The Effect of Varying Inspiratory to Expiratory Ratio on Gas Exchange in Partial Liquid Ventilation*

Chae-Man Lim, MD; Younsuck Koh, MD; Tae S. Shim, MD; Sang D. Lee, MD; Woo S. Kim, MD; Dong S. Kim, MD; and Won D. Kim, MD, FCCP

Background: In partial liquid ventilation (PLV), the nondependent lung was observed to be inflated first and the dependent lung later. The inflational time difference between the lung regions can lead to maldistribution of tidal gas and inefficient gas bubbling in the slow-inflating region during PLV. In this situation, increasing the inspiratory to expiratory (I:E) ratio of the mechanical ventilator would lessen the heterogeneity of regional ventilation and improve gas exchange possibly to a greater degree than in gas ventilation (GV).

Design and setting: Animal study at the Asan Institute for Life Sciences, Seoul, Korea

Subjects: Eighteen rabbits (2.6 ± 0.5 kg) with acute lung injury by saline solution lavage.

Interventions: Three I:E ratios were tried in GV and then in PLV. I:E ratios were changed by adjusting pause (1:2, 1:1, and 2:1; group 1) or by adjusting inspiratory flow rate (1:3, 1:1, and 2:1; group 2).

Measurements and results: With increasing I:E ratio in all animals, PaO2/FIO2 increased (80 ± 24, 143 ± 74, and 147 ± 88 mm Hg; p = 0.001), and PaCO2 decreased (74 ± 15, 66 ± 16, and 66 ± 15 mm Hg; p = 0.006). The increases of PaO2/FIO2 from 1:2/1:3 to 1:1 (p = 0.006) and from 1:1 to 2:1 (p = 0.036) were both greater in group 1 than in group 2. PaCO2 decreased with increasing I:E ratio in group 1, but not in group 2. The change of PaO2/FIO2 by varying the I:E ratio was 49 ± 65% in PLV and 14 ± 14% in GV (p = 0.003).

Conclusions: Extending the I:E ratio, especially by adding pause, improved gas exchange in PLV. Oxygenation in PLV was affected by the I:E ratio to a greater degree than in GV.

(CHEST 1999; 116:1032–1038)

Key words: gas exchange; inspiratory flow rate; inspiratory pause; inspiratory to expiratory ratio; partial liquid ventilation

Partial liquid ventilation (PLV) is one of the innovative methods of respiratory support for severe respiratory failure.1 PLV has been tested in patients with ARDS or in experimental respiratory failure, and it showed better oxygenation2–5 and less histologic injury2,6,7 when compared to gas ventilation (GV). In contrast to total liquid ventilation, in which gas exchange is done extracorporeally,8,9 gas exchange using PLV is accomplished in situ within the lung. For the in situ gas exchange to occur, gas bubbling into and out of the perfluorocarbon (PFC) liquid by the mechanical ventilator is necessary to replenish O2 and remove CO2.1,6 Despite this essential role in PLV, little is established yet about how to...
set the variables of the mechanical ventilator, including the inspiratory to expiratory (I:E) ratio.

In the first observation of PLV performed in sheep, the nondependent lung was observed to be inflated first and the dependent lung later.1 This visible difference of inflation between the superior and inferior parts of the lung, or “sequential lung inflation,” was also described later by Wolfson et al.6 As PFC is twice as dense as water and distributes preferentially to the dependent lung,5,10,11 regional inertia caused by PFC is thought to differ along the vertical axis of the lung. Gas coming from the ventilator will face less inertia in the nondependent lung but greater inertia in the dependent lung. Two consequences are possible in this situation: (1) more tidal gas would distribute to the fast-inflating region1; and (2) gas bubbling of PFC would terminate prematurely in the slow-inflating region. Considering that the dependent lung is in the greatest need of recruitment in acute lung injury (ALI),12 these consequences of sequential inflation in PLV may be disadvantageous for gas exchange.

