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Single breath CO sub 2 analysis: Description and validation of a method [Laboratory Investigation]

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Abstract

Objectives: To evaluate the performance of a newly developed single breath CO_2 analysis station in measuring the airway deadspace in a lung model (study 1), and then to quantify the bias and precision of the physiologic deadspace measurement in a surfactant-depleted animal model (study 2).

Design: A prospective bench validation of a new technique of airway deadspace measurement using a criterion standard (study 1); a prospective, animal cohort study comparing a new technique of physiologic deadspace measurement with a reference method (Bohr-Enghoff method) (study 2).

Setting: A bench laboratory and animal laboratory in a university-affiliated medical center.

Subjects: A lung model (study 1), and adult sheep with induced surfactant deficiency (saline lavage) (study 2).

Methods: The single breath CO_2 analysis station consists of a mainstream capnometer, a variable orifice pneumotachometer, a signal processor, and computer software with capability for both on- and off-line data analysis. Study 1: We evaluated the accuracy of the airway deadspace calculation using a plexiglass lung model. The capnometer and pneumotachometer were placed at the ventilator Y-piece with polyvinyl chloride tubing added to simulate increased airway deadspace. Segments of tubing were sequentially removed during each testing session to simulate decreasing deadspace. The calculated airway deadspace was derived from the single breath CO_2 plot and compared with the actual tubing volume using least-squares linear regression and paired t-tests. Study 2: The accuracy of the physiologic deadspace measurement was examined in a saline-lavaged animal model by comparing the physiologic deadspace calculated from the single breath CO_2 analysis station with values obtained using the Enghoff modification of the Bohr equation: deadspace/tidal volume ratio equals ($PaCO_2$ minus mixed expired PCO_2)/$PaCO_2$.

Measurements and Main Results: Study 1: Thirty-six measurements of calculated airway deadspace were made and compared with actual circuit deadspace during four different testing conditions. Measured airway deadspace correlated significantly with actual circuit deadspace (r^2 equals .99). The proportional error of the method was minus 0.8% with a 95% confidence interval from minus 3.6% to 1.9%. Study 2: A total of 27 pairs of measurements in four different animals were available for analysis. The derived physiologic deadspace/tidal volume ratio significantly correlated with the value obtained using the Bohr-Enghoff method (r^2 equals .84). The bias and precision of our physiologic deadspace calculation were .02 and .02, respectively, and the mean percent difference for the physiologic deadspace calculated from the single breath CO_2 analysis station was 2.4%.

Conclusions: Our initial experience with the single breath CO_2 analysis station indicates that this device can reliably provide online evaluation of the single-breath CO_2 waveform. In particular, estimation of the airway and physiologic deadspace under a variety of testing conditions was consistently within 5% of actual values. We feel that with further application and refinement of the technique, single breath CO_2 analysis may provide a noninvasive, on-line monitor of changes in pulmonary blood flow.

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The first detailed description of the use of expired CO_2 analysis to measure respiratory deadspace was by Aitken and Clarke-Kennedy in 1928 [1]. Fowler [2] further elaborated on the utility of the single breath CO_2 tracing by dividing the concentrationvolume curve into three distinct phases and relating each phase to anatomical compartments of the respiratory system. Fletcher and colleagues [3,4] reviewed the topic and described the application of single breath CO_2 analysis in patients with abnormalities of pulmonary perfusion. We recently developed a single breath CO_2 analysis station that allows on-line quantification of the airway and alveolar deadspace. This manuscript describes the technical aspects of both the hardware and software components of our system, and provides initial validation data of the device in both a lung model and an animal model.

MATERIALS AND METHODS

Description of the Technique.

The single breath CO_2 analysis station consists of a mainstream capnometer, a variable orifice pneumotachometer, a signal processor, and computer software with capability for both on- and off-line data analysis. The technical details of the individual components are provided in Appendix 1. (Tables 3 and 4) The CO_2 expirogram can be divided into three distinct phases, as first described by Fowler [2] Figure 1. Phase I represents expired gas from the conducting airways, which contains no measurable CO_2. Phase II represents the mixing of the terminal gas from conducting airways and alveolar gas from acini with the shortest transit times. Phase III represents gas from the alveoli and includes the alveolar plateau. The physiologic deadspace, the airway deadspace, and the alveolar deadspace can be reliably calculated by analysis of the expired CO_2 waveform (Figure 2, top) [5]. The details of our waveform analysis are described in Appendix 2, (Table 5) and a discussion of the potential sources of error are detailed in Appendix 3. (Table 6)

Capnometer. The CO_2 signal is provided by a mainstream, nondispersive, infrared capnometer (Capnogard®, 1265, Novametrix Medical Systems, Wallingford, CT) complete with an analog output module. This device is barometric pressure-compensated (range 550 to 780 mm Hg), with an accuracy of 5% between Pco_2 values of 41 and 100 torr (5.5 and 13.3 kPa) and 2 mm Hg between 0 and 40 torr (0 and 5.3 kPa). The capnometer operates at a sampling rate of 87 Hz, with priority reports provided to the analog module at the same rate as sample acquisition. More detailed specifications regarding this instrument have been published previously (Capnogard Model 1265 Operator's Manual, Catalogue 5552302, Novametrix Medical Systems). The calibration sequence is incorporated within the software and is a 2-point calibration at 0% and 5% CO_2 concentrations.

