CALCULATION OF DEAD SPACE - RELEVANCE IN CRITICAL CARE

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Dead space

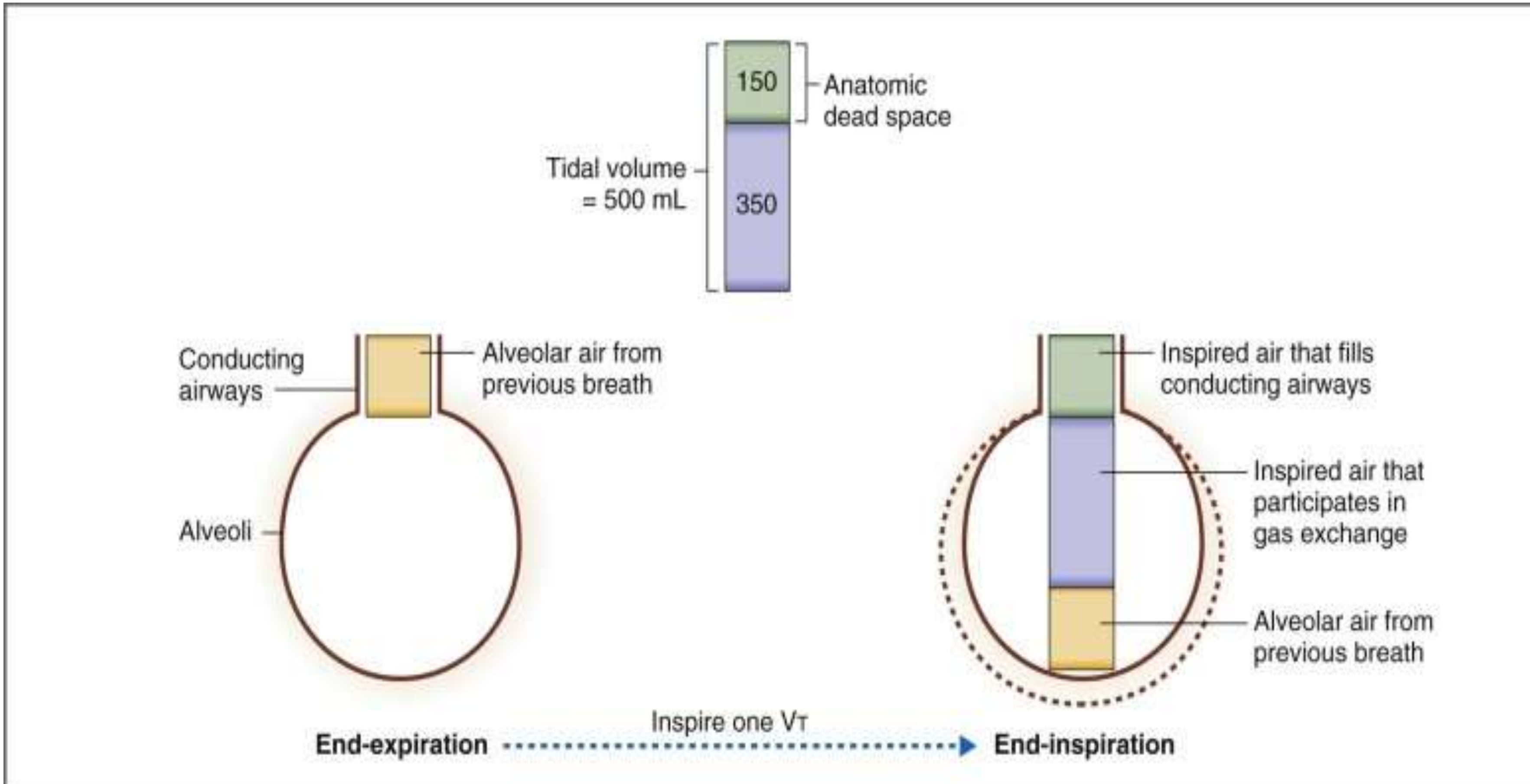
- Dead space calculation
- CO_2 measurement
- Effect of mechanical ventilation
- ARDS
- Recruitment & proning
- Pulmonary embolism
- Weaning

DEAD SPACE CALCULATION

Dead space

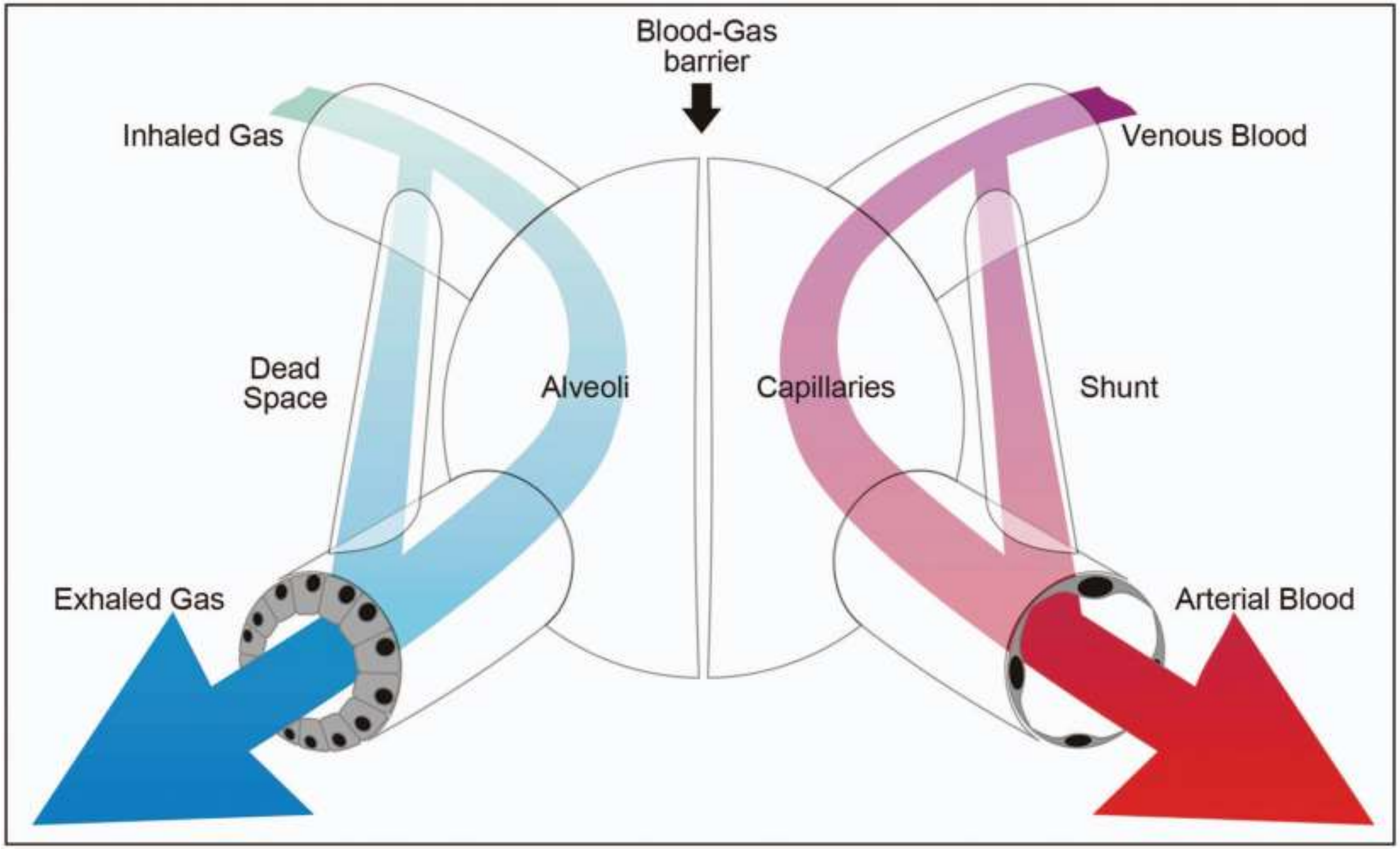
- Volume of the airways and lungs that does not participate in gas exchange
- <u>Anatomical dead space</u>
  - Volume of conducting airways
  - Upper airways, larynx, trachea, bronchi and bronchioles
  - Does not include respiratory bronchioles and alveoli
- <u>Physiologic dead space (VDphys)</u>
  - Total volume of the lungs that does not participate in gas exchange
  - Includes *anatomic* dead space plus a *functional* dead space in the alveoli

Dead space



150
Anatomic dead space
Tidal volume = 500 mL
350
Conducting airways
Alveolar air from previous breath
Alveoli
Inspired air that fills conducting airways
Inspired air that participates in gas exchange
Alveolar air from previous breath
Inspire one VT
End-expiration
End-inspiration

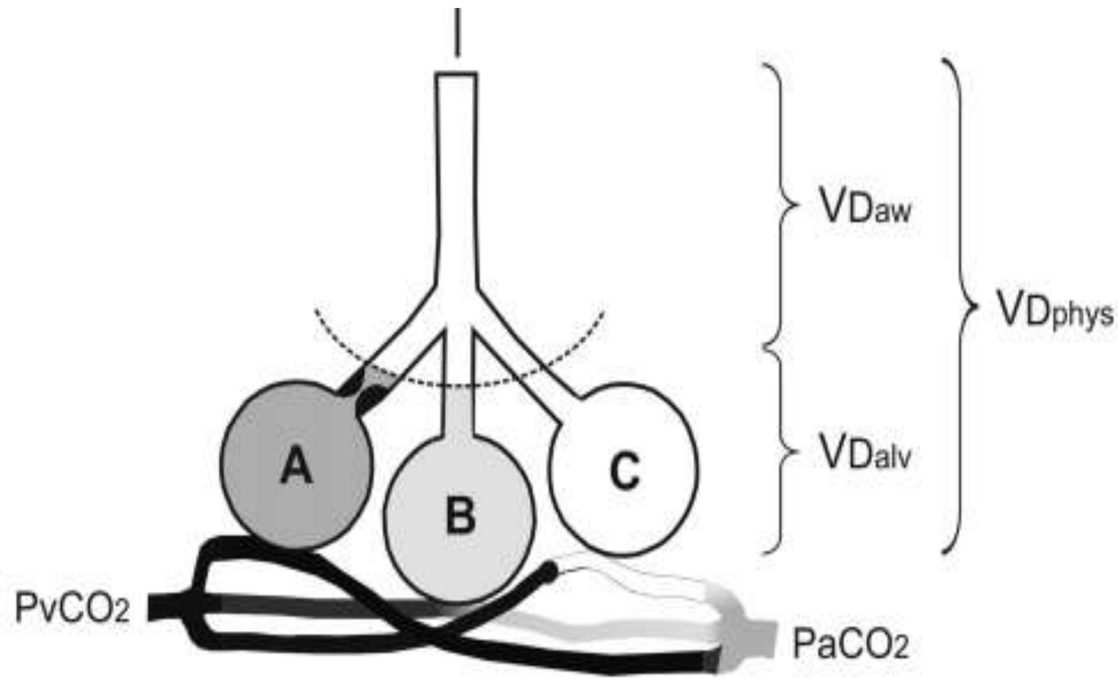
Dead space



Difference b/w expected & actual composition of the effluent media
Basis for calculating dead space and shunt

Dead space

Rileys 3 compartment model



Alveoli groups according to V/Q ratios

A – normal perfusion, no ventilation (shunt V/Q of 0)

B – normal perfusion & ventilation (shunt V/Q of 1)

C – normal ventilation, no perfusion (shunt V/Q of infinity)

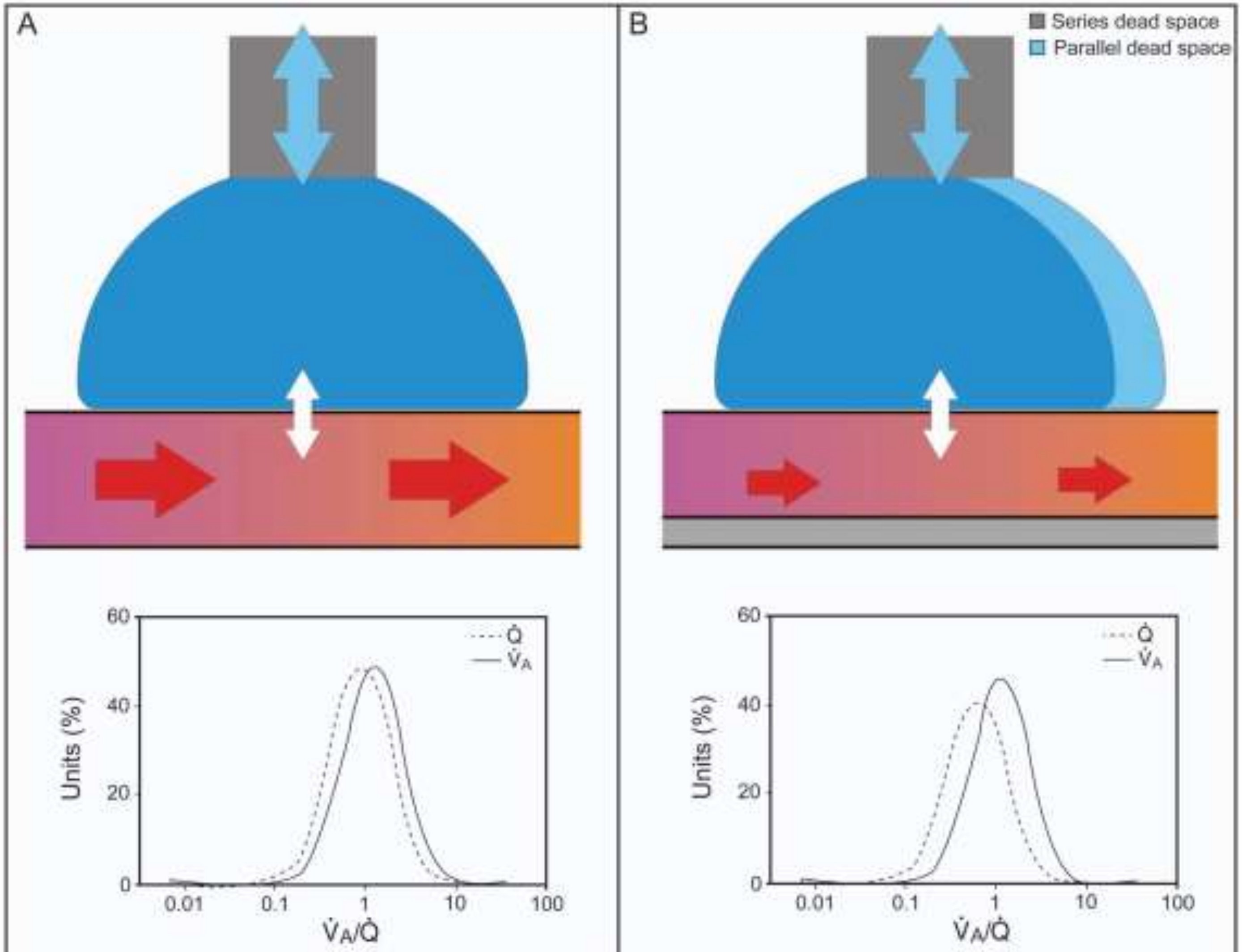
Physiological dead space (VD phys)

