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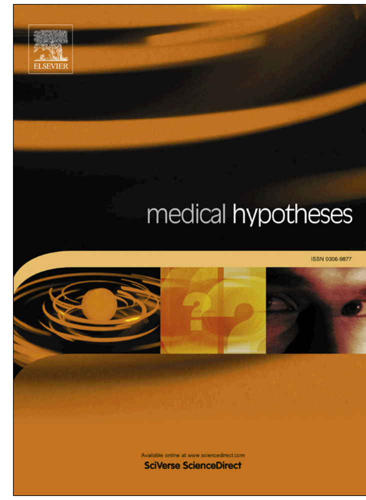

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Minimisation of dissipated energy in the airways during mechanical ventilation by using constant inspiratory and expiratory flows – flow-controlled ventilation (FCV)

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Abstract

It has been suggested that energy dissipation in the airways during mechanical ventilation is associated with an increased probability of ventilator induced lung injury (VILI). We hypothesise that energy dissipation in the airways may be minimised by ventilating with constant flow during both the inspiration and expiration phases of the respiratory cycle. We present a simple analysis and numerical calculations that support our hypothesis and show that for ventilation with minimum dissipated energy not only should the flows during inspiration and expiration be controlled to be constant and continuous, but the ventilation should also be undertaken with an I:E ratio that is close to 1:1.

Keywords

ventilator induced lung injury, lung protective ventilation, flow control, flow-controlled ventilation, energy, mechanical power

INTRODUCTION

For many years substantial effort has been made to find methods of ventilation which minimise the probability of ventilator induced lung injury (VILI) with energy being most recently suggested as a key factor [1]. As the field has developed, possible contributions from many different phenomena have been investigated, including barotrauma arising from high plateau pressures [2,3], volutrauma arising from large tidal volumes [4,5,6], atelectrauma caused by cyclic collapse and reinflation of alveoli [7,8,9,10], and various combinations of barotrauma and flow induced by high driving pressure [11,12]. All of these variables are associated with lung stress and/or strain, but no single variable or phenomenon is solely responsible for the onset of VILI. It now appears probable that a combination of mechanical effects, many of which are linked to ventilation strategy, contribute to the problem. In many cases the mechanical effects are exacerbated by conditions such as lung heterogenity and vascular pressure [13,14,15].

As the lungs expand and contract during mechanical ventilation, both stress and strain change with time. As this happens energy is applied to the lung system by the ventilator. Some of this energy is dissipated in the airways and lung tissue.

It has been suggested that an important contributor to VILI may be non-rupturing damage occurring to the lung tissues at a rate faster than the body is able to repair, as a result of the energy dissipation in the tissues [16]. Additional factors may be local stress amplification arising from lung heterogenity, leading to the initiation of significant damage despite the fact that global stress levels may appear to be well within the tolerance of the tissue [17].

For any material, the area under the stress-strain curve is the energy per unit volume applied in stretching the material [18]. If the material is subject to cyclic stress, the stress-strain curve traces out a loop and the energy dissipated in the material is proportional to the area within the loop (arising from the hysteresis) [19]. This is analogous to the pressure-volume (PV) loop during respiration, where for spontaneous breathing the work of breathing is simply the area within the PV loop [20,21]. For a ventilated patient, when the measured pressure is corrected for pressure drop in the ventilation system to give the intratracheal pressure, the area within the PV loop (when intratracheal pressure is used) is the work done by the ventilator on the patient's respiratory system. It is the energy dissipated in the patient during one breath (= respiratory cycle). This energy comes from the ventilator.

In recent years, there has been increasing interest in the potential contribution to VILI from energy applied to the patient by the ventilator during the inspiration phase of ventilation [1,22], with some evidence from work in animals to suggest that the rate at which energy is applied is indeed related to the onset of damage [23,24,25,26].

Part of the energy applied to the patient by the ventilator during inspiration is dissipated in the patient's airways and lung tissue and part is stored as potential energy by the stretching of the elastic components of the lung parenchyma and the chest. On expiration, this potential energy is released – and, now, part of this stored energy is dissipated in the patient during expiration and part is recovered, provokes the egress of gas and is finally dissipated outside the patient in the ventilator, it's associated tubing, and the atmosphere. It seems most plausible that it is not the energy applied by the ventilator (which is stored and recovered in part) but the energy dissipated in the patient's airways and lung tissue (during both inspiration and expiration) that is related to lung injury.

THE HYPOTHESIS

Because energy is also dissipated in the patient during expiration, it is almost certainly worth controlling the overall energy dissipated in the lungs during *both* inspiration and expiration phases of the respiratory cycle in order to minimise the energy dissipation that can potentially contribute to lung damage. We hypothesise that this can be achieved by controlling the flow to be constant, continuous and equal during inspiration and expiration phases, with an I:E ratio which is close to 1:1.

In the following, we use a simple model to analyse the energy dissipation during respiration. The analysis supports our hypothesis above. We illustrate this with numerical calculations. Finally, we discuss further work necessary to determine if this hypothesis is valid in patients.

THEORY

In this section, we derive mathematical expressions for the energy dissipated in a simple model of a lung unit during respiration, and show that – for a given tidal volume the energy dissipated during inspiration and expiration phases is minimised when the flows during inspiration and expiration are constant and continuous with time. We then go on to find the I:E ratio necessary to minimise energy dissipation when constant, continuous flows are used, for a given minute volume. This is very close to 1:1, rather than the values of 1:1.7 – 1:2 typically used in conventional ventilation methods.

Simple lung unit model

The simple lung unit model we use for this demonstration is shown in Figure 1. It consists of a linear resistor of resistance, R, (Pa/m^3/sec) in series with a linear compliance, C, (Pa/m^3). We have chosen SI units here rather than the more conventionally used units of mbar (pressure), l/min (flow), and ml (volume) so that the energy dissipated is calculated directly in Joules without the need to apply any conversion factors.