Pneumotachometer. The pneumotachometer is a disposable, variable orifice, differential pressure device (Accutach, Glen Medical Products, Carlsbad, CA). The response curve of each individual pneumotachometer is generated by using positive (inspiratory) and negative (expiratory) flow at 43 static intervals from 0.47 to 103.82 L/min in each direction. Since our concern is with low-flow conditions, 20 of the 43 steps were in the <10 L/min range. A characterization file was generated for each pneumotachometer with the individual flow data points and the interface analog/digital converter response count. Each level of flow was allowed to stabilize before assay and each data point contains a 2-sec average of data collected at >100 samples/sec. Each data point was plotted on a quadrant, with the x axis defining flow and the y axis defining amplifier voltage output. The amplifier output was offset such that the origin corresponded to zero volts and zero flow. A "best fit" regression line was derived and extended through the origin. Residual differences from the regression line were calculated and yielded a scaling factor for each analog/digital count. The scaling factor plot represents every possible analog/digital count and its associated scaling factor. A response binary file was generated from these data and is used by the host software during the standard calibration routine.

The calibration technique we utilized has been previously described (19). Our one-stroke calibration procedure provided an overall accuracy over the pneumotachometer flow range of ±2% with the use of pneumotachometer-specific response curves.

Signal Processing. The signal-processing hardware represents a modification of an available respiratory mechanics computer (Ventrak®, Respiratory Mechanics Monitor, Novametrix Medical Systems). The flow signal from the pneumotachometer is processed using a differential pressure transducer (163PC01D36, Microswitch, Freeport, IL) and sampled at a frequency of 100 Hz. The signal is offset and amplified to provide an output of –5 to +5 volts to the

Table 3. Appendix 1. Technical Details of the Hardware

multiplexed analog/digital converter. The analog/digital converter is a 12-bit unit with a 25-μsec maximum conversion time. The 12-bit analog/digital converter has a resolution of 4,096 counts. The 12-bit converter over the amplified flow range provides a resolution of 2.44 millivolts per analog/digital output count. Given the pneumotachometer range of ±2 L/sec, the system provides resolution of 0.00098 L/sec/analog/digital count (0.059 L/min/analog/digital count).

Pressure is measured by a differential pressure transducer referenced to atmosphere (143PC03D, Microswitch) and sampled at a frequency of 50 Hz. The signal is offset and amplified to provide an output of –5 to +5 volts to the analog/digital converter. The pressure signal is processed similarly to the flow signal. The range is –50 to +150 cm H_2O, with a resolution of 0.049 cm H_2O per analog/digital count. There are two auxiliary inputs available and the CO_2 signal is connected to one of the auxiliary inputs and sampled by the analog/digital converter at a rate of 50 Hz.

