The transient relationship between pressure and volume in the pediatric pulmonary system

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ARTICLE INFO

Article history:
Accepted 16 April 2009

Keywords:
Respiratory mechanics
Mathematical models
Structural models
Nonlinear models

ABSTRACT

An accurate understanding of the relationship between pulmonary pressure and volume is required for modeling pulmonary mechanics in a variety of clinical applications. In this study the experimental techniques and mathematical formulations used to characterize viscoelastic materials are applied to characterize transient pulmonary compliance in juvenile swine. Fixed volumes of air were insufflated into 5 swine and held constant for 45 s while the transient decay in tracheal pressure was measured. An analytical model was developed using an optimization scheme that maximized the model fit to the experimental data over the entire time convolution. The initial injected volume was varied to assess the spatial and temporal linearity of the behavior. Model performance was assessed by comparing measured and predicted pressure during insufflations of erratic volume waveforms. It is concluded that the pulmonary impedance of healthy juveniles can be adequately described over a wide volume and frequency range using a relatively simple 5-parameter model that is linear both spatially and temporally.

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1. Introduction

General characteristics of pulmonary pressure/volume curves have been long known (e.g. Mount, 1955; Radford, 1964). Pulmonary response changes with both anatomical and physiological parameters (e.g. Grossman et al., 1980), so alterations in mechanical pulmonary response, interpreted in the context of a heuristic or mechanistic model, have been studied as an indicator of pulmonary system pathology (cf. Cook et al., 1959; Matamis et al., 1984; Jonson and Svantesson, 1999). The lung has commonly been described on a system level with simple mechanical models or their electrical analogues (e.g., D’Angelo et al., 1991; Milic-Emili et al., 1990; Jonson et al., 1993; Kaditis et al., 1999, see Fig. 1) or by simple heuristic models (e.g. Hantos et al., 1992). The results obtained using these models provide a qualitative understanding of the properties of the lung and thorax during positive ventilation and passive exhalation.

Existing models have not, however, been validated over multiple respiratory cycles or for long-time transient responses, nor do they fully account for rate and frequency effects in pressure–volume histories of general pulmonary response (Nicolai et al., 1993). This limits understanding of rate effects such as pressure–volume hysteresis (c.f. Suki and Bates, 1991). Suki and Bates (1991) developed a nonlinear model based on a Volterra series and stated “nonlinear and frequency-dependent aspects of lung tissue mechanics can lead to quite a marked disparity between estimates of lung tissue resistance and elastance at a given frequency provided by different analysis techniques”. Their study does not, however, robustly show that a nonlinear model is required to capture the relevant mechanics. There are obvious benefits if simpler models can be used. The current study investigates the frequency-dependent pulmonary response of pediatric pigs ranging from functional lung inhalation volume (15 mL/kg) through total lung volume inhalation (40 mL/kg) with particular focus on the model complexity required to capture the relevant mechanics.

2. Methods

The study protocol was approved by the University of Virginia Animal Care and Use Committee. Five swine having an average whole-body mass of 23.4 kg (standard deviation 2.04 kg) were obtained for study. The trunk of these animals was similar in size to that of a 6-year-old human (Kent et al., 2006). The animals had no oral intake for at least 8 h prior to testing. Animals were sedated with a continuous infusion of propofol prior to instrumentation. Upon arrival in the laboratory, deep sedation was initiated and maintained throughout the procedure using a continuous thoracal infusion (20–30 mg/kg/h). The animals were maintained at a level of sedation where no spontaneous respirations were detected visibly or with the pressure transducers and the animals had no response to painful stimulation. Thus, the study was not impacted by any muscle

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doi:10.1016/j.jbiomech.2009.04.027
contraction of the animal. The animals were intubated and maintained on a
volume-cycled ventilator. Dextrose containing intravenous fluids were adminis-
tered at a maintenance rate during the experiment preparation. Animals were
monitored with continuous cardiac monitoring and pulse oximetry for the
duration of the experiment. A pressure transducer (model SPR-524, Millar
Instruments, Houston TX) was placed inside the endotracheal tube (Fig. 2). The
balloon on the endotracheal tube was filled with air to a pressure where no leak
occurred around the balloon. All animals received 1 mg/kg of lidocaine prior to the
procedure to minimize the risks of ventricular arrhythmias due to hypoxia or
acidosis during the experiment.

