Detecting lung overdistention in newborns treated with high-frequency oscillatory ventilation

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LUNG OVERDISTENTION HAS BEEN implicated in the development of chronic lung disease (CLD), such as bronchopulmonary dysplasia, air leaks, and cardiovascular depression, in infants with respiratory failure who require mechanical ventilation (9, 13, 31, 32). Several studies show that prolonged conventional ventilation with tidal breathing in newborn infants can lead to lung injury that can subsequently progress to CLD (6, 11, 21, 30, 41).

High-frequency oscillatory ventilation (HFOV) is an alternative mode of ventilation believed to reduce the incidence of CLD in some infants (10). HFOV uses nontidal ventilation to effect gas exchange, whereas alveolar volume is recruited and maintained by positive mean airway pressure (Paw). However, if Paw settings exceed optimal values, lung overdistention can occur with undesirable effects, such as pneumothorax, pulmonary interstitial emphysema, and CLD, as well as reduced oxygen delivery to the tissues as a result of cardiovascular depression (12, 18, 19). Moreover, the optimal Paw is itself dependent on the underlying lung mechanics, which vary with the disease process and treatments.

Therefore, a method that (1) can accurately measure changes in lung volume (ΔVl) during HFOV and (2) is sufficiently practical to allow repeated assessments in infants would be useful for clinicians managing infants with HFOV. A number of candidate methods have been investigated in the past; however, no clinically applicable method has been described to date (8, 36, 40).

Respiratory inductance plethysmography (RIP) is commonly used to assess breathing synchrony, tidal ventilation, and respiratory rate in infants (25–27, 38, 39). If direct current (DC) coupled, RIP is also able to...
continuously measure changes in static lung volume (ΔVL); i.e., changes above functional residual capacity (FRC; Refs. 7, 27, 42). The noninvasive nature of RIP and its ease of application make it especially attractive for use in critically ill neonates on HFOV. However, the accuracy of measuring Paw-induced ΔVL by using RIP has not been verified nor has a method to interpret such data been described.

The goals of this study were 1) to test whether RIP provides accurate, continuous estimates of Paw-induced ΔVL during HFOV and 2) to describe, if RIP is accurate, a method of how it may be used in clinical settings to detect and avoid lung overdistention. Here, we speculated that the Paw-ΔVL and compliance-ΔVL relationships derived from RIP data allow identification of the optimal Paw. Toward this end, we compared simultaneous whole body plethysmography and RIP measurements of ΔVL over a wide range of Paw settings in piglets with healthy and surfactant-deficient lungs.

**MATERIALS AND METHODS**

Measurements were done in five newborn piglets (age 6–15 days, weight 2.2–4.2 kg) under healthy and diseased (experimental surfactant deficiency) conditions. The animal protocol was approved and monitored by the Institutional Animal Care and Use Committee according to National Institute of Health Guide for the Care and Use of Laboratory Animals.

**Model Preparation**

Piglets were initially anesthetized with an intramuscular injection of ketamine hydrochloride (14 mg/kg). Anesthesia was maintained with pentobarbital sodium, and pancuronium bromide (0.1 mg/kg) was used to induce and maintain paralysis. Animals were placed supine on a warming blanket to maintain rectal temperature between 38 and 40°C. We inserted catheters into the animal's carotid artery to enable blood-gas sampling, medication delivery, and blood pressure monitoring. We cannulated the jugular vein for continuous infusion of fluids. A 3.0-mm (ID) endotracheal tube was inserted via tracheostomy to a depth of 4 cm. Controlled mechanical ventilation (CMV; Bear Cub Infant Ventilator, BP 2001, Bear Medical Systems, Riverside, CA) with peak inspiratory pressure of 12–15 cmH2O, positive end-expiratory pressure (PEEP) of 2–3 cmH2O, breathing rate of 40–50 breaths/min, inspiratory time of 0.5 s, and inspired O2 fraction (FiO2) of 1.0 was used to induce and maintain paralysis. As before lavage, initial Paw was maintained with pentobarbital sodium, and pancuronium bromide (0.1 mg/kg) was used to induce and maintain paralysis.