The I:E ratio in conventional GV is an important variable, either as independent or as dependent, for the ventilatory support of the lung with hypoxia. A high I:E ratio, ie, a long inspiratory time (Ti) of a given respiratory cycle, increases mean airway pressure (Pmean), generates auto-positive end-expiratory pressure (PEEP), and improves gas mixing between lung units with heterogeneous time constants.13–15 All of these effects of a high I:E ratio during GV serve to improve oxygenation in the lung with ARDS. In the context that lung inflation is regionally heterogeneous during PLV,1,6,16 the I:E ratio also can play a role in determining gas exchange in PLV. We postulated that a high I:E ratio will provide the dependent (slow-inflating) region with extended time to catch up with inflation. The longer that the dependent region is allowed to be inflated, the less the difference of regional ventilation would be. Therefore, an extended I:E ratio in PLV could favorably influence gas exchange, possibly to a greater degree when compared to GV. We also wanted to compare the efficacy of the two methods of increasing the I:E ratio on gas exchange in PLV: adding inspiratory pause (in which the inspiratory flow rate is unchanged until the pause) vs lowering the inspiratory flow rate.

**Materials and Methods**

**Animal Preparation and Instrumentation**

Eighteen New Zealand White rabbits (2.6 ± 0.5 kg) were used for this study. In group 1 (n = 9), the I:E ratio was changed by adjusting the inspiratory pause at a fixed inspiratory flow rate. In group 2 (n = 9), the I:E ratio was changed by adjusting the inspiratory flow rate. The experimental protocol was approved by the Animal Care Committee of our institute, and the rabbits were cared for and handled according to the guidelines of the National Health Institute. The rabbits were placed supine under a radiant warmer to keep rectal temperature between 38°C and 39°C. After administering ketamine, 25 mg/kg, intramuscularly on the thigh, a marginal ear vein was cannulated with a 24-gauge angiocath that was later used for the route of IV anesthesia. Under additional local anesthesia at the neck with 2% lidocaine, the rabbits were tracheostomized. After tracheotomy, a 3.5-mm cuffless endotracheal tube was inserted 3 to 4 cm deep into the trachea and firmly tied to prevent leaks of gas or liquid. The carotid artery was cannulated with an 22-gauge angiocath and connected to a pressure monitor (Escort II; Medical Data Electronics; Arleta, CA) to record pulse rate and arterial pressure referenced to the midthoracic level. Arterial blood was obtained via the carotid artery, and blood gases were analyzed within 5 min of sampling using standard blood-gas electrodes (Blood Gas System 288; Ciba-Corning; Medfield, MA). Expired gas from the rabbit was collected in a 1.0-L mixing chamber positioned distally to the expiratory valve of the ventilator, and mixed expired CO2 was measured using a side-stream infrared capnograph (Normocap; Datex; Helsinki, Finland). Anesthesia was induced with IV thiopental sodium, 20 mg/kg, given in two divided doses and maintained at 3 mg/kg/h with intermittent muscle paralysis using IV vecuronium, 0.1 mg/kg, every 30 min. The rabbits were given a solution of half saline, 5% dextrose and water IV by an infusion pump at 7.5 mL/kg/h. A mechanical ventilator (Servo 900; Siemens-Elema; Solna, Sweden) was initially set with tidal volume (VT) of 18 mL/kg and frequency of 24 breaths/min; FIO2 of 1.0; PEEP of 2 cm H2O; and an I:E ratio of 1:1 (Ti, 33% and pause 20% in group 1; Ti, 50% without pause in group 2).

**ALI**

ALI was induced by a warmed saline solution (38°C) lavage, one lavage amount being 20 mL/kg. The saline solution was allowed to remain in the lung of the rabbit while mechanical ventilation continued for 1 min or until severe bradycardia (<40 beats/min) ensued. Throughout the lavage period, peak airway pressure (Ppeak) was kept <40 cm H2O by temporarily, if necessary, lowering the VT. The saline solution was removed from the lung by gravity using a siphon that was 1 m long. Lavage was repeated two to three times at 10-min intervals; after the last lavage, 60 min was allowed for the rabbit to be stabilized in BP and PaO2. ALI was determined if the PaO2/FIO2 ratio was <100 mm Hg at the end of the stabilization period (38 ± 8 mm Hg).