For the study protocol a fixed volume of room air was injected into the
endotracheal tube using a calibrated syringe with a linear potentiometer mounted
to measure the displacement of the plunger. Since the cross-sectional area of the
syringe was constant and known, the injected volume could thus be calculated as a
function of time. The pressure and plunger displacement data were sampled
continuously at 1 kHz using National Instruments PCI-6110E data acquisition
boards and a LabView software interface.

To initiate each pulmonary characterization study, the animal was taken off
the ventilator at maximum inhalation and allowed to passively reach end
exhalation. The calibrated syringe was then used to insufflate a known volume
of air into the endotracheal tube, after which the endotracheal tube was clamped
to maintain a constant volume of air in the pulmonary system. This constant
volume was maintained for a nominal duration of 45 s, during which the transient
decay in tracheal pressure was measured. Multiple volumes of air were insufflated
so that temporal and spatial linearity could be assessed. Following the series of
ramp-hold tests on each animal, an erratic volume waveform was insufflated while
pressure was measured.

A trial was halted and resuscitation efforts were initiated if the animal's heart
rate dropped to 75% of the initial heart rate, or if the O2 saturation fell to below
75%. Following each trial, the animal was given time to stabilize on the ventilator,
and then the protocol restarted again at the next magnitude of injected volume.

After completion of the entire testing procedure, animals were euthanized using a
pentobarbital solution.

3. Model development

Biological tissues are generally viscoelastic. Thus, the entire
time history of strain, \( \varepsilon(t) \), affects the stress, \( \sigma(t) \), in the tissue. This
is reflected in a range of mechanical behaviors, including rate
sensitivity, hysteresis, stress relaxation, and creep and can be
described using a material model with a time-varying elastic
modulus, \( E(t) \)

\[
\sigma(t) = \int_{t}^{\infty} E(t - \tau) \frac{d\sigma(t)}{dt} dt. \quad (1)
\]

Furthermore, the relationship between stress and strain in
biological tissues is typically nonlinear for finite deformations.
This spatial nonlinearity is not captured by the linear viscoelastic
model of Eq. (1), so Fung (1993) proposed a quasilinear (QL)
theory that, while not completely general (Lakes, 1999), does
describe experimental observations of a variety of biological
materials and structures. In this theory, the nonlinearity of the
spatial behavior is assumed to be separable from the linear time-
dependent part. Boltzmann’s principal of superposition then
yields a convolution integral

\[
\sigma(t) = \int_{t}^{\infty} G(t - \tau) \frac{d\sigma(t)}{dt} dt \quad (2)
\]

where \( G(t) \) is a monotonically decreasing reduced relaxation
function and \( \sigma_d(\varepsilon) \) is an instantaneous elastic function, which may
have a nonlinear form.

The mathematical formulations of Eqs. (1) and (2), nominally
developed to describe the relationship between stress and strain,
have been adapted to describe transient structural behaviors
(e.g., Funk et al., 2000; Kent et al., 2003; Lucas et al., 2008) and
is a convenient formulation for characterizing the relationship
between the volume of air in the pulmonary system and the
resulting tracheal pressure. For a step increase in air volume, the
tracheal pressure exhibits decay phenomenologically identical to
the stress relaxation that results from a step in strain to a
viscoelastic material, and over a cycle of injected volume the
pressure–volume curve exhibits pronounced hysteresis. For this
study the model of Fung was adapted to

\[
P(t) = \int_{t}^{\infty} G(t - \tau) \frac{\partial P_d(V)}{\partial V} \frac{\partial V(t)}{\partial t} dt, \quad (3)
\]

where \( P(t) \) is the transient change in pressure measured by
the tracheal transducer, \( V(t) \) is the volume of air injected into the
pulmonary system after passive exhalation, and \( P_d(V) \) is the

\[
\begin{align*}
\frac{1}{k_\infty} &+ \frac{1}{k_1} + \frac{1}{k_2} = \frac{1}{c_1} + \frac{1}{c_2}, \\
V, P &+ k_\infty = c_1, \\
V &+ k_1 = c_2, \\
V &+ \infty = k_2.
\end{align*}
\]

