The dependence of measured alveolar deadspace on anatomical deadspace volume

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Background. Changes in pulmonary deadspace are indicators of disease status (e.g. pulmonary embolus, acute respiratory distress syndrome) and they have prognostic usefulness in the intensive care unit. The components of pulmonary deadspace, the alveolar and anatomical deadspaces (VDalv and VDanat), are commonly considered to be independent (i.e. the addition of airway equipment should not alter the measured VDalv). However, VDanat has been shown to affect VDalv in the absence of changes in alveolar ventilation or perfusion. We sought to quantify the variability in measured VDalv induced by changes in VDanat using a cardiorespiratory computational model.

Methods. Using the Nottingham Physiology Simulator, we examined three simulated ventilated patients with small, moderate and large ventilation–perfusion (VQ) defects. Each patient received 12.5 bpm × 500 ml. We varied VDanat between 50 and 250 ml, keeping the VQ ratio of each alveolus constant. We calculated VDalv by subtracting VDanat (measured using Fowler’s technique) from the physiological deadspace (measured using the Bohr–Enghoff equation). We calculated fresh-gas tidal volume (VTfresh) by subtracting VDanat from the exhaled tidal volume and calculated VDalv/VTfresh. In the simulated patient with the large VQ defect, we performed the same protocol with tidal volumes of 750 and 1000 ml.

Results. When VDanat increased from 50 to 250 ml (500 ml tidal volume) VDalv decreased by 48.3% (mean value across the three VQ defects) and VDalv/VTfresh decreased by 15.1%. These relationships were similar at each tidal volume studied.

Conclusions. Measured VDalv is altered by changes in VDanat despite constant VQ ratios in each alveolus. This has implications for the interpretation of deadspace measured in the clinical setting. The variability is less for the ratio VDalv/VTfresh.


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Tidal volume can be divided into a portion participating in gas exchange and a portion which does not. The latter is termed the pulmonary deadspace and comprises the anatomical deadspace (VDanat) and the alveolar deadspace (VDalv), where VDanat is the volume of the conducting airways and apparatus and VDalv is a theoretical volume which accounts for the ‘wasted ventilation’ occurring in areas of the lung that are relatively underperfused. These volumes are most commonly measured using Fowler’s technique2 (VDanat) and Enghoff’s modification of the Bohr equation (for the physiological deadspace [VDphys]). VDalv is calculated by subtracting VDanat from VDphys (the Bohr–Fowler technique); it reflects the alveolar ventilation–perfusion (VQ) configuration. VDalv and VDanat are considered as discrete and independent by most current textbooks and clinicians.1 For example, according to commonly accepted theory, the addition of equipment deadspace (e.g. a breathing system filter) to a ventilated patient would not be expected to alter the measured VDalv as long as alveolar ventilation and perfusion remained unchanged. However, previous workers have suggested that, when measured using the Bohr–Fowler technique, VDalv and VDanat are not independent, and that measured VDalv may be affected by variation in VDanat.3–5

The quantification of deadspace is an important issue. Recent work has demonstrated an association between pulmonary deadspace and mortality in the critically ill.6 In clinical practice VDalv may be used as an indicator of pulmonary disease severity and progression (e.g. pulmonary
embolus, acute respiratory distress syndrome) and the identification of changes in VDalv in critically ill patients has been highlighted in recent work.7 8

If VDalv is to be quantified, it is important that we understand the factors that may cause its variation. Coincidental variation in VDanat (e.g. through changes in breathing system configuration) may influence VDalv, and our aim in this investigation was to quantify this relationship. The apparent interdependence of the anatomical and alveolar deadspaces is not easily investigated clinically and the relationship has been only briefly considered.3 Therefore we used a detailed cardiorespiratory computational model to examine the effect of changes in anatomical deadspace on alveolar deadspace volume measured using the Bohr–Fowler technique.

