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Respirator System For Total Liquid Ventilation

Miguel A. Gómez [a], Enrique Hilario [b], Francisco J. Alvarez [c], Elena Gastiasoro [c], Antonia Alvarez [b] and Juan L. Larrabe [a]

***Abstract*—**Total liquid ventilation can support gas exchange in animal models of lung injury. Clinical application awaits further technical improvements and performance verification. Our aim was to develop a liquid ventilator, able to deliver accurate tidal volumes, and a computerized system for measuring lung mechanics. The computer-assisted, piston-driven respirator controlled ventilatory parameters that were displayed and modified on a real-time basis. Pressure and temperature transducers along with a lineal displacement controller provided the necessary signals to calculate lung mechanics. Ten newborn lambs (<6 days old) with respiratory failure induced by lung lavage, were monitored using the system. Electromechanical, hydraulic and data acquisition/analysis components of the ventilator were developed and tested in animals with respiratory failure. All pulmonary signals were collected synchronized in time, displayed in real-time, and archived on digital media. The total mean error (due to transducers, A/D conversion, amplifiers, etc.) was less than 5% compared to calibrated signals. Improvements in gas exchange and lung mechanics were observed during liquid ventilation, without impairment of cardiovascular profiles. The total liquid ventilator maintained accurate control of tidal volumes and the sequencing of inspiration/expiration. The computerized system demonstrated its ability to monitor in vivo lung mechanics, providing valuable data for early decision-making.

***Keywords*—** immature lamb, perfluorocarbon, pressure-limited, total liquid ventilation, ventilator; volume-controlled

I. INTRODUCTION

PARTIAL liquid ventilation, a relatively simple technique, has been evaluated in preterm and pediatric clinical trials [1], [2], but currently, a multicenter study of adult respiratory distress syndrome has finish to recruit patients and the results will be published shortly. Tidal or total liquid ventilation is more complex, but offers significant physiological advantages to enhance gas exchange and lung mechanics. Several total liquid ventilators have been reported, but none has been able to simultaneously deliver accurate preset tidal volumes and control ventilation during real-time monitoring of lung mechanics. Such features are essential in gas respirators to optimize ventilation processes [3], [4]. Moreover, only a limited number of total liquid prototypes have been tested in lung injury studies, or developed with safety and reliability checks that are essential in a clinical setting.

Different studies in immature lambs managed on total liquid ventilation have demonstrated that liquid ventilation can maintain an adequate gas exchange at pressures lower than those used in gas ventilation [5], [6]. Early devices were simply gravity-driven [7]-[9], with control of perfluorocarbon flows implemented either manually [8] or by automatically operated valves [7], [9]. In the former type, control of inspiratory and expiratory times was difficult to achieve, particularly if volumes had to be measured by graduated vessels. Automatic valves usually achieved higher precision over inspiratory and expiratory times and frequencies, but the problem of controlling tidal volume remained. Volumes have been measured by scales (based on weight) or displacement transducers [7]. These devices are subject to artifacts since movement and forces generated by attached devices (e.g. tubing, wires, monitors, etc…) are difficult to avoid. In more advanced liquid ventilators, pumps drive fluids and automatic valves regulate ventilation settings. This is particularly advantageous for large animals [10], [11]. In some systems, pumps regulated inlet and outlet perfluorocarbon flows [10] while in others, gravity has been used for expiration [11]. Volumes were obtained by integrating pulsatile flows, but had to be verified by weight. Thus, the problem of regulating tidal volumes remained.

The aims of the present study were to: i) develop a electromechanical liquid ventilator prototype with easily removable hydraulic components, to accurately deliver pre-set tidal volumes of perfluorocarbon; ii) develop a computerized system to measure lung mechanics able to acquire, calculate and continuously display measurements to provide operator feedback to better control ventilation; and iii) test the usefulness of the ventilator and lung mechanics-measuring system in small animals with acute lung injury. We show that lung mechanics can be accurately monitored using total liquid ventilation in real-time under physiological and acute injury conditions.

II. MATERIALS AND METHODS

A. Ventilator system

The ventilator is a time-cycled, volume-controlled,

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Miguel A. Gómez and Juan L. Larrabe are with the Department of Navigation Sciences, Engineers and Shipbuilders, High Technical School of Maritime Studies, Portugalete, Bizkaia, Spain (Miguel A. Gómez corresponding author, phone: +34946014844, e-mail: miguel.solaetxe@ehu.es

Enrique Hilario and Antonia Alvarez are with the Department of Cell Biology and Histology, Basque Country School of Medicine, Leioa, Bizkaia, Spain.