Table 4. Appendix 1. *(cont'd)*

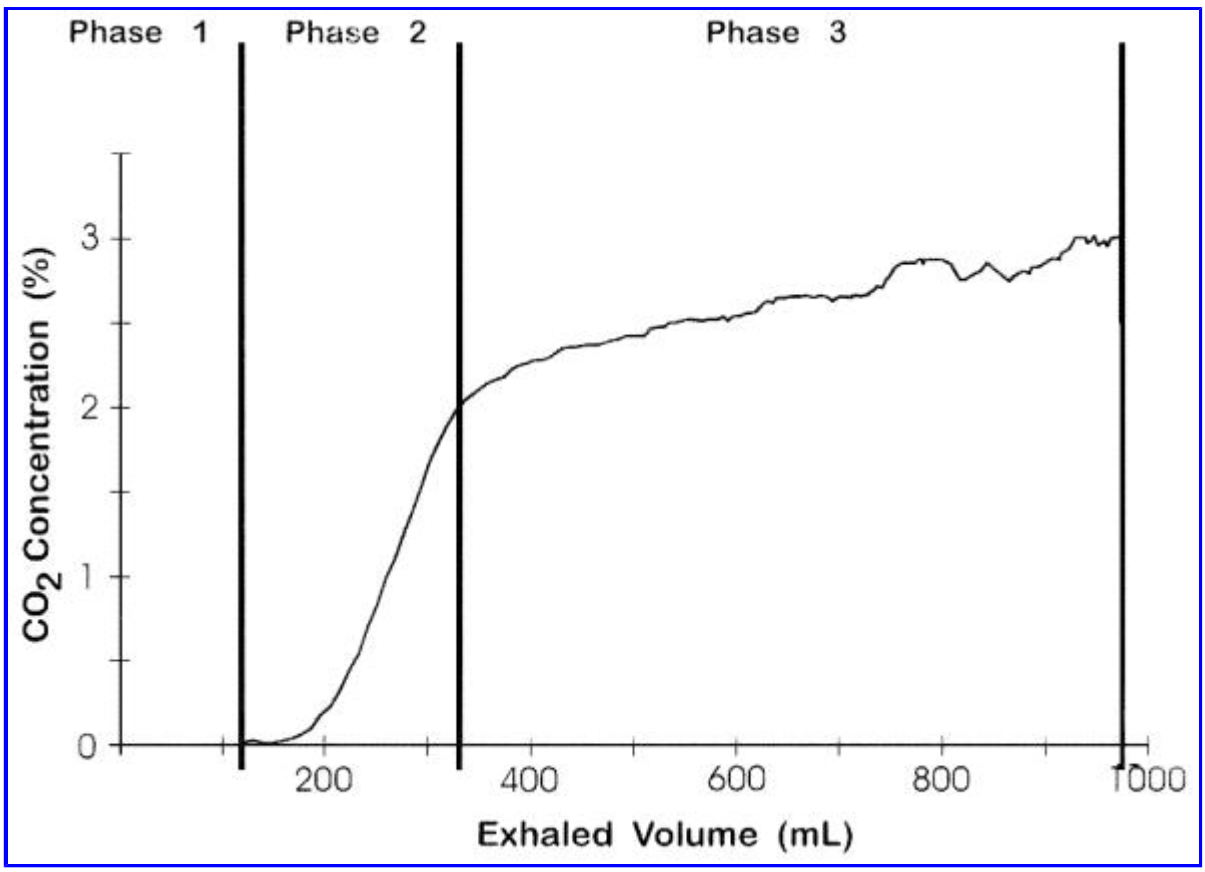


Figure 1. Three phases of the CO_2 expirogram (see Materials and Methods).

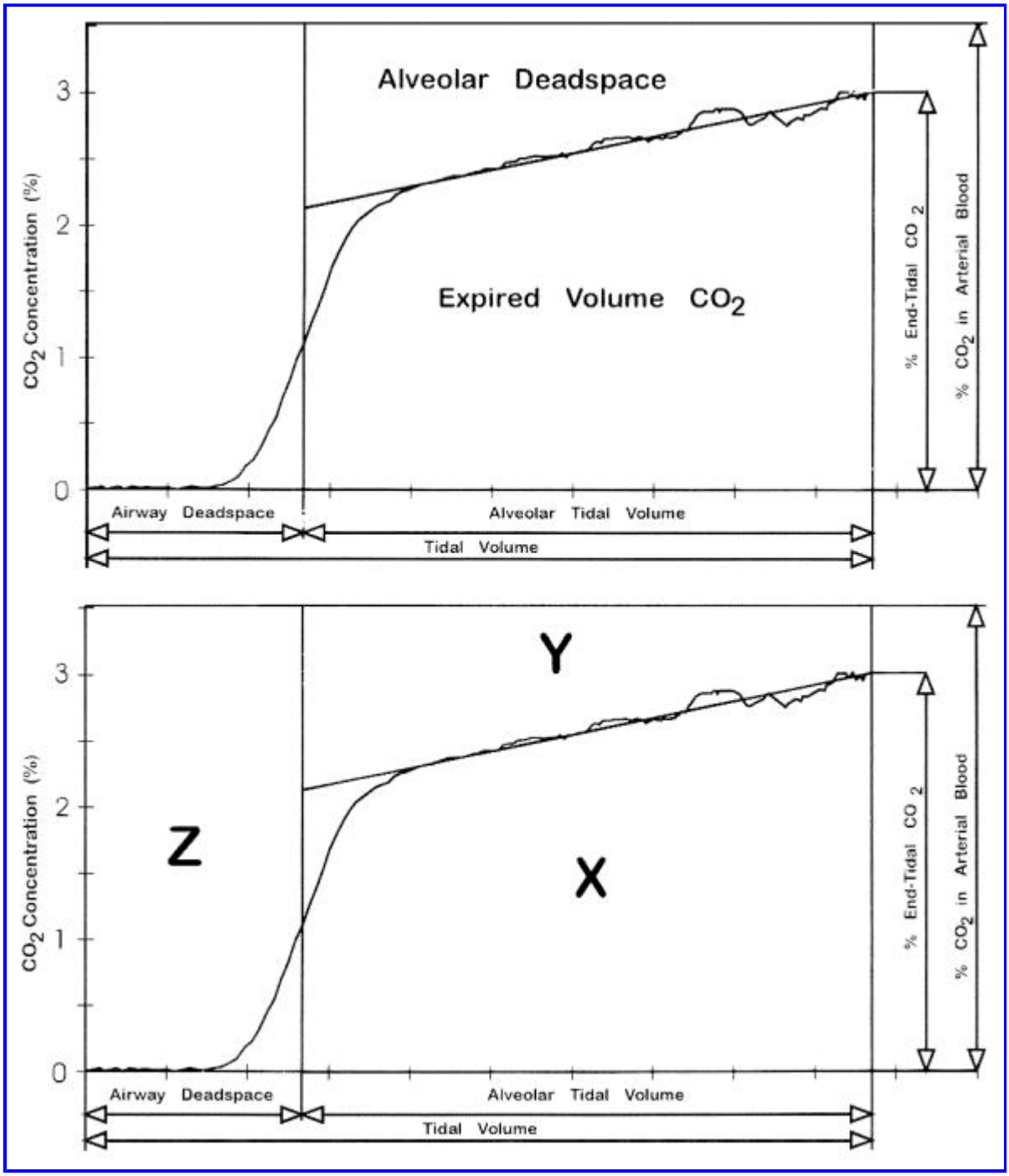
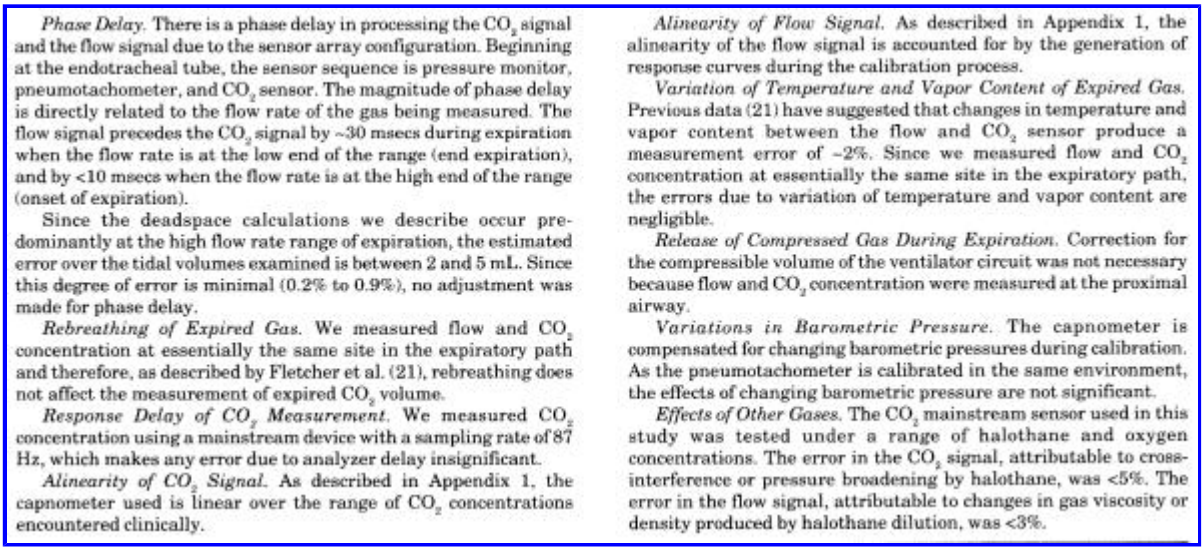


