Journal of Applied Physiology

Physiology in Medicine Paper (PIMP)

**Physiology in Medicine: Understanding Dynamic Alveolar Physiology to Minimize Ventilator Induced Lung Injury (VILI)**


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Introduction

Pulmonary physiology and pathophysiology in positive pressure mechanical ventilation have been studied for decades. Preemptive application of adequate positive end expiratory pressure (PEEP) can reduce pulmonary edema in animal models of high vascular pressure, high alveolar surface tension and high permeability-induced acute respiratory distress syndrome (ARDS). Knowing that adjustments in the mechanical ventilator settings (i.e. PEEP) can protect the acutely injured lung is key to managing the critically ill patient, since the mainstay of ARDS treatment is still supportive in the form of mechanical ventilation. Indeed, animal studies suggested that protective ventilation can reduce pathology in the acutely injured lung, which lead to a clinical trial demonstrating that protective mechanical ventilation can significantly reduce mortality. Paradoxically, the mechanical ventilator as a support strategy can have unintended effects that may accentuate lung pathology, depending on ventilator settings. The repetitive delivery of arbitrary settings will, in some patients, exacerbate the primary acute lung injury, and cause a secondary ventilator induced lung injury (VILI).

However, even though application of PEEP has been shown to prevent or reduce edema in animal models of ARDS, PEEP has not been show to improve outcome in patients with ARDS, which maybe explained by the variable amount recruitable lung with increased airway pressure in ARDS patients.

Historically there have been three main mechanical breath parameters, tidal volume (Vt), plateau pressure (Pplat) and PEEP have been used for several decades in multiple combinations in an attempt to reduce VILI. More recently the role of respiratory strain rate has also been shown to be an important contributor to VILI. Although mortality has been significantly reduced since ARDS was identified in 1967, it remains at ~40%. Since the mortality rate in ARDS patients remains unacceptably high, further analysis of the entire mechanical breath profile (MBP) (i.e. airway pressures, volumes, flows, rates and the duration at which they are applied with each breath) and how each parameter impacts at the alveolar and alveolar duct is necessary.

In the current standard of care, ventilator adjustments (Vt, PEEP, Pplat) are made on the basis of oxygenation and airway pressure, not in response to lung mechanics and VILI may or may not be averted. Although protective ventilation resulted in an initial drop in mortality it has been disappointing that the current standard of care protective ventilation strategy hasn’t further reduced mortality. (47) and (63) underscore the critical need to better understand the impact of the
mechanical breath on alveolar and alveolar duct inflation and deflation, and the mechanisms of ARDS and VILI at the alveolar level, in order to develop protective ventilator strategies that work.

What physiologic parameters can define the optimally protective mechanical breath?

The goal of the protective breath is not to optimize oxygenation but rather to minimize damage to pulmonary epithelial and vascular endothelial cells and their associated connective tissues. In order to design the optimally protective breath, we must consider: 1) the complex microanatomy of interconnected alveoli with shared alveolar walls, 2) the physiologic mechanisms of VILI in the microenvironment of the terminal airspace – the alveoli and alveolar ducts, 3) the dynamic alveolar physiology (i.e., the dynamic change in alveolar size and shape during tidal ventilation) and how changes in dynamic alveolar physiology cause tissue damage resulting in VILI and 4) apply this information to postulate an optimal mechanical breath profile (MBp), necessary to a ventilation protocol capable of blocking VILI. A mechanical breath is comprised of airway pressures, volumes, flows, rates, and the duration over which they are applied throughout inspiration and expiration. Critical consideration of VILI mechanisms and dynamic alveolar physiology can unveil MBp parameter combinations that are lung protective, thus enabling the practitioner to adjust protocols and minimize or avert VILI. Our approach is to identify an optimal combination of these physical parameters over the course of the ventilator cycle that is adaptive in real time to each individual breath.

Key Points

- Current protective mechanical ventilation strategies necessary to reduce ventilator induced lung injury (VILI) in ARDS patients have focused on three components of the mechanical breath: tidal volume, plateau pressure and PEEP.

- Although ARDS mortality has been reduced with these strategies, it remains unacceptably high at ~40%.

- To improve protective mechanical ventilation, the dynamic physiology of the alveolus in both normal and pathologic conditions must be known.