Methods

The Nottingham Physiology Simulator

The Nottingham Physiology Simulator (NPS) is an original computational model of human respiratory and cardiovascular physiology and has been described in detail previously.9–14 Briefly, the model uses an iterative numerical approach. Equilibria are resolved between compartments (e.g. alveolar gas and pulmonary capillary blood) by repeated movements of mass down a tension gradient; this process has been termed time-slicing. Mass is conserved at all steps. Aspects of the pulmonary system included in the model are as follows.

Ventilator

Ventilation is tidal. Constant-flow inspiration is provided and duty cycle, tidal volume and ventilatory frequency are adjustable. Inspired air may be warmed and humidified. The complex distribution of flow from the ventilator model through the series deadspace into the alveoli is determined by driving pressure, alveolar inlet resistance and intraluminal pressure. At any time in the ventilatory cycle, some alveoli may be inspirating, some static and some exhaling.

Anatomical (series) deadspace

The bronchial tree is modelled as a single pipe (the trachea) which branches once into 500 bronchioles; each bronchiole feeds a single alveolus. The series deadspace is modelled as non-compliant, with a fixed predetermined volume. The airway from the atmosphere down to the respiratory epithelium is modelled in a ‘stacked-plate’ formation, with 200 non-mixing gaseous laminae moving in series through the nose, trachea and proximal bronchioles. This model has been validated by comparison with clinical data.12–14

Alveoli

Each of the 500 alveolar compartments has an independently configured compliance curve and inlet (bronchiolar) resistance. Pulmonary tissue displays viscoelasticity. Each alveolar compartment has an associated pulmonary vessel which arises directly from the pulmonary arterial trunk. Each pulmonary vessel has an independently configured vascular resistance and pressure gradient. Alveolar gas exchange is resolved through time-slicing (see above), with tiny volumes of gases moving across the alveolar basement membrane until the gas tensions on each side differ by <0.1%. The time-slice used in this study was 1 ms.

Blood

Oxygen is transported in combination with haemoglobin and in solution. Details of the haemoglobin and carbon dioxide carriage models have been described previously, and have been validated.9 10 The mutually dependent effects (the carriage of carbon dioxide and oxygen and pH) are included in the model (i.e. Bohr and Haldane effects).

Tissue

Tissues are modelled as a homogeneous compartment that receives all the cardiac output through a single vessel. The body’s oxygen consumption and carbon dioxide production occur within this compartment, and equilibrium is resolved within the single capillary via a time-slicing method. Mass is conserved during equilibrium. The resultant blood gas tensions represent mixed venous blood, which is returned to the pulmonary artery.

Validation

The aspects of the model of particular relevance to this investigation have been validated.14 A brief validation of the model regarding the behaviour of VDphys during changes in tidal volume is presented in the Appendix.

Experimental set-up

The model was configured with the following parameters: height, 1.75 m; weight, 75 kg. Hypoxic pulmonary vasoconstriction was disabled to ensure a constant VQ configuration during changes in VDanat and consequent changes in arterial gas tensions. Ventilatory frequency was 12.5 bpm, inspired oxygen fraction was 0.5, respiratory ratio was 0.8, inhaled tidal volume (which was warmed and humidified) was 500 ml and exhaled tidal volume (VTexh) was 496 ml. All gas volumes were calculated at 37°C with 100% humidity and 1 atm pressure.

The following calculations were used. Fresh-gas tidal volume:

$$VT_{fresh} = VT_{exh} − VDanat.$$

Physiological deadspace (calculated using Enghoff’s modification of the Bohr equation):15

$$VD_{phys} = (1 − PE_{CO_2}/PP_{CO_2}) × VT_{exh}.$$

Alveolar deadspace volume:

$$VD_{alv} = VD_{phys} − VDanat.$$
VDanat was increased through the (clinically relevant) values 50, 100, 150, 200 and 250 ml, and the following values were recorded: VDalv, VTfresh, P_{a,o_2}, P_{a,cO_2}, and the mean and standard deviation of the alveolar VQ ratios. The purpose of recording the VQ distribution was to ensure that the VQ configuration remained constant during changes in VDanat.