Figure 2. Top: Components of the CO_2 expirogram after Fletcher [5]. Bottom: Physiologic deadspace/tidal volume ratio was defined by (area Y plus area Z)/(area X plus area Y plus area Z) after Fletcher [5].

Phase I was defined as beginning at the onset of expiration (the detection of negative flow by the pneumotachometer), and ending when the concentration of CO_2 in the expired gas increased 0.1% from baseline. Phase II was defined as beginning when the concentration of CO_2 increased 0.1% from baseline. A predictive slope for phase II was calculated at each successive data point at the time of data acquisition until the derived value was consistent and the slope maximal. The end of phase II was determined by the intersection of the predictive slope lines for phases II and III (see below). The midpoint of phase II was calculated using the methodology originally described by Fletcher and Jonson (20). Phase III began at the intersection of the predictive slope lines for phases II and III and ended at the end of expiration (the detection of positive flow by the pneumotachometer). The slope of phase III was derived from least squares linear regression using all data points collected between 50% and 70% of the integral of expired CO_2 plotted vs. volume.

Table 5. Appendix 2. Details of Waveform Analysis



Phase Delay. There is a phase delay in processing the CO_2 signal and the flow signal due to the sensor array configuration. Beginning at the endotracheal tube, the sensor sequence is pressure monitor, pneumotachometer, and CO_2 sensor. The magnitude of phase delay is directly related to the flow rate of the gas being measured. The flow signal precedes the CO_2 signal by ~30 msecs during expiration when the flow rate is at the low end of the range (end expiration), and by <10 msecs when the flow rate is at the high end of the range (onset of expiration).

Since the deadspace calculations we describe occur predominantly at the high flow rate range of expiration, the estimated error over the tidal volumes examined is between 2 and 5 mL. Since this degree of error is minimal (0.2% to 0.9%), no adjustment was made for phase delay.

Rebreathing of Expired Gas. We measured flow and CO_2 concentration at essentially the same site in the expiratory path and therefore, as described by Fletcher et al. (21), rebreathing does not affect the measurement of expired CO_2 volume.

Response Delay of CO_2 Measurement. We measured CO_2 concentration using a mainstream device with a sampling rate of 87 Hz, which makes any error due to analyzer delay insignificant.

Alinearity of CO_2 Signal. As described in Appendix 1, the capnometer used is linear over the range of CO_2 concentrations encountered clinically.