- Once we identify the alveolar pathophysiology we can modify the components of the mechanical breath necessary to normalize physiology and protect the lung.
Pathophysiology of VILI

Normal dynamic alveolar anatomy consists of interdependent, homogeneous inflated alveoli with little movement in alveolar volume during tidal ventilation (Fig 1, Animation 1). An important feature of ARDS pathophysiology is loss of surfactant function causing alveoli to either remain collapsed throughout ventilation, or sequentially collapse and reopen with each breath. This lung pathophysiology is believed to set the lung up for a secondary VILI. The mechanism of VILI is complex, with two primary mechanisms, which can subsequently contribute to two secondary mechanisms that can only occur in the presence of the primary. **Primary VILI Mechanisms:** 1) Collapsed or edema-filled alveoli that are surrounded by open alveoli causing stress-raisers (S-R) (Fig 2A-B, Animation 2) and 2) alveoli that recruit and derecruit (R/D) with tidal ventilation resulting in an increase in dynamic strain (Fig 3A-B, Animation 3). **Secondary VILI Mechanism:** 1) ARDS causes a reduction in functional lung volume by a combination of partially and fully collapsed (i.e atelectasis) alveoli. If lung volume loss is severe, even small tidal volumes can result in VILI caused by over-distension (OD) of normal alveoli and alveolar ducts, in the remaining aerated lung regions. However, if the lung is fully recruited even large tidal volumes set on the ventilator will not cause alveolar OD since this volume is shared by millions of alveoli and thus alveolar Vt remains very small and 2) stress/strain-induced injury secondary to the above mechanisms causes release of inflammatory mediators which exacerbate the physical damage termed biotrauma.

**Stress-raisers:** Although even the normal lung is not homogeneous throughout, due to variation in gas distribution, conducting airway asymmetry, and anisotropic alveolar expansion, stress transmission is still relatively well distributed in most lung tissue. However, alveolar collapse and edema results in a heterogeneous inflation pattern such that the stress during cyclic volume change becomes concentrated onto the open lung tissue adjacent to collapsed tissue. It has been shown that the homogeneous lung is stable but local atelectasis, causing stress-risers, can occur if alveolar surface tension is high and insensitive to alveolar surface area.

**Recruitment/Derecruitment:** Normal alveoli are stable and do not have marked changes in volume with each tidal breath (<4-6% change with each cycle). Thus, dynamic strain is minimal in normal alveoli. Loss of surfactant function with acute lung injury renders alveoli unstable, greatly reducing the
alveolar collapse time constant, resulting in a rapid collapse of the alveolus with each expiration.\(^{(58)}\) (Fig 3A-B, Animation 3) This leads to a large dynamic alveolar strain, which is known to be a primary VILI mechanism.\(^{(1, 17)}\) Pathologic changes in alveolar stability can be identified using a deep inflation (DI) and measuring the change in elastance (\(H\)) and hysteresivity (\(\eta\)). If \(H\) and \(\eta\) do not return to normal following a DI correlates strongly with alveolar instability viewed directly using \textit{in vivo} microscopy.\(^{(4)}\) Stabilizing alveoli and preventing derecruitment with adequate PEEP, measured directly by \textit{in vivo} microscopy, significantly reduce acute lung injury.\(^{(58)}\)

\textit{Over-Distension and Biotrauma}: In a homogenous, stable lung, it is postulated that alveolar OD sufficient to cause VILI histopathology does not exist in the absence of S-R or R/D, unless extremely high airway pressures are delivered. We hypothesize that due to interdependence (Fig 1), alveolar OD can only occur adjacent to collapsed or unstable alveoli.\(^{(42, 55)}\) Mead demonstrated that the shared alveolar walls would be stretched in response to a single over-distended or collapsing alveoli.\(^{(42)}\) We have seen that loss of interdependence (i.e collapse of one or more alveoli) can cause instability and OD of adjacent alveoli, using \textit{in vivo} microscopy. Animation 4 depicts the collapse of a single ‘alveolus’ results in instability and OD of adjacent alveoli, stressing the importance of maintaining a fully recruited lung. Biotrauma occurs secondary to alveolar S-R and R/D-induced tissue trauma causing a release of inflammatory mediators. Thus, VILI will be minimized if both S-R and R/D are blocked. OD of a fully inflated lung can cause airways to rupture (e.g. pneumothorax) if sufficiently elevated yet does not cause lung histopathology typical of VILI.\(^{(56)}\) Alveolar ducts, rather than alveolar sacs, may be the site of OD and the possible site of airway rupture in a heterogeneously ventilated lung.\(^{(36)}\) In summary, VILI is minimized in an open and stable lung, even with high lung volumes and pressures. In summary, VILI has most often been viewed as an alteration of the barrier between the alveolar space and capillary, which is closely associated with an increase in inflammation (Biotrauma). However, physical failure of the load bearing cells and tissues during ventilation is now understood to also play a major role in VILI.\(^{(60)}\)

\textit{Key Points}

- \textit{VILI can occur when the normal, homogenous lung becomes heterogeneous.}
- \textit{The heterogeneous lung is a combination of normal alveoli, alveoli flooded with edema, and unstable alveoli that collapse and reopen during tidal ventilation.}
The primary mechanism of VILI is an alteration of normal dynamic alveolar physiology resulting in excessive alveolar volume change (strain) with each breath.

