Expiratory Asynchrony in Proportional Assist Ventilation

Hong-Lin Du, Mikiya Ohtsuji, Masaki Shigeta, David C. Chao, Katsunori Sasaki, Yutaka Usuda, and Yoshitsugu Yamada

Clinical Research Department, Newport Medical Instruments Inc., Newport Beach, California; Department of Anesthesiology, The University of Tokyo Hospital, Tokyo, Japan; Emergency Life-saving Technique Academy of Tokyo, Tokyo, Japan; Barlow Respiratory Research Center, Los Angeles, California; and Department of Anesthesiology, Yokohama City University School of Medicine, Yokohama, Japan

One of the proposed advantages of proportional assist ventilation (PAV) has been the automatic synchrony between the end of the patient's inspiratory effort and the ventilator cycle (i.e., expiratory synchrony). However, recent clinical studies have shown a prolonged ventilator inspiratory time or even a "runaway" phenomenon with the normal use of PAV. We hypothesize that control-system delay may account for this, because in reality there is always some degree of delays between control-system's input and output in all ventilators. Computer simulation study to date has not taken into account the potential effect of control-system delay on expiratory synchrony. We therefore created a computer model in which the parameter of control-system delay time was introduced. We found that significant expiratory asynchrony may occur with this more realistic model of PAV. The ventilator flow termination may fall behind the completion of the patient inspiration by as long as 0.33 seconds under the selected simulation conditions. The inspiratory termination delay time is in proportion to the control-system delay time, the respiratory time constant, and the assist gain settings. In conclusion, this model indicates that due to the unavoidable control-system delay in the ventilators, expiratory asynchrony may be an inherent shortcoming associated with PAV.

Keywords: mechanical ventilation; patient-ventilator synchrony; proportional assist ventilation; computer simulation

Expiratory asynchrony has been shown to be a clinical issue in the patients with partial support ventilation (1–5). Under the condition of expiratory asynchrony, the termination of the ventilator flow occurs either before or after patients stop their inspiratory effort. Expiratory asynchrony not only causes discomfort to patients but also induces unnecessary inspiratory and expiratory work on the part of patients (6). Proportional assist ventilation (PAV) is a ventilatory mode that partially supports patients' spontaneous inspiratory effort. In theory, with PAV, ventilator pressure output (airway pressure, P_{aw}) is proportional to the instantaneous patient effort (inspiratory muscle pressure, P_{mus}). It is thus assumed that there is automatic synchrony between the end of the patient's effort and of the ventilator cycle (7–9). To validate this assumption, Younes (10) has conducted a computer simulation study on PAV, showing a well-synchronized breath ending, with some assumptions and simplifications built into his computer model. So far, there are no clinical data available that directly support this assumption of expiratory synchrony. Although patients/volunteered subjects feel more comfortable with PAV than with pressure support ventilation (11–13), it does not necessarily mean a complete synchronized breath ending between the ventilator and the patient with PAV (i.e., expiratory synchrony). In fact, a close scrutiny on some patient data with PAV may indicate a sign of expiratory asynchrony. In a study on a group of patients with chronic obstructive pulmonary disease (COPD) and acute respiratory failure, Ranieri and coworkers have observed the occurrence of the "runaway" phenomenon when PAV was used with a flow-assist gain setting of $\sim$ 80% and a volume-assist gain setting of $\sim$ 45% (14). This "runaway" phenomenon (i.e., delayed ventilator flow ending) cannot be explained by PAV theory because the volume-assist is well below the patients' passive elastance and the flow-assist is also less than respiratory resistance (7, 8). Other clinical studies on PAV also indicate a tendency of delayed inspiratory ending with high assist levels (9, 15). In a study on patients with acute respiratory failure, Navalesi and coworkers (15) have shown some data indicating a clear tendency of prolonged ventilator inspiratory time as volume-assist level was increased from 20% to 60% and 80%. Although the prolonged ventilator inspiratory time may be caused by many possible reasons, the absence of a simultaneous change in expiratory time in most cases suggests a possibility of the delayed breath ending with PAV. In a patient study published by Giannouli and coworkers (9), ventilator inspiratory time with PAV was statistically significantly prolonged in proportion to assist levels, whereas expiratory time was changed only insignificantly. Carefully reviewing the waveforms in the Figure 1 of the same study (9) reveals that, although there appears to be no phase delay between the completion of patient inspiratory effort (as judged by the esophageal pressure waveforms) and the completion of the ventilator inspiratory flow at a low assist level (i.e., 37%), such phase delay approximates 0.25 to 0.30 seconds at an assist level of 75%.