Francisco J. Alvarez and Elena Gastiasoro are with the Research Unit on Experimental Pulmonary Physiology and Neonatal Intensive Care Unit, Department of Pediatrics, Hospital of Cruces, Basque Country School of Medicine, Bizkaia, Spain.

pressure-limited system with multiple rigid cylinder-piston devices on a sliding platform moved by a linear actuator with an electric synchronous motor [12]. The motor (OSY71STH, Sew Eurodrive, Bilbao, Spain) was controlled by applying a "resolver" with 4096 steps per revolution. It was possible to select the type of movement (e.g. linear ramps, square waves, and sinusoidal oscillations) as well as speed (and acceleration) by adjusting the step rate to the motor.

During inspiration, pinch valves (Z110A, Sirai, Milan, Italy) were used to drive flows from the inspiratory reservoir to the lungs. During the expiratory cycle, perfluorocarbon flows were driven from the lungs to the expiratory reservoir. Reservoirs, valves and tubing were all placed at the same level to avoid the introduction of parasitic hydrostatic forces (other than those produced by the linear actuator).

Perfluorocarbon was recirculated in a feedback circuit from an auxiliary reservoir through a heat exchanger (ECMO-Therm, Avecor, Plymouth, MN, USA) and a membrane oxygenator (0800A, Avecor, Plymouth, MN, USA) by means of a roller pump (10-150, Stockert, Munchen, Germany).

Operator control of ventilatory processes was performed via a graphic interface. Settings that were selected at the start of liquid ventilation included: patient body weight (bw; kg), inspiratory-expiratory ratio (I:E), ventilatory frequency (f; cycles·min-1), standardized tidal volume (VT; mL·kg-1), standardized functional residual capacity (FRC; mL·kg-1). In order to control delivered volumes from different cylinder-pistons, volume (mL) and diameter (mm) must be also set. All settings could subsequently be adjusted as needed.

B. Lung Mechanics System

Pulmonary mechanics measurements were calculated on a breath-by-breath basis. Breath-by-breath data were used to calculate derived pulmonary parameters including: minute ventilation ($\dot{V}_E$), mean airway pressure ($\overline{P_{AW}}$), quasi-static peak inspiratory pressure (PIP), quasi-static positive end expiratory pressure (PEEP), mean airway resistance (R_{AW}), dynamic lung compliance (C_{dyn}) and work of breathing (W_R). Since the sampling rates of all signals were constant, each respiratory cycle had a number of samples (n) that was related to respiratory frequency (>100 points in all cases).

Mean airway pressure ($\overline{P_{AW}}$), expressed in cmH_2O, was calculated as the mean value of airway pressure during one breath.

$$\overline{P_{AW}} = \frac{1}{n}\sum_{i=1}^{n} Paw_i \quad (1)$$

Standardized tidal volume, expressed in mL·kg-1, was the normalized volume of one breath.

Quasi-static peak inspiratory pressure (PIP) and quasi-static positive end-expiratory pressure (PEEP), expressed in cmH_2O, were calculated as the mean pressure at the end of the inspiratory and expiratory cycles by a proximal airway occlusion for 500 ms. These were determined when sample-to-sample increments of instantaneous volume were less than 0.01 mL (i.e. perfluorocarbon flow was close to zero and airway pressure was considered equal to alveolar pressure). If n' and n'' are the number of pressure samples during inspiration and expiration respectively, then PIP and PEEP can be computed as:

$$PIP = \frac{1}{n'}\sum_{i=1}^{n'} Paw_i \quad (2)$$

$$PEEP = \frac{1}{n''}\sum_{i=1}^{n''} Paw_i \quad (3)$$

Standardized dynamic lung compliance (C_{dyn}), expressed in $mL \cdot cmH_2O^{-1} \cdot kg^{-1}$, was calculated as maximum difference in volume normalized by the pressure difference and body weight [13].

$$C_{dyn} = \frac{\Delta V}{\Delta P \cdot bw} = \frac{Vmax - Vmin}{(PIP - PEEP) \cdot bw} \quad (4)$$

The airway resistance (R_{AW}), expressed in $cmH_2O \cdot L^{-1} \cdot s^{-1}$ was calculated at different levels of inflation volume using the method of Mead and Whittenberger [14] as:

$$R_{AW} = \frac{P_{ins} - P_{exp}}{\dot{V}_{ins} + |\dot{V}_{exp}|} \quad (5)$$

The pressure difference between inspiratory (P_{ins}) and expiratory pressure (P_{exp}) was obtained for each step of volume change from the P-V loop. Inspiratory ($\dot{V}_{ins}$) and expiratory flows ($|\dot{V}_{exp}|$) were measured at the same volume.