Airway dead space (VD aw)

Alveolar dead space (VD alv)

Riley RL et al, J App Physiol 1949

Dead space


A
B
Series dead space
Parallel dead space
60
40
20
0
Units (%)
0.01
0.1
1
10
100
$\dot{Q}$
$\dot{V}_A$
$\dot{V}_A/\dot{Q}$

Bohrs dead space

- Danish physiologist Christian Bohr in 1891
- Mass balance calculation dilution of the expired gas by the inspiratory gas filling the conductive airways

$$V_T = V_A + V_D$$

$$V_T \times F_{ECO_2} = V_A \times F_{ACO_2} + V_D \times F_{DCO_2}$$

$$\boxed{V_D/V_T = (F_{ACO_2} - F_{ECO_2})/F_{ACO_2}}$$

FACO2 -
mean alveolar CO2 concentration sample of gas collected late in exhalation

FECO2
fractional CO2 concentration in the total mixed exhaled breath

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012

Bohrs dead space

- Fractions or partial pressures of CO2 are used interchangeably
- $FACO_2$ is the mean value of CO2 within the alveolar compartment
- $FE\ CO_2$ is calculated using formula

$V_{CO2}/V_T \times (P_b - P_{H2O})$

H.Thomas Robertson, Eur Respir J 2015;45
Tusman G et al, Anesth Analg 2012

Bohrs dead space

- Direct measurement of $PACO_2$ has not been validated until volume capnography
- $PACO_2$ was replaced by its surrogate parameter end-tidal CO2 ($PET\ CO_2$) assuming both are same
- $PACO_2 = FACO_2 = PET\ CO_2$

- $VD/VT = (PET\ CO_2 - PE\ CO_2)/\ PET\ CO_2$

H.Thomas Robertson, Eur Respir J 2015; 45

Bohrs dead space

- $PACO_2$ / PET CO_2 used in Bohrs equation is determined by many factors
  - non-uniform V/Q distributions
  - diffusion coefficients
  - tidal fluctuations in alveolar gas composition
  - alveolar expiratory time constants

H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012

Bohrs dead space

<u>Draw backs</u>

- End tidal CO_2 does not reflect the mean alveolar CO_2 in diseased lungs
- In exercise & hyperventilation the difference increases by more than 4-6 mm Hg
- Usage of ET CO_2 overestimates the true VDphys

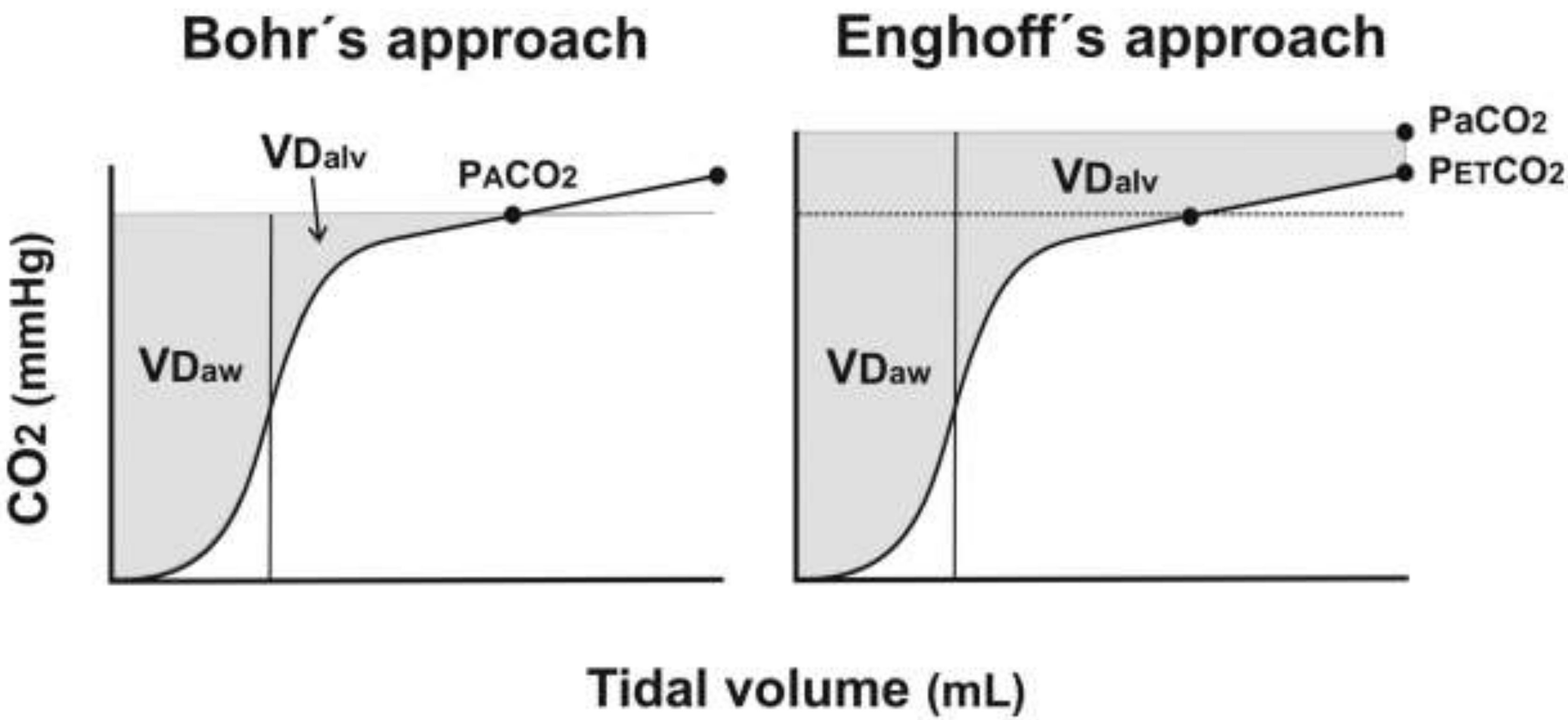
H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012

Enghoffs modification

- Enghoff proposed the substitution of $PaCO_2$ by $PACO_2$ in Bohrs equation in 1938
- Difficulty in identifying mean $PACO_2$ is avoided
- Always be greater than classical Bohrs dead space as $PaCO_2$ is always greater than $PACO_2$
- It is sensitive to range of gas exchange abnormalities

H.Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012

Enghoffs modification



Tusman G et al, Anesth Analg 2012

	Bohrs approach	Enghoffs approach
Formula	VD Bohr $= \frac{(PACO2 – PECO2)}{PACO2}$	VD B-E $= \frac{(PaCO2 - PECO2)}{PaCO2}$
Type of V/Q analysed	V /Q of infinity (units C) High V /Q > 1 but < infinity	V /Q of infinity (units C) High V /Q > 1 but < infinity V /Q of 0 (unit A) Low V /Q < 1 but > 0
Type of measurement	Noninvasive, continuous, breath by breath	Invasive, discontinuous provides information only when arterial blood samples are obtained
Physiological factors influencing parameter	Alveolar overdistension by excessive PEEP or VT pulmonary embolism hypovolemia pulmonary hypotension	Idem Bohr's approach plus all causes of shunt and low V /Q ˙: atelectasis, pneumonia, COPD, asthma

*** ENGHOFFS MODIFICATION REPRESENT GLOBAL INDEX OF V/Q MISMATCH**

Kuwabara's correction of Enghoff equation

$$V_D/V_T = \frac{\left(PvCO_2 - \frac{PvCO_2 - PaCO_2}{1 - Qs/Qt}\right) - PECO_2}{\left(PvCO_2 - \frac{PvCO_2 - PaCO_2}{1 - Qs/Qt}\right)}$$

$PvCO_2$ – partial pressure of CO2 in mixed venous blood
Qs/Qt – right to left shunt

Dead space

- True dead space can only be determined by Bohrs equation
- Bohrs formula cant detect what is happening at the alveolocapillary membrane
- But Enghoffs approach is clinically useful – good global estimate of lung's state of V/Q

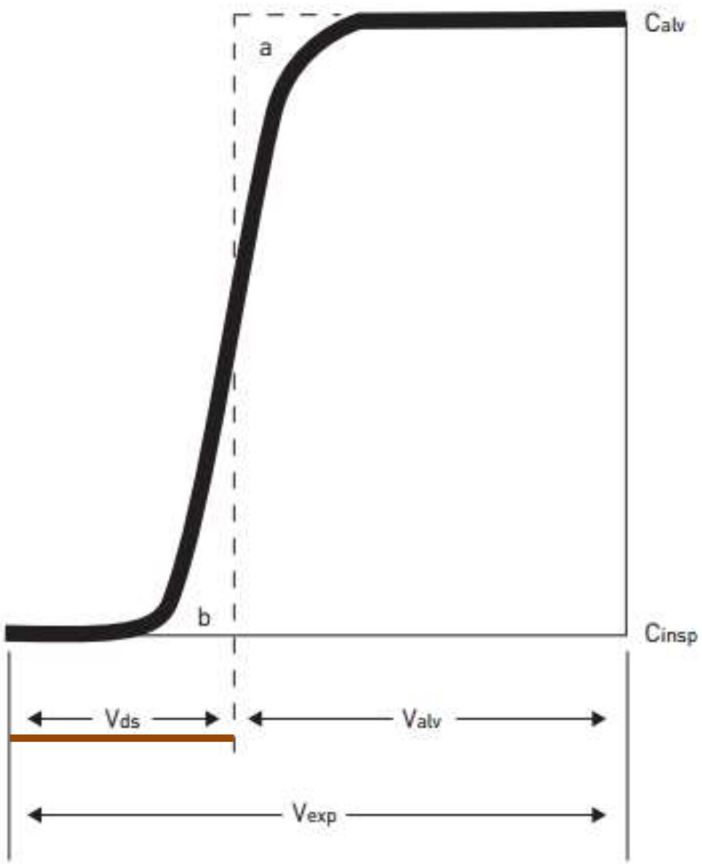
H. Thomas Robertson, Eur Respir J 2015; 45
Tusman G et al, Anesth Analg 2012

Fowlers dead space

- Ward Fowler calculated physiological dead space in late 1940's
- It is now described as anatomical dead space
- Measurements of exhaled N_2 concentrations immediately following the inspiration of a breath of 100% O_2
- Volume of the exhaled air was plotted against the exhaled N_2 concentration

FowlerWS, Am J Physiol 1948

Fowlers dead space



Expired gas concentration vs tidal volume curve

Phase I, contains no N_2
Phase II, progressively ↑ concentration of N_2
Phase III, N_2 concentration in alveolar gas

The vertical dashed line is positioned so that a and b subsume equal areas, and intersection of the dashed line with the exhaled volume axis defines "Vds"

Fowler WS, Am J Physiol 1948

Fowlers dead space

- Anatomical dead space in cubic centimetres roughly equalled a subject's IBW in pounds
- Difference between measurements made at different end-inspiratory lung volumes (avg 100 cm^3 difference in dead space between the largest and smallest starting volumes)
- Measured dead space would decrease if a 20-s breath-hold preceded the exhalation

FowlerWS, Am J Physiol 1948

Fowlers dead space

<u>Draw backs</u>

- Analysis by geometrical methods
- Doubtful results since the junction of the phases II and III is difficult to define in disease, especially during tidal breathing

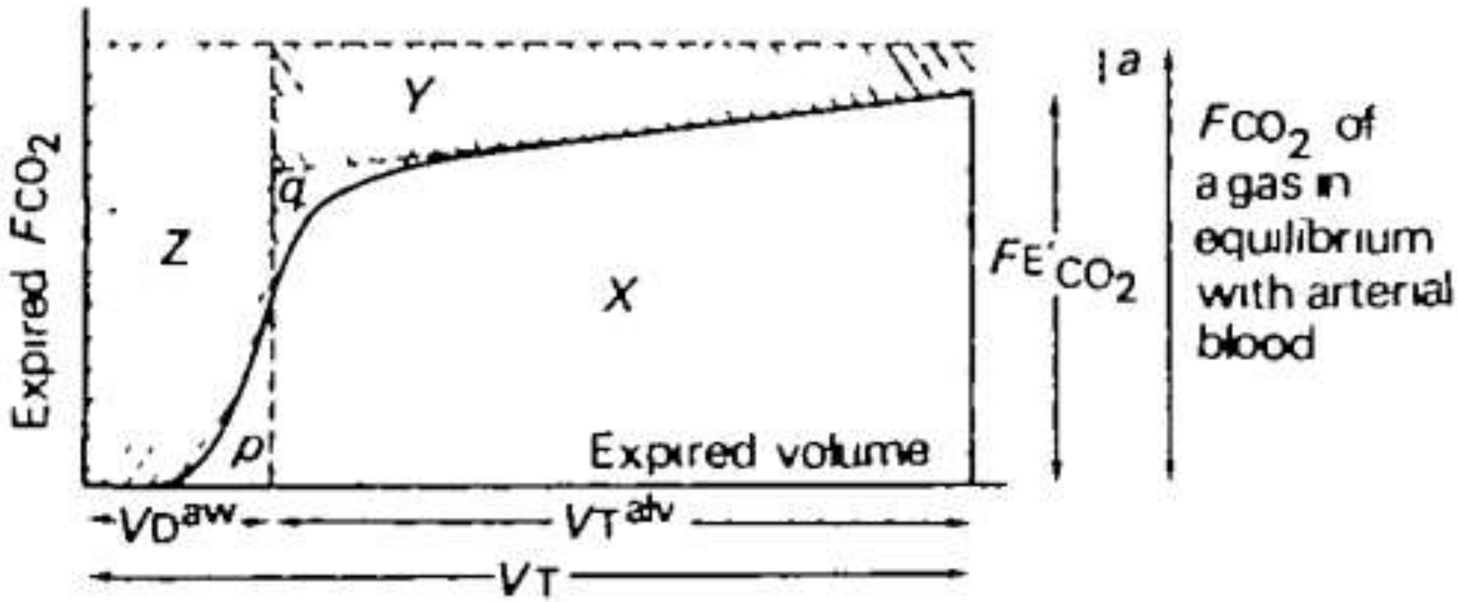
FowlerWS, Am J Physiol 1948

Single breath test CO_2

- CO2 can be substituted for expired N2 and plotted against tidal volume
- In contrast to the use of N2 washout in the it is not necessary to first ventilate with 100 % O2 because the "marker", which in this case is CO2, is already in the alveoli
- Basis for volumetric capnography