**Data Acquisition and Analysis**

RIP volume data was computed from the sum of the rib cage and abdominal data. Each was sampled at 50 Hz and collected by using the Somnostar PT (model 105–042–01, SensorMedics). Changes in plethysmograph pressure (Pplefth) were similarly sampled and collected by using an auxiliary analog channel on the Somnostar. These were then used to indicate absolute ΔVL on the basis of a linear calibration. Plethysmograph and RIP measurements were simultaneously calibrated by using a five-point (0, 10, 20, 30, and 40 ml) volume calibration before each change in Paw (Fig. 1). A sufficient interval of time was allowed to elapse between consecutive volume injections to allow for a semblance of a plateau in both RIP and Ppleth. Ppleth and RIP data were adjusted by their respective calibration factors to provide volume data in milliliters.
An example of ΔVt data in a healthy piglet measured with both methods in response to a Paw of 14 cmH2O is shown in Fig. 1. Before analysis, these data were digitally low-pass filtered (characteristic frequency $\approx 2$ Hz, $\approx 92$ dB Blackman) to remove the superimposed oscillatory ventilation effects on both signals (MP 100, BioPac Systems, Santa Barbara, CA) as illustrated in Fig. 1. Accuracy of transient and steady-state ΔVt estimated by RIP ($\Delta V_{LRIP}$) was then verified as follows.

**Transient volume changes.** We compared the time-dependent rise in lung volume $[\Delta V_l(t)]$ as estimated by RIP $[\Delta V_{LRIP}(t)]$ vs. plethysmograph $[\Delta V_{Lpleth}(t)]$ using standard linear regression analysis (Fig. 2). In addition, the between-method bias and limits of agreement analysis were determined from the difference function $[\Delta V_{LRIP}(t) - \Delta V_{Lpleth}(t)]$ according to the method of Bland and Altman (5). These comparisons were repeated for each change in Paw in each piglet before and after lung lavage.

**Maximal or steady-state volume changes.** After every change in Paw, lung volume increased in a time-dependent fashion until it reached a maximal plateau or steady-state value ($\Delta V_{Lmax}$; see example in Fig. 1). The $\Delta V_{Lmax}$ estimated from each method and those for all Paw settings were combined and contrasted by using linear regression analysis. Here also, between-method $\Delta V_{Lmax}$ bias and limits of agreement were estimated as per Bland and Altman (5).

### Lung Recruitment and Mechanics

As Paw settings were modified, changes in lung mechanical properties were quantified by deriving the following relationships before and after lung lavage: 1) $\Delta V_{Lmax}$ vs. Paw, 2) effective compliance ($C_{eff}$, in ml/cmH2O) vs. Paw, and 3) $C_{eff}$ vs. $\Delta V_{Lmax}$.

$C_{eff}$ is computed as the ratio of $\Delta V_{Lmax}$ (ml) to Paw (cmH2O). It primarily reflects the mechanical properties of the respiratory tissues ($C_{ti}$) and to a lesser extent that of the alveolar gas volume ($C_{g}$); or $C_{eff} = C_{ti} + C_{g}$ with $C_{ti} > C_{g}$.

Note that the change in $C_{g}$ relative to Paw = 0 may be approximated as follows

$$\Delta C_{g} = \Delta V_{Lmax}(P_{atm} - P_{H_2O})$$  \hspace{1cm} (1)

where $P_{atm}$ and $P_{H_2O}$ are the atmospheric (1,033 cmH2O) and vapor pressures (64 cmH2O), respectively.

### Lung Overdistention

When the lung is derecruited after lavage, $C_{eff}$ should decrease relative to its healthy or prelavage value. In contrast, as more alveolar volume is recruited at higher Paw, one...
expects that C_{eff} should increase as a result of 1) the necessary increase in C_{g} and 2) a greater C_{ti}. The latter is true except when overdistention occurs. Thus interpreting changes in C_{eff} in terms of Paw (or equivalently \Delta V_{L,max} is the main element of how \Delta V_{l} measurements may be used to avoid overdistention during HFOV (Fig. 3).