Standardized work of breathing (W_R), expressed in $g \cdot cm \cdot kg^{-1}$, was calculated for each breath using the following equation [3]:

$$W_R = \frac{\int P_{aw} dV}{bw} = \frac{\int P_{aw} \frac{dV}{dt} dt}{bw} = \frac{\int P_{aw} \dot{V} dt}{bw} \quad (6)$$

This value is the area enclosed by the hysteresis loop formed by plotting pressure versus volume.

C. Calibrations

Circuit compliance (Ccircuit) was determined in the hydraulic components (i.e., piston cylinders, tubing, fittings, etc.) of the ventilator at constant volume increments (1 mL). Determinations of Ccircuit were repeated 10 times.

Calibrations of volume, pressure and temperature were performed at atmospheric pressure and room temperature (25°C and 101.4±0.7 kPa). Under these conditions, the perfluorocarbon (FC-75, 3M, St. Paul, MN, USA) used in this study has the following physical and chemical properties: 157 mL CO_2·100 mL, 52 mL O_2·100 mL, surface tension 0.015 $N \cdot m^{-1}$, vapor pressure 7.87 kPa, dynamic viscosity 8·10-4 Pas.

The accuracy of measuring delivered volumes was assessed using 5, 10 and 50 mL glass syringes (Hispano ICO SA, Barcelona, Spain). In each case, the cylinder-piston device of the ventilator was serially connected to calibration syringes in which the measured volumes were recovered, and later compared to volumes established by the computer for lung mechanics (5, 10, 20, 30, 40 and 50 mL).

Pressure signals were calibrated with a U-tube water manometer (3T294, Fisher Scientific, Chicago, IL, USA). Atmospheric pressure was considered a zero reference point.

Upper and lower pressures were expressed as relative values (-30, -20, -10, 10, 20 and 30 cmH_2O).

Temperature signals were compared to digital thermometers with a resolution of 0.1 ºC (Digi-Sense, Cole-Parmer Instr. Co., Chicago, IL, USA) at 25, 37 and 45 °C.

The accuracy of time-dependent ventilatory settings (i.e. inspiratory and expiratory times, I:E ratio and frequency) was compared using traces recorded by a polygraph (7P, Grass Instr., Quincy, MA, USA). Computerized and polygraph records were closely examined over five consecutive respiratory cycles (n=5). To calibrate I:E ratios (3:1, 2:1, 1:1, 1:2 and 1:3) and inspiratory (T_I) and expiratory (T_E) times (3-12 s), physiological V_T (15 $mL \cdot kg^{-1}$), animal weight (4 kg) and frequency (5 $cycles \cdot min^{-1}$) were maintained constant. Conversely, in order to calibrate frequency (1, 2, 5, 8 and 10 $cycles \cdot min^{-1}$); V_T (15 $mL \cdot kg^{-1}$), animal weight (4 kg), I:E ratio (1:1) were maintained constant.

The absolute (ΔValue = Valuemeasured - Valuereference) and percent relative errors (δValue = 100·ΔValue / Valuereference) were determined at each increment of volume, pressure, temperature and time [15]. A mean calibration error was calculated for each set of values.

D. In vivo experiments

Experimental protocols met all regulations for animal research (EU Directive 86/609) and were approved by the Institutional Experimental Research Committee. The study was carried out on 10 healthy newborn lambs less than 6 days old with a mean bw (± SD) of 3.21±0.75 kg.

Lambs were sedated, anaesthetized and paralyzed as previously described [16]. A tracheotomy was performed and animals were placed on a conventional gas ventilator. Rectal temperature was monitored and kept constant with a radiant warmer. Catheters were placed in the left femoral and pulmonary arteries to determine pH, partial pressures of oxygen (P_{aO2}) and carbon dioxide (P_{aCO2}), systemic arterial and pulmonary artery pressures, and cardiac output computed from a mean of three random determinations [17].