During the inspiration phase of respiration a time-varying flow, $Q_i(t)$, is input into the system. During the expiration phase a time varying flow, $Q_e(t)$, is extracted from the system. For convenience, we write these flows as the sum of a constant component in each case (q_i,q_e) and a fluctuating component ($\Delta q_i(t)$,$\Delta q_e(t)$) as follows:

$$Q_i(t) = q_i + \Delta q_i(t) \quad (1)$$

$$Q_e(t) = q_e + \Delta q_e(t) \quad (2)$$

Energy dissipation during inspiration

We first consider the inspiration phase. The tidal volume, V_T, is simply the integral of the input flow over the inspiration time, $tinsp$:

$$V_T = \int_0^{tinsp} Q_i(t)dt = q_i tinsp + \int_0^{tinsp} \Delta\, q_i(t)dt \quad (3)$$

We wish to ventilate to a constant tidal volume, V_T. In order to achieve this, we arrange that the integral of the fluctuating component of input flow is zero, that is:

$$\int_0^{tinsp} \Delta\, q_i(t)dt = 0 \quad (4)$$

The tidal volume, V_T, is then:

$$V_T = q_i tinsp \quad (5)$$

At any instant during inspiration, the power dissipated in the resistance, $P_i(t)$, is simply the product of the resistance value, R, and the square of the flow through it, $Q_i(t)^2$:

$$P_i(t) = RQ_i(t)^2 = R\big(q_i + \Delta q_i(t)\big)^2 \quad (6)$$

The energy dissipated during the whole of the inspiration phase, E_i, is then the integral of this power, $P_i(t)$, over the inspiration time, $tinsp$:

$$E_i = \int_0^{tinsp} R\,\big(q_i + \Delta q_i(t)\big)^2 dt \quad (7)$$

When we expand the squared term on the right-hand side of this equation and factor out constant terms, we find:

$$E_i = Rq_i^2 tinsp + 2Rq_i \int_0^{tinsp} \Delta\, q_i(t)dt + R\int_0^{tinsp} \Delta\, q_i(t)^2 dt \quad (8)$$

The right-hand side of this equation has three terms. We consider each of these in turn:

First term: $Rq_i^2 tinsp$

This is simply the energy dissipation we would see in the resistance were only the mean flow, q_i, to pass through it for the whole of the inspiration phase. It is independent of the fluctuating flow. However, the fluctuating flow *does* appear in the other two terms.

Second term: $2Rq_i \int_0^{tinsp} \Delta\, q_i(t)dt$

This term represents an additional energy dissipation which fluctuates with the fluctuating component of the flow. However, we know from equation (4) that $\int_0^{tinsp} \Delta\, q_i(t)dt = 0$ and so the energy dissipation due to this term is equally positive and negative over the inspiration. This term averages to zero over the inspiration.

Third term: $R\int_0^{tinsp} \Delta\, q_i(t)^2 dt$

This term represents a further additional energy dissipation which fluctuates with the fluctuating component of the flow. However, this term does *not* average to zero over the inspiration, because the fluctuating component of the flow is squared here, and so the additional energy dissipation due to this term is *always* positive. No matter what the type of flow fluctuation, this term always adds additional energy dissipation during inspiration.

We can therefore write the energy dissipation during inspiration using only the first and third terms of Equation (8) as:

$$E_i = Rq_i^2 tinsp + R\int_0^{tinsp} \Delta\, q_i(t)^2 dt \qquad (9)$$

The first term on the right-hand side of this equation is constant – independent of the fluctuating component of the flow. The second term is the additional energy dissipation during inspiration arising from the flow fluctuations, and it is always positive. In order to minimise the energy dissipation during the inspiration phase, we must therefore ensure that $\Delta q_i(t)$ is zero – that is, that there is no fluctuation in the flow. This is because the *increase* in energy dissipation that occurs when the flow increases by a certain amount above the mean flow is greater than the *decrease* in energy dissipation that occurs when the flow is reduced by the same amount below the mean flow.

For minimum energy dissipation during the inspiration, the flow should therefore be constant, and in this case, the energy dissipation over the inspiration will be:

$$E_{imin} = Rq_i^2 tinsp \qquad (10)$$

Example calculation of reduction of energy dissipation during inspiration when constant flow is used

We demonstrate this with a simple example. Consider a situation where the airway resistance of the lung unit is 5.9 mbar/l/s (this corresponds to an airway pressure drop of 588.4 Pa/l/s) and the inspiration time, $tinsp$, is 2 seconds. Assume that the flow during inspiration starts at a high value of 60 l/min (1 l/s), and then decays exponentially so that at the end of inspiration – 2 seconds later – 500 ml (0.5 l) has flowed into the lung unit. These would be typical values for a reasonably healthy patient ventilated non-aggressively with pressure-controlled ventilation (PCV).

We can represent the input flow as a constant flow component of 15 l/min (0.25 l/s) upon which is superimposed with an exponentially fluctuating flow component which varies from +45 l/min (+0.75 l/s) at the beginning of the inspiration to -13.8 l/min (-0.23 l/s) at the end of the inspiration. This is illustrated in Figure 2a.

We then calculate the power dissipated in the lung unit airway resistance in this example as a function of time from the beginning of inspiration. We do this for both the case of constant flow at 15 l/min, and the case of exponentially varying flow as described above. Note that the tidal volume is the same in both cases: 500 ml (0.5 l).

Figure 3a shows how the power dissipation varies as a function of time from the beginning of inspiration for the two cases. Note that the exponentially varying flow produces a large power peak at the beginning of inspiration which then falls off rapidly, while the power dissipation in the constant flow case is constant through the inspiration, at a value which is approximately 1/16th of the peak value for the exponential flow case.

We can now calculate the energy dissipated in the lung unit airway resistance by integrating the power dissipation with respect to time. If we do this through the inspiration, we obtain the accumulated energy that is dissipated in the airways as a function of time through the inspiration. This is shown for the two flow cases in Figure 3b. For the constant flow case, the energy accumulated in the airway tissue rises linearly with time – in this example the energy dissipated by the end of the inspiration is 0.075 J. Equation (9) shows that this is the minimum energy that could be dissipated in the airways and lung tissue whilst achieving this tidal volume (500 ml) over this inspiration time (2 sec) in this example. If the flow fluctuates, the energy dissipation will inevitably rise.

The situation is substantially different for the exponentially varying flow case. Here, the dissipated energy accumulates rapidly in the airways at the beginning of the inspiration (when the power dissipation is highest), and the rate of accumulation then falls off. By the end of the inspiration, the energy dissipated in the airways is 0.16 J – substantially higher than the energy dissipation necessary to achieve the same tidal volume (500 ml) over the same inspiration time (2 sec) at constant flow.

Energy dissipation during expiration

Now we consider the expiration phase: Equations which are exactly analogous to Equation (3) – (10) can be written for expiration, with the mean flow during inspiration, q_i, replaced by the mean flow during expiration, q_e, and the inspiration time, $tinsp$, replaced by the expiration time, $texp$. Note that energy is also dissipated in the airways during expiration and by analogy with Equation (9), the dissipated energy during expiration, E_e, is:

$$E_e = Rq_e^2 texp + R\int_0^{texp} \Delta\, q_e(t)^2 dt \qquad (11)$$

Again, in order to minimise this energy dissipation, it is necessary for the expiration flow to be controlled to be constant and continuous. Just as for inspiration, any fluctuation in flow during expiration, $\Delta q_e(t)$, will increase the dissipated energy during the expiration phase.