The secondary mechanism of VILI is alveolar over-distension and generation of inflammatory mediators caused by excessive alveolar strain.

Dynamic changes in alveolar volume

Although a great deal of literature has been devoted to understanding the physiology of normal and abnormal alveolar mechanics (i.e. the dynamic change in alveolar size and shape during tidal ventilation), there is still no consensus on alveolar size change in the normal lung with each breath.(26) It is well accepted that alveolar microanatomy is complex, with alveoli sharing walls in a honeycomb fashion forming a structurally stable design [Fig 1].(42) Due to this alveolar interdependence and to the fact that alveolar walls are only one or two cells thick (a vascular endothelial cell and an alveolar epithelial cell), it is proposed that that alveolar volume change is not simply stretching and contracting, similar to a rubber balloon, although this has never been directly proven with the more likely mechanism being folding and unfolding like a paper bag.(62) The three most logical mechanisms by which alveoli and alveolar ducts can change size during ventilation are: 1) an all or none alveolar opening and closing during each breath, such that there are more open alveoli at inspiration than at expiration, 2) fluctuations in alveolar size owed to crumpling and uncrumpling of alveolar walls, similar to how a paper bag would change volume, and 3) change in the size of the alveolar duct with minimal change in alveolar size.(26, 50)

Alveolar volume change is often perceived to be elastic in nature such that for a given force causing stress (i.e. tidal volume - Vt), alveoli would be expected to change size (i.e. strain) immediately on both inspiration and expiration. However, alveoli do not behave as an elastic structure but, rather, as a viscoelastic system. A viscoelastic system would not exhibit an immediate change in alveolar size during tidal ventilation.(11, 19, 31, 40, 59) The delay in strain following the applied force induced stress is represented graphically as a hysteresis in the stress (σ)/strain (ε) curve. Direct visualization of the whole lung and subpleural alveoli during lung inflation have demonstrated this lag between the time that the Vt force delivers the stress until the time alveoli actually begin to expand or recruit (strain) [Movie 1].(3) Similar assessment of alveolar mechanics and stability have been previously published.(61)
vivo microscopy to is one of the few methods to measure the dynamic change in alveolar size during ventilation in real time it must be remembered that subpleural alveoli are unique in that they are not totally surrounded by alveoli and thus they may inflated or deflate differently than the majority of alveoli that comprise the lung. Also, measuring dynamic inflation and deflation of a single alveolus in an animal ARDS model demonstrated that there was no significant reduction in alveolar size until airway pressure fell from 13mmHg to 6mmHg.(46) A second time lag would be generated by collapsed alveoli with different opening pressure/duration constants such that for ‘sticker’ alveoli would require a higher pressure or longer duration at a pressure would be necessary for recruitment. This would generate a time lag from when the pressure was applied and when the alveolus recruited. Thus \textit{Time} is a critical component in determining alveolar inflation and deflation during each mechanical breath.

\textbf{Alveolar Viscoelasticity – the Spring and Dashpot:} The change in alveolar size with ventilation is complex and has been depicted as viscoelastic in nature. This viscoelasticity has been described on a molecular basis using a mathematical framework.(20, 59) In this paper we will use a very basic model to analyze viscoelastic behavior using a spring attached to a dash in a filled pot. [Animations 5] Using this model the force, which in the case of the lung would be the pressure generated with the Vt, is applied to the tissue represented by the spring and dashpot. In response to this stress Animation 5 shows that in a viscoelastic system such, the spring would move rapidly whereas there would be a significant delay and a much slower movement of the dashpot. Conversely, when the stress is released (expiratory phase of lung ventilation), the spring compresses rapidly followed by a slow reverse strain of the dashpot [Animation 4], Using this spring and dashpot model to describe dynamic alveolar inflation we can postulate that the rate of dashpot movement on both inspiration and expiration could be altered by lung pathology. For example, with loss of surfactant function during ARDS, collapsed alveoli would be very ‘sticky’(25) and thus it would take a great deal of stress over time to recruit them. This would be depicted by a very slow moving dashpot. Once these surfactant depleted alveoli open they would be unstable and derecruit very rapidly during expiration,(28) this would be represented by a fast collapsing dashpot.