With no study that exclusively explores in depth the patient–ventilator interaction during the transition from inspiration to expiration during PAV, it remains unclear whether or not an expiratory synchrony always exists. Although Younes' study with a computer model (10) indicated a well-synchronized breath ending in PAV, ventilating a patient using a real ventilator with PAV may mean something different. In particular, unlike a computer model such as the one that Younes used, any ventilator has a delay in the control system, or ventilator response time. From a control system standpoint, a ventilator needs to measure the airway pressure and flow from a pressure sensor and a flow sensor (i.e., mechanical delay), to use filters to reduce high-frequency noise in signals so as to reduce the potential for system oscillation, and to send the signals to an analog–digital converter (i.e., electronic delay). The processor in the ventilator then needs to process the signals, integrate the flow into volume, and make a decision on the flow rate for the next time point (i.e., software control delay). To

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Correspondence and requests for reprints should be addressed to Yoshitsugu Yamada, M.D., Department of Anesthesiology, Yokohama City University, Yokohama, Japan or Hong-Lin Du, M.D., Clinical Research Department, Newport Medical Instruments Inc., P.O. Box 2600, Newport Beach, CA 92658. E-mail: yamaday@med.yokohama-cu.ac.jp or HLDu@nmitkb.com

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further complicate the matter, in a servo-controlled system, to deliver a predetermined flow rate a time delay also occurs because the command to the inspiratory flow valve that is predetermined by the processor does not necessarily result in exactly the same flow rate as expected, thus requiring time for adjustment. In the case of PAV, another delay exists because the target for the control system is not the flow, but the pressure, a function of the combination of flow, respiratory mechanics, and patient spontaneous effort. In the ventilator used for PAV as described by Younes and coworkers, the control system delay is at least 20 to 40 milliseconds to maintain a stable control system (8, 16).

To understand expiratory synchrony in PAV with the condition closer to reality, we introduced the parameter of control system delay time into a computer simulation model. We hypothesized that the control system delay may play a role in expiratory synchrony during PAV. Using this computer model, we analyzed the mechanisms governing the expiratory asynchrony in PAV. The data from the computer model were further validated using a mechanical lung setup and in healthy volunteers.

METHODS

During PAV, the motion of the respiratory system can be represented by the single first-order differential Equation 1, assuming that inertial losses are negligible and that the pressure–flow and pressure–volume relationships are linear in the range of tidal ventilation:

$$P_{aw}(t) + P_{mus}(t) = R\cdot\dot{V}(t) + E\cdot\Delta V(t) \quad (1)$$

where at any instant t, the volume displacement $\Delta V(t)$ from the end-expiratory level and instantaneous flow $\dot{V}(t)$ are determined by the total driving pressure applied to the respiratory system, i.e., the time varying airway pressure P_{aw}, and patient-generated inspiratory muscle pressure P_{mus}. R and E represent the resistance and elastance of the respiratory system.

When PAV is applied through a mechanical ventilator, the ventilator assists the patient spontaneous effort with a flow-assist gain (K_f) and a volume-assist gain (K_v). For the purpose of the analysis, both K_f and K_v are expressed as the percent of the patient airway resistance and respiratory elastance, respectively. Thus, the pressure output from the ventilator at any instant, $P_{aw}(t)$, is adjusted by the ventilator control-system according to the following equation:

$$P_{aw}(t) = K_f \times R \times \dot{V}(t) + K_v \times E \times \Delta V(t) \quad (2)$$