\( G(t) = \frac{1}{t} e^{\frac{-t}{\tau}}, \) affects the stress,
\( \sigma_d(t) \), in the tissue. This

\[
\text{Fig. 1. Viscoelastic model of lung (D'Angelo et al., 1991; Milic-Emili et al., 1990;}
\text{Kaditis et al. 1999). The independent variable is lung volume, and the dependent}
\text{variable is lung pressure.}
\]

\[
\text{Fig. 2. Schematic of experimental setup.}
\]
function describing the pressure response to a step increase in volume.

For this study, the reduced relaxation function was described as the Prony series

\[ G(t) = \sum_{i=1}^{n} G_i e^{-\Delta t_i} + G_\infty, \]

where \( \beta_i \) are time constants with associated weights \( G_i \) and \( G_\infty \) defines the steady-state response. The maximum value of the reduced relaxation function occurs at time \( t = 0 \) and is equal to

\[ \sum_{i=1}^{n} G_i + G_\infty = 1. \]

Both linear and nonlinear equations were considered for \( P_i(V) \).

The linear model had a single coefficient

\[ P_i(V) = A^* \cdot V, \]

while the QL model used an exponential form of the instantaneous elastic function

\[ P_i(V) = A e^{B V} - 1. \]


4. Parameter identification

A set of parameters was identified for each ramp-hold volume of air insufflated into each animal. The experimental data were filtered using a 60-Hz low-pass 8-pole Butterworth filter and a numerical convolution scheme was used to solve simultaneously for the model coefficients that best fit the experimental data. The numerical convolution can be developed by combining Eqs. (3) and (4), discretizing the time step, and stepping forward in time to determine at each time step the steady-state component of the pressure, \( P_\infty \), and the transient component, \( P_i \),

\[ P_\infty(t + \Delta t) = P_\infty(t) + G_\infty [P_i(t + \Delta t) - P_i(t)], \]

and the transient component, \( P_i \),

\[ P_i(t + \Delta t) = \xi_i P_i(t) + (1 - \xi_i) \left( \frac{G_i}{\Delta t} \right) \left( \frac{P_i(t + \Delta t) - P_i(t)}{\Delta t} \right), \]

where

\[ \xi_i = e^{-\beta_i \cdot \Delta t}. \]

The total change in pressure at each time point is then the sum

\[ P_i(t) = P_\infty(t) + \sum_{i=1}^{n} P_i(t). \]

Several values of \( n \) were investigated to identify the required model complexity. The generalized reduced gradient nonlinear optimization scheme employed by the Microsoft Excel Solver was used to solve simultaneously for the parameters (\( A^* \) or \( A^* \), \( B \), \( G_\infty \), \( \beta_1 \), \( G_\infty \)) that maximized the model fit to each experiment. The objective function to minimize was the sum of the squared error between the measured pressure and the model-predicted pressure over the entire time history.

5. Model assessment

An erratic volume waveform was generated manually by depressing and extending the syringe plunger in an erratic pattern. The animal-specific model was used to calculate the output pressure (Eq. (3)). This calculated pressure was compared to the measured pressure–time history to assess the model's ability to predict the response to an input volume waveform containing a range of frequencies and having characteristics much different than the ramp-hold waveform used to develop the model coefficients. Further a test of temporal linearity was performed by fitting models to the same animal with different magnitudes of insufflated volume.

6. Results

A typical set of experimental data (Tests 5.1, 5.2, and 5.3) is shown in Fig. 3. Two input ramp–hold waveforms with the resulting pressure used for parameter identification are shown. The bottom set of plots shows the erratic input volume waveform and the resulting pressure history used to assess model performance. Fig. 4 shows the pressure–volume cross-plots for a parameter identification test and for a model assessment test. The complete test matrix with maximum measured values is shown in Table 1.