Fletcher R et al, Br J Anesth 1981

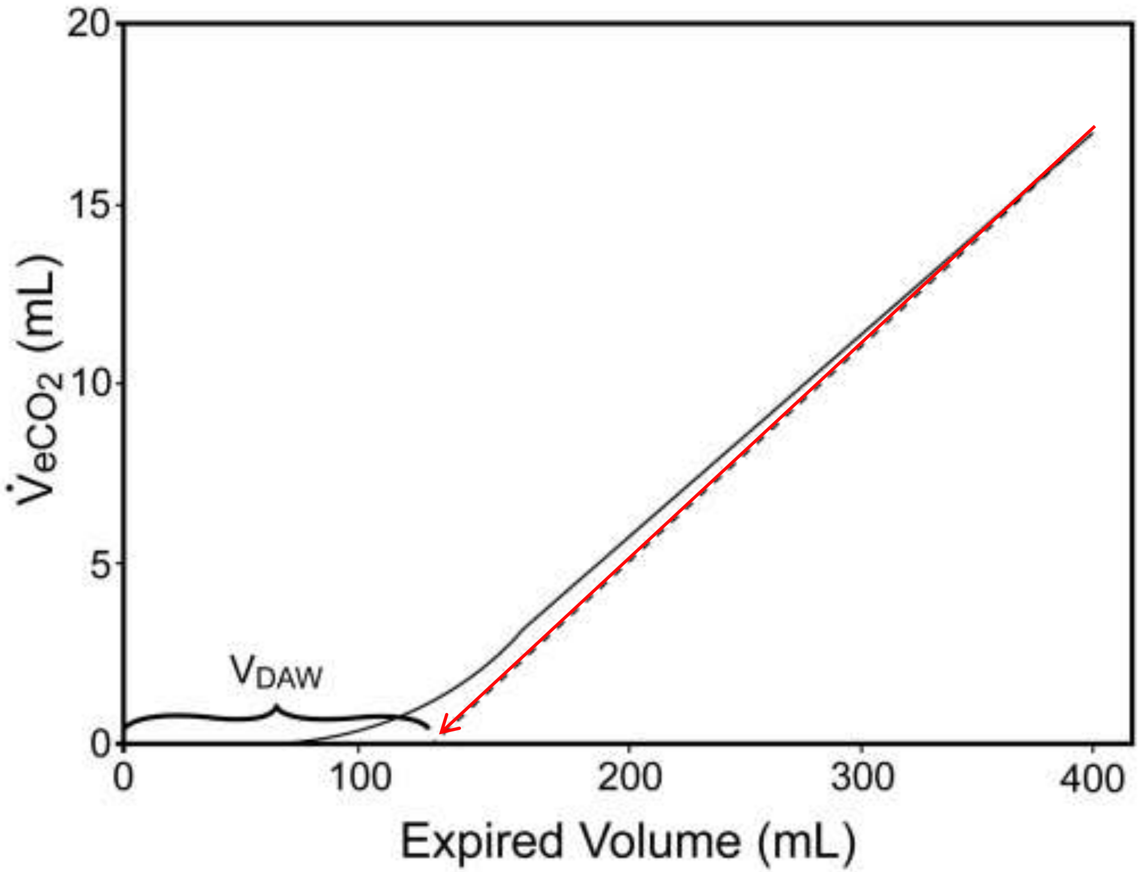
Single breath test CO_2



Fletcher R et al, Br J Anesth 1981

Langleys method

Volume of
CO2 elimination
per breath (ml)



Total expired volume (ml)

Re arranged alveolar equation

- Estimated VD/VT was calculated using re arranged alveolar gas equation for $PaCO_2$
- PaCO2 = 0.863 x VCO2 / VA
- VCO2 = PaCO2 x VA /0.863
- VCO2 = PaCO2 x (VE – VD) /0.863
- VD = 1- [(0.86 x VCO2est) / (VE x PaCO2)]

Re arranged alveolar equation

- VCO2est - estimated production of CO_2 calculated from predicted resting energy expenditure equation (REE)
- VCO2est = (HBpred x hf x 0.8) / 6.8644

- HBpred is gender specific

For females = $655.1 + (6.56 \times Wt_{Kg}) + (1.85 \times Ht_{cm}) - (4.56 \times age)$

For males = $66.45 + (13.75 \times Wt_{Kg}) + (5 \times Ht_{cm}) - (6.76 \times age)$

- hf is hyper metabolic factors (1.13 per °C over 37°C, 1.2 for minor surgery, 1.35 for major trauma and 1.6 for severe infection)

Re arranged alveolar equation

- Rapid bedside estimation
- Uses only routine clinical data
- Shown to be predictor of mortality in ARDS

<u>Draw backs</u>

- No studies comparing it with actual Vd/Vt
- REE by Harris Benedict equation in critically ill not evaluated

Siddiki et al. Critical Care 2010,14:141
Blanch et al. Critical Care 2016, 20 :214

MIGET

- Multiple inert gas élimination technique
- Characterises gas exchange abnormalities
- Quantify the ventilation perfusion inequality, shunt and dead space fractions
- Partial pressures of six intravenously infused inert gases are measured in arterial and mixed venous blood and mixed expired gases
- MIGET software program used for calculation

Peter D Wagner , Intensive Care Med 2008, 34:994–1001

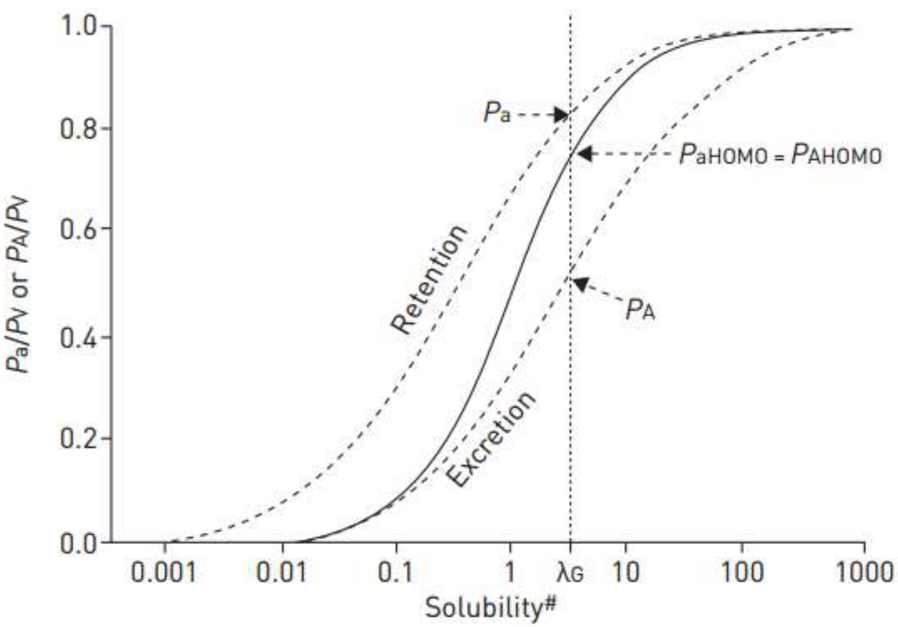
MIGET

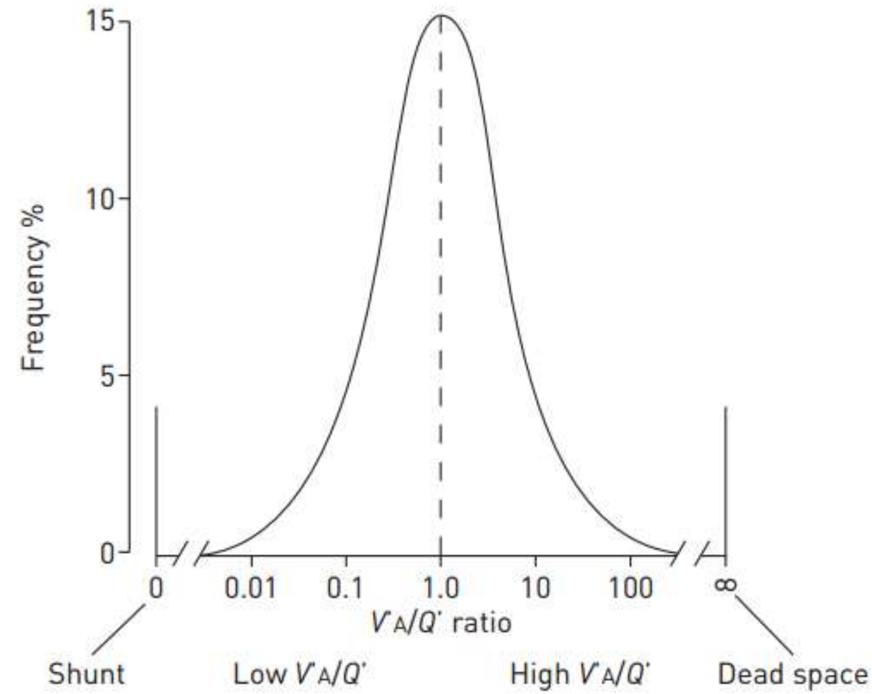
- The fraction of inert gas that is not eliminated is a simple function of the partition coefficient (λ) and the VA/Q ratio
- Retention of inert gas, $R = Pa/Pv = \lambda/[\lambda + VA/Q]$
- Similarly excretion of inert gas is also measured
- VA/ Q distributions are measured either from the excretion or the retention solubility curves

Peter D Wagner , Intensive Care Med 2008, 34:994–1001

MIGET

Retention (and excretion)/solubility curves
and corresponding distributions of ventilation and blood flow





H. Thomas Robertson, Eur Respir J 2015; 45

MIGET

- Research tool rather than a clinical test
  - Operational complexity
  - Not evaluated as a clinical tool
  - Provides more information than we can currently use clinically in patient management and therefore is difficult to justify

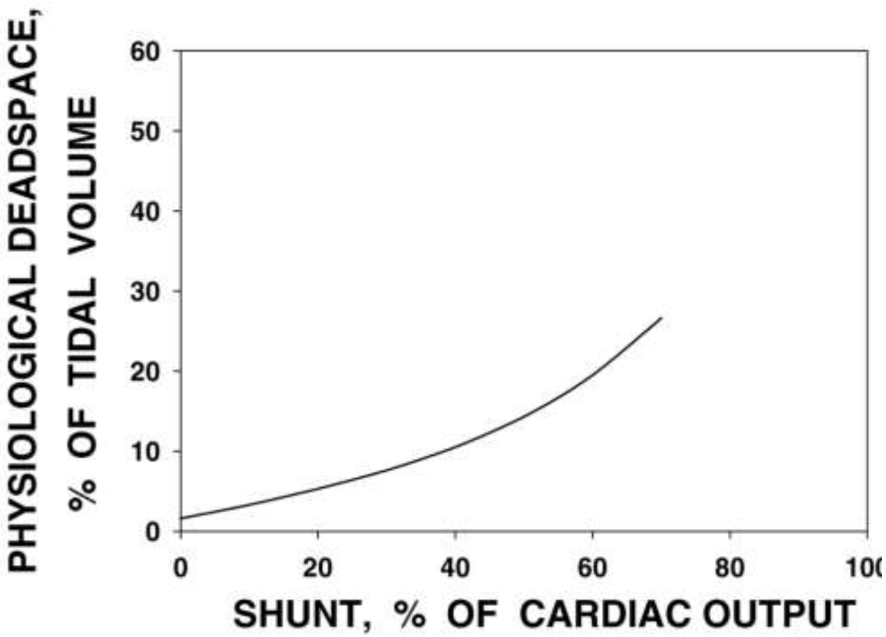
Peter D Wagner , Intensive Care Med 2008, 34:994–1001

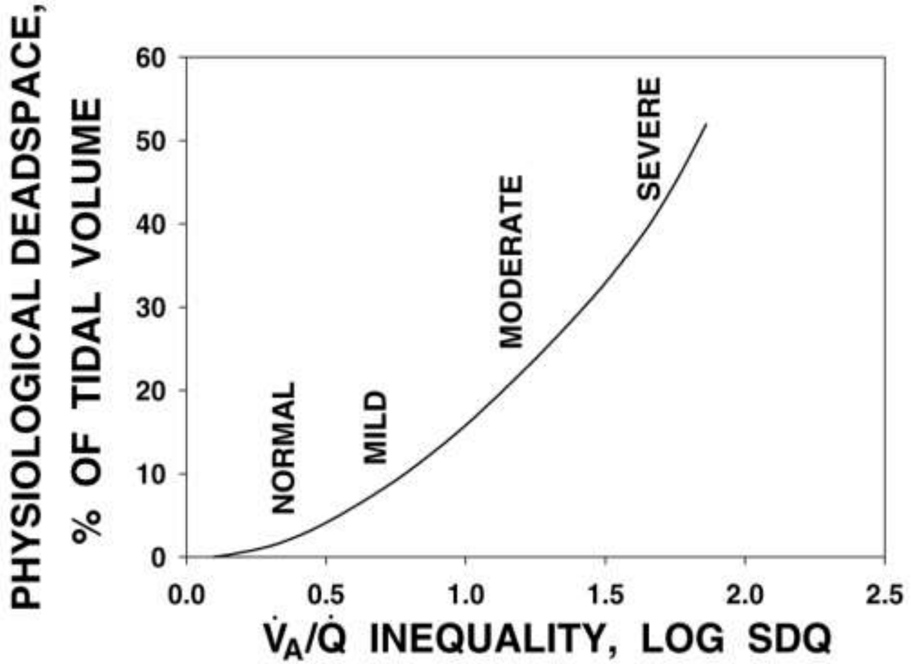
Dead space

- Relationship b/w shunt and physiological dead space is nonlinear
- Effect of shunt on dead space increases as the shunt fraction exceeds 50 %, importance of shunts of < 30% is not great
- Many perturbations commonly seen in ICU influence the effect of shunt on calculated dead space like low cardiac output, metabolic acidosis, anemia and hyperventilation

Niklason L et al, Critical Care 2008, 12:R53

Dead space





V /Q inequality generally is a cause of greater physiological dead space than shunt

PD Wagner, Critical care 2008, 12:48

CO_2 MEASUREMENT

CO2 measurement

- Douglas bag – measures PE CO_2
- Calorimeter method - measures PE CO_2
- Volume capnography – measures both PE CO_2 & PA CO_2

*Bohrs dead space – only by Vcap
Enghoffs dead space – Vcap, Dbag, calorimeter

CO2 measurement

Douglas bag

- Expired air was collected during 2 to 3 minutes into a non permeable rubber bag of 50 to 100 L capacity
- PECO2 was determined using a sample taken from bag
- Time consuming & laborious
- Prone to handling errors