Alinearity of Flow Signal. As described in Appendix 1, the alinearity of the flow signal is accounted for by the generation of response curves during the calibration process.

Variation of Temperature and Vapor Content of Expired Gas. Previous data (21) have suggested that changes in temperature and vapor content between the flow and CO_2 sensor produce a measurement error of ~2%. Since we measured flow and CO_2 concentration at essentially the same site in the expiratory path, the errors due to variation of temperature and vapor content are negligible.

Release of Compressed Gas During Expiration. Correction for the compressible volume of the ventilator circuit was not necessary because flow and CO_2 concentration were measured at the proximal airway.

Variations in Barometric Pressure. The capnometer is compensated for changing barometric pressures during calibration. As the pneumotachometer is calibrated in the same environment, the effects of changing barometric pressure are not significant.

Effects of Other Gases. The CO_2 mainstream sensor used in this study was tested under a range of halothane and oxygen concentrations. The error in the CO_2 signal, attributable to cross-interference or pressure broadening by halothane, was <5%. The error in the flow signal, attributable to changes in gas viscosity or density produced by halothane dilution, was <3%.

Table 6. Appendix 3. Analysis of Potential Sources of Error

Study 1: Validation of Airway Deadspace Estimation.

We evaluated the accuracy of the airway deadspace calculation using a Plexiglas lung model. The lung model consisted of two compartments filled with water and separated by a perforated divider that allowed variable resistance to be applied to the system. The Plexiglasenclosed water was perfused with a continuous supply of CO_2 to simulate a minute CO_2 production of 300 mL/min. The test lung was ventilated using a Servo 900C Registered Trademark Ventilator (Siemens, Solna, Sweden) at an inspiratory time of 1.25 secs with frequency adjusted to provide an end-tidal PCO_2 between 35 and 45 torr (4.7 and 6.0 kPa). We varied the set tidal volume between separate testing sessions in order to provide some variation in the dead-space/tidal volume ratio. A premeasured length of 1/2 times 3/32 double prime polyvinyl chloride tubing (Tygon Registered Trademark, Norton Performance Plastics, Akron, OH) was placed between the ventilator Y-piece and the inlet to the test lung using two 15 times 15-mm adaptors to simulate increased airway deadspace. The volumes of the tubing and adaptors were measured using water and a graduated cylinder. The protocol consisted of sequential removal of 3-inch segments of tubing to simulate decreasing airway deadspace. The precise length of tubing removed at each step was measured and converted to a volume (3.2 mL/inch) to calculate the actual airway deadspace. At the end of each test, the volume of the remaining tubing was measured using water and a graduated cylinder to verify the accuracy of the tubing deadspace calculation. In all cases, the accuracy of the tubing deadspace calculation compared with the actual circuit volume was within 1%. The airway deadspace was calculated using the average values derived from ten successive single breath CO_2 curves once equilibration had occurred (15 mins), following removal of a known volume of deadspace.

Study 2: Validation of Physiologic Deadspace Measurement.

The accuracy of the physiologic deadspace measurement was examined in a saline-lavaged animal model by comparing the physiologic deadspace calculated from the single breath CO_2 analysis station with values obtained using the Enghoff modification of the Bohr equation: deadspace/tidal volume ratio equals ($PaCO_2$ minus mixed expired PCO_2)/$PaCO_2$ [6]. This protocol was approved by the Animal Care and Use Committee of Children's Hospital, and the animals were handled according to the Guidelines for the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Council (DHHS Publication No. [NIH]

85-23, 1985).

Induction of anesthesia in the adult sheep was produced with intramuscular ketamine (20 to 30 mg/kg) and the animals were intubated orally with a 7.5-mm inner diameter endotracheal tube (Mallinckrodt, Glenn Falls, NY). After adequate intravenous access was established, maintenance anesthesia was provided by the administration of halothane (0.5% to 1.0% inspired), and muscle relaxation was achieved by giving pancuronium (0.2 mg/kg/hr). Controlled ventilation was provided by a piston-driven ventilator (3MV-Ped, Emerson Equipment, Cambridge, MA) at standardized ventilator settings (FIO_2 equals 0.50, tidal volume 10 mL/kg, with rate adjusted to achieve a $PaCO_2$ between 35 and 45 torr [4.7 and 6.0 kPa]).

In order to produce abnormalities of the deadspace/tidal volume ratio over a clinically relevant range, the animals underwent repetitive lung lavage using warmed physiologic saline, as has been previously described [7]. During lavage, the animals were ventilated with an FIO_2 of 1.0, and 35 to 40 mL/kg of warmed normal saline were instilled in 60-mL aliquots via the endotracheal tube. Instillation lasted approximate 3 to 5 mins, and the lavage fluid was then allowed to drain passively with the animal placed in a 10 degrees head-down tilt. The animals were then ventilated with an FIO_2 of 1.0, at the same rate and tidal volume as prelavage, for a period of 5 mins. Lavage was repeated until the PO_2 was less than 100 torr (less than 13.3 kPa) with an FIO_2 of 1.0 (usually two or three repetitions). In the first animal, lavage was followed by 1 hr of equilibration. Serial measurements of the physiologic deadspace were made over a 4-hr period. Expired tidal volumes were continuously measured and the delivered tidal volume was adjusted to maintain a constant expired tidal volume of 10 mL/kg.