We propose that a simple method to arrive at optimal Paw settings during HFOV may be based on C_{eff} vs. \Delta V_{L,max} relationships. These curves can be determined by methodically increasing Paw over a physiologically relevant range and allowing for a stable \Delta V_{l} plateau after each change. If alveoli are recruited without overdistention, the change in C_{eff} (\Delta C_{eff}) should exceed the increase in C_{g} (\Delta C_{g}) due to the alveolar volume change (Fig. 3); i.e., \Delta C_{eff} > \Delta C_{g}. This would also reflect an increase in C_{ti}. Alternatively, a relative drop in C_{ti} would result if overdistention of respiratory tissues is present, and hence a \Delta C_{eff} < \Delta C_{g}. Consequently, the C_{eff} vs. \Delta V_{L,max} relation would exhibit a C_{eff}, relative to the previous or lower Paw setting, that is either 1) decreased, 2) unchanged, or 3) increased by less than \Delta C_{g} (Fig. 3).

### RESULTS

**Validation of RIP**

**Transient volume changes.** Results of the between-methods comparison for estimating transient volume changes, or time response, induced by increasing Paw are summarized in Table 1. First, the range of Paw settings varied slightly between piglets mainly 1) because of different initial (or lowest) Paw needed in each piglet before and after lavage to maintain normal blood-gas limits, and 2) to provide for a range of Paw settings for evaluation.

Our analysis indicated that, in all piglets, the transient lung volume changes estimated by both techniques [\Delta V_{L,RIP}(t) and \Delta V_{L,pleth}(t)] were similar for all Paw. Averaged linear regression results (Table 1) dem-

![](image_url)

**Fig. 3.** A cartoon depicting the separate contributions of mechanical properties of respiratory tissue (C_{ti}) and of gas volume (C_{g}) to effective respiratory system compliance (C_{eff}) as lung volume is increased by alveolar recruitment (i.e., \Delta V_{L,max}). C_{g} is always an increasing function (linear as per Eq. 1), reflecting the increased alveolar gas volume. Alternatively, C_{ti} will increase with \Delta V_{L,max} until the respiratory tissues become overstretched, or true overdistention (OD_{actual}). C_{eff} is the algebraic sum of C_{ti} and C_{g} and hence may continue to increase with further lung recruitment despite tissue OD (see C_{ti}). Indeed, detection of OD based on C_{eff} (OD_{observed}) is necessarily delayed until the decrease in C_{ti} is of greater magnitude than the increase in C_{g}, au, Arbitrary units.