CO2 measurement

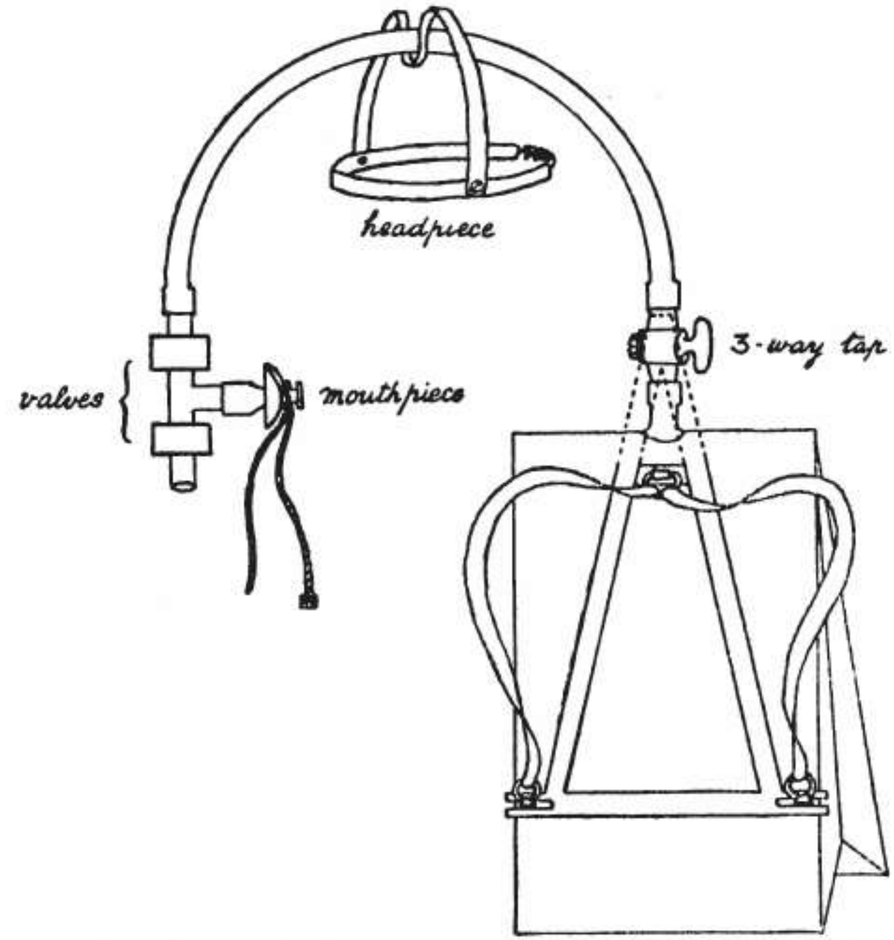


FIG. 17.—Douglas's respiration apparatus. From "Journal of Physiology" (Cambridge University Press).

CO_2 measurement

<u>Metabolic monitor</u>

- Measure pulmonary O_2 uptake and CO_2 production (VO_2 & VCO_2)
- Used for measuring resting energy expenditure and dead space

CO_2 measurement

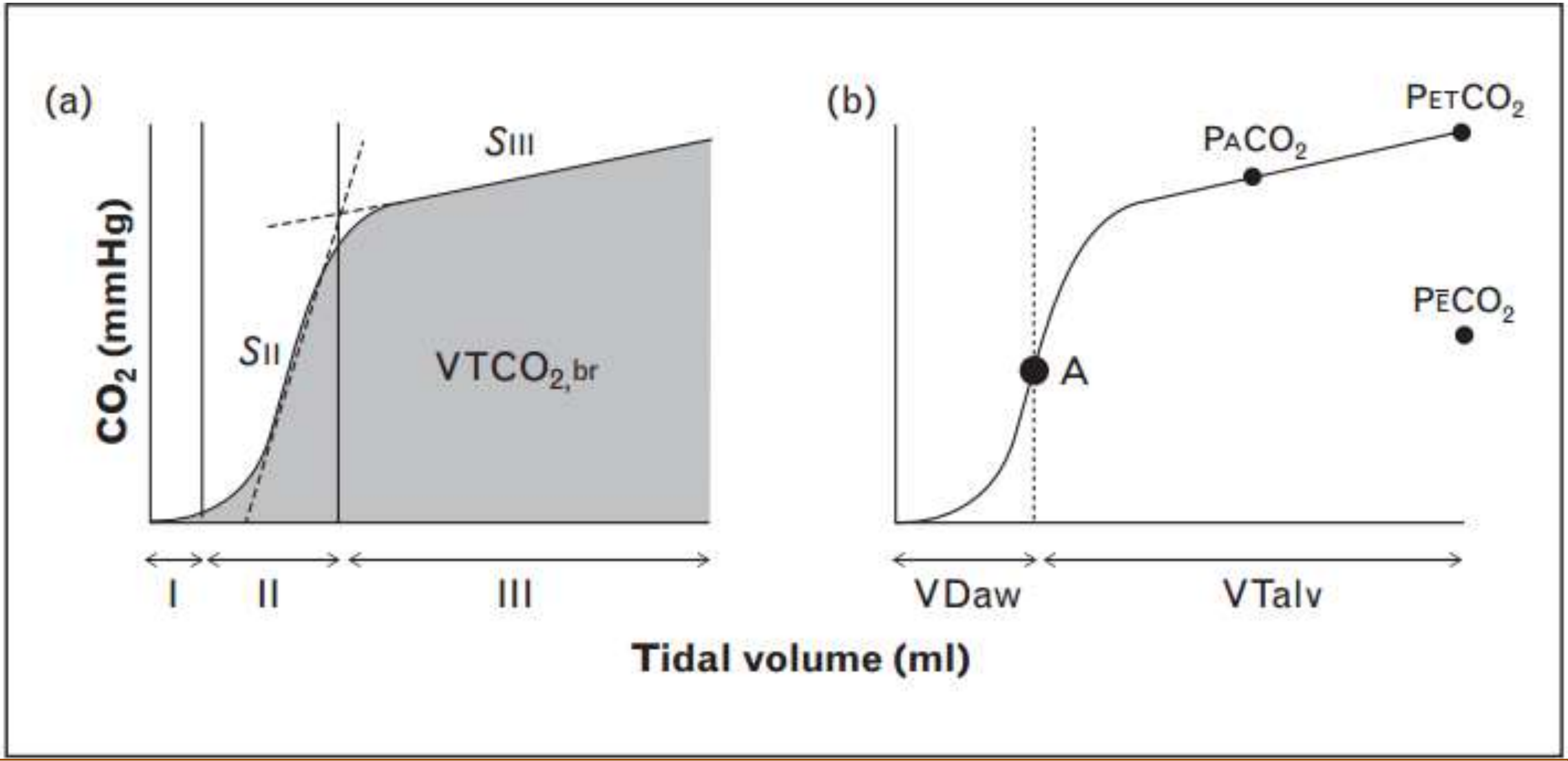
- In both the methods of CO_2 measurement, the expired gas is diluted by the compressed air within the ventilator circuit and bias flow
- Leads to overestimation of true V_D/V_T due to lowering of P_ECO_2
- Requires correction factor based on circuit compliance and peak inspiratory pressure

CO_2 measurement

Volume capnography - Standard now for dead space measurement

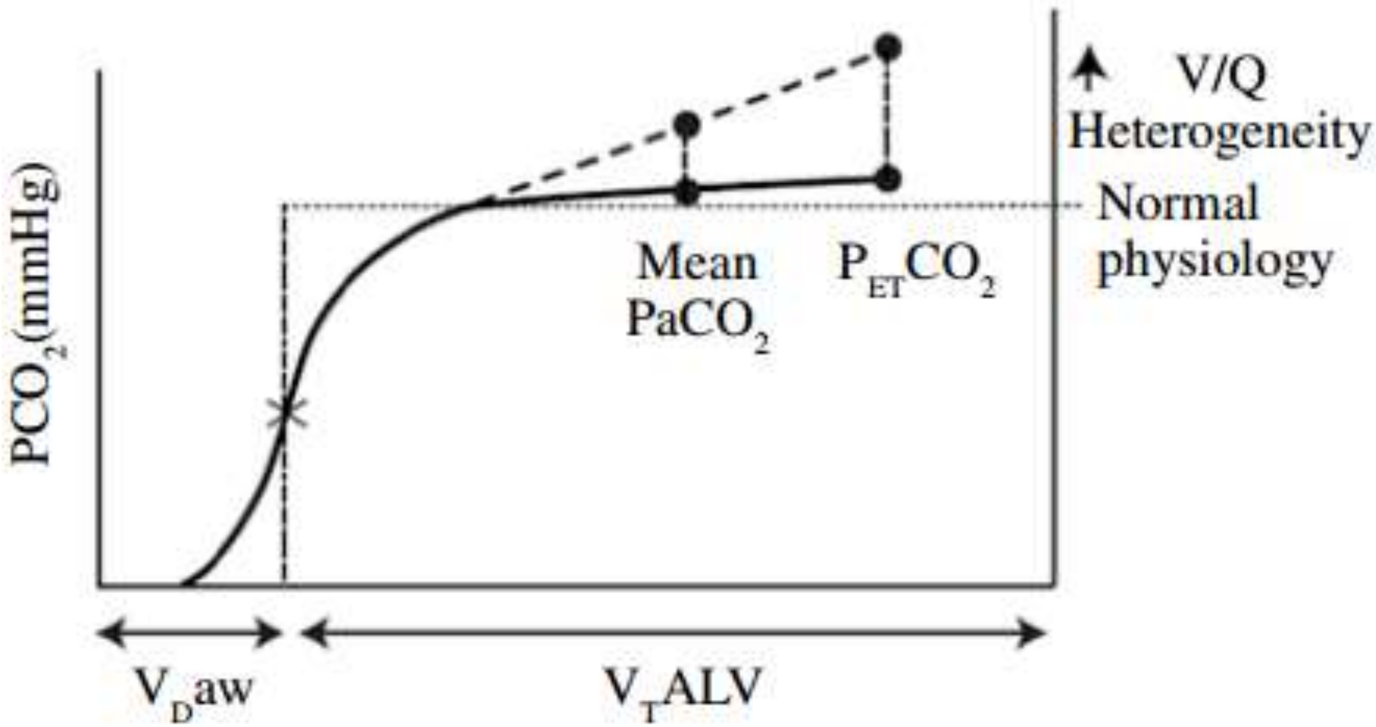
- Fast CO_2 sensors and pneumotachographs
- Measures flow and CO_2 with mainstream or side stream sensors placed at the airway opening
- Vcap determined on a breath to breath basis

CO2 measurement



The slope of Phase III (SIII) - exclusively by gas from the alveolar compartment
Always positive and reflects the different time constants of emptying alveoli and the continuous influx of CO2 from the pulmonary capillaries

CO2 measurement



CO_2 measurement

- $PACO_2$ was the main limitation in calculating true dead space initially
- $PACO_2$ could theoretically be obtained from the midportion of phase III of the Vcap, resulting in reliable measurements of true VDPhys from Vcap
- This concept has been validated against the MIGET studies

CO_2 measurement

- P_ECO_2 and VD/VT measured by calorimeter and Vcap were compared
- 90 readings in 23 ARDS subjects

	Uncorrected Delta trac	**Corrected Delta trac**	**NICO monitor**
P_eCO_2 (mm Hg)	15.7 ± 4.7	18.5 ± 5.7	17.5 ± 5.5
VD/VT	0.64 ± 0.11	0.58 ± 0.14	0.60 ± 0.12

VD/VT measured by volumetric capnography was strongly correlated with uncorrected ($r^2 = 0.93$, $p < 0.0001$) & corrected ($r^2 = 0.89$, $p < 0.0001$) measurements made using the metabolic monitor technique

RH Kallet et al, Resp Care 2015

EFFECT OF MECHANICAL VENTILATION ON DEAD SPACE

Effect of mechanical ventilation

- Numerous pulmonary and extrapulmonary factors affect interpretation of dead space variation at bedside
- Mechanical ventilation makes it more difficult to understand
- Tidal volume, PEEP, inspiratory time, flow pattern all affect the calculation of dead space

Tidal volume

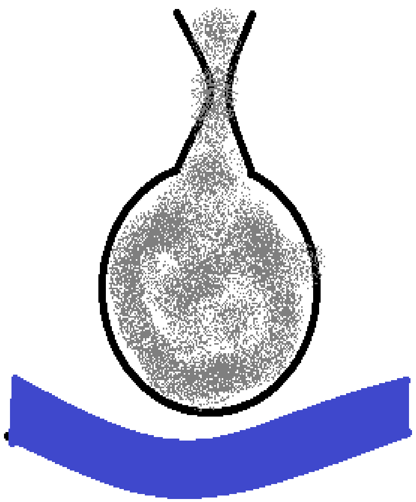
- In normal subjects, increasing tidal volume increases ventilatory efficiency, decrease dead space

- In ARDS, no much change in dead space was observed with increasing VT
  - VT in ARDS may not recruit lung areas effectively
  - recruited diseased alveoli may not contribute to alteration of dead space

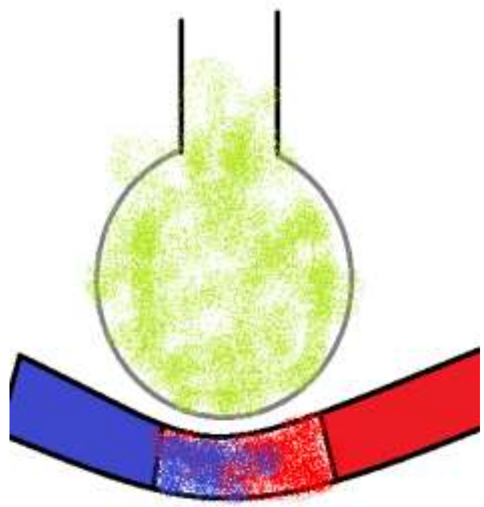
Romero PV et al, Eur Respir J 1997

PEEP

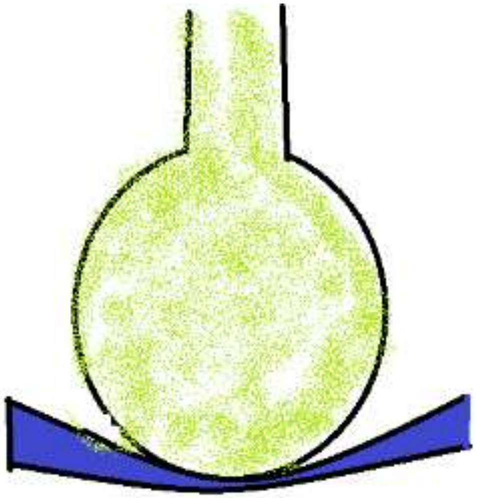
With less PEEP: Collapse aka SHUNT



With optimum PEEP



With high PEEP: over distention aka DEAD SPACE



PEEP

Increasing PEEP

- Recruits the collapsed alveoli
- Increase the airway dead space
- Decrease the cardiac output