It was found that a fully linear model with two time constants \( (n = 2) \) represented the pressure response well over the convolution of the entire time history, with a mean correlation coefficient \( (R^2) \) of 0.890 for all model fits (Table 2). The QL model generated virtually identical correlations. A typical model fit is shown in Fig. 5. The two time constants identified in the optimization were approximately 2 orders of magnitude apart, with the higher-rate time constant, \( \beta_1 \), averaging 34.8 s\(^{-1} \) for all model fits and the other time constant, \( \beta_2 \), averaging 0.079 s\(^{-1} \). The coefficient associated with \( \beta_1 \) was much greater \( (G_1 = 0.816 \pm 0.110) \) than the coefficient associated with \( \beta_2 \) \( (G_2 = 0.080 \pm 0.029) \), indicating pronounced pressure relaxation early in the event, well before the insufflation was complete. The long-time relaxation was substantial, with the steady-state pressure only approximately 10% of the instantaneous response \( (G_\infty = 0.104 \pm 0.092) \). The proportionality constant relating instantaneous pressure and volume was found to be reasonably consistent among subjects \( (A^* = 0.150 \pm 0.060 \text{ cmH}_2\text{O mL}^{-1}) \).

7. Model assessment

In all cases, the model coefficients based on the ramp-hold tests predicted well the same animal's response to an erratic waveform \( (R^2 = 0.875 \text{ average over all tests}) \). The measured pressure response to the erratic volume input waveforms, with the corresponding model-predicted responses, are shown in Fig. 6.

The assessment of temporal linearity revealed slight dependence of \( G(t) \) on the insufflation volume. The coefficient associated with the short time constant, \( G_1 \), was slightly smaller for the larger volume insufflations (average of 0.756) than for the smaller volumes \( (0.888, p = 0.05) \), and the coefficients associated with the long-time response were greater. The coefficient \( G_2 \) increased from 0.060 to 0.100 \( (p = 0.03) \) and \( G_\infty \) increased from 0.052 to 0.148 \( (p = 0.08) \) (Fig. 7). These variations have minimal effect on the resulting model.

8. Discussion

This study developed a time-dependent mechanical model for predicting tracheal pressure from insufflation volume using a porcine model of the pediatric chest. Experimental and analytical methods commonly applied to the development of viscoelastic material models were adapted for this application. This allowed for an assessment of required model complexity, both in terms of
linearity and the number of coefficients necessary for capturing the behavior adequately. A quasilinear (QL) formulation was considered, and the number of required time constants was minimized to retain model applicability over a range of input frequencies while generating the simplest model. A linear model, containing only 5 parameters, can be used to adequately model pulmonary compliance over a frequency range likely to encompass any clinical application and over a range of inhalation...
volumes up through total lung capacity. The model strength is highlighted in its ability to predict tracheal pressure during an erratic insufflation of air.

Mechanical models of the pulmonary system have been studied by Bates et al. (e.g. D’Angelo et al., 1991; Milic-Emili et al., 1990), among others, and have been represented as shown in Fig. 1 by a spring and a dashpot in parallel with a Maxwell element with a single time constant \( t = c_1/k_1 \). The isolated dashpot \( c_2 \) may be interpreted as a Maxwell element with an infinitely large spring constant (so that \( t \approx 0 \)). The parameters in these models have been estimated using pressure response to volumetric step inputs and constant flow inputs. For respiratory response in anesthetized children, Kaditis et al. (1999) found different estimates of model parameters than those seen in adults (D’Angelo et al., 1991). Further, this model has been used to characterize the simple viscoelastic response of young and adult pigs (De Robertis et al., 2001) and static to slow dynamic response in pigs (Bitzen et al., 2004).