### Table 1. Summary of RIP vs. plethysmograph linear regression and bias analysis results

<table>
<thead>
<tr>
<th>Piglet</th>
<th>Paw, cmH_{2}O</th>
<th>Slope</th>
<th>Intercept, ml</th>
<th>r^2</th>
<th>Bias, ml</th>
<th>SD, ml</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Prelavage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>6–12</td>
<td>0.90–1.15</td>
<td>−0.4–0.5</td>
<td>0.95–0.99</td>
<td>−2.8–2.3</td>
<td>0.7–1.9</td>
</tr>
<tr>
<td>2</td>
<td>7–13</td>
<td>0.89–1.10</td>
<td>0.1–0.4</td>
<td>0.99</td>
<td>2.1–3.1</td>
<td>1.0–3.6</td>
</tr>
<tr>
<td>3</td>
<td>8–14</td>
<td>0.83–1.04</td>
<td>1.7–1.2</td>
<td>0.99</td>
<td>−1.3–2.0</td>
<td>1.3–2.5</td>
</tr>
<tr>
<td>4</td>
<td>6–14</td>
<td>0.91–1.01</td>
<td>0.4–2.4</td>
<td>0.99</td>
<td>−1.1–0.1</td>
<td>0.5–1.5</td>
</tr>
<tr>
<td>5</td>
<td>5–13</td>
<td>0.85–1.11</td>
<td>0.6–1.4</td>
<td>0.97–0.99</td>
<td>−2.3–1.2</td>
<td>0.6–0.9</td>
</tr>
<tr>
<td>Range</td>
<td>5–14</td>
<td>0.85–1.15</td>
<td>−0.4–3.0</td>
<td>0.95–0.99</td>
<td>−2.8–3.1</td>
<td>0.5–3.6</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>0.99±0.04</td>
<td>1.3±0.9</td>
<td></td>
<td>−0.9±0.8</td>
<td>1.1±0.3</td>
</tr>
<tr>
<td><strong>Postlavage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>10–22</td>
<td>0.97–1.12</td>
<td>−0.5–2.4</td>
<td>0.98–0.99</td>
<td>−2.7–2.0</td>
<td>0.5–1.6</td>
</tr>
<tr>
<td>2</td>
<td>14–24</td>
<td>0.90–1.06</td>
<td>0.3–3.6</td>
<td>0.99</td>
<td>−4.3–2.1</td>
<td>1.1–1.5</td>
</tr>
<tr>
<td>3</td>
<td>14–24</td>
<td>1.00±0.07</td>
<td>2.2±1.3</td>
<td>0.99</td>
<td>−1.3–2.6</td>
<td>1.7±0.8</td>
</tr>
<tr>
<td>4</td>
<td>14–20</td>
<td>0.94–1.01</td>
<td>1.3±0.6</td>
<td>0.99</td>
<td>−1.4±1.5</td>
<td>0.8±0.4</td>
</tr>
<tr>
<td>5</td>
<td>15–23</td>
<td>0.87–0.98</td>
<td>1.7±2.9</td>
<td>0.99</td>
<td>−3.1–3.0</td>
<td>0.8±0.9</td>
</tr>
<tr>
<td>Range</td>
<td>10–24</td>
<td>0.87–1.12</td>
<td>2.3±0.8</td>
<td>0.98–0.99</td>
<td>−4.3–2.1</td>
<td>0.2–2.6</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td></td>
<td>0.98±0.04</td>
<td>1.6±0.6</td>
<td></td>
<td>−1.0±0.9</td>
<td>1.1±0.4</td>
</tr>
</tbody>
</table>

Values are ranges and means ± SD. RIP, respiratory inductive plethysmography; Paw, airway pressure.
onstrated a slope of nearly 1 (0.99 ± 0.04 prelavage and 0.98 ± 0.04 postlavage); small intercept values of 1.3 ± 0.9 ml before and 1.6 ± 0.6 ml after lavage; and \( r^2 \) > 0.95. Furthermore, the average between-method bias (−0.9 ± 0.8 ml prelavage and 1.0 ± 0.9 ml postlavage) and the SD (1.1 ± 0.3 ml prelavage and 1.1 ± 0.4 ml postlavage) that describe the limits of agreement or accuracy between RIP and plethysmography were also small for both healthy and diseased lungs.

Maximal or steady-state volume changes (\( \Delta V_{L_{\text{max}}} \)). As expected, \( \Delta V_{L_{\text{max}}} \) increased as Paw was increased to higher settings (Fig. 4). \( \Delta V_{L_{\text{max}}} \), or the effective change in lung volume with Paw, did not differ for plethysmography and RIP throughout the range of Paw settings both pre- and postlavage [Fig. 5A; \( \Delta V_{L_{\text{RIP}}} \) (ml) = 1.01 × \( \Delta V_{L_{\text{pleth}}} \) (ml)−0.35; \( r^2 \) = 0.95]. Here also, the between-method difference in \( \Delta V_{L_{\text{max}}} \) indicated a near-zero (0.07 ml) bias and with relatively small upper (5.0 ml) and lower (−4.9 ml) limits of agreement (Fig. 5B). Consequently, the similarity of \( \Delta V_{L_{\text{max}}} \) obtained from both plethysmography and RIP lead to essentially identical lung mechanics results or \( \Delta V_{L_{\text{max}}} \) vs. Paw, Ceff vs. Paw, and Ceff vs. \( \Delta V_{L_{\text{max}}} \) relationships.

Lung Mechanics and Detection of Overdistention

The RIP-derived \( \Delta V_{L_{\text{max}}} \) vs. Paw relationships before and after lung lavage are shown in Fig. 6. Note that the range of Paw values used and the maximal lung recruitment were both expectedly higher postlavage. In either case, however, \( \Delta V_{L_{\text{max}}} \) was generally an increasing nonlinear function of Paw.