Global effect on physiologic VD/VT varies with PEEP & amount of lung injury

Inspiratory time

- Mean Distribution Time -the portion of inspiration available for alveolar gas mixing and diffusion
- Optimal MDT causes a proximal shift in the fresh-gas: respiratory zone interface up to the point of minimal CO_2 diffusion
- Prolonging MDT (either by increasing Ti or EIP) had similar positive effects on $VTCO_2$

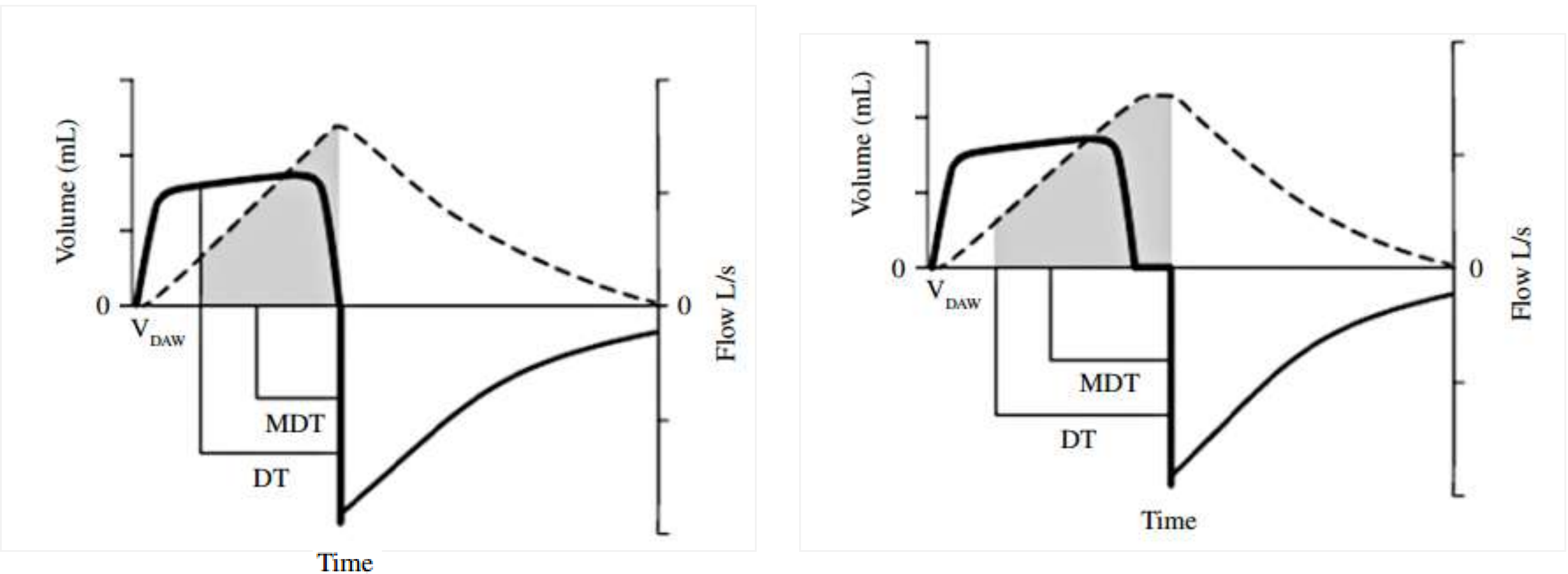
Astrom E et al, Intensive Care Med 2008

Inspiratory flow waveforms

- Square flow form is better than descending ramp
- Impact on CO_2 excretion distinct from MDT; thought to be related to the effects of flow oscillations on diffusion
- Abrupt flow cessation cause high frequency oscillations that may resonate down to the respiratory zone and enhance gas mixing

Astrom E et al, Intensive Care Med 2008

End inspiratory pause



Increase in EIP from 0 to 30 % resulted in increased MDT from 0.2 to 0.8s

Significant increase in $PACO_2$ and $VTCO_2$

Aboab J et al, Clin Physiol Funct Imaging 2007;27:2-6

Inspiratory pattern

- Inspiratory pattern with long MDT and end inspiratory flow (abrupt cessation)
- Optimal inspiratory pattern minimises the dead space ventilation with enhanced CO2 elimination
- Results in reduction of tidal volume – facilitating lung protective ventilation

"Short insufflation followed by a long post inspiratory pause"

Aboab J et al, Crit Care. 2012; 16(2): R39

DEAD SPACE ARDS

Dead space ARDS

- Vascular lesions include thrombotic, fibroproliferative, and obliterative changes leading to pulmonary vascular destruction
- Pulmonary hypertension due to hypoxic vasoconstriction, vascular compression & parenchymal destruction
- Alveolar filling leading to increased venous admixture and shunt

Pierrakos et al, J Clin Med Res. 2012 Feb; 4(1): 7–16

Dead space ARDS

- Responsible for CO_2 retention in severe ARDS
- Increase in minute ventilation requirement
- Lung regions with low V/Q usually coexist with high V/Q regions
- Correlate with severity of ARDS

Pierrakos et al, J Clin Med Res. 2012 Feb; 4(1): 7–16

Dead space ARDS

- Gas exchange in ARDS by MIGET studies
- Shunt
- Low V/Q regions
- Increased overall V/Q heterogeneity
- Isolated high V/Q regions are infrequent despite severe elevations in physiologic Vd/Vt

Main contribution - raised VDphys

H. Thomas Robertson, Eur Respir J 2015; 45

Dead space ARDS

Over all dead space fraction was 0.58 ± 0.10

179 subjects of ARDS	Survived (n=104)	Died (n=75)	*P*
PaO2 : FiO2	163 ± 63	123 ± 51	<0.001
Quasistatic respiratory compliance (ml/cm H2O)	33.6 ± 12.0	27.2 ± 8.5	<0.001
Lung-injury score	2.2 ± 0.6	2.6 ± 0.6	<0.001
Dead-space fraction	0.54 ± 0.09	0.63 ± 0.09	<0.001
Absolute dead space — ml/kg	6.0 ± 1.3	7.2 ± 1.3	<0.001

**** Dead space was calculated 10.9 hrs after insult using Enghoff modification of the Bohr equation, Metabolic monitor method of CO2 measurement***

TJ Nuckton et al, NEJM 2002; 346 : 1281-6

Dead space ARDS

	Odds ratio	**95% CI**	***P***
Dead-space fraction (per increase of 0.05)	1.45	1.15 – 1.83	0.002
SAPS II (per 1-point increase)	1.06	1.03 – 1.08	<0.001
Static compliance (per↓ of 1 ml/cm of H2O)	1.06	1.01 – 1.10	0.01

***Variables independently associated with risk of death**

TJ Nuckton et al, NEJM 2002; 346 : 1281-6

Dead space ARDS

- 80 patients of ARDS
- Vd/Vt in early (within 3 days) and intermediate phase of ARDS (8 – 10 days)
- $PECO_2$ measured by Douglas bag method for 5 min

Dead-space fraction	Survived	Died	*P*
Early phase (n 45 vs 35)	0.53 ± 0.11	0.64 ± 0.09	<0.001
Intermediate phase (n 31 vs 18)	0.50 ± 0.10	0.62 ± 0.09	<0.001

Raurich et al, Respir care 2010, vol 55 :3

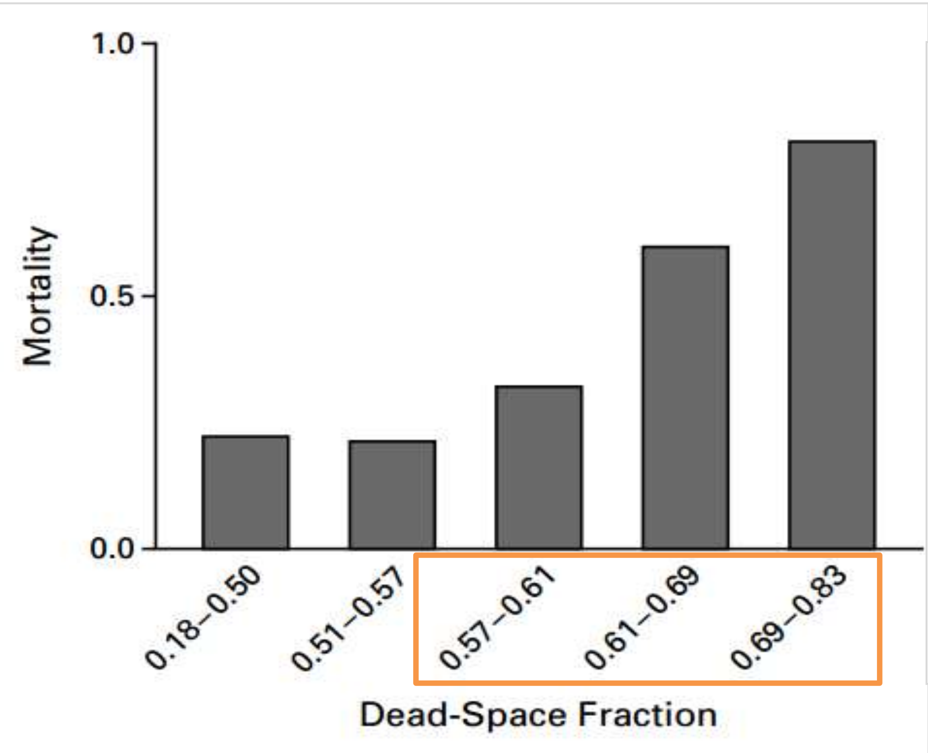
Dead space ARDS

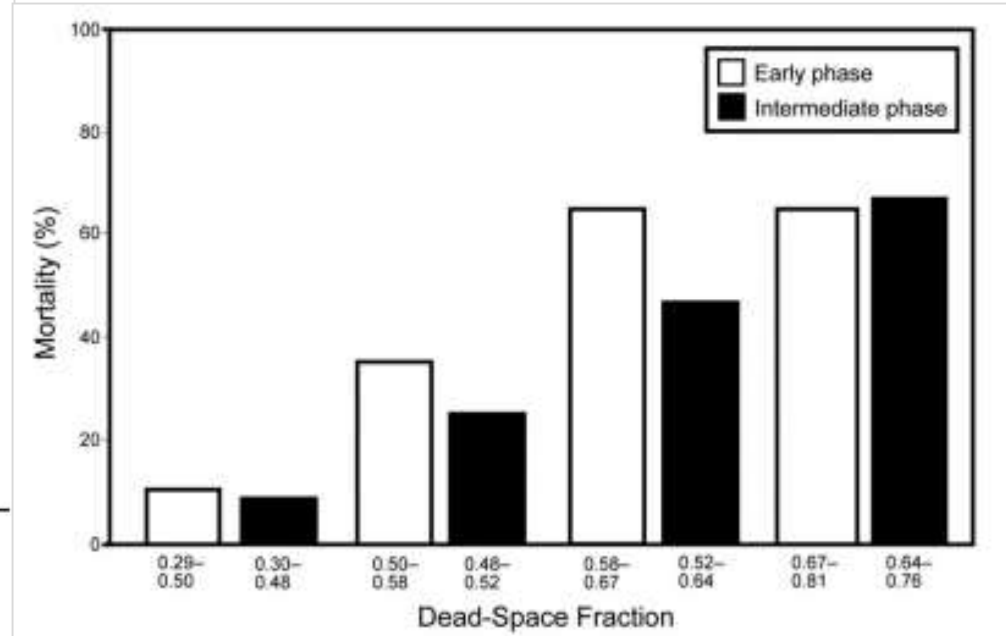
Dead-space fraction (per increase of 0.05)	**Odds ratio**	**95% CI**	***P***
Early phase	1.59	1.18 – 2.16	0.003
Intermediate phase	2.87	1.36 – 6.04	0.005

- Dead-space fraction of ≥ 0.60 is associated with more severe lung injury
- Sustained dead-space elevation is characteristic in non-survivors

Raurich et al, Respir care 2010, vol 55 :3

Dead space ARDS





TJ Nuckton et al, NEJM 2002; 346 : 1281-6
Raurich et al, Respir care 2010, vol 55 :3

Dead space ARDS

Study	Population	Method	Survived vs dead
Cepkova et al, CHEST 2007	Prospective 42 ALI patients	Enghoffs equation Volume capnography Early phase of ALI	0.53 ± 0.10 (n=15) Vs 0.61 ± 0.09 (n=27) $p = 0.02$
Kallet et al, Respir Care 2004	Prospective 59 ARDS patients	Enghoffs equation Metabolic monitor Day 1, 2, 3 & 6	**D1** 0.54 ± 0.08 vs 0.61 ± 0.09 ($p < 0.05$) **D2** 0.53 ± 0.09 vs 0.63 ± 0.09 **D3** 0.53 ± 0.09 vs 0.64 ± 0.09 **D6** 0.51 ± 0.08 vs 0.66 ± 0.09 ($p < 0.001$)

Dead space ARDS

- 109 pts in Mayo cohort, 1896 pts in ARDS-net cohort
- Estimated Vd/Vt - rearranged alveolar gas equation
- Both day 1 (OR = 1.07, 95% CI 1.03 to 1.13) and day 3 (OR = 1.12, 95% CI 1.06 to 1.18) estimated Vd/Vt predicted hospital mortality for 0.05 change
- Estimated Vd/Vt had weak correlation with PaO2/FiO2 and OI
- Independent predictor of poor prognosis

Siddiki et al. Critical Care 2010,14: 141

Dead space ARDS

- VD/VT in early phase of ARDS is an independently predicts the mortality than oxygenation indices
- Sustained elevation of VD/VT in acute and subacute phases of ARDS was seen in non survivors
- VD/VT of 0.55 during first 6 days of ARDS was a/w significantly higher mortality risk
- It weakly correlates with P/F ratio & Oxygenation Index