<table>
<thead>
<tr>
<th>Test no.</th>
<th>Subject</th>
<th>Test type</th>
<th>Max. insufflated volume (mL)</th>
<th>Max. tracheal pressure (cmH₂O)</th>
<th>Time to max. volume and pressure (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1</td>
<td>03-P-1</td>
<td>1</td>
<td>812.7</td>
<td>26.3</td>
<td>0.41</td>
</tr>
<tr>
<td>5.2</td>
<td>03-P-1</td>
<td>1</td>
<td>400.1</td>
<td>13.0</td>
<td>0.22</td>
</tr>
<tr>
<td>5.3</td>
<td>03-P-1</td>
<td>2</td>
<td>809.7</td>
<td>25.5</td>
<td>0.46</td>
</tr>
<tr>
<td>5.16</td>
<td>03-P-2</td>
<td>1</td>
<td>652.2</td>
<td>19.5</td>
<td>0.39</td>
</tr>
<tr>
<td>5.17</td>
<td>03-P-2</td>
<td>1</td>
<td>314.9</td>
<td>11.5</td>
<td>0.22</td>
</tr>
<tr>
<td>5.19</td>
<td>03-P-2</td>
<td>2</td>
<td>664.4</td>
<td>28.3</td>
<td>0.53</td>
</tr>
<tr>
<td>5.32</td>
<td>03-P-3</td>
<td>1</td>
<td>333.1</td>
<td>14.3</td>
<td>0.24</td>
</tr>
<tr>
<td>5.33</td>
<td>03-P-3</td>
<td>1</td>
<td>647.0</td>
<td>27.6</td>
<td>0.25</td>
</tr>
<tr>
<td>5.62</td>
<td>03-P-6</td>
<td>1</td>
<td>320.1</td>
<td>17.5</td>
<td>0.15</td>
</tr>
<tr>
<td>5.77</td>
<td>03-P-6</td>
<td>1</td>
<td>649.8</td>
<td>36.9</td>
<td>0.24</td>
</tr>
<tr>
<td>5.78</td>
<td>03-P-6</td>
<td>1</td>
<td>319.0</td>
<td>21.5</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Table 1
Test matrix and selected maxima.

Table 2
Model coefficients.

<table>
<thead>
<tr>
<th>Test No.</th>
<th>( G_1 )</th>
<th>( G_2 )</th>
<th>( G_\infty )</th>
<th>( A^* ) (cmH₂O mL⁻¹)</th>
<th>( \beta_1 ) (s⁻¹)</th>
<th>( \beta_2 ) (s⁻¹)</th>
<th>( R^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.1</td>
<td>0.676</td>
<td>0.118</td>
<td>0.206</td>
<td>0.063</td>
<td>12.354</td>
<td>0.088</td>
<td>0.991</td>
</tr>
<tr>
<td>5.2</td>
<td>0.857</td>
<td>0.048</td>
<td>0.094</td>
<td>0.156</td>
<td>47.195</td>
<td>0.063</td>
<td>0.986</td>
</tr>
<tr>
<td>5.16</td>
<td>0.819</td>
<td>0.059</td>
<td>0.122</td>
<td>0.136</td>
<td>50.157</td>
<td>0.358</td>
<td>0.894</td>
</tr>
<tr>
<td>5.17</td>
<td>0.842</td>
<td>0.089</td>
<td>0.068</td>
<td>0.139</td>
<td>45.020</td>
<td>0.071</td>
<td>0.875</td>
</tr>
<tr>
<td>5.18</td>
<td>0.906</td>
<td>0.075</td>
<td>0.019</td>
<td>0.192</td>
<td>56.723</td>
<td>0.027</td>
<td>0.579</td>
</tr>
<tr>
<td>5.32</td>
<td>0.792</td>
<td>0.072</td>
<td>0.136</td>
<td>0.102</td>
<td>9.759</td>
<td>0.029</td>
<td>0.947</td>
</tr>
<tr>
<td>5.33</td>
<td>0.898</td>
<td>0.077</td>
<td>0.025</td>
<td>0.205</td>
<td>50.756</td>
<td>0.065</td>
<td>0.619</td>
</tr>
<tr>
<td>5.62</td>
<td>0.859</td>
<td>0.111</td>
<td>0.030</td>
<td>0.167</td>
<td>21.852</td>
<td>0.028</td>
<td>0.987</td>
</tr>
<tr>
<td>5.63</td>
<td>0.886</td>
<td>0.064</td>
<td>0.050</td>
<td>0.216</td>
<td>30.617</td>
<td>0.043</td>
<td>0.984</td>
</tr>
<tr>
<td>5.77</td>
<td>0.551</td>
<td>0.126</td>
<td>0.323</td>
<td>0.052</td>
<td>7.075</td>
<td>0.064</td>
<td>0.960</td>
</tr>
<tr>
<td>5.78</td>
<td>0.893</td>
<td>0.038</td>
<td>0.069</td>
<td>0.227</td>
<td>51.578</td>
<td>0.039</td>
<td>0.967</td>
</tr>
</tbody>
</table>