Figure 7 illustrates the dramatic decrease in respiratory system compliance after lung lavage in two example piglets. In one of these piglets (postlavage), increasing Paw beyond 21 cmH2O resulted in a slightly lower Ceff despite the greater volume recruitment. Such a drop in Ceff as Paw is increased probably reflects overdistention of lung tissues, and it certainly indicates that HFOV at these Paw or lung volumes is disadvantageous and may compromise gas exchange.

Ceff and \( \Delta V_{L_{\text{max}}} \) from all piglets were averaged for the same Paw setting (independent variable). The resulting Ceff vs. \( \Delta V_{L_{\text{max}}} \) relationships exhibited strong nonlinear characteristics both pre- (\( r^2 \) = 0.98) and postlavage (\( r^2 \) = 0.99) that were best approximated by the following sigmoid equations (Fig. 8)

\[
\text{Ceff(prelavage)} = 2.1 + 1.0/[1 - \exp^{-1(\Delta V_{L_{\text{max}}}-8.9)/1.3}] \quad (2)
\]

\[
\text{Ceff(postlavage)} = 1.6 + 1.5/[1 - \exp^{-1(\Delta V_{L_{\text{max}}}-13)/2.5}] \quad (3)
\]

where Ceff is in units of ml/cmH2O and \( \Delta V_{L} \) in units of ml/kg.

Ceff for the same lung recruitment, or \( \Delta V_{L_{\text{max}}} \) was significantly lower postlavage. This is explained by the derecruitment, or lower starting lung volumes at Paw = 0, in the surfactant-deficient lungs. Otherwise, pre- and postlavage Ceff-\( \Delta V_{L_{\text{max}}} \) curves had similar char-
acteristics: 1) Ceff is lowest at the lower ΔVl_{max} values (or effective lung volumes); 2) Ceff increased as lung volume increased until it reached a maximum value; 3) the average Ceff appears to peak at nearly 3.1 ml/cmH2O in both healthy (for ΔVl_{max} > 12 ml/kg) and surfactant deficient (for ΔVl_{max} > 18 ml/kg) piglets. The latter probably reflected the reduced compliance (i.e., over-distention) at higher Paw settings in some piglets (see example in Fig. 6). The same maximal Ceff before and after lavage also suggests that the net effect of the lavage was alveolar derecruitment with no changes in the intrinsic tissue properties.

**DISCUSSION**

Many infants who are born before term require mechanical ventilation for respiratory failure because of respiratory distress syndrome (RDS) (17). Advances in the management of sick neonates during the past two decades have decreased the mortality associated with RDS (1, 17, 20). However, despite decreased mortality in very-low-birth-weight infants (500–1,500 g), the incidence of CLD remains unchanged (20, 28, 31). CLD is caused, in part, by the lung injury inflicted by mechanical ventilation and the use of supplemental oxygen (31).

HFOV in neonates is widely used today. Evidence is mounting that HFOV is less likely to induce lung injury in infants than CMV (10, 16, 19, 34, 35, 37). The most commonly used high-frequency oscillator operates using a bidirectional piston that functions near the resonance frequency of the infant lung (10–15 Hz). Tidal volume may be less than the volume of the anatomic dead space, and lung volume is higher than FRC. Applying HFOV to infants carries a substantial risk of lung overdistention because, as the infant's lung compliance improves, lung volume may increase to harmful levels, resulting in alveolar and/or bronchiolar rupture (36). A method to estimate lung volume during HFOV is needed to alert clinicians as lung volume increases.

Gas dilution techniques (helium dilution and nitrogen washout) have been widely used in the pulmonary function laboratory setting to measure lung volume (22). In mechanically ventilated patients, these techniques are cumbersome, are not readily available, and at best provide discrete lung volume measurements. More importantly, they require prolonged interruption.
of HFOV and hence cannot provide information about Paw-induced lung recruitment and lung mechanics to detect and avoid overdistention during HFOV.

Whole body plethysmography has been widely used in cooperative adults and in animal research to measure thoracic gas volume, from which FRC can be calculated (14, 15, 29). Although this method can be used to measure ΔVl during HFOV (as we did in this study), it is rarely employed in infants, particularly those who are intubated and require intravenous infusions. This method limits access to the infant for some period and is difficult to perform (22). For change in lung volume to be continuously assessed, infants would need to remain in a leak-free plethysmograph, which is not clinically feasible or safe.