From the ventilator control system standpoint, the ventilator makes a decision of its output according to the input information, i.e., the measured flow and pressure. As described earlier, however, between the input and output there are always several components that cause the control system delay. For the convenience of the study, these components are grouped as system delay time, T_d. Thus, from the start of inspiration until T_d, P_{aw} will remain at zero. Once the time after the onset of inspiration exceeds T_d, P_{aw} can be described as:

$$P_{aw}(t) = K_f \times R \times \dot{V}(t - T_d) + K_v \times E \times \Delta V((t - T_d)\ (t \geq T_d) \quad (3)$$

The time course of P_{mus} during neural inspiratory phase, on the other hand, can be approximated by the following second-order polynomial function (17):

$$P_{mus}(t) = c \times t - d \times t^2 \ (0 < t < T_I) \quad (4)$$

This equation can be solved mathematically (*see* online data supplement), yielding

$$P_{mus}(t) = P_{mus\ max} \times \left(\frac{t}{T_I}\right) \times \left(2 - \frac{t}{T_I}\right)\ (0 \leq t < T_I) \quad (5)$$

Physiologically, the cessation of P_{mus} is not instantaneous after the end of neural inspiration. Rather, the inspiratory muscle activity generally extends into expiratory phase, resulting in residual inspiratory P_{mus} during neural expiration (18). In this model, therefore, P_{mus} is considered to decline exponentially with a time constant of $\tau_{E\ mus}$ during neural expiratory phase following the completion of inspiration. Accordingly,

$$P_{mus}(t) = P_{mus\ max} \times e^{-(t - T_I)/\tau_{E\ mus}} \ (t \geq T_I) \quad (6)$$

As it appears impossible to analytically solve the above-described differential equations, we solved the equations numerically using the fourth-order Runge–Kutta method (19). Thus, the ventilator flow rate at any instant from the start of inspiration through an entire breath cycle, $\dot{V}(t)$, can be calculated by iteration with an incremental step of one millisecond.

The computation of $\dot{V}(t)$ was conducted with a computer program written in a Microsoft Excel file. The ventilator termination delay time was used as an indicator of expiratory asynchrony and was calculated as the time lag between the end of neural inspiration and the return of the ventilator flow to zero. It was calculated under the following selected conditions: airway resistance, R: 5, 20 cm H_2O/L/s; lung compliance, C_L: 80, 40, 20 ml/cm H_2O; chest wall compliance, C_{cw}: 200 ml/cm H_2O; neural inspiratory time, T_I: 1.0 s (with a breath frequency of 20 breaths/min); maximal inspiratory muscle pressure, $P_{mus\ max}$: 10 cm H_2O; flow-assist gain, K_f: 0%, 50%, 80%; volume-assist gain, K_v: 0%, 50%, 80%.

To evaluate the effect of the control system delay (T_d) on the expiratory synchrony during PAV, three levels of the control system delay time were chosen: 5, 20, and 40 milliseconds (8, 16). The time constant of the P_{mus} decay from the $P_{mus\ max}$ during expiration ($\tau_{E\ mus}$) was assumed to be 0.15 seconds on the basis of the data published by Behrakis and colleagues (18).

Although it has been recognized that the intrinsic pressure–flow relationship of the respiratory system in normal subjects appears to be nearly linear (20), it is well known that the pressure–flow relationship of the endotracheal tubes is curvilinear (21). Because many patients with PAV have an endotracheal or tracheostomy tube in place, we further evaluated the effect of the addition of endotracheal tube characteristics into the above-mentioned model. The pressure–flow relationship of the endotracheal tube was modeled as:

$$\text{Pressure} = a \times \dot{V}^b \quad (7)$$

To simplify the computation and presentation, the effect of addition of endotracheal tube was evaluated under the following conditions: R of 5 or 20 cm H_2O/L/s; C_L of 80, 40, or 20 ml/cm H_2O; C_{cw} of 200 ml/cm H_2O; T_I of 1.0 s; $P_{mus\ max}$ of 10 cm H_2O; flow-assist gain of 0% or 80%; volume-assist gain of 0% or 80%; and T_d of 40 ms. The values of a and b in Equation 7 were assumed to be 4 and 2, respectively. These values approximate the resistive characteristics of endotracheal tube size of 8.5 mm (21).

This computer model was further validated both in a mechanical lung model and in healthy volunteers. For detailed information on the method, *see* online data supplement.