DEAD SPACE – PEEP, RECRUITMENT & PRONING

PEEP and recruitment

PEEP

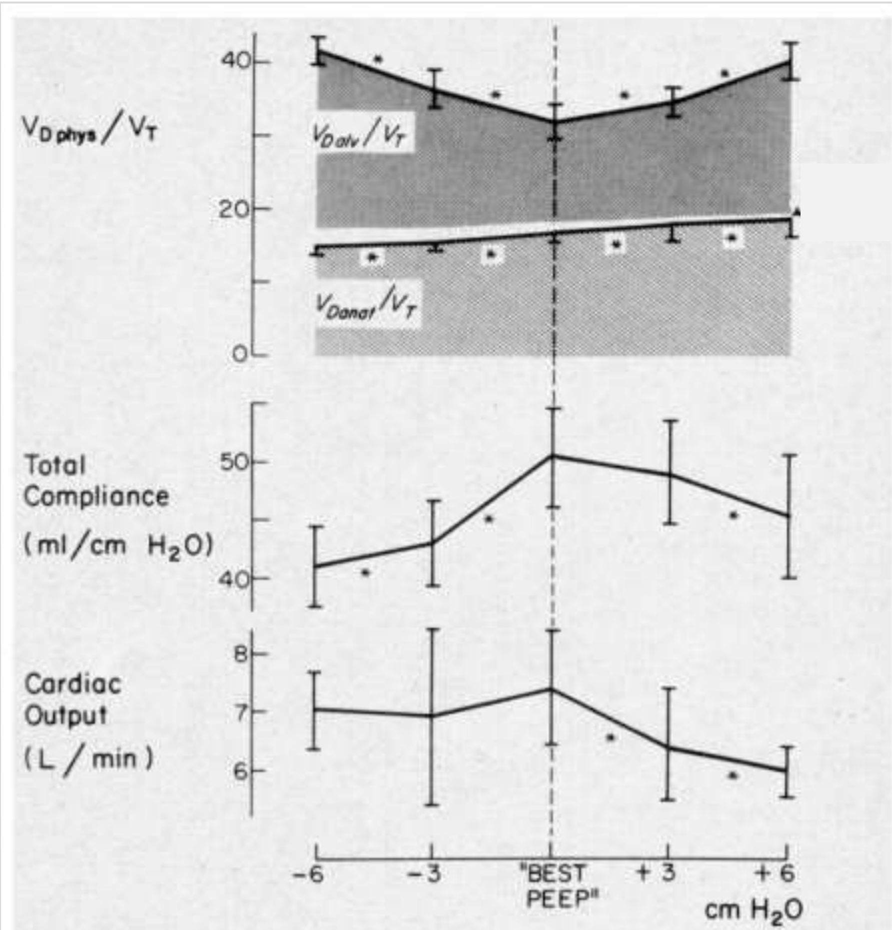
- Recruits atelectatic areas
- Increase FRC
- Increase compliance
- Increase arterial O2 concentration

High PEEP

- Overdistension of alveoli
- Increase in physiological dead space
- Decreased compliance
- Decrease in cardiac output

In ARDS, ideal PEEP titration achieves a balance between maintaining optimal alveolar recruitment and reasonably avoiding lung overdistension

PEEP and recruitment



- Best PEEP- greatest O2 transport

VDalv

- Low levels of PEEP- VDalv decreased due to expansion of atelectatic areas
- Higher levels - VDalv increased due to more alveolar overdistension and under perfusion (raised intraalveolar pressure and decrease in cardiac output)
- Negative correlation with compliance

VDanat

- Increases due to distension of conducting airways

Suter et al, NEJM 1975

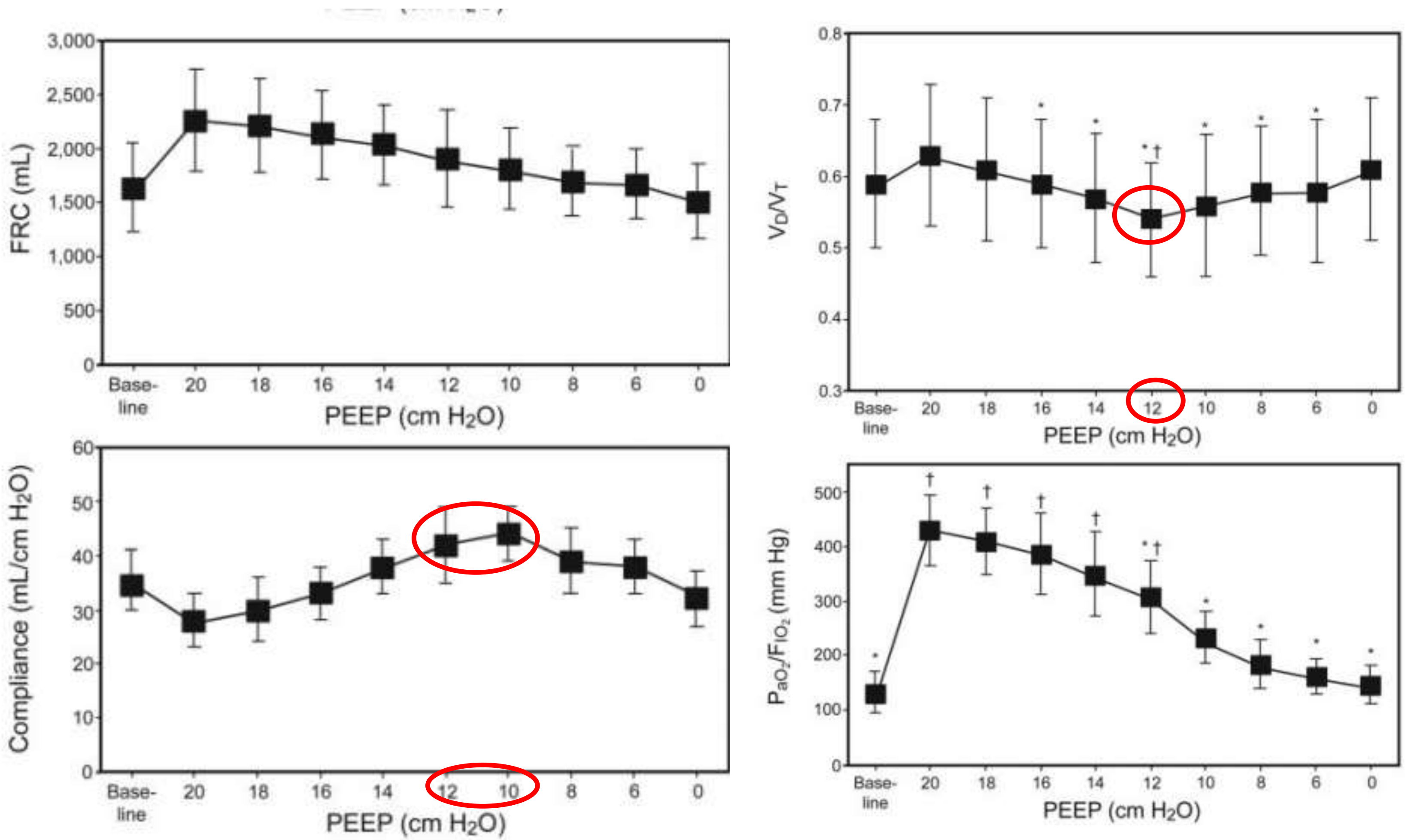
PEEP and recruitment

Stefan Maisch et al, Anesth Analg 2008	
Participants	20 anesthetised patients , normal lungs undergoing maxillofacial surgery
Intervention	PCV mode of ventilation Stepwise increase of PEEP/inspiratory pressures (0/10, 5/15, 10/20, 15/25 cm H2O, each level lasting for 20 min) A recruitment manoeuvre (at 20/45 cm H2O for a maximum of 20 min) was performed, followed by a stepwise pressure reduction in similar way At each level, FRC, compliance, Pao2, and dead space fraction measured
Results	All measured variables had better values after recruitment than before At 10/20 cm H2O, compliance was highest with lower dead space While paO2 and FRC were highest at the maximal pressure 15/25 cm H2O but deterioration of compliance and dead space worsened
Conclusion	FRC and Pao2 were insensitive to alveolar over-distension Compliance and dead space fraction were indicators for efficient ventilation at an optimal PEEP

PEEP and recruitment

Guo Fengmei et al, Respiratory Care 2012	
Participants	23 ARDS patients ventilated in VCV mode
Intervention	Sustained inflation (40 cm H_2O, 30 s) used as a recruitment manoeuvre, followed by decremental PEEP changes from 20 to 6 cm H2O, in steps of 2 cm H2O, and then to 0 cm H2O VD/VT, FRC, compliance and resistance were measured at each level
Results	VD/VT was significantly lower at 12 cm H2O and compliance of the static respiratory system (CRS) was significantly higher at pressure step 12/10 cm H2O Arterial oxygenation values and functional residual capacity were reduced gradually during PEEP, decreasing from 20 cm H2O to 0 cm H2O
Conclusion	Monitoring of VD/VT was useful for detecting lung collapse and for establishing open-lung PEEP after a recruitment manoeuvre

PEEP and recruitment



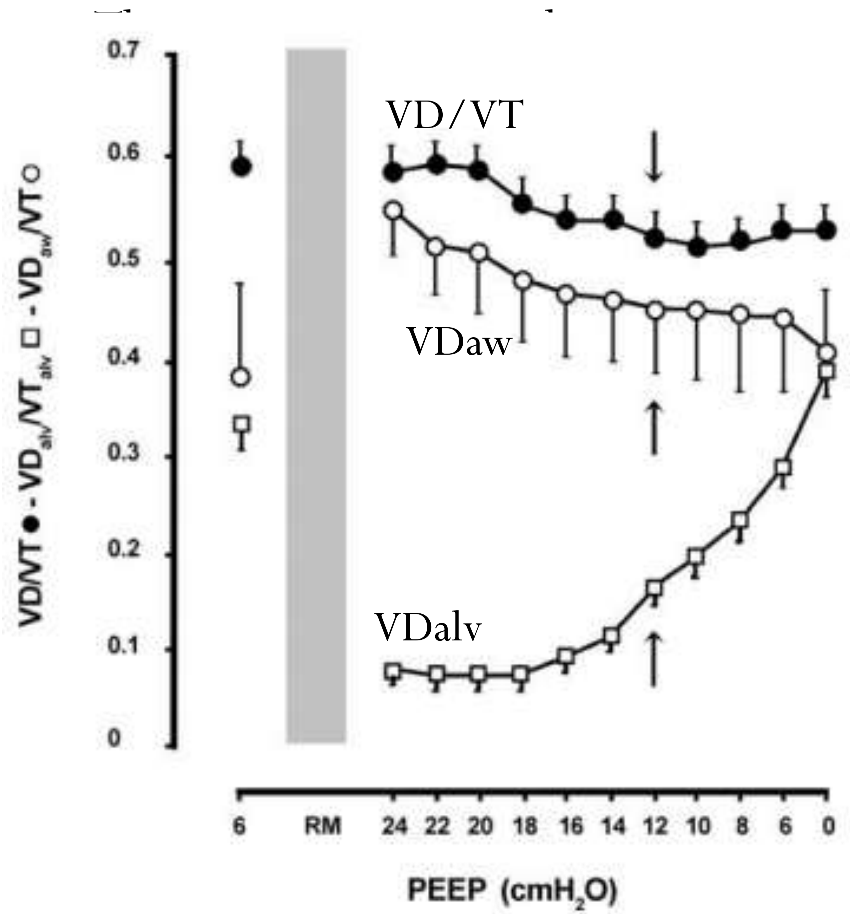
Guo Fengmei et al, Respiratory Care 2012

PEEP and recruitment

- In a decremental PEEP model after lung recruitment in 8 lung lavaged pigs
- Dead space variables during each PEEP level were correlated with CT aeration and oxygenation
- **Vdalv, VDalv / VTalv, and Pa-etCO2** showed a good correlation with PaO2 & normally aerated areas
- Monitoring of dead space was useful for detecting lung collapse and for establishing open-lung PEEP after a recruitment manoeuvre

Tusman et al, Intensive Care Med 2006

PEEP and recruitment



- VD/VT is a more global ratio is "contaminated" by the effect of PEEP on airway dead space
- VDalv/VTalv is not influenced by Vdaw
- Dead space portion of the alveolar gas provides more meaningful information than the classical VD/VT ratio when monitoring of the lung collapse-recruitment phenomena

Tusman et al, Intensive Care Med 2006

PEEP and recruitment

Study	Subjects	Methods	Results	
Boyden L et al, Intensive care Med 2002	10 ALI patients	Stepwise increment of PEEP from zero to 15 cm H_2O Lung mechanics and Vd/ Vt were measured Vcapnography	VDalv does not vary systematically with PEEP in patients with various degrees of ALI Subjects in whom oxygenation improved with PEEP showed a concurrent decrease in VDalv and vice versa VD fractions are independent of compliance	
Blanch L et al, ERJ 1999	8 normal 9 ALI 8 ARDS	Random change of PEEP (0, 5, 10 and 15 mH2O) at 4 levels Physiological measurements were made by volume capnography	VD/VT ALI patients > control patients ARDS patients > ALI patients PEEP had no effect on VD/VT in any group	

PEEP and recruitment

- VD/VT - no relation with PEEP in both the studies
- Few subjects in both the studies
- No recruitment was performed in both
- Different effect of PEEP in patients with various degrees of lung injury (or)
- in positive PEEP responders, the reduction in alveolar dead space compensated
- for the concurrent increase in airway dead space

PEEP and recruitment

- PaO_2 depends on hemodynamic and metabolic state as well, non specific for judging the recruitment
- PaO_2 determination is insensitive to the over-distension of alveoli, verified by reduced compliance and increased dead space fraction
- VD/VT as a marker of V/Q matching appears to be better suited for titrating PEEP than PaO2

PEEP and recruitment

- Recruitment of lung results in better dead space fraction values as compared to pre recruitment
- Vd/Vt monitoring cane be used to detect early lung collapse - derecruitment in decremental PEEP trial
- Can only be used in PEEP responders of ARDS

Response in proning

- Both PaO_2/FiO_2 and $PaCO_2$ improve with prone positioning in ARDS
  - Decreased $PaCO_2$ was inversely related to lung recruitment
  - $PaCO_2$ responders had better survival than PaO_2 responders
- VDalv may be the consequence of non perfused or poorly perfused lung areas in ventilated anterior areas, but also of a slow compartment partially excluded from ventilation

Gattinoni L et al, Critical care Med 2003

Protti et al, Intensive Care Med 2009

Response in proning

- Relevance of dead space measurement in proning in ARDS in 13 patients of severe ARDS (P/F <100)
- Persistent hypoxemia after 48 hr of ventilation
- PCO2, VD/Vt, P/F ratio, Crs were recorded in supine and 3, 6, 9, 12, 15 hrs after proning
- Responders to PP were defined after 15 hrs of PP either by an increase in PaO2/FiO2 ratio > 20 mmHg or by a decrease in PaCO2 > 2 mmHg