Viscoelastic physiology implies that the \textit{Time} at inspiration and expiration is a key MBP parameter that has the potential to ‘\textit{open the lung and keep it open’}.(37) Unfortunately, time has been overlooked in most protective ventilation strategies.(9) An
extended duration at inspiration would apply the pressure to the alveolus for a longer
period of time, gradually ‘nudging’ open alveoli with each breath [Animation 5, Movie 1].
Minimal duration at expiration would quickly release the pressure, allowing for ventilation
and CO₂ removal, but minimize alveolar collapse because the dashpot would not have
time to move [Animation 6]. Using this physiologic knowledge, a mechanical breath that
may better open and stabilize the lung can be constructed.

Considering viscoelasticity as a key component of dynamic alveolar mechanics is
critical when undertaking the design of a mechanical breath that will minimize VILI. Since
the two primary mechanisms of VILI are alveolar R/D and S-R, a protective breath must
be designed to prevent or treat both of these pathologies. Considering that alveoli are
viscoelastic, we postulate that a mechanical breath with an extended inspiratory and
short expiratory duration would recruit alveoli with each breath [Animation 5], as well as
prevent alveolar collapse during expiration [Animation 6]. This would minimize VILI by
reducing both S-R and alveolar R/D [Figs 2,3; Animations 2,3]. Thus, our protective
mechanical breath strategy uses the component of time, in addition to the airway
pressures, volumes and flows being delivered with each breath, to block VILI. If lung
volume increase were slow the corresponding pressure would be near the elastic limit of
the tissue. Higher ventilation rates would generate higher stresses exacerbating tissue
injury and if this were true it would offer a second benefit of the extended inspiratory
duration.

Key Points

• Alveoli do not inflate and deflate in an ideal elastic spring-like fashion (elastic) but
  rather are a viscoelastic system.
• In a viscoelastic system there is a time lag between the time the force (Vt) is
  applied or removed and when the alveolus opens or collapses
• This knowledge of dynamic alveolar physiology suggests that an extended time
  at inspiration would recruit alveoli and a minimal time at expiration would prevent
  alveolar collapse.
• Recruiting alveoli and preventing their collapse would convert the heterogeneous
  lung to homogeneous ventilation and reduce VILI.

Translating Dynamic Alveolar Physiology to the Bedside
The current standard of care protective mechanical ventilation in patients with established ARDS uses low Vt and a sliding scale of PEEP based on oxygenation.(9) This strategy is based on the knowledge that a significant volume of lung is either collapsed or edema filled and thus if a normal Vt was forced into this lung the remaining normal lung tissue would be injured by over-distension. We showed evidence earlier that OD does not occur in the homogeneously ventilated lung and thus it seems a better strategy would be to initially opening the lung, which would eliminate heterogeneous ventilation and stress-risers (33, 43). PEEP would then be applied to keep the newly recruited alveoli open, eliminating the final mechanical mechanism of VILI, that of alveolar R/D. Indeed, this strategy of initially recruiting the ARDS lung has been shown to improve oxygenation and driving pressure without detrimental effects on mortality, ventilator-free days or mortality in a pilot study.(32) In this study a decremental PEEP trial was conducted as the pressure in the recruited lung was decreased in 2cmH_2O increments with the optimal PEEP identified by the best dynamic lung compliance.(32) A meta-analysis has recently shown that this open lung approach significantly reduces the mortality in ARDS patients.(38)