The minimum dissipated energy that is achievable during expiration is given by the first term in Equation (11) and is:

$$E_{emin} = Rq_e^2 texp \qquad (12)$$

We demonstrate the expiratory phase – again with an exponentially varying flow – in Figure 2b. Here the airway resistance of the lung unit is again 5.9 mbar/l/s (as for the inspiration calculation described above) but the expiration time, $texp$, is 3 seconds corresponding to an I:E ratio in this example of 1:1.5. The tidal volume is the same and so the mean flow during expiration is 10 l/min. The peak flow at the start of expiration remains 60 l/s and the tidal volume is still 500 ml. Figure 3c shows the power dissipations calculated during expiration for the two flow cases, and Figure 3d shows the accumulation of dissipated energy in the airway. The exponential flow case gives a large power peak at the beginning of expiration (compare this to the constant flow case where the power is very much lower and constant over the whole expiration) and – again substantially higher overall energy dissipation over the full expiration (0.15 J) than for the constant flow case (0.049 J).

Optimum I:E ratio for minimum energy dissipation

During normal ventilation, the expiration phase usually lasts for longer than the inspiration phase. However, this is not optimal to minimise energy dissipation over the whole ventilation cycle. This is because the flow during inspiration then necessarily has to be greater than that during expiration, and this leads to an increase in energy dissipation by the higher inspiratory flow which is not matched by the decrease in energy dissipation by the lower expiratory flow. In consequence, the net dissipated energy over the complete ventilation cycle is higher than optimal. We therefore wish to find the value of I:E ratio that gives the minimum energy dissipation in the airways over one complete ventilation cycle.

We assume that the flows during inspiration and expiration are maintained constant at q_i and q_e. From Equation (10) and (12) the energy dissipated over one complete ventilation cycle, E_{cycle}, is then:

$$E_{cycle} = Rq_i^2 tinsp + Rq_e^2 texp \qquad (13)$$

The respiratory exchange ratio (RER) is usually less than one, so that the volume of gas leaving the lung unit during expiration is slightly less than that entering it during inspiration. We shall assume that the expiratory volume is K times the inspiratory volume, where K is a factor slightly less than 1. We can then write:

$$q_e texp = K q_i tinsp \text{ or } q_e = K q_i \frac{tinsp}{texp} \qquad (14)$$

Using Equation (5) we can write this expression in terms of the tidal volume as:

$$q_e = K \frac{V_T}{texp} \qquad (15)$$

Let the time for one cycle be T so that

$$texp = T - tinsp \qquad (16)$$

We use this expression to substitute for $texp$ in Equation (15) and then substitute the resulting expression for q_e into Equation (13). This gives:

$$E_{cycle} = RV_T^2 \left(\frac{1}{tinsp} + \frac{K^2}{(T - tinsp)} \right) \qquad (17)$$

We now find the value of $tinsp$ which minimises dissipated energy by differentiating Equation (17) with respect to $tinsp$, setting the differential to zero, and solving for $tinsp$ to find the value of $tinsp$ which gives minimum energy dissipation over the complete cycle. This is:

$$t_{insp}(MinimumEnergy) = \frac{T}{1+K} \qquad (18)$$

The corresponding value of $texp$ is:

$$t_{exp}(MinimumEnergy) = T \frac{K}{1+K} \qquad (19)$$

and the I:E ratio for minimum energy dissipation, $I{:}E(MinimumEnergy)$, is:

$$I{:}E(MinimumEnergy) = 1{:}K \qquad (20)$$

This result indicates that ventilation for minimum energy dissipation requires both constant, continuous and equal flows during inspiration and expiration, and this requires a substantially different I:E ratio to that normally used. The oxygen consumption for an adult at rest is normally taken as around 250 ml/min. At a RER of 0.8 this would produce 200 ml/min of CO_2. If we take 5 l as a typical minute volume, then the volume of gas leaving the lungs during expiration is 0.99 times the volume of gas entering during inspiration, that means K in the equations above is 0.99. For minimum energy dissipation it is therefore necessary to ventilate with an I:E ratio of around 1:0.99, that means a slightly inverse I:E ratio rather than the ratios of 1:1.7 – 1:2 that are normally used. Note that at the I:E ratio giving minimum energy dissipation, the flows during inspiration and expiration are inevitably equal. This is clearly a very different mode of ventilation to conventional pressure-controlled or volume-controlled ventilation (PCV/VCV). In what follows we shall call this new ventilation mode FCV, or (bidirectionally) flow-controlled ventilation.

Non-linear compliance

In the analysis above we have assumed that the lung unit compliance is linear, that means the pressure in the lung unit is linearly related to the volume of gas it contains. In practice the lung compliance curve usually has a sigmoidal shape with a reduced gradient at low pressures caused by the collapse and reinflation of alveoli, a roughly linear region at normal operating pressures and a reduced gradient again at high pressure arising from the onset of overextension of the lung tissue [27].

The pressure in the lung unit can only have indirect effect on the power dissipation, inasmuch as it might change the flow when the lung unit is connected to a ventilator system.

In the analysis above, we have assumed the flow is fully controlled by the ventilator system, and so the pressure in the lung unit (and therefore any non-linear compliance characteristic) cannot affect our conclusion that for minimum energy dissipation the unit should be ventilated using constant, continuous and equal flows during the inspiration and expiration phases.

Non-linear airway resistance

Ventilation of the lung unit at constant flow gives minimum energy dissipation in the example above because the power dissipation is related to the square of the flow (Equation (6)). If at any point during the cycle the flow rises above the mean flow necessary to achieve the required tidal volume, then at a subsequent point in the cycle it must fall below the mean flow by an equal amount. The flow must average to $\frac{V_T}{tinsp}$. As already mentioned above, the power dissipation increases as the square of the flow and so the increase in energy dissipation during the periods when the flow is above the mean value is greater than the decrease in energy dissipation during the periods when the flow is below the mean value and, in consequence, the overall energy dissipation has to rise.

If we represent the airway resistance using Rohrer's expression [28]:

$$R = k_1 + k_2 Q(t) \qquad (21)$$

the power dissipation now becomes:

$$P(t) = k_1 Q(t)^2 + k_2 Q(t)^3 \qquad (22)$$

In addition to the square-law relationship between power and flow, there is now also a cubic component. This exacerbates the increase in power dissipation if the flow rises above average and further reduces the decrease in dissipation when the flow falls below average. Compared to the linear resistance case, the effect of this is to exacerbate the overall increase in energy dissipation if the flow fluctuates. With a non-linear airway resistance, it becomes even more critical to maintain a constant and continuous flow in order to minimise energy dissipation. The constant flow condition is necessary for minimum energy dissipation in all cases where the pressure drop across the airway resistance depends on flow – that is in all situations found in practice.

Multi-compartment lungs and viscoelastic effects

The model used for the derivation above is that of a simple single-compartment. Real lungs consist of many such compartments linked in a complex network. In addition, lung tissue displays a degree of viscoelasticity exhibiting time-dependant strain, stress relaxation and creep. We may model both the multi-compartment nature of the lungs and viscoelasticity using a variant of the Maxwell-Weichert model [29] as shown in Figure 4, consisting of a network of units similar to that used in the analysis above – but with each unit having a different time constant.