Pulmonary hypoperfusion, produced by graded hemorrhage, has previously been shown to produce progressive increases in the physiologic deadspace when tidal volumes remain constant [8]. In three subsequent animals, we attempted to produce a range of values for the physiologic deadspace by progressively impeding venous return to the right atrium using an adjustable constrictor placed around the inferior vena cava. In these animals, following saline lavage, a left thoracotomy was performed at the fifth to sixth intercostal space, using sterile surgical technique. The left internal mammary artery was cannulated after careful dissection, and a hydraulic constrictor (Hazen Everett, Teaneck, NJ) was placed around the inferior vena cava at the atrial-caval junction. The arterial pressure waveform and electrocardiogram were continuously displayed throughout the protocol. Incremental injections of 0.2 mL of normal saline were made until the animal manifested systemic hypotension or metabolic acidosis (usually four to six injections, totaling 0.8 to 1.2 mL). Expired tidal volumes were continuously measured and the delivered tidal volume was adjusted to maintain a constant expired tidal volume of 10 mL/kg. Measurements were made after a 15-min equilibration period following each injection.

In all animals, a 5-min recording of the single breath CO_2 expirogram was saved on disk for subsequent off-line analysis. Arterial blood gases were sampled at the end of this period and immediately analyzed using a standard laboratory blood gas analyzer (278 Blood Gas System, Ciba Corning Diagnostics, Medfield, MA) with automatic temperature correction. The protocol included calibration of the CO_2 analysis station to a standard calibration gas (10% CO_2), according to the PCO_2 value displayed on the blood gas analyzer. This calibration procedure was repeated at the beginning of each testing sequence.

The physiologic deadspace/tidal volume ratio was derived from averaging the terminal 60 secs of each recording (Figure 2, bottom). We compared the physiologic deadspace/tidal volume ratio derived from the CO_2 expirogram with the respiratory deadspace value derived from the Bohr-Enghoff equation. The mixed expired PCO_2 was obtained by analysis of a 10-mL sample obtained from a 4-min collection of expired gas collected in a gas-impermeable bag (6030, Hans Rudolph, Kansas City, MO). Mixed expired PCO_2 was quantified using the same blood gas machine used for all other gas tension measurements and calibration. The values for deadspace/tidal volume ratio obtained by the two methods were compared using linear least-squares regression. The bias and precision were evaluated using the mean and standard deviation of the differences between the measures. The differences between the methods of deadspace measurement (bias) were plotted against the average of the two methods. The bias measures systematic error between the methods, and the precision quantifies the random error or variability [9]. The limits of agreement were defined as the mean difference plus minus 2 SD and describe the range that includes 95% of the differences between the measures. The percent difference was calculated from the following formula: percent difference (%) equals 100 times (difference between the methods)/mean deadspace measurement.

RESULTS

Study 1: Validation of Airway Deadspace Estimation.

Four separate tests were performed at varying tidal volumes and inspiratory pressures Table 1. Thirty-six measurements of calculated airway deadspace were made and compared with actual circuit deadspace using least-squares linear regression and paired t-tests to estimate proportional error, constant error, and random error, as described by Westgard and Hunt [10]. Measured airway deadspace correlated significantly with actual circuit deadspace (r^2 equals .99, p less than .0001) (Figure 3, top). The proportional error (slope of the regression line) of the method was minus 0.8% with a 95% confidence interval from minus 3.6% to 1.9%. The constant error (y intercept) of the measurement was 1.6 mL, and the random error (standard error of the estimate) was 2.8 mL. In addition, the bias (mean difference) was 0.2 mL with a 95% confidence interval from minus 0.57 mL to 0.97 mL; the precision (standard deviation of the difference) of the measurement of airway deadspace was 2.3 mL.

	V_T (mL)	PIP (cm H_2O)	RR (breaths/min)	$Petco_2$ (torr)	Deadspace Range (mL)
Test 1	848 (825–871)	17	10	38 (33–41)	166–252
Test 2	774 (761–787)	20	10	35 (33–37)	152–243
Test 3	551 (530–558)	10	10	34 (32–38)	165–252
Test 4	543 (537–548)	10	10	35 (33–36)	165–252

V_T, tidal volume; PIP, peak inspiratory pressure; RR, respiratory rate; $Petco_2$, end-tidal CO_2 tension.
Values are means with ranges in parentheses.