Fumey et al. (15) have reported using a planimetric method for estimating lung volume from chest radiographs in infants with CLD. Measurements using their planimetry method closely correlated with plethysmographic measurements of thoracic gas volume in infants with CLD. Although promising, this technique depends on the availability and timeliness of chest radiographs. Other methods of estimating lung volume from chest radiographs have been reported (3, 4, 33), but their clinical value is controversial.

Clinicians assess lung volume using periodic chest radiographs. The optimum position of the dome of each hemidiaphragm is between the top of the eighth rib and the bottom of the ninth rib (40). As the position of the diaphragms varies, Paw is increased or decreased to maintain lung inflation at the desired level. This technique may provide a crude estimate of lung volume; however, it is not continuous, is not immediately available, and exposes infants to radiation. More important, recent evidence suggests a poor correlation between this radiographic assessment and actual measurements of lung volume using helium dilution (40). Dramatic ΔVl leading to air leaks may ensue before lung volume can be assessed by radiography.

Measuring ΔVl with RIP

RIP is a commonly used method for assessing and quantifying thoracoabdominal asynchrony in infants and children (25–27, 38, 39). When DC coupled, the RIP signal carries information on how the static lung volume is changing above FRC (25). Several investigators have used RIP to measure ΔVl in adult patients and normal volunteers. Valta and co-workers (42) studied alveolar recruitment with changes in PEEP using RIP. Chandra et al. (7) used RIP estimates of ΔVl and breathing synchrony to study the effects of hyperpnea on PEEP-induced alveolar recruitment. Although these investigators have used RIP to estimate ΔVl, to our knowledge no studies have validated RIP for measuring ΔVl during HFOV.

In piglets with both healthy and surfactant-deficient lungs, we found that Paw-induced ΔVl during HFOV estimated by RIP over a wide range of settings were in excellent agreement with those independently provided by whole body plethysmography. Indeed, both methods provided similar estimates of the overall recruitment as a function of Paw (ΔVlmax, Fig. 5) as well as of the transient change in lung volume between FRC and FRC + ΔVlmax (Fig. 2; Table 1). In both cases, the bias and limits of agreement between RIP and plethysmography were relatively small. This agreement was obtained despite 1) the fact that RIP (unlike plethysmography) measurements depend on incomplete sampling of the thorax (one rib cage and one abdominal RIP band), 2) varying effects of extraneous noise such as cardiogenic oscillations on RIP compared with plethysmography (Fig. 1), and 3) the possibility of very slow undetectable leaks within the plethysmograph.

Besides its noninvasiveness and apparent accuracy for measuring lung volume changes, other aspects of RIP make it highly attractive for the proposed use with HFOV. First, RIP bands are easy to use and should not interfere with the medical care of patients. Ensuring that these bands are correctly placed and do not move during the assessment on HFOV is, however, critical.

Second, RIP bands exhibit a linear quality over the physiological range of ΔVl values (see Fig. 1), and hence the nontrivial task of absolute calibration of RIP measurements to units of volume (ml) may not be necessary for the purpose of detecting overdistention. This is because the latter is determined from the change in Ceff as Paw is increased rather than from absolute Ceff values. Calibration of RIP requires additional equipment and measurements (e.g., flow/volume) to be done on infants while HFOV is discontinued. Calibration is also possible by briefly switching to conventional ventilation, in which tidal ventilation and RIP data may be combined to determine calibration coefficients. Absolute calibration, though, is advantageous because it provides 1) physiologically meaningful recruitment (ml/kg) and Ceff (ml/cmH2O) values for comparison to healthy values and 2) a mathematical separation of changes in Cti and Cg from measured Ceff changes.

Finally, unlike volume measurements derived from flows at the proximal airway (e.g., pneumotachography), RIP measurements reflect volume changes at the chest wall and hence are unaffected by airway leaks at the endotracheal tube-airway interface. When airway leaks are present, flow measurements at the proximal endotracheal tube can be substantially inaccurate in infants. Worse, the relative magnitude of the airway leak will depend on the load impedance, which will change as the lung is recruited.