RESULTS

Computer Simulation

When both flow-assist and volume-assist are used together. When both flow-assist and volume-assist are used together with the same assist gain, the ventilator inspiratory termination delay time during PAV is in proportion to the control system delay time and respiratory time constant (Figure 1). At control system delay time of five milliseconds, there is no significant expiratory asynchrony. As control system delay time increases to 20 or 40 milliseconds, however, the termination of the ventilator flow during PAV falls behind the end of "patient" inspiratory effort, by as long as 0.33 seconds at a high respiratory time constant (e.g., R20C80). There is a clear correlation between the termination delay time and respiratory time constant, with the correlation coefficient between the two being > 0.98 under all simulated conditions. The termination delay is also affected by the assist gain. The termination delay is longer with 80% gain than with 50% gain.

When flow-assist alone or volume-assist alone is used. The pattern of expiratory asynchrony with flow-assist alone or volume-assist alone behaves differently from that when both

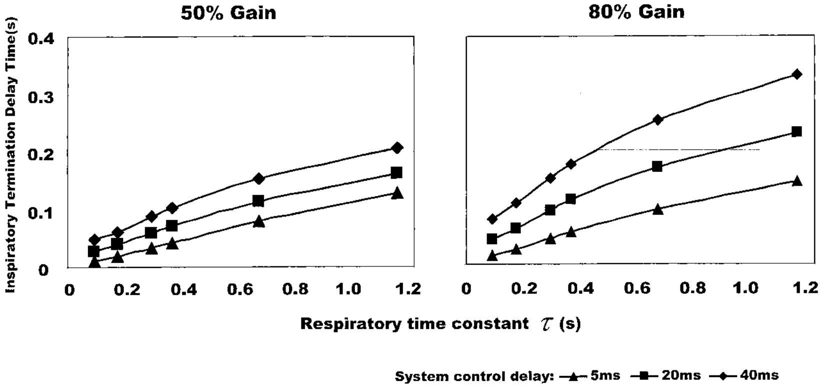

Figure 1. Ventilator inspiratory termination delay time at different levels of PAV assist gain and respiratory time constant.

flow-assist and volume-assist are used together (Tables 1–3). Using flow-assist alone without simultaneous volume-assist does not cause any significant expiratory asynchrony at any level of control-system delay times (termination delay time $\leq$ 0.1 seconds). Using volume-assist alone without simultaneous flow-assist, however, results in significant delay in the inspiratory flow termination. The termination delay with volume-assist alone is related to the respiratory time constant. The termination delay time when volume-assist alone is applied is even longer than when both flow-assist and volume-assist are used together. In other words, the expiratory asynchrony when both flow-assist and volume-assist are used together is the result of volume-assist, not flow-assist.

Effect of the addition of endotracheal tube with curvilinear resistive characteristics. Table 4 shows the inspiratory termination delay time when the effect of endotracheal tube with curvilinear resistive characteristics was taken into account. In comparison to the values in Table 3 when no endotracheal tube was added into the model, addition of the endotracheal tube did not change the pattern of expiratory asynchrony during PAV. The inspiratory termination delay time remained almost the same as that without endotracheal tube.

Validation Data

Mechanical lung model. The inspiratory termination delay times from the mechanical lung model were shown in Figure 2. As with the data from the computer simulation study, the delay in the inspiratory termination from the mechanical lung model was longer with 80% assist level than with 50% assist level. The delay time increased when the airway resistance was increased or when the compliance was increased, with the longest delay time at the longest time constant of the respiratory system. Because the mechanical lung model has ~ 50 milliseconds time lag between the onset of the driving pressure (P_{mus}) and the onset of the airway flow of the dependent lung, the absolute values of the termination delay time from the mechanical lung model were compared with those from the computer model with a total system delay time of 90 milliseconds (i.e., 50 milliseconds mechanical lung model delay plus 40 milliseconds system delay). As shown in Figure 3, in the Bland and Altman plot (22), there was a favorable consistency between the values from the computer model and mechanical lung model (at 80% assist level: $r^2 = 0.97$, $p < 0.01$, bias: 0.09 ± 0.10 seconds, mean ± SD; at 50% assist level: $r^2 = 0.97$, $p < 0.01$, bias: 0.07 ± 0.03 seconds).