Table 1. Testing conditions for validation of airway deadspace measurements

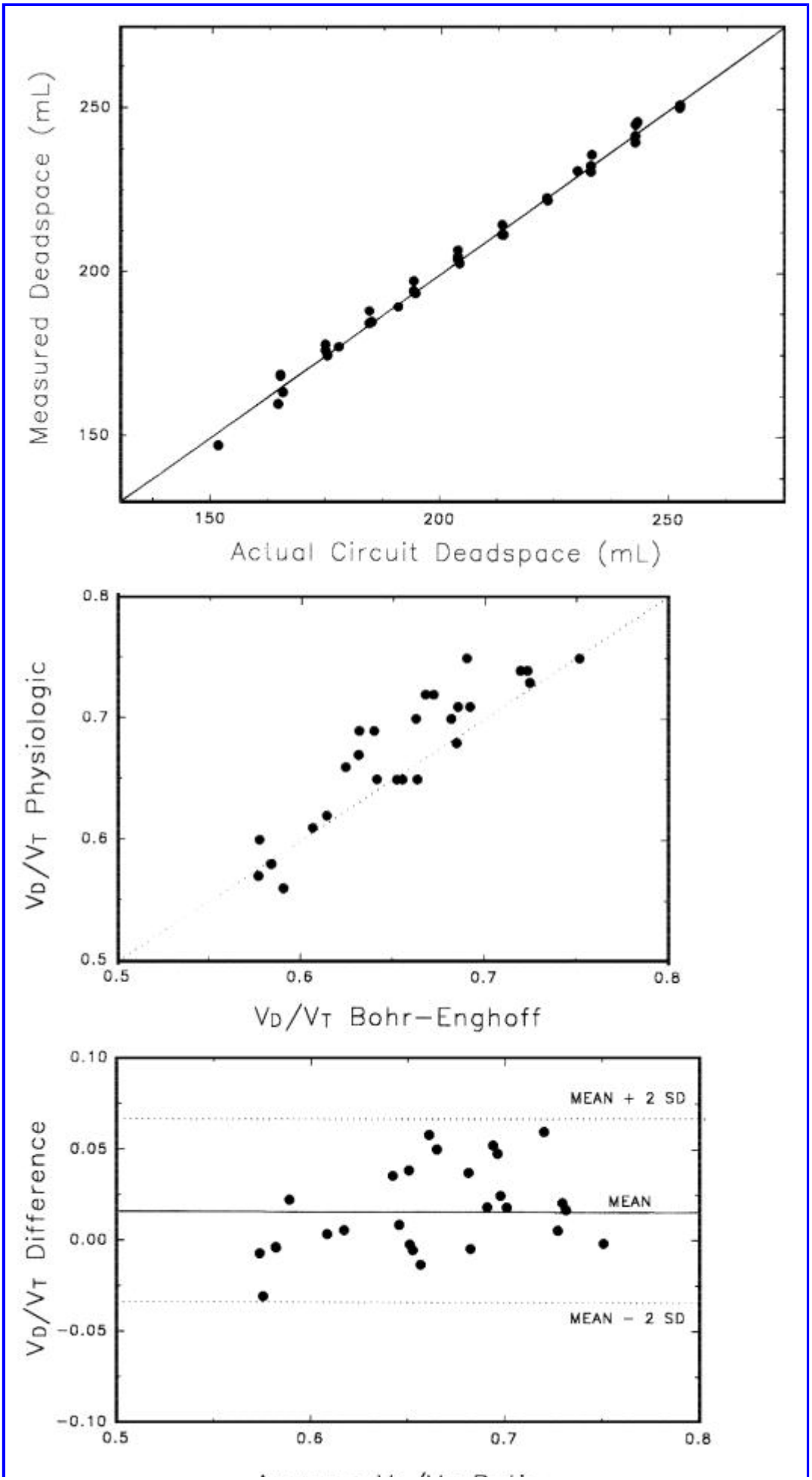


Figure 3. Top: Measured airway deadspace measurements plotted against actual circuit deadspace (r^2 equals .99, p less than .0001). The line represents the line of identity, y equals x. Middle: Measured physiologic deadspace (VD/VT) measurements plotted against the Bohr-Enghoff method (r^2 equals .84, p less than .0001). The line represents the line of identity, y equals x. Bottom: Bias of the physiologic deadspace (VD/VT) measurement plotted against the average deadspace/tidal volume ratio. The mean difference is .02, and the limits of agreement are minus .03 and .07 (mean difference plus minus 2 SD).

An error analysis for each individual test demonstrates that both proportional error and constant error were relatively constant across all testing conditions Table 2. The proportional error, as measured by the slope of the regression line, ranged between minus 7.7% and 6.3%. The constant error, as measured by the mean bias, ranged between minus 0.3 and 1.5 mL.

		m	b (mL)	Sy (mL)	Bias (mL)	SD_d	*t*	r^2
Test 1	(n = 10)	0.996	7.4	3.9	–0.3	1.9	0.54	.99
Test 2	(n = 7)	0.923	15.9	2.3	–0.9	3.0	0.78	.99
Test 3	(n = 9)	1.058	–13.3	4.8	1.5	2.1	2.09	.99
Test 4	(n = 10)	1.063	–13.4	2.8	0.3	2.0	0.52	.99
Overall error	(n = 36)	0.991	1.6	2.8	0.2	2.3	0.53	.99

m, slope of the regression line; b, y intercept; Sy, standard error of the estimate; SD_d, standard deviation of the difference; *t*, paired student's *t*-test statistic; *r*, Pearson's correlation coefficient.