In this model we note the following:

1. In order to minimise the overall energy dissipation, it is necessary to minimise the energy dissipation in each individual unit.
2. The analysis given above holds for each individual unit. In order to minimise energy dissipation the flows to and from the unit during inspiration and expiration should be constant, continuous and very nearly equal (governed by the RER).
3. If constant flow is applied to or extracted from the network, the flow in each unit will also be constant.

If the inspiration and expiration phases of the ventilation cycle were infinitely long and the flows applied to and extracted from the network were constant and continuous, the energy dissipated in each unit of the network would be minimised and given by Equation (10) and (12) above. However, when the flow changes direction, a transient phenomenon occurs as gas is redistributed between units in the network with different time constants. During the transient the flows in the units are not constant and so the net effect is to raise the dissipated energy above the minimum that would be achievable if each unit was ventilated individually at constant flow. Unfortunately, it is impossible to impose this condition by adjusting the single flow rate at the input to the network.

Indeed, any deviation from constant flow at the network input during inspiration or expiration can only either increase the rate of gas redistribution between units of different time constants when the flow changes direction, or increase the time over which the redistribution occurs. In either case, the energy dissipation in each lung unit is increased above that occurring with constant flow. With constant flow at the network input, variations in flow occur in each unit for a short time after the flow changes direction and the energy dissipation is greater than the minimum achievable if each unit was ventilated at constant flow individually. However, the variations in flow in each unit are nonetheless minimised and the energy dissipation in the entire network is therefore the minimum practically achievable.

Effect on the PV loop

Ventilation using constant flow during inspiration and expiration substantially changes the shape of the PV loop. In conventional PCV the flow varies substantially during both inspiration and expiration phases. This causes a time-varying pressure drop across the airway resistance which appears as a deviation in airway pressure from the static compliance curve of the lungs. The deviation in pressure varies substantially with lung volume and is largest at the beginning of the inspiration/expiration phase where a substantial change in pressure but only a small change in volume has to be noted. The deviation is positive during inspiration and negative during expiration.

In VCV the flow is constant (and relatively low – typically 15 – 20 l/min depending on the I:E ratio) during inspiration (here we are referring to the inflation but not the plateau phase), but again varies substantially (typically from a peak of roughly 60 l/min) during expiration as gas is driven out of the lungs by the elastic relaxation of the chest wall and lung parenchyma. During inspiration the deviation of airway pressure from the static compliance curve of the lungs is therefore constant and positive. During expiration the deviation of airway pressure from the static compliance curve varies substantially (being largest at the beginning of the expiration phase) and is negative – mirroring what happens during the expiration phase of PCV.

When constant, continuous and identical flows are used during both inspiration and expiration, the deviation of airway pressure from the static compliance curve is constant and positive during inspiration and constant and negative during expiration.

We illustrate this in Figure 5, which shows the result of calculations of PV loops arising during PCV, VCV, and FCV under roughly comparable ventilation conditions. The lung model used in this calculation was a two-compartment lung model with complex impedance representative for a typical healthy adult. At a respiratory rate of 10 breaths per minute the compliance was 58 ml/mbar and the airway resistance was 5.6 mbar/l/s. The endotracheal tube resistance coefficients used in the calculation were values for an 8 mm (inner diameter) tube taken from Flevari et. al.[30]. The ventilator circuit resistance used was 0.784 mbar/l/s.

We calculated PV loops based on both the pressure at the proximal end of the endotracheal tube (usually defined as airway pressure) and the intratracheal pressure using the network solving routines in the Quite universal circuit simulator [31]. The calculations for the three ventilation cases were set up as follows:

1. The PEEP level (in the trachea) was set to 4.8 mbar in all cases.
2. For the PCV calculation:
   a. The I:E ratio was set to 1:1.7.
   b. The respiratory rate was set to 10 breaths per minute.
   c. The peak inspiratory pressure was then adjusted to achieve a minute volume of 6.3 l.
3. For the VCV calculation:
   a. The I:E ratio was set to 1:1.7.
   b. The respiratory rate was set to 10 breaths per minute.
   c. The peak inspiratory pressure was then set to 18.1 mbar (the same value used in the FCV case below)
   d. The flow rate was adjusted to achieve a minute volume of 6.3 l (without a plateau phase during inspiration).
4. For the FCV calculation:
   a. The I:E ratio was set to 1:1.
   b. The flow rate was adjusted to achieve a minute volume of 6.3 l.

c. The peak inspiratory pressure was then adjusted to achieve a respiratory rate of 10 breaths per minute (identical to the PCV case).

This procedure was followed in order to ensure that the ventilation parameters pertinent to gas exchange in the three cases were identical. This was also necessary because the multi-compartment lung model simulates the creep and relaxation phenomena found in real multi-compartment lungs with viscoelastic properties. It therefore responds differently to PCV (where the flow pauses and the lungs then have time to come to a pressure equilibrium with a stable volume), VCV, and FCV (where the flow is never zero and the lungs are therefore moving continually during the ventilation cycle).

With PCV the PV loop calculated at the proximal end of the endotracheal tube displays the typical large pressure deviations from the static compliance curve of the lungs at the beginnings of the inspiration and expiration phases, where the flow is highest and there is the greatest pressure drop across the combination of endotracheal tube resistance and equivalent ("anatomical") airway resistance. This gives a broad loop. The loop calculated using intratracheal pressure is narrower – because the pressure deviations from the static compliance curve of the lungs are caused only by flow through the equivalent ("anatomical") airway resistance, rather than by flow through both the equivalent airway resistance and the endotracheal tube. The area of the loop based on intratracheal pressure gives the energy dissipated in the equivalent ("anatomical") airway resistance – that is the energy dissipated in the lung/chest system.

With VCV, the inspiratory phase of the loop is modified because of the constant flow throughout the inspiration (here without a plateau phase), but the expiratory phase of the loop mirrors that seen in PCV. Again, the loop using intratracheal pressure is narrower for the same reason given above.

For FCV the PV loops calculated for both the proximal end of the endotracheal tube and the intratracheal pressure are both much narrower than their PCV counterparts – indicating substantially less dissipated energy as predicted by the mathematical development outlined above. Table 1 compares the energy dissipation in the lung/chest system for the three cases.

It is worth noting that the volumes of gas in the lungs at the beginning and end of inspiration differ between the calculation for PCV and for FCV. Overall, the volume of gas retained in the lungs is greater in FCV than in PCV. This occurs because of the properties of the two-compartment lung model as it mimics the creep and relaxation effects occurring due to viscoelasticity. Because gas is moving slowly and continuously throughout the whole ventilation cycle in FCV, the lungs never have time to 'catch up' with the ventilator – and the net result are more 'open' lungs for the same values of PEEP and tidal volume. Additionally, although the lungs are inflated somewhat quicker during PCV, the average residence time of any parcel of respired gas within the lungs under FCV is longer than that for PCV because of the controlled flow during expiration. For both reasons, more 'open' lungs and longer residence time, it therefore appears likely that – for similar ventilation parameters – oxygenation in particular will be better for FCV because there is more time for gas exchange to take place across the alveolar membrane during the ventilation cycle.