TABLE 1. INSPIRATORY TERMINATION DELAY TIME (IN SECONDS) DURING PAV: CONTROL SYSTEM DELAY TIME OF FIVE MILLISECONDS

	R5C20 (τ = 0.09)	R5C40 (τ = 0.17)	R5C80 (τ = 0.29)	R20C20 (τ = 0.36)	R20C40 (τ = 0.66)	R20C80 (τ = 1.14)
FA + VA	0.02	0.03	0.05	0.06	0.10	0.15
VA Only	0.05	0.10	0.15	0.17	0.25	0.32
FA Only	0.01	0.01	0.01	0.01	0.02	0.03

Definition of abbreviations: C = lung compliance in ml/cm H_2O; FA = flow-assist; R = respiratory resistance in cm H_2O/L/s; VA = volume-assist. τ = respiratory time constant (in seconds) that is a product of R and respiratory compliance (C_{rs}).

The gains of both FA and VA used are 80%. C_{rs} is calculated by $1/C_{rs} = 1/C + 1/C_{cw}$, where C_{cw}, chest wall compliance is assumed to be 200 ml/cm H_2O.

Healthy volunteers. All three volunteers experienced a delayed inspiratory flow termination during PAV when the respiratory resistance (thus, the respiratory time constant) was increased by the addition of a resistor R20 at the airway opening (Table 5). The inspiratory termination of the ventilator was delayed by up to 0.86 seconds. At the baseline airway resistance, the inspiratory termination was obviously delayed in two of the three subjects at the assist gain of 80% during PAV. There was no apparent termination delay when the gain of 50% assist was applied at the baseline airway resistance. The pattern of the change in the inspiratory termination delay time in the volunteers is consistent with that from the computer simulation.

DISCUSSION

This computer simulation study showed that there might be an expiratory asynchrony between the ventilator and patient during PAV due to the control system delay time in ventilators. This finding was further validated and supported by the data both from our mechanical lung simulation and from healthy volunteers.

As with any analytic modeling of physiologic behaviors, certain simplifications and assumptions are necessary in its development. In computer simulation study, we assumed that the ventilator is triggered as soon as the patient inspiratory effort begins, without taking trigger delay into account. To simplify model and data presentation, we assumed that there is no active expiration or intrinsic PEEP (which may be a result of

TABLE 2. INSPIRATORY TERMINATION DELAY TIME (IN SECONDS) DURING PAV: CONTROL SYSTEM DELAY TIME OF 20 MILLISECONDS

	R5C20 (τ = 0.09)	R5C40 (τ = 0.17)	R5C80 (τ = 0.29)	R20C20 (τ = 0.36)	R20C40 (τ = 0.66)	R20C80 (τ = 1.14)
FA + VA	0.04	0.06	0.09	0.11	0.17	0.23
VA Only	0.07	0.12	0.17	0.19	0.26	0.33
FA Only	0.02	0.02	0.03	0.03	0.04	0.07

For definitions of abbreviations *see* Table 1.

TABLE 3. INSPIRATORY TERMINATION DELAY TIME (IN SECONDS) DURING PAV: CONTROL SYSTEM DELAY TIME OF 40 MILLISECONDS

	R5C20 (τ = 0.09)	R5C40 (τ = 0.17)	R5C80 (τ = 0.29)	R20C20 (τ = 0.36)	R20C40 (τ = 0.66)	R20C80 (τ = 1.14)
FA + VA	0.08	0.11	0.15	0.18	0.25	0.33
VA Only	0.10	0.14	0.19	0.22	0.29	0.36
FA Only	0.04	0.04	0.05	0.05	0.06	0.11

For definitions of abbreviations *see* Table 1.