The investigation was performed three times, each time in the presence of a different VQ mismatch (small, moderate and large defects); the defects were created by varying the compartmental bronchiolar and pulmonary capillary resistances. The resulting VQ distributions are summarized in the Results section and presented in Figure 1. Next, inhaled tidal volume was increased to 750 and 1000 ml in the simulated patient with the large VQ defect. The protocol of increasing VDanat and data recording was repeated at each tidal volume.

The Nottingham Physiology Simulator can be obtained (free of charge) from the authors.

Results

Tidal volume 500 ml in three distinct VQ defects

Changes in the measured values of VDalv induced by changes in VDanat are shown in Figure 2A and changes in VDalv/VTfresh are shown in Figure 2B. Mean reduction in VDalv during the increase in VDanat from 50 to 250 ml was 48.3% (range 41.3–52.9%). Mean reduction in VDalv/VTfresh during the increase in VDanat was 15.1% (range 12.3–16.3%).

Mean VQ ratios were as follows: small VQ defect, 2.44 (SD 2.39); moderate VQ defect, 3.44 (3.40); large VQ defect, 5.06 (5.21). These values varied by <2% during changes in VDanat.

P_{a,o_2} varied from 39 to 26 kPa and P_{a,cO_2} varied from 4.5 to 10.5 kPa.

Increased tidal volume applied to a single baseline VQ defect

The response of measured VDalv to VDanat at inhaled tidal volumes of 750 and 1000 ml was qualitatively similar to that
at 500 ml. Changes in measured values of VDalv induced by changes in VDanat are shown in Figure 3A and changes in VDalv/VTfresh are shown in Figure 3B. Mean reduction in VDalv during the increase in VDanat from 50 to 250 ml was 39.3% (range 28.1–53.1%). Mean reduction in VDalv/VTfresh during the increase in VDanat was 11.7% (range 8.3–16.3%).

Discussion

Our results suggest that measurement of VDalv is affected by coincidental variation in VDanat, even when alveolar ventilation and perfusion are constant. This has implications for the use of VDalv in clinical practice. For example, addition of a breathing system filter, which would increase VDanat but would not affect the lung state, would cause a decrease in measured VDalv. Clearly, this is misleading. Our results also suggest that the ratio VDalv/VTfresh varies substantially less than VDalv when VDanat varies. Since it is necessary to measure VDanat in order to calculate VDalv (VDalv = VDphys−VDanat), no additional investigation is required to calculate VDalv/VTfresh compared with VDalv, and so it seems prudent to represent alveolar deadspace as VDalv/VTfresh rather than VDalv to minimize spurious variation induced by VDanat.

We postulate that the variation of VDalv caused by variation of VDanat relates to the volume of gas re-inhaled from the anatomical deadspace. This re-inhaled gas has already taken part in gas exchange, and its re-inhalation does not contribute significantly to gas exchange. Thus the fresh-gas ventilation of the alveoli is reduced by a volume equal to VDanat, thereby reducing VDalv (which is the tidal volume wasted, rather than a static volume). The reduction in VTfresh by VDanat is only approximately equal to VDanat because at the end of exhalation VDanat contains not only gas that has undergone exchange, but also some gas exhaled from areas of relatively poor perfusion that has had its inspired composition modified only slightly and still retains some residual gas-exchanging potential.

It was the above theory that prompted us to examine the variability of VDalv/(VT−VDanat). Our finding that the new calculation does not correct VDalv perfectly for variation in VDanat demonstrates the complexity of the process, but it is clear that this new calculation provides a more robust assessment of alveolar ventilation and perfusion than consideration of VDalv alone.

We disabled the computational model’s hypoxic pulmonary vasoconstriction during this investigation to avoid changes in VQ configuration during changes in VDanat. These would inevitably cause changes in alveolar and pulmonary capillary PO2. We demonstrated the stability of the pulmonary VQ configurations during changes in VDanat by measuring the mean and standard deviation of alveolar VQ ratios; these varied by <2%. To avoid the effect of PO2 on carbon dioxide dissociation and consequent changes in measured deadspace we used an inspired oxygen fraction of 0.5. This resulted in PaO2 values between 36 and 29 kPa, which would be unlikely to affect our findings.