The flow is constant throughout the inspiration phase for FCV, whereas in PCV the flow has fallen essentially to zero by the end of the inspiration. There is therefore a pressure drop across the "anatomical" airway right to the end of the inspiration phase in FCV. This adds on to the alveolar pressure and so the intratracheal pressure is higher at the end of the inspiration phase in FCV than in PCV even though the alveolar pressures might be the same. This is apparent in the PV loops.

Note that in table 1, the tidal volume given is that calculated at the ventilator output, whereas the minute volume is that actually entering the simulated lung system. The effects of circuit compliance can be seen in the PCV and VCV cases (tidal volume slightly higher than expected as it is also filling up the circuit compliance). This is not present in FCV because the FCV system precisely controls flow into the lungs through a low compliance circuit (see below for a description of a system that can apply FCV in practice).

DISCUSSION

Our analysis of the energy dissipated in the airways during ventilation as well as our numerical calculations indicate that energy dissipation may be substantially reduced by controlling the ventilation flow to be constant and continuous during both inspiration and expiration and by ventilating at an I:E ratio very close to 1:1 (determined by the RER) – that is by using FCV.

Recent work in pigs [26] in which the variation in flow during expiration was partially reduced tends to support the hypothesis that lung injury may be reduced by controlling flow. However, the expiratory flow was not constant in these experiments and no calculation of energy dissipation was made. In order to fully test our hypothesis we suggest that it is most appropriate to undertake ventilations on living subjects under conventional (PCV and VCV) ventilation modes, and FCV, and then measure PV loops using the intratracheal pressure. This would enable direct calculation of the energy dissipated in the subject's airways from the area of the loop. Note that the areas of PV loops obtained using the pressure at the proximal end of the endotracheal tube give an overestimate of the energy dissipated in the airways [32] because the resistance of the tube causes substantial widening of the loop as we have demonstrated in our calculations shown in Figure 5. Therefore (direct) measurement or proper calculation of the intratracheal pressure is mandatory.

Ideally, tests should be made to compare the loops obtained with conventional ventilation modes (PCV and VCV) with those obtained using FCV under conditions where the parameters pertinent to gas exchange are identical.

At present, we know of only one ventilation system, which is capable of both closely approximating FCV while simultaneously providing a direct readout of intratracheal pressure. This is the Evone ventilator (Ventinova Medical, Eindhoven, The Netherlands) used with a novel small-bore endotracheal tube, which incorporates an intratracheal pressure measurement lumen (Tritube; Ventinova Medical, Eindhoven, The Netherlands) [33].

Measurement of intratracheal pressure during ventilation using conventional ventilators is more difficult and less reliable. Guttmann et al. [34] have used a technique where the pressure at the proximal end of the endotracheal tube is measured and then compensated for pressure drop across the tube due to the flow using previously measured tube resistance coefficients. Litwarck-Aschoff et al. [35] have compared intratracheal pressure estimates made using a similar technique with pressure measurements obtained using a catheter and found good agreement for short-term measurements. However, these methods are potentially susceptible to variations caused by effects such as different flow patterns occurring when the tube is used in a patient compared to the flows and resistance coefficients pertaining when resistance coefficients measured *in-vitro* [36]. Attempts to overcome these problems include the work by Sondergard et al. [37] who used a fibreoptic Fabry-Perot interferometer to measure intratracheal pressure in paediatric respiratory monitoring.

Notwithstanding these difficulties and some other limitations resulting from different technical layout, we suggest that comparison of PV loops obtained with conventional ventilation modes applying mathematical tube compensation (or, if feasible, direct tracheal pressure measurement) and with FCV using a system like the Evone ventilator would be a valuable first step in validating our hypothesis. It would be possible to intubate the subject with a conventional wide-bore endotracheal tube to obtain data using a conventional ventilator and then to insert the small-bore Tritube inside the conventional tube to obtain data for the FCV case. Whilst not providing an exact comparison, it is nonetheless likely that the approximate comparison available using this method would provide enough information to evaluate our energy dissipation hypothesis.

When ventilating lungs with multiple compartments with different time constants, it is clear that the volume distribution between the compartments will be the most even if the flow is as low as possible. This gives the compartments with long time constants time to ‘catch up’ with the compartments which have shorter time constants. For a given tidal volume and respiration time, the lowest peak flow is necessarily achieved if the flow is constant over the inspiration or expiration time, and so ventilation with constant flow not only minimises the energy dissipation, but is also likely to result in the lung compartments of differing time constants being more uniformly inflated over the greatest portion of the ventilation cycle, that is, the lungs will be more ‘open’ [38]. Concomitantly, the distribution of dissipated energy within the lungs will also be more uniform with FCV. The rapid variations in flow which occur during both phases of the cycle in PCV, and during the expiratory phase in VCV are less than ideal in terms of maintaining the lung ‘open’ for the full cycle. Additionally, during inspiration, non-uniform inflation of the different lung compartments gives a higher probability of regional overinflation if peak pressures are increased in an attempt to achieve sufficient tidal volume – especially if the lungs are compromised due to disease.

For the reasons given above we suggest that – for given ventilation parameters – oxygenation in particular may be better in the FCV case and this has been observed in an animal model [39]. This could be tested by comparing arterial blood gas measurements obtained under FCV with those obtained for the same ventilation conditions using conventional ventilation modes.

Conflict of interest statement

D. Enk: inventor of EVA technology (Ventrain, Tritube, Evone), royalties for EVA technology (Ventrain, Tritube, Evone), patent applications on minimising dissipated energy and on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical

D. van Asseldonk: patent application on calculating and displaying dissipated energy, CEO Ventinova Medical

T. Barnes: patent application on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical

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Table 1

	Minute volume (l)	Tidal volume (ml)	Energy dissipated per litre of gas ventilated (J)
Pressure-controlled ventilation (PCV)	6.3	639	0.36
Volume-controlled ventilation (VCV)	6.3	646	0.248
Flow-controlled ventilation (FCV)	6.35	635	0.169

Captions for Figures

Figure 1

The simple lung unit model used to develop the flow-controlled ventilation (FCV) theory

Figure 2

The exponentially varying flow used to demonstrate the increase in dissipated energy during (a) inspiration and (b) expiration when the flow varies

Figure 3

The variation of power and accumulated energy dissipated in the lung unit airway resistance during inspiration and expiration for two cases: Exponentially varying flow (shown in red), constant flow at a value equal to the mean flow in the exponential (shown in green)