TABLE 4. INSPIRATORY TERMINATION DELAY TIME (IN SECONDS) DURING PAV WHEN ENDOTRACHEAL TUBE WAS ADDED INTO THE MODEL: CONTROL SYSTEM DELAY TIME OF 40 MILLISECONDS

	R5C20 (τ = 0.09)	R5C40 (τ = 0.17)	R5C80 (τ = 0.29)	R20C20 (τ = 0.36)	R20C40 (τ = 0.66)	R20C80 (τ = 1.14)
FA + VA	0.11	0.17	0.24	0.20	0.27	0.36
VA Only	0.12	0.18	0.24	0.22	0.29	0.36
FA Only	0.04	0.04	0.07	0.05	0.08	0.13

Note: The conditions were the same with this table and Table 3, except that an endotracheal tube with curvilinear resistive characteristics was added into the model.

dynamic hyperinflation and/or fast breath frequency). Because intrinsic PEEP ($PEEP_i$) is a threshold value that needs to be overcome by inspiratory muscle pressure development before inspiratory flow begins, P_{mus} contributing to airway pressure development will actually be (P_{mus} – $PEEP_i$). Therefore, the presence of $PEEP_i$ will decrease actual percentage of flow assist and volume assist to P_{mus}, and thus tend to decrease the ventilator termination delay by the magnitude of its effect of decreasing actual % assist. We also assumed that the pressure–flow and pressure–volume relationships of the respiratory system are linear in the range of tidal ventilation, whereas the pressure–flow relationship of the endotracheal tube is curvilinear. In terms of P_{mus}, only one level of $P_{mus\ max}$ was selected in this study. The reason for this simplification was the consistent observation during simulations that any change in $P_{mus\ max}$ only affects the vertical magnitude of the breath assist outcomes (e.g., P_{aw} and tidal volume), but not the time phase of each parameter.

With these assumptions and simplifications being kept in mind, this computer simulation study revealed that expiratory asynchrony may happen with PAV. The ventilator flow termination may fall behind the completion of the patient neural inspiration by as long as 0.33 seconds under the selected conditions of simulation. The ventilator termination delay is in proportion to the control system delay time, respiratory time constant, and assist gain (Figure 1). This explains why it was concluded that there is automatic synchrony between the end of the patient's effort and ventilator cycle in the Younes' computer simulation study, in which the control system delay was not taken into account (10). From the control system standpoint, the targeted output of a ventilator cannot be achieved instantaneously with the input. As illustrated in Figure 4, a typical servoid pressure control system is composed of many components, all of which are inherent with a delay time. There may be mechanical delay, electronic delay, and software control delay between the input and output. In the case of PAV, in order for the ventilator to achieve a targeted level of pressure, the ventilator needs to measure airway pressure and airway flow through a pressure sensor and a flow sensor. This may cause a delay due to the flow and pressure signal transmissions at the sound wave speed as well as the response time of the sensors. The signals will then be conditioned by filters and amplifiers. When the signals contain high frequency noise that causes an unstable control system (i.e., system oscillation), filters are usually used to stabilize the system (16). The use of filters may cause a significant delay in the control system, as shown in Figure 5. Depending on the frequency and characteristics of the filters, a phase lag of 20–50 milliseconds may occur when a 30- or 10-Hz filter is used. Although the conditioned pressure signal is directly used by the processor, the flow signal needs to be integrated either before the processor or inside the processor to obtain volume information. The processor will then make a decision on the magnitude of the command to the inspiratory flow valve, on the bases of these inputs. Although a single loop in the control software in modern generation of mechanical ventilators usually ranges between 3–20 milliseconds, very often the targeted flow/pressure cannot be achieved by one loop. In this study, we selected three levels of control system delay time: 5, 20, and 40 milliseconds. These levels were conservatively selected based both on what Younes described in their publications using the Winnipeg ventilator (8, 16) and on our own experiences.