Lung lavage was performed as previously reported [18] to obtain a severe and stable respiratory failure with P_{aO2}<100 mmHg, P_{aCO2}>50 mmHg, pH<7.2, 50% decrease in Cdyn and 50% increase in pulmonary artery pressure. At least 30 minutes were allowed to ensure that additional substantial changes in physiological parameters did not occur. Baseline levels were determined at this point (i.e. post-injury). After lung lavage, lambs received an intratracheally-instilled volume of 30 $mL \cdot kg^{-1}$ as perfluorocarbon FRC, and then placed on liquid ventilation for 3 hours. All series of parameters were recorded every 30 min.

During gas ventilation, C_{dyn}, R_{AW}, $\overline{P_{AW}}$ and $\dot{V}_E$ were calculated by a computerized system (PEDS, MAS, Hatfield, PA, USA), as previously described [16]. During total liquid ventilation, lung mechanics parameters were determined using the computerized system and equations described above. All pulmonary mechanics studies during gas and liquid ventilation were performed on 10 consecutive breaths over a period when there were no changes in ventilation strategy (i.e. constant f, V_T, I:E ratio, etc).

Statistical Analyses.

Values are expressed as mean ± SD. Simple linear regression analyses were performed to describe the relationship between calibrated and monitored signals (e.g. temperature, frequency) and to describe relative errors. Comparisons of physiological data were tested with one-factor analysis of variance with Bonferroni-Dunn's correction as function of time (StatView SE+Graphics; Abacus Concepts Co., Orlando, FL, USA). A p-value <0.05 was accepted as significant.

III. RESULTS

A. Ventilatory Performance

The respirator prototype was assembled on a portable and compact frame that could be easy managed and that facilitated making correct connections with animals. During ventilation, accessibility by the operator was made as convenient as possible to enable the checking and management of circuit components as well as to respond quickly to warning signals. Tubing, fittings and cylinder-piston seals did not show perfluorocarbon leakage over physiological ranges of pressures (-20 to 50 cmH_2O) and temperatures (25 to 45°C).

When the total liquid ventilator is turned on, the computer positions cylinder-pistons and valves in the inspiratory phase, avoiding the generation of potentially harmful pressures. This is maintained until operator commands are entered to begin respiratory control.

The respirator system incorporates adjustable airway pressure safety limits for inspiration (50 cmH_2O) and active expiration (-20 cmH_2O). During the expiration cycle, if the lower airway pressure limit is reached, the current cycle is automatically stopped and a new inspiration started. Similarly, during inspiration, if upper airway pressure is achieved, the input flow into the lungs is arrested and an expiration cycle initiated. However, typical maximum inspiratory and minimum expiratory pressures were between 10 and 25 cmH_2O, and between -5 and -15 cmH_2O, respectively.

B. Calibration assays of signals

A primary advantage of total liquid ventilation is the relative incompressibility of the fluids and solid structures on the ventilator side of the pulmonary circuit. Since the compliance of the hydraulic component is negligible compared to other elastic elements (i.e. the lungs), volume variations within the ventilator pistons are directly transmitted to the lungs. The hydraulic circuit compliance was 8.3 10^{-3} ± 0.7·10^{-3} $ml \cdot cmH_2O^{-1} \cdot kg^{-1}$.

Pressure signals were measured over a range from -20 to 50 cmH_2O during in vivo studies involving 10 newborn lambs. The system is capable of monitoring a range from -543 to 650 cmH_2O. Calibration experiments involving pressure signals resulted in a mean error of -1.0±0.8%. No single measurement produced a pressure error greater than 4%.

The delivered volume signal was varied over the range from

0 to 120 mL during in vivo studies. The system is capable of delivering and monitoring a range from 0 to 320 mL. Calibration procedures demonstrated a mean error in delivered volumes of 0.9±1.7%.

Temperature signals had a physiological range of 25-45 °C during in vivo studies. The system is capable of measuring a range from near 0 to 100 cmH_2O. The regression coefficient between electrical signals provided by the temperature probes and its conversion to °C was R^2=0.999 ($p<0.001$). Therefore, the error in temperature measurement was considered negligible.

The ability of the computerized system to make temporal measurements was assessed by having the system take readings from well-defined control signals. Mean absolute error of T_I and T_E at different I:E ratios are summarized in Figure 1. Errors from manually derived data using polygraph traces showed higher mean values than those obtained with computerized calibrations. In all cases, the absolute and relative errors compared to polygraph determinations were less than 100 ms and 2.56 %. Computerized measurements demonstrated the lowest mean errors (100 ms and -1.66%).