Figure 4

The multi-compartment / viscoelastic lung model

Figure 5

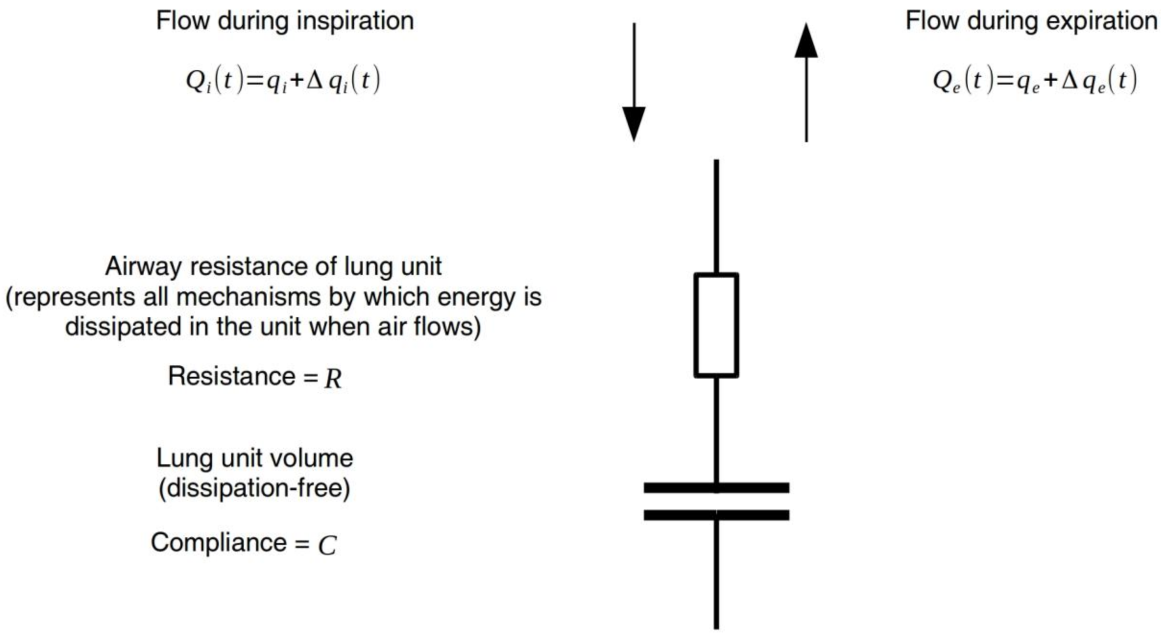
The lung and ventilator circuit model used to demonstrate the reduction of dissipated energy when flow-controlled ventilation (FCV) is used, together with PV loops comparing calculated results from FCV (shown in green) with pressure-controlled ventilation (PCV; shown in red) and volume-controlled ventilation (VCV; shown in black). The additional pressure drop across the “anatomical” airway caused by the constant flow in FCV at the end of the inspiration phase can be clearly seen. (PV loops were calculated both at the proximal end of the endotracheal tube and in the trachea.)