The open lung approach makes sound physiologic sense as a method to minimize the mechanisms of VILI at the alveolar level. Indeed a link has been shown between optimal compliance/elastance and alveolar over-distension and instability in an animal model(6) and the role of driving pressure, which is calculated using compliance, as an indicator of mortality in ARDS patients,(5) However, using compliance/elastance does not take advantage of the viscoelastic component of alveolar inflation and deflation. In theory an extended time at inflation would progressively recruit alveoli and a short time at expiration would prevent alveolar collapse. There are three FDA-approved mechanical breath strategies that incorporate an extended inspiratory and minimal expiratory duration: 1) Inverse inspiratory:expiratory (I:E) ratio,(12, 43) 2) High Frequency Oscillatory Ventilation (HFOV),(22, 66) and 3) Airway Pressure Release Ventilation (APRV).(27, 30) Relatively little study has been directed at inverse I:E in ARDS and the results have been mixed.(12, 43) HFOV has been extensively studied, however recent work has shown that HFOV may increase mortality in ARDS patients,(22, 65) although the reasons for this failure may not be due to the impact of HFOV on alveolar mechanics.(41) The failure of HFOV to reduce mortality may be due to a misdistribution of ventilation in the heterogeneously injured lung.(29) A very specific strategy of personalized APRV(30) has been shown effective at stabilizing alveoli(35, 36) and protecting form the
development of ARDS in a clinically applicable porcine model. In a meta-analysis this personalized APRV strategy significantly reduced ARDS incidence and mortality in a Surgical Intensive Care Unit but has not been tested in a prospective clinical trial. It is also possible that a novel method of multifrequency oscillatory ventilation (MFOV) that would better personalize the HFOV breath to the patient’s lung pathology would improve outcome.

Key Points

- Ventilation strategies that: 1) greatly extend the inspiratory time would continually recruit the alveoli with slow opening time constants and 2) dramatically reduce expiratory duration to a time less than the alveolar collapse time constant, would be lung protective based on our knowledge that dynamic alveolar physiology is viscoelastic in nature.

Conclusions

Although controversy still exists there is strong evidence suggesting that the two primary mechanisms of VILI at the alveolar level are: stress-raisers and repetitive alveolar opening and collapsing. If these primary injury mechanisms are left untreated they will result in a secondary mechanical mechanism of injury, alveolar over-distension. All three mechanical injuries cause inflammation resulting in Biotrauma, which is the forth component of the VILI tetrad. Logic dictates that if a mechanical breath can be applied that eliminates both of these primary VILI mechanisms, lung tissue damage would be significantly reduced. Thus, the goal for protective mechanical ventilation is to ‘open the lung and keep it open’ or if applied early ‘never let the lung collapse’.

The normal lung on mechanical ventilation inflates via increased pressure delivered by the ventilator and deflates passively due to elastic lung recoil. Alveolar inflation and deflation are viscoelastic and thus there is a short but distinct time lag between the time that the force of airway pressure is delivered and time that alveolar inflation occurs. Conversely, there is a distinct time lag between the point that stress is removed during lung deflation and when alveoli begin to collapse. In the acutely injured lung with loss of surfactant function, a longer time is required at inspiration to open alveoli and a much shorter time at expiration to prevent alveolar collapse.
Understanding that alveoli are viscoelastic structures suggests that a greatly extended inspiratory duration would open alveoli and a very short duration at expiration would keep alveoli open. By modifying the time of the applied breath during both inspiration and expiration in an attempt to maintain a homogeneously ventilated lung, the incidence of VILI may be reduced, which may significantly lower the morbidity and mortality associated with ARDS.

Disclosures: PLA, GFN, and NMH have presented and received honoraria and/or travel reimbursement at event(s) sponsored by Dräger Medical Systems, Inc., outside of the published work. PLA, GFN, NMH and LAG have lectured for Intensive Care Online Network, Inc. (ICON). NMH is the founder of ICON, of which PLA is an employee. NMH holds patents on a method of initiating, managing and/or weaning airway pressure release ventilation, as well as controlling a ventilator in accordance with the same, but these patents are not commercialized, licensed nor royalty-producing. The authors maintain that industry had no role in the design and conduct of the study; the collection, management, analysis, or interpretation of the data; nor the preparation, review, or approval of the manuscript.

Legends

Figure 1. Interdependent alveoli with shared alveolar walls represented as hexagons. This homogeneous anatomical design assists in stabilizing alveoli preventing collapse during expiration and over-distension during inspiration, since there is no pressure (arrows) gradient between alveoli (opposing arrows of equal force). Only about a 2% change in alveolar area is measured between inspiration (A) and expiration (B) using in vivo microscopy (Animation 1).8

Figure 2. Heterogeneous alveolar injury depicted as a cluster of collapsed alveoli in the center of the field (H) surrounded by open interdependent alveoli (hexagons). Note the
distortion and over-distension of the patent alveoli adjacent the collapsed alveolar cluster (asterisks), with more over-distension alveoli at expiration (B) as compared with inspiration (A). The large change is size of these alveoli with each breath the larger the dynamic strain-induced tissue damage. These dynamic changes can be seen in Animation 2.

