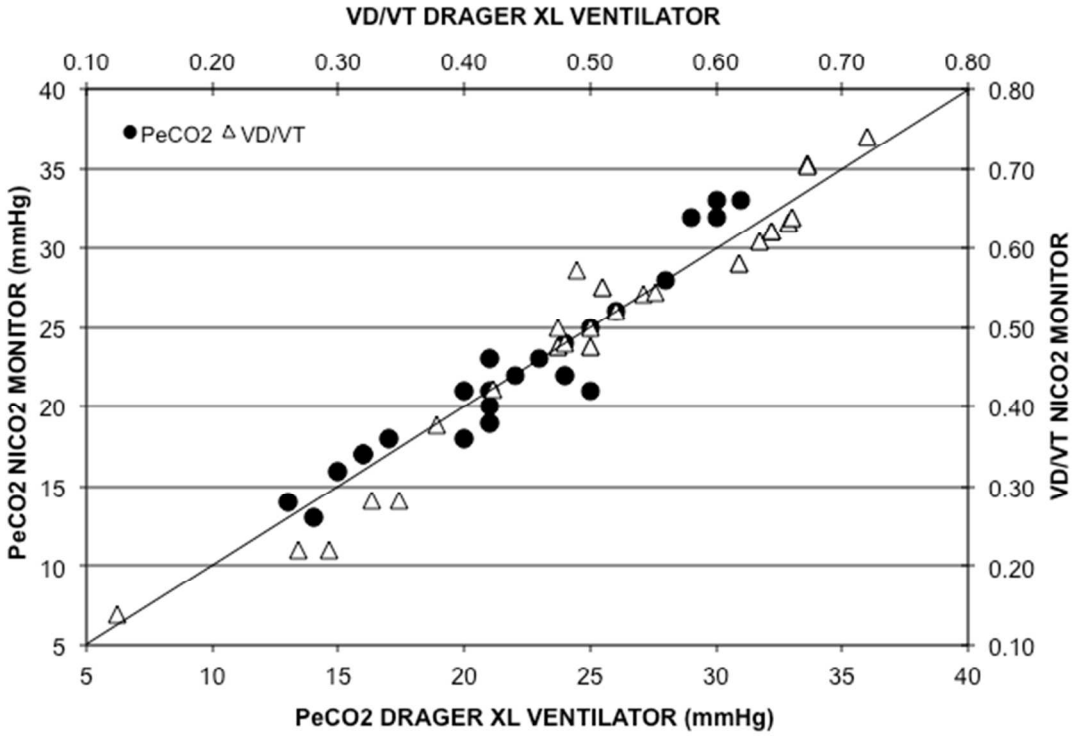

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Figure 5

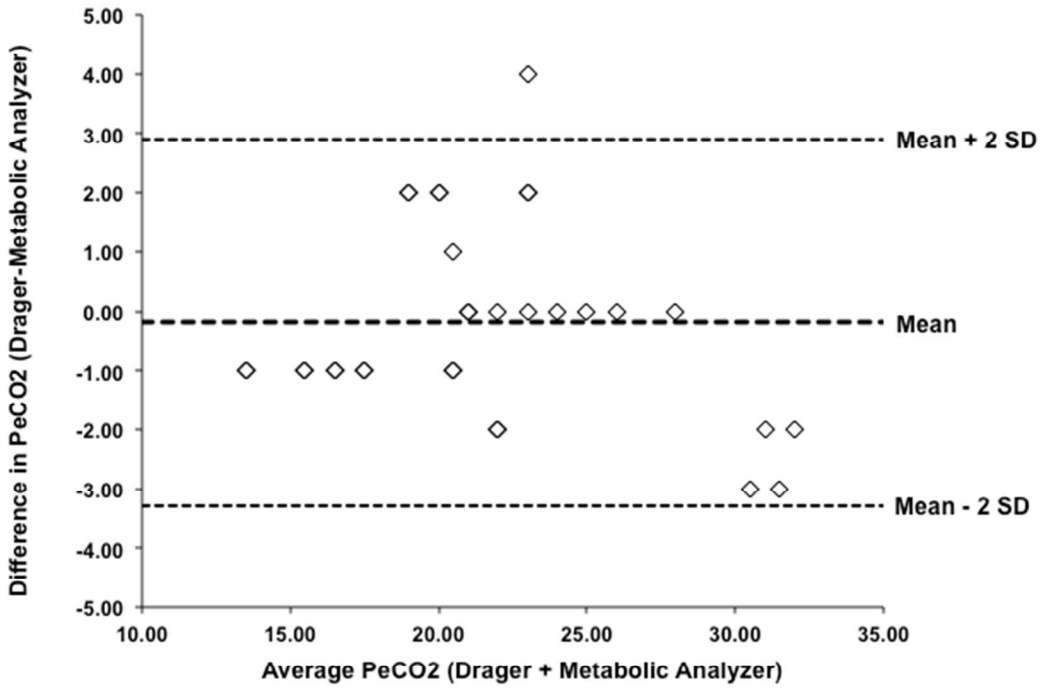

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Figure 