Avg. ± S.D. | 0.816 ± 0.110 | 0.080 ± 0.029 | 0.104 ± 0.092 | 0.150 ± 0.060 | 34.8 ± 19.0 | 0.079 ± 0.095 | 0.890 ± 0.149 |

Fig. 5. Model fit (bold line) to experimental data (typical, test 5.78 shown). Long (left) and short (right) time windows are shown.
The linear model of the current study can be expressed as a discrete lumped-parameter model with constant coefficients with a form as shown in Fig. 1 and compared with the pediatric model of Kaditis et al. (1999) (Table 3). One characteristic of the Kaditis model, and the models of Bates et al. (1985), is that the presence of the isolated dashpot introduces a Dirac delta function into the model’s transfer function. The effect of this can be illustrated by inputting a 400-mL peak, 2-Hz triangular waveform to both the Kaditis model and the model developed here. The Kaditis model predicts an instantaneous pressure rise initially and an instantaneous drop when the volume input peaks. According to Suki and Bates (1991), lung “pressure–volume data do not show any features that could be described mathematically as discontinuities”. In contrast to the Kaditis model, the model developed here generates a more realistic onset by placing a spring with finite stiffness in series with the dashpot (Fig. 8a). Another important difference between the models can be illustrated by applying a sinusoidal volume waveform of the form

$$V(t) = B \sin(2\pi \omega t - \pi/2) + B$$

(12)

to both over a frequency range from $\omega = 0.01$ to 2 Hz where $B = 200 \text{ mL}$. As shown in Fig. 8b, both the current model and the Kaditis model exhibit rate sensitivity and hysteresis, and at frequencies around 1 Hz the models are similar. There are, however, important divergences at higher and lower frequencies. First, the Kaditis model predicts less rate sensitivity.

Fig. 6. Model assessment using erratic volume inputs (dashed line) to compare model-predicted pressure (bold solid line) to measured pressure (thin solid line).

Fig. 7. Trends in relaxation function coefficients as an assessment of temporal linearity using repeated trials with different insufflation volumes on the same animal.
Over the range from 0.01 to 2 Hz, the pressure at peak volume increases by only approximately 20% in the Kaditis model, while it nearly doubles in our model. Second, the Kaditis model predicts virtually no hysteresis at 0.01 Hz, while our model exhibits pronounced dissipation even at this low frequency. The isolated dashpot in the Kaditis model provides no pressure relaxation for a constant volume (the associated time constant is zero), and the time constant associated with the Maxwell element in the Kaditis model is 0.75 s. Thus, the model reaches a steady-state response faster than does the pulmonary system. This can be illustrated by fitting the Kaditis model to the porcine pressure–relaxation data from our experiments. Fig. 8c shows the Kaditis model fit to our data from test 5.78. It is apparent that pressure relaxation occurs over a longer time regime than that captured by the Kaditis model. Despite these limitations in the model, however, our data confirm that the Kaditis model predicts the pressure response.

Table 3
Discrete model parameters compared to those in the literature.

<table>
<thead>
<tr>
<th>Subject mass (kg)</th>
<th>k₁ (cmH₂O/mL/kg)</th>
<th>k₂ (cmH₂O/mL/kg)</th>
<th>c₁ (cmH₂O/mL/s kg⁻¹)</th>
<th>c₂ (cmH₂O/mL/s kg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study*a</td>
<td>23.4±2.0</td>
<td>0.365</td>
<td>2.865024</td>
<td>0.280986</td>
</tr>
<tr>
<td>D’Angelo*b (Adults)</td>
<td>64.8</td>
<td>0.49–0.56</td>
<td>0.15±0.05 (IV)</td>
<td>0.17±0.03 (IF)</td>
</tr>
<tr>
<td>Kaditis (Children)</td>
<td>15.0±2.8</td>
<td>0.47–0.63</td>
<td>0.12</td>
<td>0.088</td>
</tr>
</tbody>
</table>

*a Average coefficients listed on Table 2, restated in terms of a lumped parameter model and scaled by subject mass, as proposed by D’Angelo et al. (1991) and Kaditis et al. (1999).
*b IF: isoflow conditions; IV: isovolume conditions.