VTfresh has been described previously as VTalv, but this term has also been used to describe the difference between VDphys and tidal volume. Furthermore, variation in VDanat does not actually alter the alveolar tidal volume; rather, it alters the composition of this volume. Therefore we preferred the term ‘VTfresh’ to represent the volume of gas entering the alveoli that has not already participated in gas exchange.

This investigation has been conducted using a computational model and may be criticized as being entirely theoretical. However, the computational model is detailed in replicating human physiology, and we have attempted to convey some of this detail in our description. The validation presented in the Appendix and our previous extensive published validations of the model provide assurance of the model’s lifelike behaviour.9–14 We acknowledge that this model is in constant development, but before any new investigation the current version of the model is verified against our previous published validations. One such validation that has particular relevance to this investigation provides considerable reassurance that the model used provides a meaningful and accurate simulation of respiratory deadspace and carbon dioxide elimination.14 In addition, the
computational model is publicly available, and our methodology and results can be verified. Therefore we believe that a model-generated artifact is unlikely to be responsible for our results. Our ability to explain our findings using established physiological theory lends them credibility and suggests that they are not artifactual. Indeed, our findings are in general agreement with those of Petrini and colleagues who used a simple mathematical model and anaesthetized dogs to examine this issue.

Confirmation of these findings in human subjects would enhance their credibility. Such an investigation could comprise Bohr–Fowler measurement of VDalv while maintaining tidal volume and adding equipment deadspace. However, VDalv in human subjects varies over time, and the addition of equipment deadspace may itself alter airway flow and consequently VDalv. Thus significant data noise would inevitably be introduced. This temporal heterogeneity and physiological sensitivity typifies the problems of conducting such investigations in vivo. Conversely, modelling investigations allow isolated variation of the variable of interest, greatly reducing data noise. In addition, such an in vivo investigation would require mechanically ventilated subjects to ensure constant tidal volume, and ethical considerations would be likely to prohibit such a study.

Recent work has demonstrated that nitric oxide reduces measured VDalv in ventilated critically ill patients. Nitric oxide probably has its predominant effect on the alveoli, but one cannot exclude effects upon VDanat caused by changes in airway pressure. This variation in VDanat could significantly influence measured VDalv. It is clear that if a measurement technique based upon Bohr’s and Fowler’s techniques is used, the parameter measured may not be VDalv but, rather, a mathematical combination of VDanat and VDalv.

Further recent work has suggested that an increase in total deadspace is associated with increased mortality in the critically ill. While this association may represent the contribution of factors that affect deadspace to eventual mortality, it is likely that disturbed VQ matching contributes to mortality. If this is the case, then VDalv may be more strongly associated with mortality than total deadspace. Clearly, this relationship needs to be quantified and we would suggest that examination of VDalv/VTfresh will provide a clearer quantification of the contribution of VQ mismatch than will examination of VDalv.

Appendix

A brief validation exercise was performed to establish the validity of the model’s behaviour with respect to published theories on the behaviour of deadspace. The model was configured with the large VQ defect described above, VDanat was set to 60 ml and VDalv was measured. Tidal volume was then increased to 750 and 1000 ml and VDanat and VDalv were remeasured. Model-derived data were compared with the findings of Nunn and Hill, who examined various deadspace volumes in anaesthetized humans in 1960. These authors did not alter tidal volume within individuals, but gathered data from numerous subjects, inferring the relationship between tidal volume and VDphys, VDalv and VDanat.

The results of this exercise are presented in Figure A1. Elements of the model’s behaviour can be compared with that described by Nunn and Hill.

1. VDanat is relatively unaffected by tidal volume.
2. VDalv increases linearly with tidal volume, and the gradient of this increase is similar to that found by Nunn and Hill. The upward displacement of the model-derived data from the clinical data represents the larger VQ defect used in this validation exercise.

![Figure A1](image-url)
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