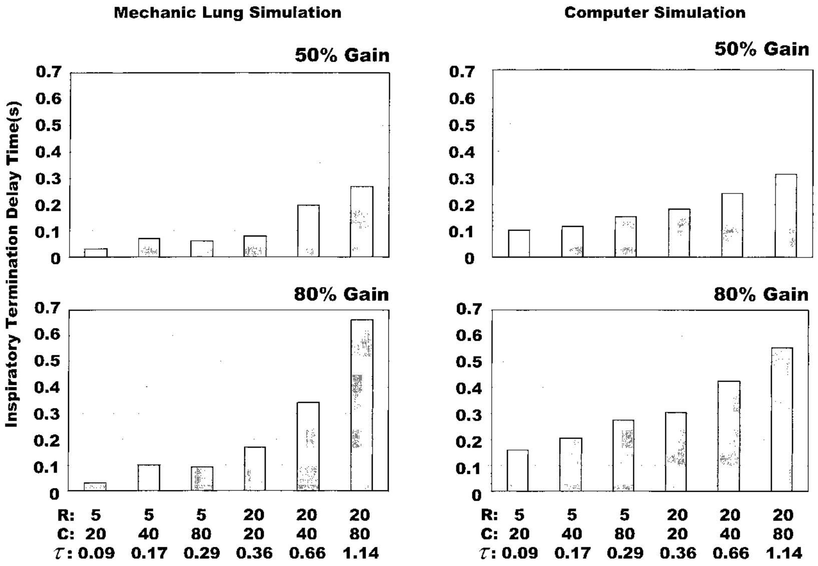

Figure 2. The ventilator inspiratory termination delay time both from the mechanic lung simulation and computer simulation. R: respiratory resistance in cm H_2O/L/s; C: lung compliance in ml/cm H_2O. τ: respiratory time constant (in seconds) that is calculated with assumption of chest wall compliance of 200 ml/cm H_2O.

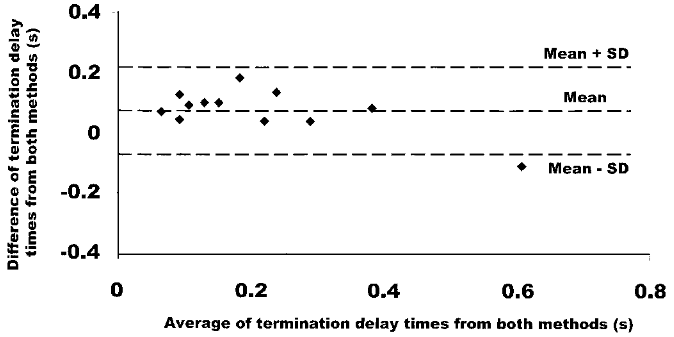

Figure 3. Bland and Altman plot between the inspiratory termination delay times measured from mechanical lung simulation and calculated from computer simulation.

Although there is no significant expiratory asynchrony with the control system delay of five milliseconds when both flow-assist and volume-assist are used simultaneously, termination delay time becomes longer when the control system delay is 20 or 40 milliseconds (Figure 1). At the control system delay of 20 or 40 milliseconds, the termination delay time in PAV is related to the respiratory time constant and the level of assist gain (Figure 1). The termination delay time increases with the respiratory time constant. It is longer with a higher assist gain (e.g., 80% gain) than with a lower assist gain (e.g., 50% gain). This is consistent with the data from the patient studies in which the ventilator inspiratory time was prolonged with the assist level of PAV (9, 15). In a patient study published by Giannouli and coworkers (9), ventilator inspiratory time with PAV was statistically significantly prolonged in proportion to the assist levels (from the minimal assist level of 31% volume-assist with 55% flow-assist to the maximal assist level of 78% volume-assist with 76% flow-assist), whereas expiratory time was changed only insignificantly. Navalesi and colleagues (15), in their study on PAV in patients with acute respiratory failure, also showed a set of data that indicate a tendency of prolonged ventilator inspiratory time as PAV assist level was increased.

Many researchers have advocated the use of both volume-assist and flow-assist together for the best benefits of PAV (7, 14, 15); however, some have tried the use of volume-assist alone during PAV (11). Our results indicate that using volume-assist alone without simultaneous flow-assist is accompanied by a significant delay in the inspiratory flow termination. The pattern of expiratory asynchrony with volume-assist alone is different from that when both flow-assist and volume-assist are used together. The termination delay time with volume-assist alone is somewhat independent of the control system delay, and flow-assist seems to partially offset the termination delay during volume-assist alone (Tables 1–3). In other words, the expiratory asynchrony when both flow-assist and volume-assist are used is the result of volume-assist, not flow-assist. In fact, Ranieri and colleagues (14) also found in their patients that volume-assist alone significantly increased ventilator inspiratory time to total breathing cycle time ratio (T_I/T_{tot}), whereas flow-assist alone did not modify ventilator inspiratory time or T_I/T_{tot}. In a patient study from Navalesi and coworkers (15), the authors demonstrated that high levels of volume-assist alone were accompanied by the increased ventilator inspiratory time while the expiratory time remained unchanged, indicating a possibility of delayed ventilator flow termination.