**Trial of Different I:E Ratios in GV and PLV**

From the baseline ratio of 1:1 in GV, the I:E ratio was then randomly changed to 1:2 or 2:1 (in group 1) or to 1:3 or 2:1 (in group 2) by flipping of a coin. After the completion of GV, PLV was started at a ratio of 1:1, which was altered likewise in GV. PLV was done using perfluorodecalin (perfluor-decalin, C20F38; Fluka Chemie AG; Buchs, Switzerland); 9 mL/kg. This somewhat lower dose of PFC was deliberately chosen to amplify the unequal distribution of liquid between the nondependent and dependent lung regions. The PFC liquid was warmed to 38°C in an incubator before instillation. Each dose of perfluorodecalin was instilled into the lung over 20 to 30 s via a swivel connector positioned between the endotracheal tube and
the Y connector of the ventilator circuit. The dose of PFC was halved, and each half was given with the rabbit in the left or right lateral decubitus position, respectively. The evaporative loss of perfluorodecalin was not replaced because the total PLV time was < 1 h and the application of different I:E ratios was randomized.

In group 1, the I:E ratio was varied by adding inspiratory pause at the same inspiratory flow rate (Ti fixed at 33%; pause time varying 0%, 20% and 30%, resulting in I:E ratios of approximately 1:2, 1:1 and 2:1, respectively). In group 2, the I:E ratio was varied by adjusting inspiratory flow rate (Ti varying 25%, 50% and 67%, resulting in I:E ratios of 1:3, 1:1 and 2:1, respectively).

**Physiologic Measurements**

Hemodynamic data (mean arterial pressure and pulse rate) and respiratory data (Ppeak, inspiratory pause pressure [Ppause], Pmean, total PEEP [PEEPt], and blood gases) were determined at the establishment of ALI, and at 15 min of each I:E trial in GV and PLV. Ppause was measured by an inspiratory hold of 5 s. PEEPt was measured by an end-expiratory hold of 5 s. Physiologic dead space ventilation (Vd/Vt) was calculated according to the Enghoff’s modification of the Bohr’s equation.17

**Statistics**

All data are expressed as mean (± SD), unless otherwise stated. Friedman’s nonparametric analysis of variance was performed for the two groups in PLV, with a Wilcoxon signed rank sum test for the comparison among the different I:E ratios. An unpaired t test was used for the overall change of variables between GV and PLV. A p value < 0.05 was considered significant.

**Results**

With increasing I:E ratio in all animals, PaO2/FiO2 increased (50 ± 24 mm Hg at 1:2/1:3; 143 ± 74 mm Hg at 1:1; and 147 ± 88 mm Hg at 2:1; p = 0.001) and PaCO2 decreased (74 ± 15 mm Hg, 66 ± 16 mm Hg, and 66 ± 15 mm Hg, respectively; p = 0.006). With an increasing I:E ratio in group 1, PaO2/FiO2 increased (p = 0.001) and PaCO2 and Vd/Vt decreased (both p < 0.05; Table 1). In group 2, on the other hand, PaO2/FiO2 at 2:1 was lower than at 1:1 (p < 0.05), and PaCO2 and Vd/Vt did not change (Table 2). Increases of PaO2/FiO2 from 1:2/1:3 to 1:1 (p = 0.006) and from 1:1 to 2:1 (p = 0.036) were both greater in group 1 than in group 2 (Fig 1).

In all animals, the amount of change in PaO2/FiO2 by varying I:E ratios was 49 ± 65% in PLV and 14 ± 14% in GV (p = 0.003). Changes of PaO2/FiO2 from 1:2/1:3 to 1:1 (p = 0.023) or from 1:1 and 2:1 (p = 0.038) were both greater in PLV than in GV (Fig 2). The change of PaCO2 in all animals was 11 ± 7% in PLV and 11 ± 9% in GV (p = 0.912). Changes of PaCO2 from 1:2/1:3 to 1:1 (11 ± 6% vs 12 ± 10%; p = 0.668) or from 1:2 to 2:1 (11 ± 8% vs 9 ± 9%; p = 0.543) were not different between PLV and GV.