Fig. 8. Assessment of Kaditis model relative to the model developed in this paper. (a) Model responses to a 400-mL peak, 2-Hz triangular waveform; (b) Lissajous curves for the model developed here (left) and the Kaditis model (right). Input is 3 cycles of the sine wave of Eq. [12]; (c) Kaditis model compared to measured long-time relaxation behavior.
very well for input frequencies around 1 Hz and is therefore adequate for many clinical applications. We did not identify significant spatial or temporal nonlinearities over the range of conditions considered here. Indeed, the repeatability of the response and the response for random variable insufflation histories argues against nonstationarity of systemic response. This does not imply, however, that the constitutive behavior of lung tissue does not contain pronounced nonlinearity. Most biological materials exhibit nonlinearity at finite strains, and the complex micro- and macro-structure of lung tissue suggests that it is in this class of materials. For example, a recent study of lung contusion due to blunt impact (Stitzel et al. 2005) employed a nonlinear constitutive model in a finite element simulation of staged impacts to rat lung. It appears from our experiments, however, that even large values of insufflation volume either do not strain the lung tissue sufficiently to generate significant nonlinearity, or are dominated by gross structural mechanics that are sufficiently linear as to mask any nonlinearity in the material behavior. The insufflation volumes used in this study did include values quite high relative to normal respiration for these swine, as evidenced by the fact that venous return was severely hampered during the hold portion of the tests involving larger volumes. Therefore, even if the lung material is nonlinear at finite strains, it appears that a relatively simple linear model of tracheal pressure as a function of insufflation volume can capture the behaviors likely to be of interest in most clinical settings. These long-time behaviors include recruitment and de-recruitment of lung elements during insufflation and apneia, and other physiology and gas mechanics. There may be, of course, higher-order phenomena associated with some pathologies, and more complex models may reveal factors that aid in diagnosis. The work here has focused only on healthy subjects of similar weight. Further study will be necessary to describe how the parameter values or overall model response change across various species, sizes, lung pathologies, and thoracic and abdominal pathologies.

Another limitation of this study is the neglect of any change in air volume in the lungs due to gas exchange. An estimate of the volume change during the hold portion of our input waveform can be made using results from human breath holding experiments (Parkes, 2006). For breath holding, gas exchange results in lung contraction as buildup of alveolar CO2 removes the partial pressure gradient driving CO2 exchange, so the O2 extracted is not replaced by an equal molar volume of CO2 (Hong et al. 1971) found a lung volume decrease of 145 mL (2.6%) over 45 s of breath holding in nine subjects with 5450 ± 305 mL total lung volume. This suggests that the effect of lung volume change owing to gas exchange in our experiments was small.

9. Conclusions

This paper has presented an experimental and analytical framework for characterizing pulmonary mechanics. The framework is based on a viscoelastic and nonlinear model often used to describe the constitutive behavior of biological materials. This framework was applied to 5 healthy juvenile swine to identify the simplest model that could describe a range of behaviors. It was found that the relationship between insufflated volume and tracheal pressure could be modeled over a wide range of frequency (0 Hz up to approximately 35 Hz) and volume magnitude (0 to ~40 mL/kg) using a linear viscoelastic model with two time constants (5 total model parameters). This relatively simple model accurately described the measured response to ramp-hold and erratic applied volume waveforms, and, in contrast to an existing linear model, generated realistic tracheal pressure responses to both triangular and sinusoidal input volumes.

Conflict of interest statement

No author has a conflict of interest.

Acknowledgements

Dr. Sanford Feldman, Jeremy Gatesman, and Gina Wimer at the UVA Center for Comparative Medicine for their tireless assistance and expertise. Funding sources: US Department of Transportation, University of Virginia Department of Emergency Medicine faculty development grant.

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