Clinical and Physiological Implications of RIP-derived ΔVl

Given the validity of RIP derived estimates of ΔVlmax, we were able to construct ΔVlmax vs. Paw (Fig. 6), Ceff vs. Paw (Fig. 7), and Ceff vs. ΔVlmax (Fig. 8) relationships before and after lung lavage. The obtained curves conveyed important physiological information about the underlying lung mechanics (healthy vs. diseased) and also provided a quantitative basis for detection of lung overdistention. Specifically, we show
how the characteristics of the Ceff vs. Paw, or equivalently Ceff vs. ΔVLmax, curves can be used to indicate overdistention. This aspect of using RIP has important clinical implications as to how such measurements can be used to determine optimal HFOV settings and how these settings ought to be changed during weaning of HFOV support.

On the basis of our findings, we propose that a method to arrive at optimal HFOV settings is possible from consideration of the changes in Ceff as Paw is methodically increased over its physiologically relevant range of values. Briefly, Ceff vs. Paw and Ceff vs. ΔVLmax relationships are then derived by allowing for a stable plateau for lung recruitment after each Paw change.

An increase in ΔCeff is advantageous provided that it exceeds the expected rise in alveolar gas compression compliance (i.e., ΔCg) alone at the higher lung volume. A ΔCeff < ΔCg indicates a relative decrease in Cti or lung tissue overdistention. A decreased or unchanged Ceff at higher Paw (or ΔVLmax) also suggests overdentention for the same reason. Arguably, removing the chest wall component of Cti would increase the sensitivity of this method to parenchymal overdistention. This, however, is only possible at the price of inserting an invasive esophageal balloon and additional equipment requirement so that separation of lung and chest wall mechanical properties is facilitated.

In conclusion, we have shown that DC-coupled RIP can accurately estimate lung recruitment (i.e., ΔVLmax) during HFOV and that combining RIP-derived ΔVLmax and Paw data can provide important insight on changes in lung mechanics via Ceff vs. Paw and Ceff vs. ΔVLmax relationships. These relationships were then used to develop a possible clinically useful method for detecting and avoiding lung overdentention, with or without absolute calibration of RIP. According to this method, the optimal HFOV settings are those that maximize lung volume and compliance via Paw-induced alveolar recruitment without overdentention of the parenchymal tissues. Oxygenation is also promoted as lung volume is increased provided that the deleterious effects of overdentention on the pulmonary vascular bed, and hence gas exchange, are avoided.

Although this method offers a promising approach for optimizing HFOV management in infants, some technical and clinical factors must be addressed to facilitate its clinical use. First, currently available RIP devices provide volume change data only. Integration of RIP measurements with HFOV and automation of the proposed assessment procedure (e.g., sweeping through Paw values) including computation and plotting of the change in all compliance values (Ceff, Cti, and Cg) are essential steps if this method is to be widely implemented in nurseries (see Fig. 3).

Other factors not addressed in this study may affect the optimal HFOV settings. Overdentention stemming from the superimposed oscillatory ventilation is plausible, but this risk is small given the amplitude of these oscillations and may be accounted for during recruitment. Finally, the implicit assumption that the lungs are expanded as a homogenous mechanical unit is not always accurate, particularly in the surfactant-deficient lung during treatment. Although RDS affects the infant fairly homogeneously, delivery of exogenous surfactant in the prematur infant lung is almost invariably nonuniform (2) and will lead to nonhomogeneous lung mechanical properties. Arguably, overdentention of healthier lung units (or those with the highest regional compliance) may go undetected if a cumulative or single-compartment measure such as Ceff is used. Related to this is the fact that, even if inhomogeneity is not present, overdentention may occur at lower Paw as the lungs become healthier during treatment. Conversely, if the disease worsens, applied HFOV settings may become suboptimal. We believe that these scenarios are best avoided, or minimized, by periodic (and perhaps frequent) application of the proposed method for determining appropriate support levels. Consequently, future efforts should attempt 1) to refine the proposed technique to account for lung inhomogeneity and 2) to automate this technique so that its clinical implementation is facilitated.

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