**Discussion**

In at least two animal studies, the superior lung and the inferior lung were observed to be inflated in sequence during PLV.1,6 The current study was intended to evaluate the effect of an increased I:E ratio on gas exchange in this situation of sequential lung inflation. In our results, extending the I:E ratio in PLV increased oxygenation and decreased PaCO2 of acutely injured rabbit lung. In the application of a high I:E ratio in PLV, adding inspiratory pause was superior to lowering inspiratory flow for both oxygenation and CO2 elimination. The impact of a changing I:E ratio on oxygenation was greater in PLV compared to GV.

Although the conventional mechanical ventilator is an integral part of PLV, little is established about a ventilating strategy, including the I:E ratio, for improving the efficiency of gas exchange mediated by PFC. In the first experiment of PLV by Fuhrman et al, an I:E ratio of 1:3 was used. The I:E ratio in succeeding studies of PLV ranged from 1:3 to 1:118–23 or was varied as a dependent variable.4 To our knowledge, no systematic study has yet been reported concerning the role of the I:E ratio on gas exchange during PLV. Our results showed that oxygenation of acutely injured lung in PLV improved as the I:E ratio was increased, which was more pronounced when compared to GV. The superiority of 1:1 over 1:3 or 1:2 agrees to the finding of Hernan et al23 that an I:E of 1:1 was better than their previous ratio (1:3) for oxygenation (although data was not presented). Interestingly, auto-PEEP did not develop in our rabbits in PLV despite an increasing I:E ratio up to 2:1. Conceivably, the column of incompressible PFC (liquid auto-PEEP) not only stabilizes alveoli, but also prevents noncartilaginous small airways from tidal collapse during the expiratory phase. Therefore, expiratory flow limitation as might occur in GV can be circumvented, and the shortened expiratory time would not be translated into the elevation of end-expiratory alveolar pressure. Lack of auto-PEEP development in our rabbits suggests that the mechanism of improved oxygenation at high I:E ratio in PLV differs from that in GV. It seems to rest with the inspiratory phase rather than with the curtailed expiratory time. It is likely that longer I:E ratios (1:1 and 2:1) have provided the slow region (the dependent lung) with longer Ti, which could have lessened the heterogeneity of ventilation between the nondependent and dependent regions.

Increases of PaO2/FiO2 with a change of the I:E ratio from 1:2/1:3 to 1:1, and from 1:1 to 2:1 were both greater by adding pause (group 1, unchanging inspiratory flow rate) than by lowering the flow rate (group 2; Fig 1). Especially, the mean change of PaO2/FiO2 from 1:1 to 2:1 in group 2 was negative.
Table 1—Effects of Varying the I:E Ratio by Adding Pause Time on Gas Exchange and Respiratory Mechanics in PLV vs GV for Rabbit ALI Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>PLV</th>
<th></th>
<th></th>
<th>Friedman Test</th>
<th></th>
<th></th>
<th></th>
<th>Friedman Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1:2</td>
<td>1:1</td>
<td>2:1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAO₂/FIO₂, mm Hg</td>
<td>87 ± 27</td>
<td>160 ± 68†</td>
<td>201 ± 59†</td>
<td>p = 0.003</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PACO₂, mm Hg</td>
<td>77 ± 17</td>
<td>67 ± 17†</td>
<td>62 ± 14‡</td>
<td>p &lt; 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vn/Vt</td>
<td>7.18 ± 0.12</td>
<td>7.22 ± 0.13</td>
<td>7.26 ± 0.13‡</td>
<td>p = 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>5.0 ± 0.03</td>
<td>5.0 ± 0.04‡</td>
<td>5.0 ± 0.04‡</td>
<td>p = 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base excess, mEq/L</td>
<td>-2.7 ± 6.4</td>
<td>-2.6 ± 6.3</td>
<td>-1.2 ± 6.2‡</td>
<td>p = 0.045</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ppeak, cm H₂O</td>
<td>18.3 ± 2.0</td>
<td>17.9 ± 1.7</td>
<td>17.7 ± 2.0‡</td>
<td>p = 0.029</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pmean, cm H₂O</td>
<td>16.1 ± 1.2</td>
<td>16.1 ± 1.9</td>
<td>16.2 ± 2.0</td>
<td>p = 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP, cm H₂O</td>
<td>5.6 ± 0.2</td>
<td>8.5 ± 0.6‡</td>
<td>9.9 ± 1.1‡</td>
<td>p &lt; 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEET, cm H₂O</td>
<td>1.8 ± 0.4</td>
<td>2.1 ± 0.3</td>
<td>1.9 ± 0.3</td>
<td>p &gt; 1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD.
†p < 0.05 compared to 1:2 by paired t test.
‡p < 0.05 compared to 1:1 by paired t test.