**Figure 3.** Alveoli depicted as hexagons are homogeneously inflated at inspiration (A). Acute lung injury can cause heterogeneous collapse of a group of alveoli during expiration (B, star), while the remaining alveoli remain open. Collapsed alveoli are depicted in the center of the field (B, star). Alveolar instability causes alveoli to open (A, all alveoli homogeneously recruited) and collapse (B, central alveoli collapse causing heterogeneous ventilation) with each breath. Alveolar instability results in excessive dynamic shear stress on alveolar walls of the unstable alveoli (B, star). In addition, alveoli adjacent to the collapsing area are over-distended during expiration with significant dynamic strain during each breath (arrows). These dynamic changes can be seen in Animation 3.

**Animations:**

**Animation 1.** Normal homogeneous alveolar ventilation with interconnected alveolar walls (hexagons) and approximately a 2% change in alveolar areas measured by *in vivo* microscopy (unpublished observations). This interdependent alveolar design with each alveolus sharing a wall with the adjacent alveolus renders alveoli very resistant to over-distension or collapse since there is equal pressure across alveolar walls. Loop the animation for the optimal effect.

**Animation 2.** In a heterogeneous lung injury, which is typical in ARDS, stress-concentrators develop around areas of collapsed alveoli seen in the center of the field. Note how the patent alveoli (hexagons) adjacent to the collapsed alveoli change volume greatly with each breath (i.e. high dynamic strain) and are much larger than normal resulting in over-distension. Also of interest is that patent alveoli adjacent to collapsed alveoli are over-distended to the greatest extent during expiration. Loop the animation for the optimal effect.
Animation 3. Alveoli can become unstable follow with acute lung injury resulting in alveolar collapse during expiration and reopening during inspiration. Alveoli in the center of the animation are unstable and recruit and derecruit with each breath. This causes shear stress-induced cellular damage secondary to a high dynamic strain. Note that patent alveoli adjacent to collapsing alveoli over-distend during expiration. Loop the animation for the optimal effect.

Animation 4. In our ‘spring and dashpot’ model of dynamic alveolar physiology the applied force (i.e. tidal volume) generating the stress is depicted by the Red-T moving up (inflation) or down (deflation). The Red-X represents the time at inspiration (top of cycle) and at expiration (bottom of cycle). The resultant strain caused by this stress is not linear but has a fast (Spring) and slower (Dash in the pot) component. Note if the applied force is held (Red-X at the top of the cycle) during inflation, the spring component rapidly reaches maximum whereas the dash in the pot component continues to rise slowly without additional force being added. With release of the force reducing the stress, the spring component rapidly collapses, with a significant time lag before the dash in the pot component begins to move and this movement continues slowly even after the stress is totally released (Red-X at bottom of the cycle). Loop the animation for the optimal effect.

Animation 5. Using our ‘spring and dashpot’ model to assess the impact of inspiratory time on dynamic alveolar inflation. There is a slow continual inflation, represented by the dash in the pot movement, as long as the lung is at peak inspiration (Red T at the top of the cycle). The green circle turning red represents the duration of the applied force (tidal volume), which is held at peak inspiration (large red arrow) for an extended period of time. The dash in the pot continues to move slowly even though the force remains constant. This suggests that the longer the force can be applied during each breath (i.e. the longer the inspiratory time) the more alveoli that will be recruited. Loop the animation for the optimal effect.

Animation 6. Using this ‘spring and dashpot’ model to assess the impact of expiratory time on dynamic alveolar deflation. If the force (i.e. tidal volume) represented by the Red-T is released from peak inspiration (top of cycle) and then reapplied after a very short time at expiration (bottom of cycle) the dash in the pot does not have sufficient time...
to move. The green circle turning red represents the short duration of expiration, which ends before the dash in the pot has time to move (green check mark over the circle). This suggests that a very short expiratory duration would prevent alveolar collapse. Loop the animation for the optimal effect.

Movies:

Movie 1. An excised rat lung with Tween-induced ARDS. The heterogeneous injury can be seen as areas of dark red collapsed lung tissue and areas of normally inflated lung, which are pink in color. The lung is being exposed to a recruitment maneuver of 40cmH$_2$O for 40 seconds. Note that although the pressure does not change (40cmH$_2$O airway pressure applied immediately and not changed) that alveoli continually recruit (tissue changes from dark red to pink) for the full 40 seconds. This demonstrates the time dependency of alveolar recruitment (Copied with permission). Loop the movie for the optimal effect.