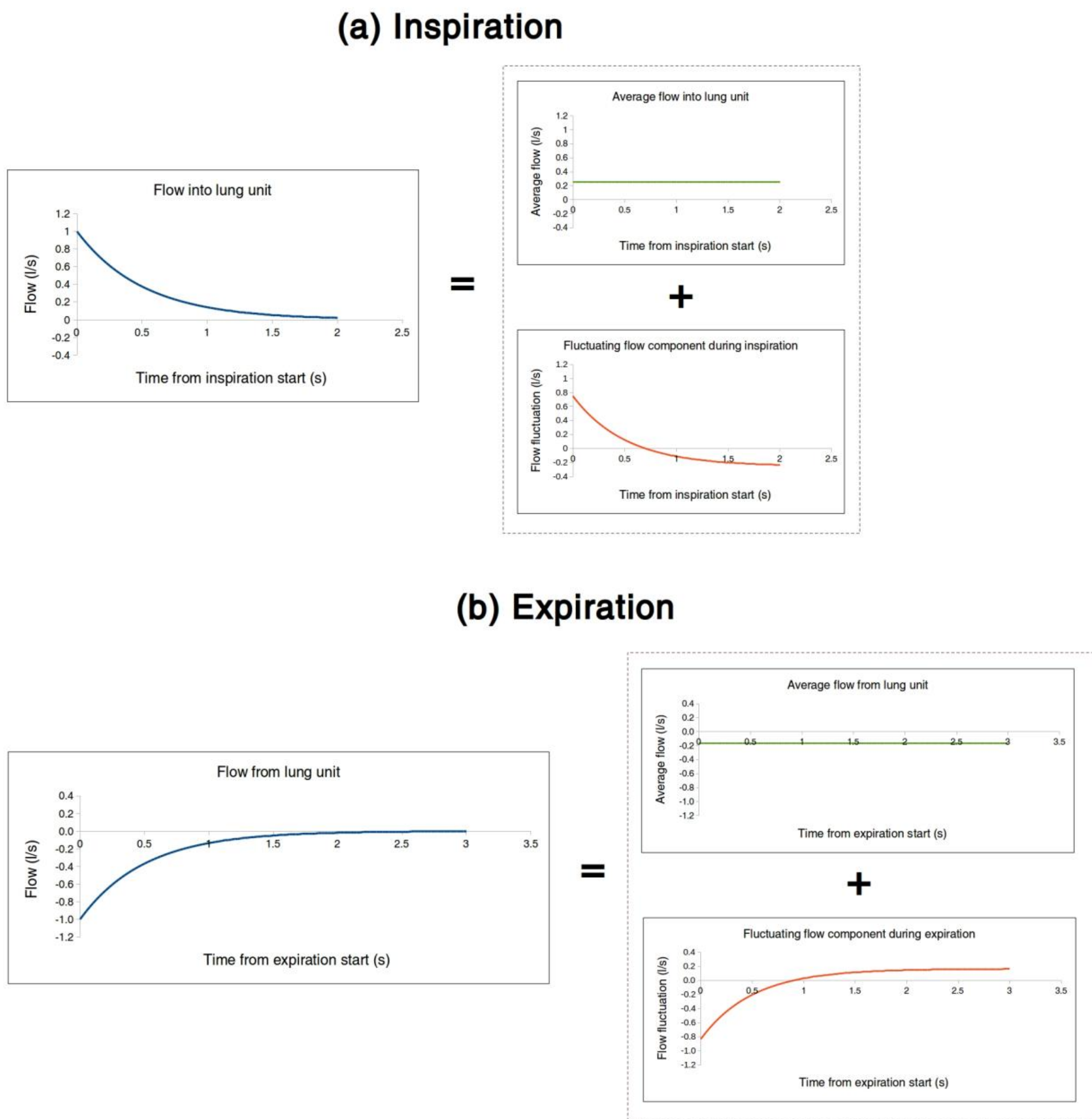
Conflict of interest statement

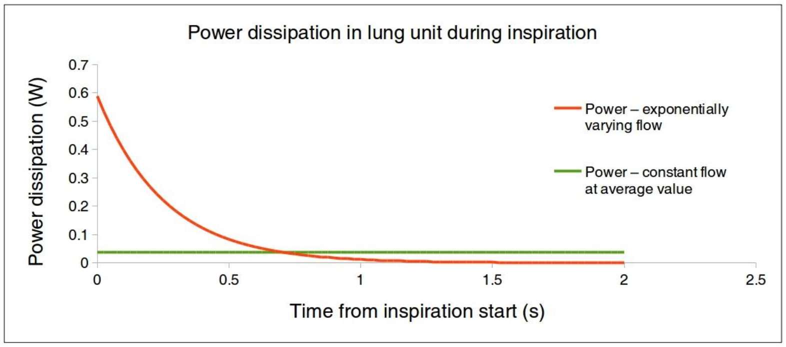
D. Enk: inventor of EVA technology (Ventrain, Tritube, Evone), royalties for EVA technology (Ventrain, Tritube, Evone), patent applications on minimising dissipated energy and on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical

D. van Asseldonk: patent application on calculating and displaying dissipated energy, CEO Ventinova Medical

T. Barnes: patent application on calculating and displaying dissipated energy, (paid) consultant to Ventinova Medical

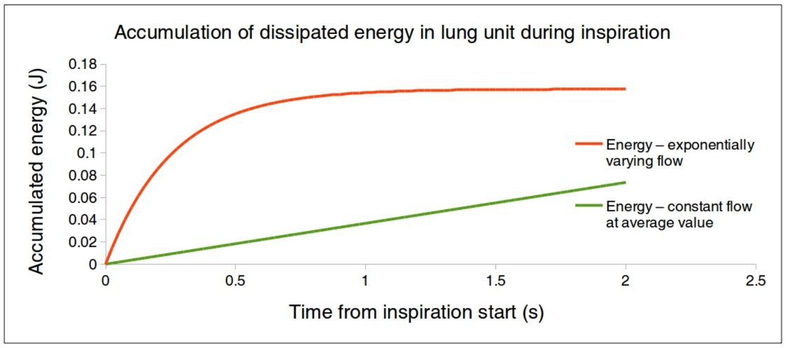

Flow during inspiration
$Q_i(t)=q_i+\Delta q_i(t)$
Flow during expiration
$Q_e(t)=q_e+\Delta q_e(t)$
Airway resistance of lung unit
(represents all mechanisms by which energy is dissipated in the unit when air flows)
Resistance = R
Lung unit volume
(dissipation-free)
Compliance = C


(a) Inspiration
Flow into lung unit
Flow (l/s)
Time from inspiration start (s)
=
Average flow into lung unit
Average flow (l/s)
Time from inspiration start (s)
+
Fluctuating flow component during inspiration
Flow fluctuation (l/s)
Time from inspiration start (s)
(b) Expiration
Flow from lung unit
Flow (l/s)
Time from expiration start (s)
=
Average flow from lung unit
Average flow (l/s)
Time from expiration start (s)
+
Fluctuating flow component during expiration
Flow fluctuation (l/s)
Time from expiration start (s)



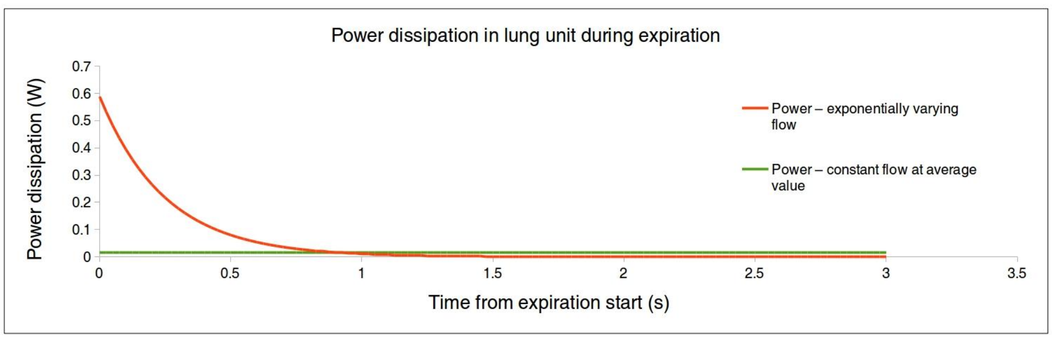
Power dissipation in lung unit during inspiration
Power dissipation (W)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
Time from inspiration start (s)
Power – exponentially varying flow
Power – constant flow at average value

(a)



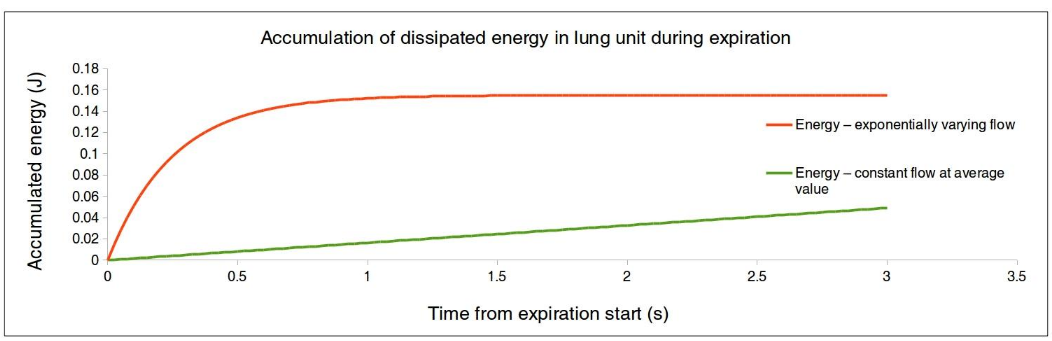
Accumulation of dissipated energy in lung unit during inspiration
Accumulated energy (J)
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.5
1
1.5
2
2.5
Time from inspiration start (s)
Energy – exponentially varying flow
Energy – constant flow at average value

(b)