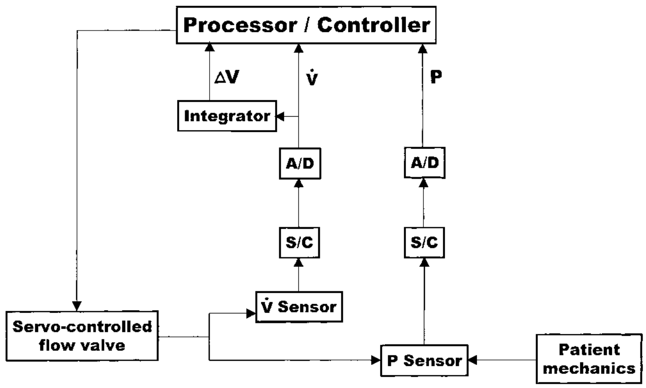

Figure 4. Schema of a typical servo-control system for pressure targeted ventilation. A/D: analog-digital converter; S/C: signal conditioner; P: pressure; V̇: flow; ΔV: volume.

It is unclear why the delayed breath termination is associated more with volume-assist than with flow-assist. One of the explanations might be that when the breath approaches the end of inspiration, the volume-related elastic recoil pressure will approach its maximum. Meanwhile, the flow-related pressure becomes minimal as the flow has tapered down toward zero. Therefore, at the end of inspiration, any delay caused by volume-assist will take more effect, whereas any delay caused by flow-assist will be virtually minimal.

Because the expiratory asynchrony during PAV is related to the control system delay in a PAV ventilator system, the development of a faster control system in PAV ventilators may reduce expiratory asynchrony. However, some delays, such as valve-opening delay and sound wave speed could not be abolished. Other delays in the control system (e.g., delay caused by filters) are technically unavoidable. Furthermore, in some patients, there may be a significant mechanical delay inside the patient from onset of inspiratory muscle pressure to the onset of the airway flow due to the respiratory time constant (23, 24). This delay cannot be removed by improving ventilator de-

TABLE 5. INSPIRATORY TERMINATION DELAY TIME (IN SECONDS) DURING PAV IN HEALTHY VOLUNTEERS

Subject no.	Baseline Mechanics	With Baseline Resistance 50% Assist	With Baseline Resistance 80% Assist	With Addition of R20 50% Assist	With Addition of R20 80% Assist
1	R: 6.5 E: 15.7	0.05	0.44	0.28	0.86
2	R: 10.3 E: 9.8	0.16	0.33	0.48	0.74
3	R: 10.1 E: 10.2	0.03	0.06	0.35	0.72

Data are the average of three consecutive breaths. R: The measured airway resistance in cm H_2O/L/s; E: the measured elastance of respiratory system in cm H_2O/L.

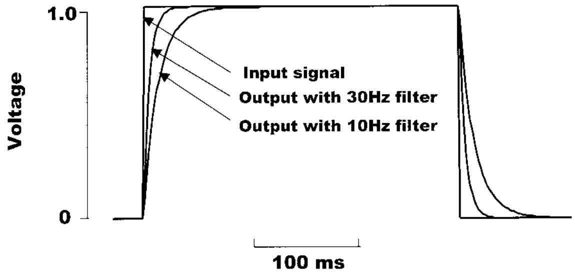

Figure 5. Example of the effects of the filters on the phase delay between the input signal and output signals.

sign and may cause additional ventilator termination delay, thus deteriorating expiratory asynchrony.

Due to the limited number of the subjects in our validation data from healthy volunteers, we did not conduct any statistical analysis on the volunteer data. However, the data from the healthy volunteers and from mechanical lung models support the conclusions arisen from our computer model. It will be worthwhile to examine more closely on expiratory synchrony in patients under PAV.

In conclusion, our computer model study indicates that, due to the unavoidable control system delay in the ventilators, expiratory asynchrony may be an inherent shortcoming with PAV.

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