Charron et al. Critical Care 2011, 15:R175

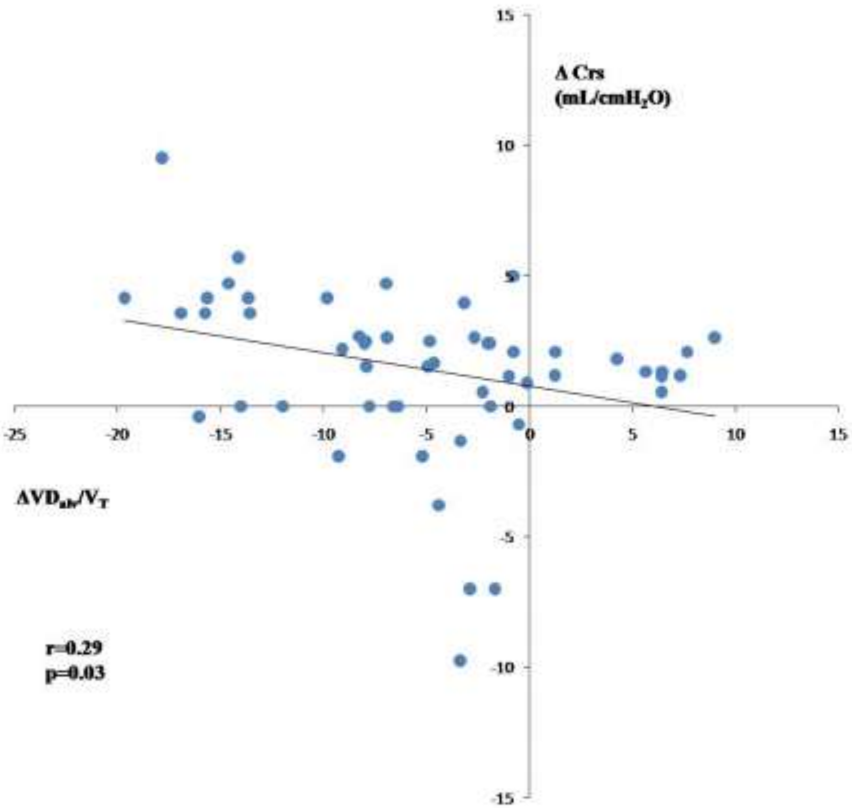
Response in proning

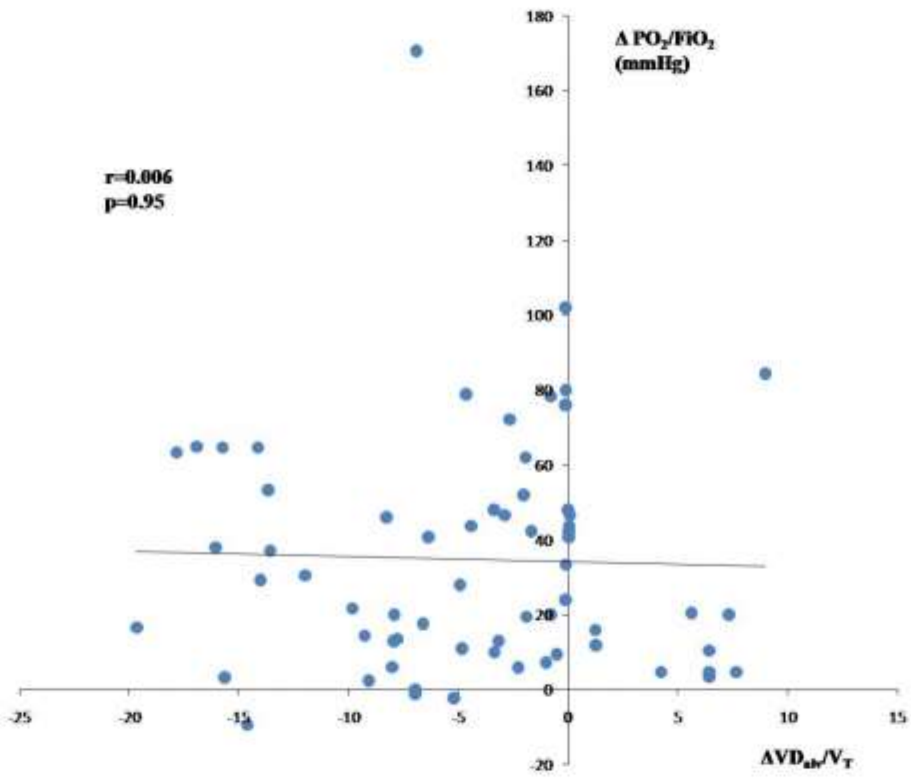
- Maximal improvements in VD/ VT and PaCO2 tended to occur earlier (6 and 9h respectively) compared to maximal improvements in PaO2/FiO2 (15 h)
- PaCO2 responders has greater decrease in VDalv/VT ratio and in Pplat and a greater increase in Crs than P/F responders
- PaCO2 response is better associated with lung recruitability than PaO2

Charron et al. Critical Care 2011, 15:R175

Response in proning

- Changes in dead space correlated with compliance and no correlation was found with oxygenation





Charron et al. Critical Care 2011, 15:R175

Response in proning

- Measuring dead-space may be a particularly expedient method for assessing the effectiveness of prone positioning in ARDS
- Using PaCO2 changes rather than PaO2/FiO2 changes to define the respiratory response to PP appeared more relevant

Charron et al. Critical Care 2011, 15:R175

DEAD SPACE – PULMONARY EMBOLISM

Pulmonary embolism

- Spatial differences in blood flow between respiratory units in the lung cause inefficient gas exchange that is reflected as increased alveolar VD
- The mechanical properties may not be greatly affected, so these alveoli empty in parallel with other respiratory units with similar time constants
- Because ventilation to the affected alveoli continues unabated, PCO_2 in these alveoli decreases
- Exhaled dead space volume dilutes the amount of CO_2 in exhaled breaths relative to PaCO2

Nausherwan K Burki, Am Rev Respir Dis 1986

Pulmonary embolism

- Wide variety of pulmonary disorders in which V_D/V_T is increased - potentially less specific
- $V_D/V_T < 40\%$ makes the diagnosis of PE extremely unlikely
- V_D/V_T value $> 40\%$ in the presence of a normal spirogram is highly suggestive of PE and was comparable with lung perfusion scan

Nausherwan K Burki, Am Rev Respir Dis 1986

Pulmonary embolism

- Combination of D dimer assay and alveolar dead space fraction can be used as screening test for PE

Subjects of suspected PE (n =380)	Results of D dimer and Vdalv/Vt	
PE confirmed (n= 64)	40 both abnormal 20 abnormal D dimer 3 abnormal VDalv/Vt 1 had both normal	Sensitivity 98.4 % (95 % CI 91.6 -100) Specificity 51.6 % (95 % CI 46.1 -57.1)
No PE (n = 316)	26 both abnormal 104 abnormal D dimer 75 abnormal VDalv/Vt 163 both normal	

Kline JA et al; REPE study, JAMA 2001

Pulmonary embolism

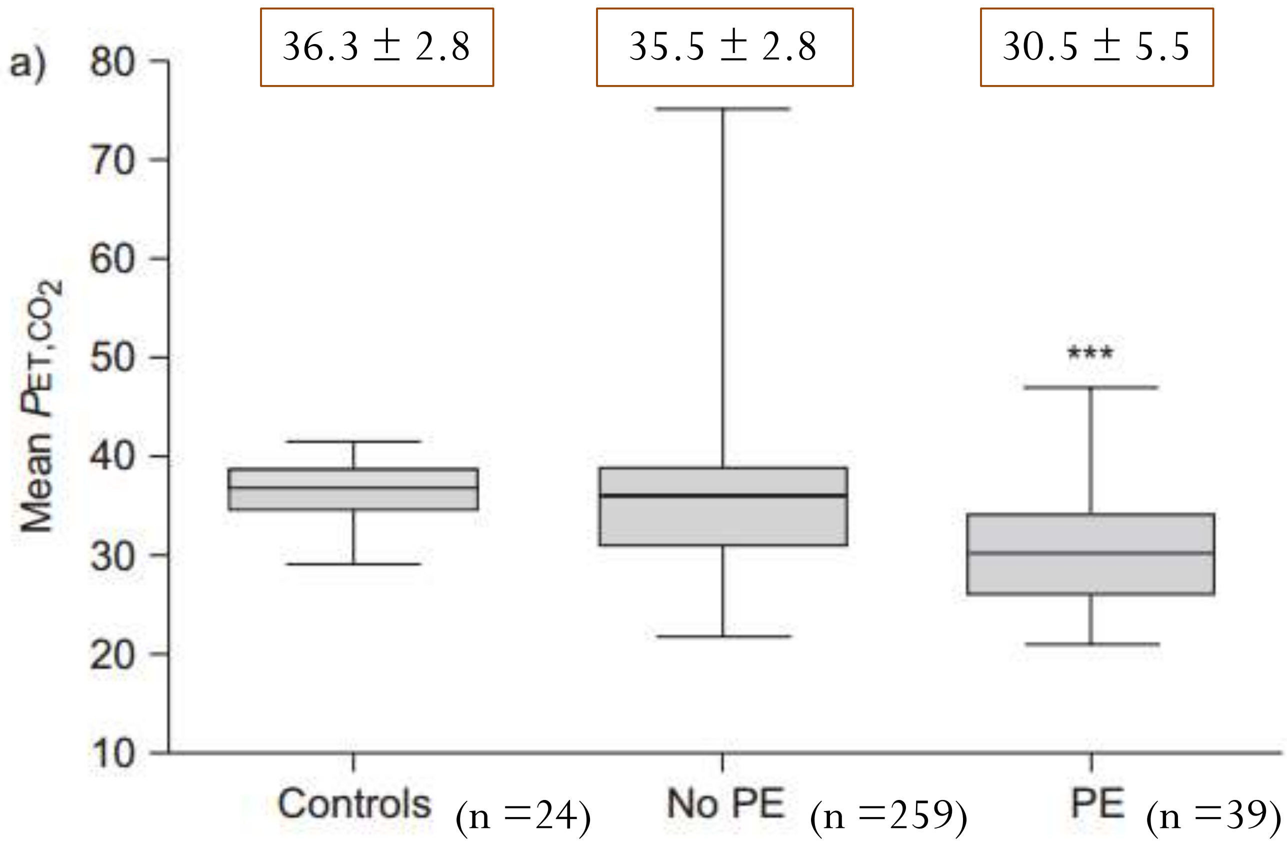
- Subjects with PE who died within a month had significantly higher dead space compared with who survived
- Dead space was significantly greater in subjects with high probability V/Q scan than other V/Q readings

Kline JA et al; REPE study, JAMA 2001

Pulmonary embolism

- End-tidal carbon dioxide tension (PET,CO2) is a physiological surrogate for vascular obstruction from PE and dead space ventilation
- 298 patients who underwent imaging for suspected PE were studied. PET,CO2 was measured within 24 after the imaging

A.R. Hemnes et al, Eur Respir J 2010



A PET CO2 of ≥ 36 mmHg - a negative predictive value of 96.6%, which increased to 97.6% when combined with Wells score < 4

A.R. Hemnes et al, Eur Respir J 2010

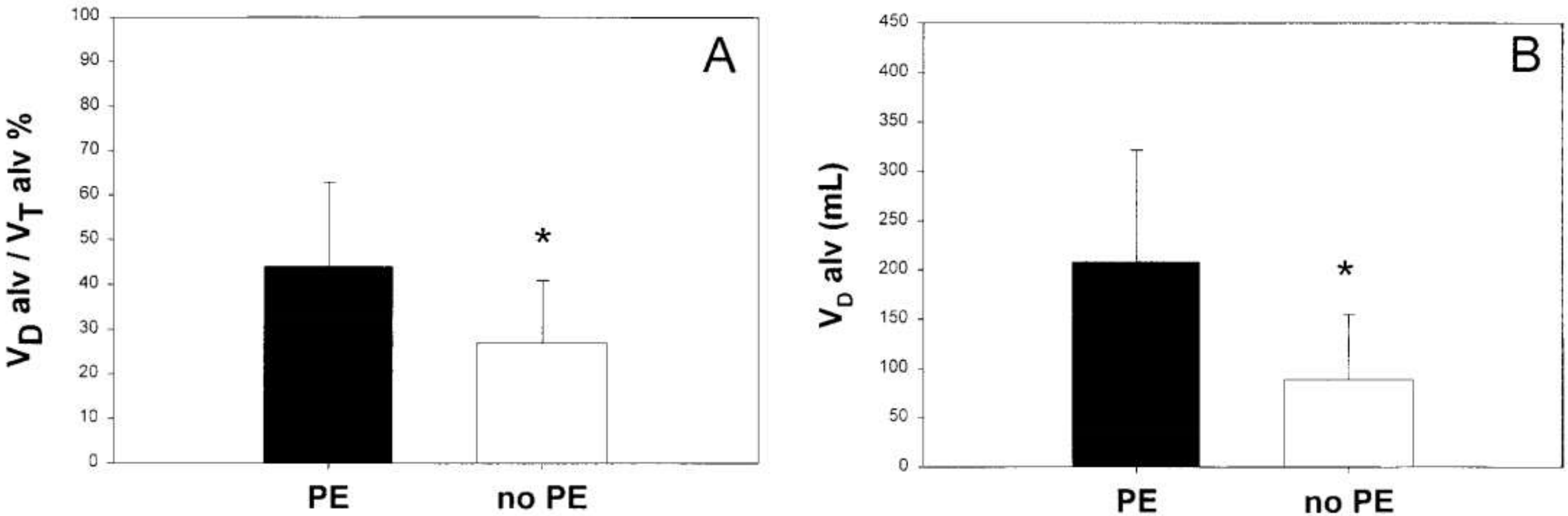
Pulmonary embolism

- Prospective study - 53 subjects of suspected hemodynamically stable PE
- Confirmed in 33 subjects by V/Q scan or CTPA
- Correlation between perfusion defect and VDalv/Vt

	Confirmed PE (n = 33)	**No PE (n = 20)**
Perfusion defect	38 ± 22 %	-
VDalv	208 ± 115 mL	89 ± 66 mL
VDalv/Vt	43 ± 18%	27 ± 14 %
Mean SPAP	44 ± 17 mm Hg	34 ± 10 mm Hg

Kline JA et al, Acad Emerg Med 2000

Pulmonary embolism



Regression of VDalv/VT vs perfusion defect yielded $r^2 = 0.41$
Regression of VDalv/VT vs pulmonary artery pressures yielded $r^2 = 0.59$