Table 2. Summary of statistical results for airway deadspace measurements

Overall, the mean bias of 0.2 mL for all testing conditions represents an error of 0.1% of the mean value of actual tubing volume used during the bench validation. For a 200-mL actual airway deadspace, the measured value using the single breath CO_2 analysis station would be 199.9 mL with a 95% confidence interval of 199.1 to 200.6 mL.

Study 2: Validation of Physiologic Deadspace Measurement.

Four adult sheep (mean weight 43.3 kg, range 40.0 to 46.6) were anesthetized and instrumented. Baseline arterial blood gases and CO_2 expirograms were obtained 30 mins after completing the surgical preparation. Incremental injections of the constrictor were performed as described, with analysis of blood gas tensions and recording of the CO_2 expirogram after 15 mins to allow equilibration. In the first animal, lavage was followed by 1 hr of equilibration. Seven serial measurements of the physiologic deadspace were made without inflating the constrictor over a 4-hr period. In three subsequent animals, lavage was followed by 1 hr of equilibration and five incremental injections of the hydraulic constrictor. Expired tidal volumes were continuously measured, and the delivered tidal volume was adjusted to maintain a constant expired tidal volume of 10 mL/kg.

A total of 27 pairs of measurements were available for analysis. The physiologic deadspace/tidal volume ratio, as calculated from the single breath CO sub 2 analysis station, ranged between .56 and .75 (mean value .67). The derived physiologic deadspace/tidal volume ratio significantly correlated with the value obtained using the Bohr-Enghoff method

(r^2 equals .84, p less than .0001) (Figure 3, middle). The bias and precision of our physiologic deadspace calculation were .02 and .02, respectively (Figure 3, bottom). The 95% confidence interval for the bias was .01 to .03. The limits of agreement were minus .03 and .07. The mean percent difference for the physiologic deadspace calculated from the single breath CO_2 analysis station was 2.4%.

DISCUSSION

Our initial experience with the single breath CO_2 analysis station indicates that this device can reliably provide on-line evaluation of the single-breath CO_2 waveform. In particular, estimation of the airway and physiologic deadspace under a variety of testing conditions was consistently within 5% of either actual values, or the values obtained from the best available methodology. Defining the largest acceptable difference between two methods of measurement is a complex issue that has been reviewed by LaMantia and colleagues [11]. These authors point out that the minimal differences required to suggest clinically relevant differences in cardiac output based on triplicate thermodilution measurements has been estimated to be 13% [12]. Our data demonstrate that for determination of airway deadspace, the limits of agreement (mean difference plus minus 2 SD) represent 2.2% of the mean value of the actual circuit deadspace. Furthermore, the limits of agreement for the physiologic deadspace measurement represents 7.3% of the mean value of the physiologic deadspace derived using the Bohr-Enghoff method. We feel that this degree of accuracy is well within "reasonable" limits when evaluating new techniques and devices in the clinical setting [9].

We [13] reported the utility of respiratory deadspace measurements in neonates with profound abnormalities of gas exchange. In our study [13] of infants undergoing extracorporeal membrane oxygenation, the mean deadspace/tidal volume ratio decreased from .53 after the institution of extracorporeal membrane oxygenation to .42 just before discontinuation of extracorporeal membrane oxygenation, which corresponded to significant improvement in the gasexchanging efficiency of the lung. More recent experience [14] in a group of infants with congenital diaphragmatic hernia suggests that respiratory deadspace measurements may provide important prognostic information in these patients. In this series of highrisk infants with congenital diaphragmatic defects, there was a significant difference between the highest deadspace/tidal volume ratio measured in survivors vs. nonsurvivors. Furthermore, a deadspace/tidal volume ratio of more than equals .60 predicted mortality with a positive predictive value of 80%, a negative predictive value of 79%, and an odds ratio of 15.

These clinical reports, however, describe changes in the physiologic deadspace that may reflect alterations in either the airway deadspace or reflect abnormalities of the alveolar deadspace. Single breath CO_2 analysis offers the precision to differentiate the alveolar deadspace from the airway deadspace, and previous data [15] suggest that quantification of the alveolar deadspace may be directly related to effective pulmonary perfusion.

Beyond estimation of the airway or alveolar deadspace fractions, a number of recent studies have described the utility of CO_2 waveform analysis in evaluating abnormalities of gas exchange in a variety of settings. In a surfactant-depleted animal model, the slope of phase III has been correlated with the degree of lung injury as quantified by the functional residual capacity [16]. The same group of investigators [17] also demonstrated a difference in phase III slope between normal adults and those individuals with adult respiratory distress syndrome.

Another intriguing possibility is the speculation that changes in phase III slope may reflect alveolar development and lung growth in normal infants and children [18].

We feel that with further application and refinement of the technique, single breath CO_2 analysis may provide a noninvasive, on-line monitor of changes in pulmonary blood flow. This technique represents a particularly important advance in understanding the physiology of pulmonary hypertension and may allow the development of specific therapies designed to optimize pulmonary blood flow.

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