6

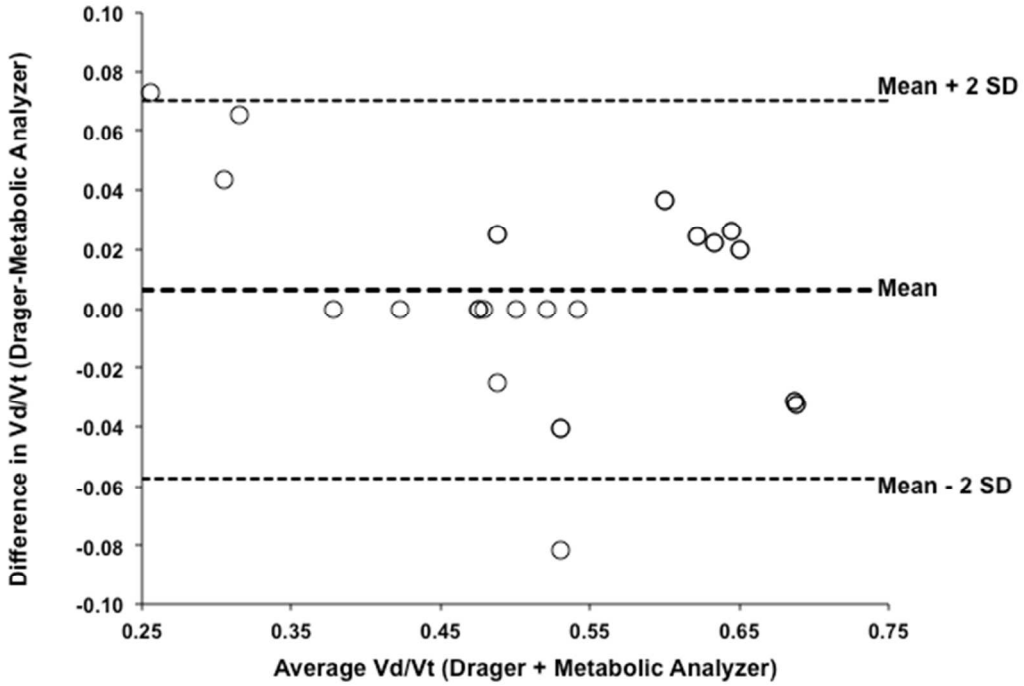

Figure 7

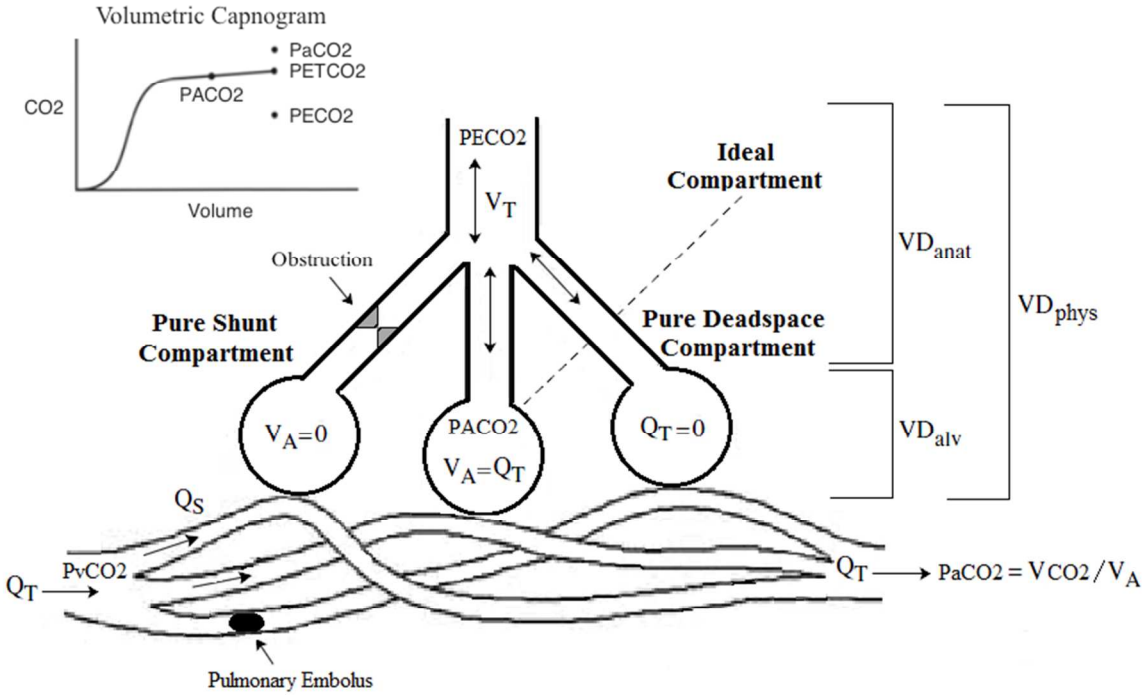

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Figure 8