* $P < 0.001$

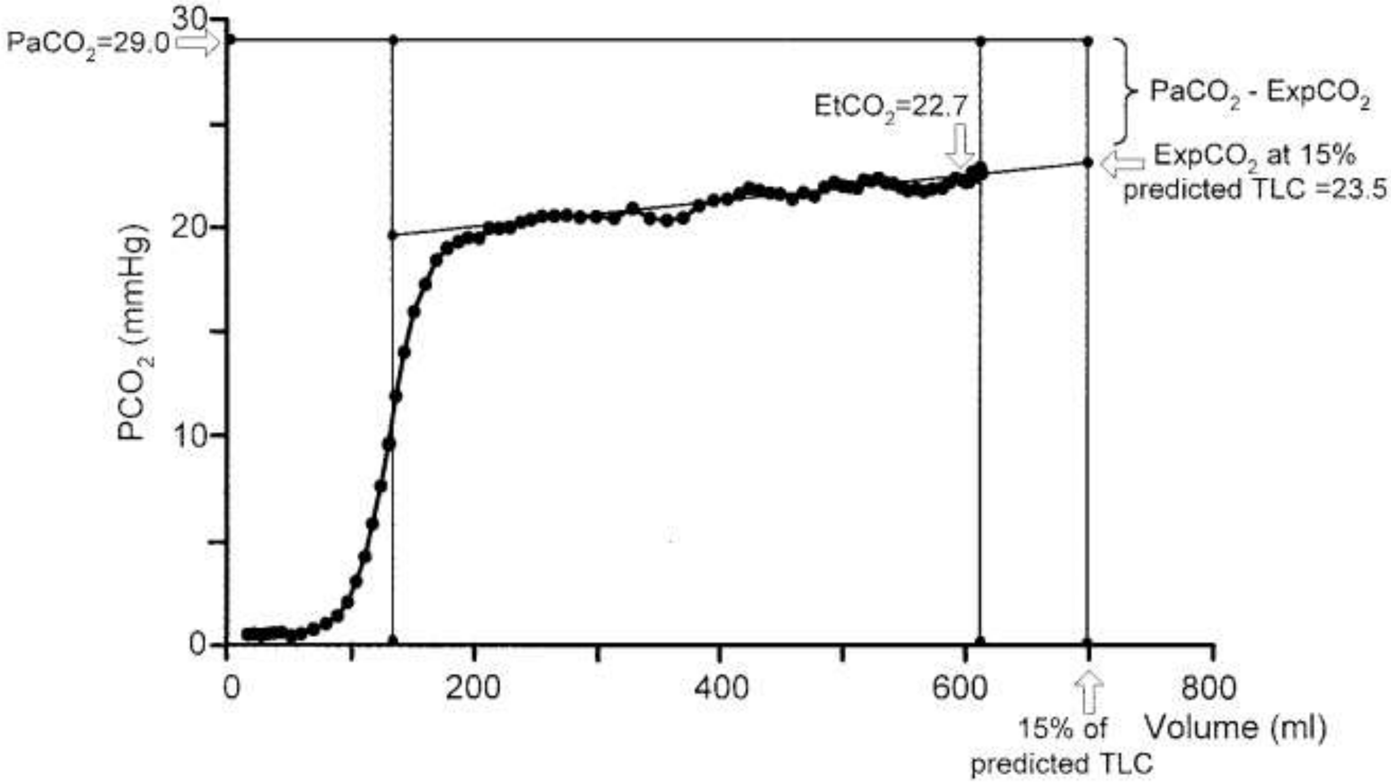
Kline JA et al, Acad Emerg Med 2000

Pulmonary embolism

- 10 subjects had perfusion defect > 50 % and mean VDalv/Vt was > 0.60 in that subgroup
- 7 subjects had VDalv/Vt > 0.60, 3 of them died
- PE increases the VDalv proportionately to the severity of pulmonary vascular obstruction
- Potential for VDalv to quantify the embolic burden of PE

Kline JA et al, Acad Emerg Med 2000

FDlate



Lung embolism causes a difference between arterial and expired CO_2 even at the end of a long expiration (15% of pred TLC) while the normal lung & in airway disease it reaches $PaCO_2$

FDlate cutoff of 12% correlated significantly with the angiographic findings in PE

Erikkson et al, CHEST 1989; 96:357-62

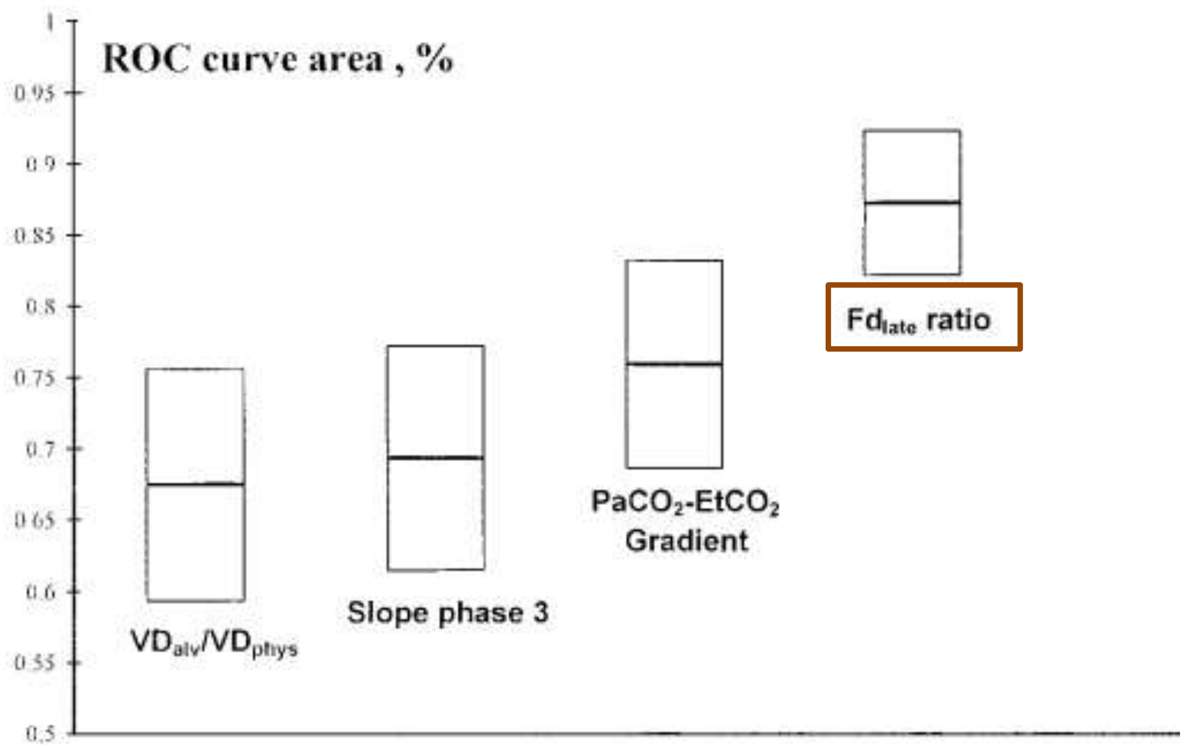
FDlate

- Improves the specificity of the dead space measurement by separating patients with obstructive lung diseases from those with PE, both conditions being frequently associated with an increased Paco2- EtCO2 gradient
- It corrects for falsely positive CO2 gradient due to an incomplete diffusion time in patients with high respiratory rates or low VT values

Erikkson et al, CHEST 1989; 96:357-62

Pulmonary embolism

45 outpatients of suspected PE and high D dimer > 500 ng/ml
18 patients had confirmed PE



Verschuren et al, CHEST 2004; 125:841–850

Pulmonary embolism

- Dead space measurement can be **used to exclude PE** in conjunction with D dimer levels
- Can predict the severity of embolic burden
- FDlate had better diagnostic performance than P(a-ET) CO2 gradient or VD/VT in PE
- **Not sensitive in cases of peripheral PE** or in cases of adaptation of the V /Q ratio mismatches due to pulmonary infarction, atelectasis,or a potential hypocarbic bronchoconstrictive reflex

DEAD SPACE WEANING

Success of extubation

- Vd/Vt in extubation success ($n = 59$) vs failure ($n = 17$) groups calculated prior to extubation 0.48 vs 0.65, $p < 0.0001$ in 76 adult extubated patients
- Significant association between the *V*d/*V*t and extubation failure, with OR = 1.52 (1.11 - 2.09, *P* = 0.008) for each 0.01 of Vd /Vt
- Vd/Vt of 0.58 - best sensitivity & specificity for predicting extubation failure

A. González-Castro et al, Medicina Intensiva 2011

Success of extubation

45 children in Paediatric ICU
Who met criteria for extubation
20 min on PSV to tidal volume of 6ml/kg – dead space was calculated

Vd/Vt	n	Successful extubation
≤ 0.50	25	24 (96%)
0.50 – 0.65	10	6 (60%)
> 0.65	10	2 (20 %)

Hubble CL et al, Crit Care Med. 2000 Jun;28(6):2034-40.

Success of extubation

	Comparison	Subjects	Success vs failure
Ozylimaz et al, Tuberk Toras 2010	Baseline Vd/Vt with extubation success	35 adults	25 (71 %) vs 10 (29%) 0.54 vs 0.66 ($p < 0.05$)
Albert Bousso et al, Jornal de Pediatria - 2006	Pre extubation data vs extubation success	86 children	65 (76 %) vs 21 (24 %) 0.62 vs 0.65 ($p = 0.4$)
A. González-Castro et al, Medicina Intensiva 2011	Pre extubation data vs extubation success	76 adults	59 (78 %) vs 17 (22 %) 0.48 vs 0.56 ($p < 0.0001$)

Success of extubation

- Dead space was measured before and after tracheostomy in 42 patients in SICU
- No significant change of Vd/Vt was seen before and after the procedure (50.7 vs 51.9)
- No significant difference in Vd/Vt is seen b/w who were weaned within 72 hrs & who were weaned > 5 days post tracheostomy
- Change in dead space does not predict the weaning outcome

Mohr et al, J Trauma 2001; 51

Success of extubation

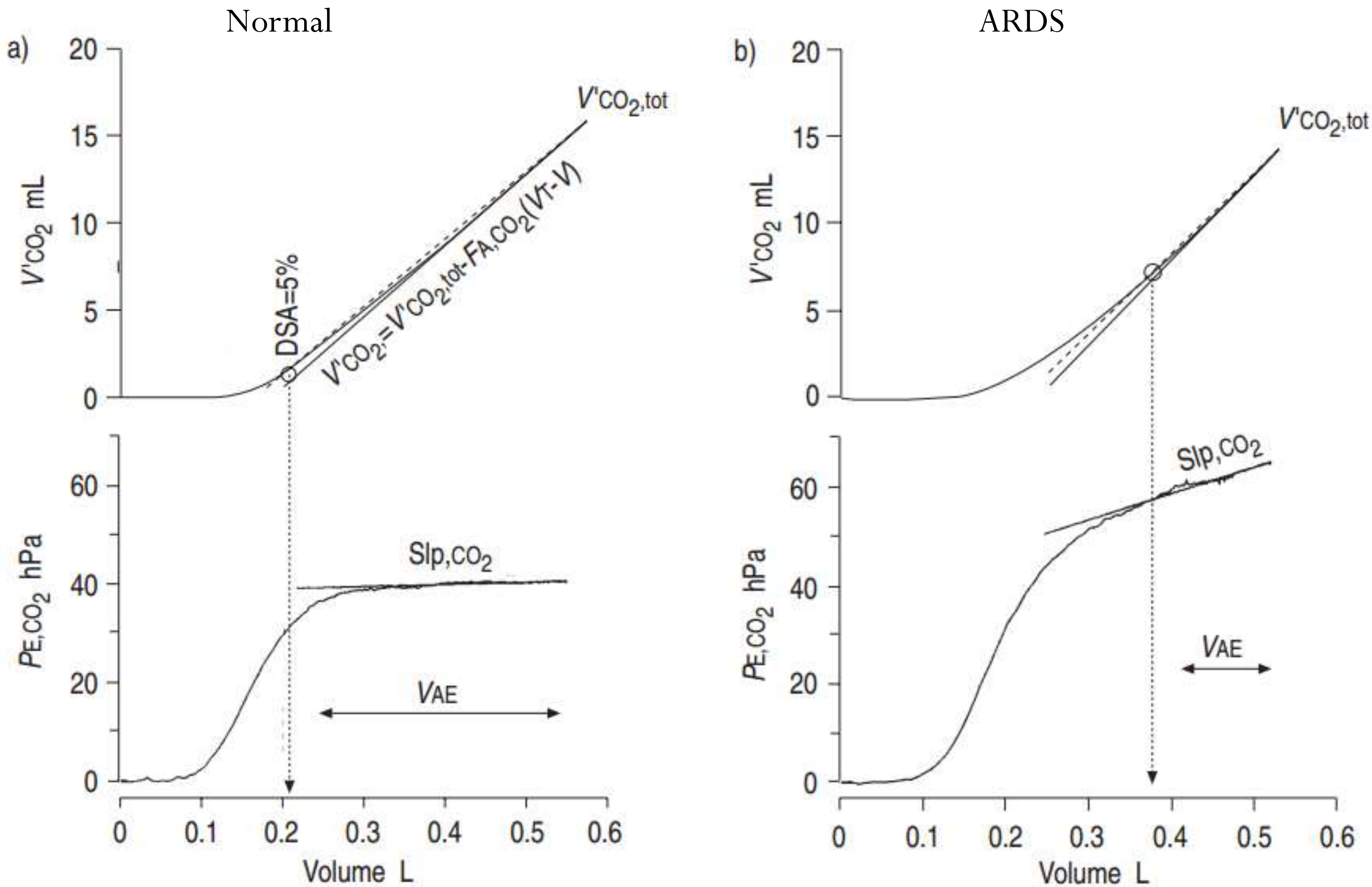
- Dead space measurement can predict the success of extubation
- Elevated VD/VT may be useful for predicting the need for NIV after extubation and therefore the potential for averting the need for re-intubation

V_{AE}/V_T – new variable

- Alveolar ejection volume
- Volume of the pure alveolar gas with minimum dead space contamination
- Represent an index of alveolar inhomogeneity
- It is unaffected by the variations in the tidal volume and set ventilatory pattern in acute lung injury

PV Romero et al, Eur Respir J 1997; 10: 1309–1315

VAE/VT



Normal
ARDS
a)
b)
V'CO2,tot
V'CO2=V'CO2,tot-FA,CO2(VT-V)
DSA=5%
V'CO2 mL
PE,CO2 hPa
Slp,CO2
VAE
Volume L

VAE/VT

- Best correlated with mechanical alterations in ARDS (parallel inhomogeneity)
- Best predictor of outcome among all other capnographic indices(VD Bohr /VDPhys) in ARDS

Take home message

- ✓ Enghoffs approach - global gas exchange status
- ✓ Dead space calculated varies with the ventilator settings
- ✓ High dead space in ARDS predicts in hospital mortality
- ✓ Low dead space can be used for excluding PE along with D dimer values
- ✓ VD/VT as a marker of V/Q matching appears to be better suited for titrating PEEP than PaO2
- ✓ Better variable to detect response to proning and weaning from mechanical ventilation

Thank you