Table 2—Effects of Varying the I:E Ratio by Adjusting the Inspiratory Flow Rate on Gas Exchange and Respiratory Mechanics in PLV vs GV for Rabbit ALI Model

<table>
<thead>
<tr>
<th>Variables</th>
<th>PLV</th>
<th></th>
<th></th>
<th>Friedman Test</th>
<th></th>
<th></th>
<th></th>
<th>Friedman Test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1:3</td>
<td>1:1</td>
<td>2:1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PAO₂/FIO₂, mm Hg</td>
<td>75 ± 20</td>
<td>128 ± 80</td>
<td>99 ± 56†</td>
<td>p = 0.014</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PACO₂, mm Hg</td>
<td>70 ± 12</td>
<td>64 ± 16</td>
<td>69 ± 16</td>
<td>p = 0.072</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vn/Vt</td>
<td>0.89 ± 0.02</td>
<td>0.86 ± 0.03</td>
<td>0.86 ± 0.03</td>
<td>p = 0.121</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pH</td>
<td>7.20 ± 0.10</td>
<td>7.19 ± 0.10</td>
<td>7.21 ± 0.13</td>
<td>p = 0.452</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Base excess, mEq/L</td>
<td>-2.7 ± 4.6</td>
<td>-4.9 ± 6.4</td>
<td>-2.4 ± 4.7</td>
<td>p = 0.147</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ppeak, cm H₂O</td>
<td>20.1 ± 2.1</td>
<td>18.1 ± 1.1‡</td>
<td>17.8 ± 1.1‡</td>
<td>p &lt; 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pmean, cm H₂O</td>
<td>17.2 ± 2.1</td>
<td>16.8 ± 2.0‡</td>
<td>16.7 ± 1.4</td>
<td>p = 0.048</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEEP, cm H₂O</td>
<td>5.3 ± 0.5</td>
<td>7.4 ± 0.8‡</td>
<td>9.0 ± 0.9‡</td>
<td>p &lt; 0.001</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PEET, cm H₂O</td>
<td>2.1 ± 0.3</td>
<td>2.0 ± 0.5</td>
<td>2.1 ± 0.4</td>
<td>p &gt; 1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Data are given as mean ± SD.
†p < 0.05 compared to 1:3 by paired t test.
‡p < 0.05 compared to 1:1 by paired t test.
As the changes in Pmean and PEEPt from 1:1 to 2:1 were not different between the two groups, the different response of oxygenation to inverse ratio (2:1) may be attributable to different inspiratory flow rates. In view of the need of gas bubbling by the mechanical ventilator in PLV, extending inspiratory phase from 1:1 to 2:1 at the expense of the inspiratory flow rate could have deteriorated the efficiency of oxygenation of PFC itself. Regarding the efficiency of CO₂ elimination, PaCO₂ decreased stepwise with adding inspiratory pause, while it did not change with lowering the inspiratory flow rate. Because other factors governing PaCO₂ (minute ventilation and the metabolic rate of the rabbit) were controlled in both groups, inspiratory phase characteristics might have been also responsible for the difference in the level of PaCO₂. From the comparisons of gas exchange between the two methods of I:E change, maintaining an adequate flow rate along with an extended Ti was thought to be more desirable in PLV than merely having a long Ti at a compromised flow rate.