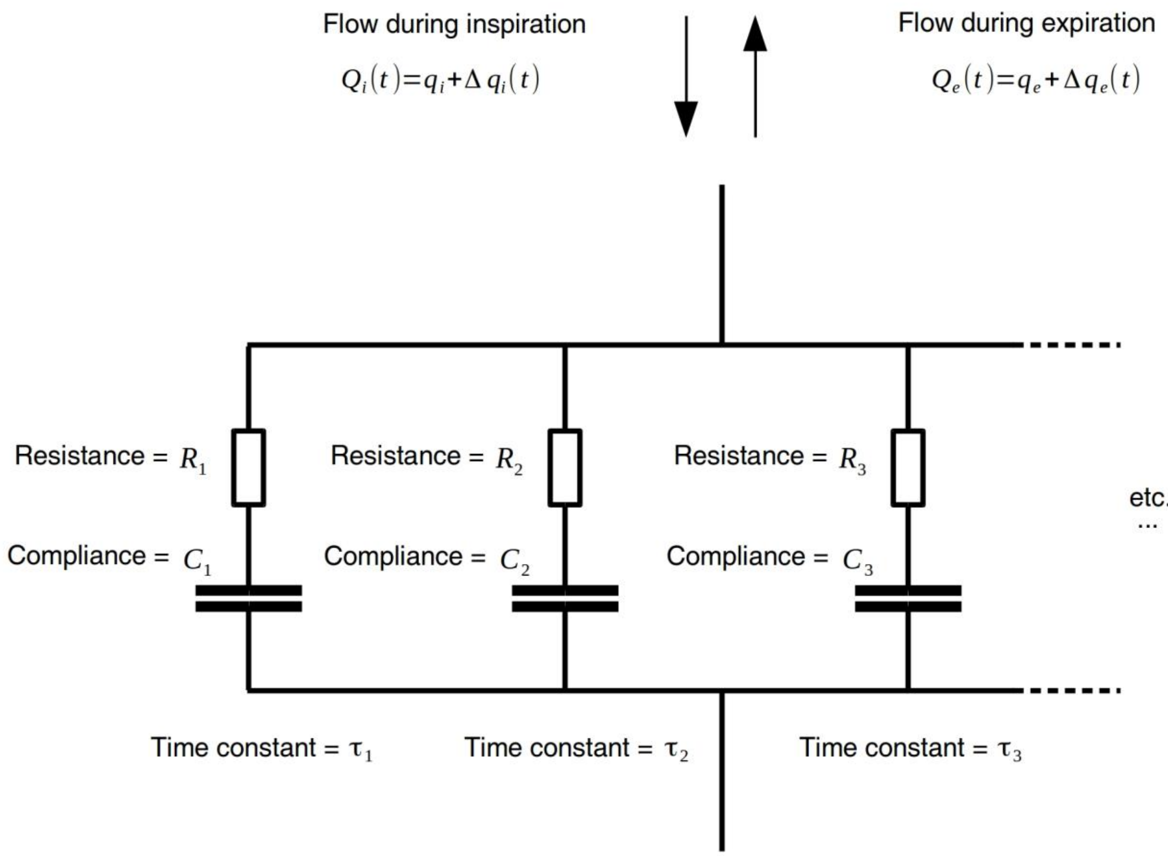
Power dissipation in lung unit during expiration
Power dissipation (W)
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.5
1
1.5
2
2.5
3
3.5
Time from expiration start (s)
Power – exponentially varying flow
Power – constant flow at average value

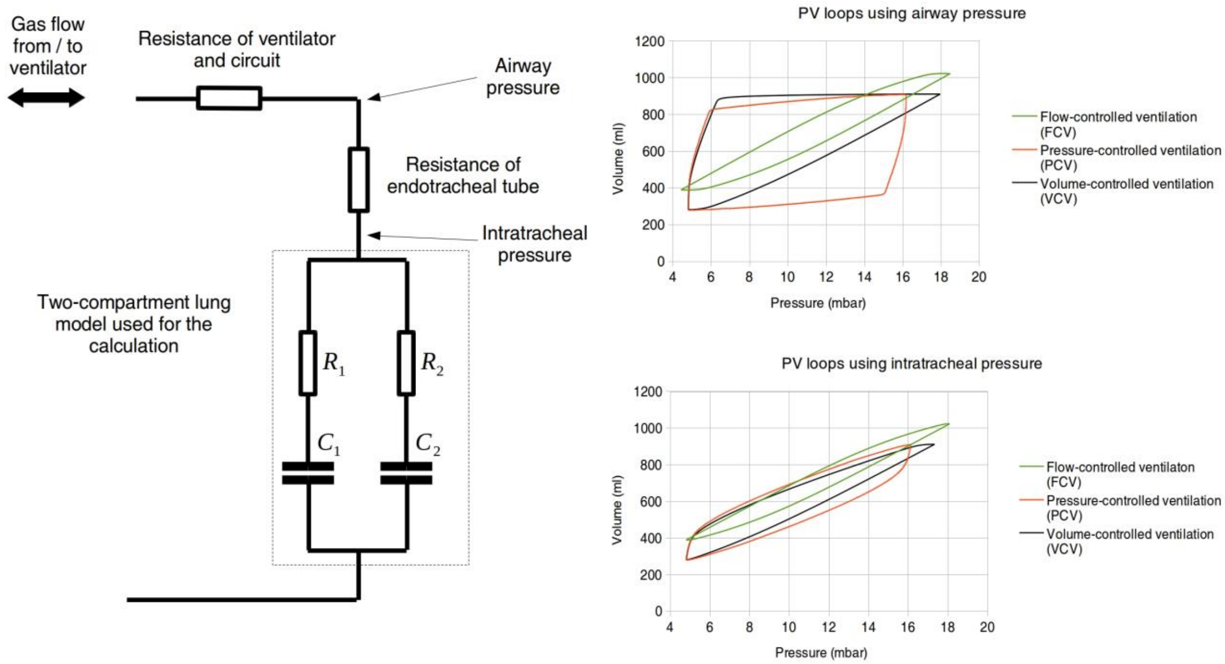
(c)



Accumulation of dissipated energy in lung unit during expiration
Accumulated energy (J)
0.18
0.16
0.14
0.12
0.1
0.08
0.06
0.04
0.02
0
0
0.5
1
1.5
2
2.5
3
3.5
Time from expiration start (s)
Energy – exponentially varying flow
Energy – constant flow at average value

(d)


Flow during inspiration
$Q_i(t)=q_i+\Delta q_i(t)$
Flow during expiration
$Q_e(t)=q_e+\Delta q_e(t)$
Resistance = R_1
Resistance = R_2
Resistance = R_3
etc.
...
Compliance = C_1
Compliance = C_2
Compliance = C_3
Time constant = τ_1
Time constant = τ_2
Time constant = τ_3


Gas flow from / to ventilator
Resistance of ventilator and circuit
Airway pressure
Resistance of endotracheal tube
Intratracheal pressure
Two-compartment lung model used for the calculation
R_1
R_2
C_1
C_2
PV loops using airway pressure
Volume (ml)
Pressure (mbar)
Flow-controlled ventilation (FCV)
Pressure-controlled ventilation (PCV)
Volume-controlled ventilation (VCV)
PV loops using intratracheal pressure
Volume (ml)
Pressure (mbar)
Flow-controlled ventilaton (FCV)
Pressure-controlled ventilation (PCV)
Volume-controlled ventilation (VCV)