Compared to GV, oxygenation in PLV was affected by the I:E ratio to a greater degree. This can be anticipated, considering the exaggerated inflational time difference between lung regions during PLV. PaCO₂ was affected to a similar degree between PLV and GV. Although the influence of varying the I:E ratio on PaCO₂ and Vd/Vt were not different, the values of PaCO₂ and Vd/Vt were significantly lower in PLV than in GV at all of the tested I:E ratios. Elimination of CO₂ from the alveoli may be different in PLV than in GV. In GV, after CO₂ is released into the alveoli from pulmonary capillaries, it undergoes convective dilution along the conducting airways. In PLV, on the other hand, CO₂ readily dissolves in PFC (140 to 210 mL/100 mL), which is found from the alveoli to the conducting airways, and the phenomenon of

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21932/)  
**Figure 1.** A comparison of the change in PaO₂/FIO₂ with a varying I:E ratio from 1:2/1:3 to 1:1 (p = 0.006; left, a) and from 1:1 to 2:1 (p = 0.036; right, b) between group 1 and group 2 in PLV.

![Figure 2](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21932/)  
**Figure 2.** A comparison of the amount of change in PaO₂/FIO₂ (mean ± SE) with a varying I:E ratio from 1:2/1:3 to 1:1 (p = 0.003; left, a) and from 1:1 to 2:1 (p = 0.023; right, b) between PLV and GV.

![Figure 3](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21932/)  
**Figure 3.** A capnogram of one of the rabbits during GV (upper panel) and during PLV (lower panel). Note the indentation of the expired CO₂ curve at midexpiration in GV (arrow) and its disappearance in PLV.
convective dilution can be theoretically reduced. This was supported by the capnogram taken during PLV, in which the midindentation of CO₂ rise seen during GV disappeared (Fig 3).

In testing our hypothesis, we confined our study to the volume-controlled mode. Although extended Ti can be achieved in the pressure-controlled mode as well, an alteration in inspired Vt will confound the oxygenation response in PLV. Vd/Vt as determined by the Bohr’s equation turned out to be very high in our study. We used an adult ventilatory circuit, the bore of which was obviously too large for the rabbit. Considering that the Vt of the rabbit was around 50 mL, the compression volume of the ventilator circuit could have diluted expired CO₂ in the mixing chamber, causing Vd/Vt values to be calculated high. In comparing the two methods of varying I:E ratio in PLV, the shortest I:E ratios were not identical between group 1 (1:2) and group 2 (1:3). This was inevitable with the volume-controlled mode on the Servo 900C. This limitation, however, does not seem to invalidate our results, because the overall change in PaO₂/FiO₂ and PaCO₂ showed the same trend when the two groups were analyzed separately. Also in comparing the two groups, the more favorable results of gas exchange were obtained in group 1, in which the change of the I:E ratio was relatively smaller than in group 2. Although 5 s of expiratory pause hold was long enough for the animal we used, the pause method adopted from GV may not hold true in a lung filled with a variable amount of liquid. The concept and/or measurement of auto-PEEP may need to be redefined in liquid ventilation. In interpreting gas exchange with a varying I:E ratio, the change in the distribution of pulmonary blood flow should be taken into consideration. Pulmonary blood flow during PLV is known to favor the nondependent lung regions in a vertical plane and the apical regions on a transverse plane in the normal lung. It is not yet known how pulmonary blood flow is altered in diseased lung during PLV. Our results, therefore, are currently not amenable to interpretation in terms of pulmonary blood flow change accompanying sequential inflation or a varying I:E ratio. The latter issue, however, needs to be investigated in view of the increasing interest about the different dosing of PFCs and about the combination of PFC with PEEP.

In conclusion, extending the I:E ratio in PLV improved gas exchange of acutely injured rabbit lung. In increasing the I:E ratio, the method of adding inspiratory pause was superior to the method of lowering the inspiratory flow rate for both oxygenation and CO₂ elimination. The impact of a changing I:E ratio on oxygenation was greater in PLV compared to GV. These findings suggest that an appropriate adjustment of the variables on the mechanical ventilator (synchronization of the inflation between the dependent and nondependent lungs, and providing an adequate inspiratory flow rate) are necessary for optimal gas exchange in PLV.

**References**