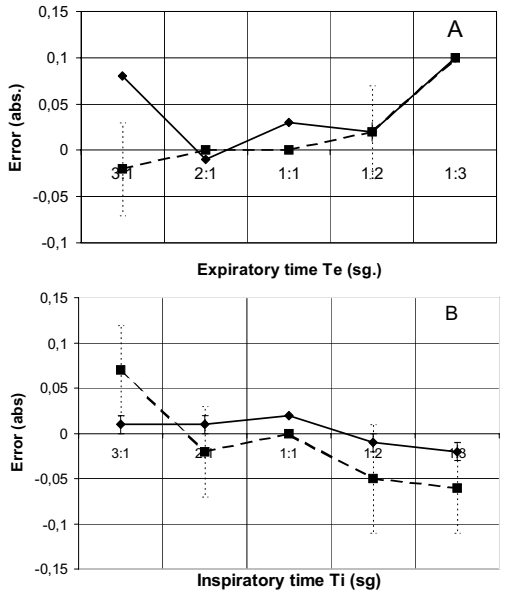

Fig. 1 Temporal errors in polygraph traces (♦) versus computerized (■) assessment of expiratory (A) and inspiratory (B) times with different I:E ratios. Mean ± SD. Te: expiratory time, Ti: inspiratory time, (abs.): absolute error.

C. Lung Mechanics System

The system can calculate dynamic compliance (C_{dyn}) from raw signals (volume and pressure) using equation (4), with a range from near 0 to 100 $ml \cdot cmH_2O^{-1} \cdot kg^{-1}$. In the 30 procedures performed (3 per animal, after 1, 2 and 3 hours), a physiological range of 1.04±0.02 to 2.68±0.01 $ml \cdot cmH_2O^{-1} \cdot kg^{-1}$ was measured. Scatter of C_{dyn} for each procedure (dispersion) showed a maximum range of 16.68% (-7.37 to 9.31%) and minimum of 0.84% (-0.55 to 0.29%). The maximum standard deviation expressed as a percentage was 4.83% (Figure 2A).

The system can calculate airway resistance (R_{AW}) from raw signals (pressure and flow) using equation (5), with a range from 0 to 11500 $cmH_2O \cdot L^{-1} \cdot s^{-1}$. The physiological range during *in vivo* studies involving 10 newborn lambs was 107±4 to 1659±21 $cmH_2O \cdot L^{-1} \cdot s^{-1}$. Scatter of R_{AW} for each study had a maximum range of 15.18% (-8.56 to 6.62%) and minimum of 2.42 % (-1.47 to 0.95%). The maximum standard deviation was 5.00 % for all studies (Figure 2B).

The system can calculate standardized work of breathing (W_R) from raw signals (pressure, volume) using equation (6), with a range from 0 to 12300 $g \cdot cm \cdot kg^{-1}$. The physiological range during in vivo studies involving 10 newborn lambs was 62±1 to 1177±40 $g \cdot cm \cdot kg^{-1}$. Scatter of W_R for each study had a maximum range of 14.10% (-8.49 to 5.61%) and minimum of 1.03% (-0.46 to 0.57%). The maximum standard deviation was 4.91% for all studies (Figure 2C).

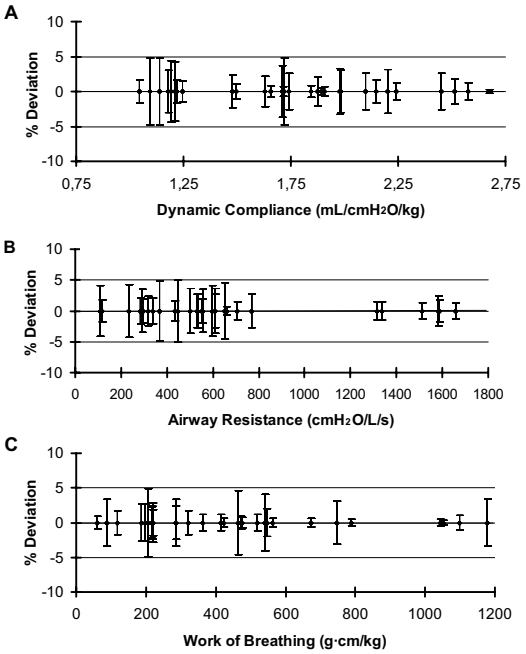

Fig. 2 Range of computed lung mechanics parameters. Values for C_{dyn} (A) ranged from 1.04 to 2.68 $mL \cdot cmH_2O^{-1} \cdot kg^{-1}$, R_{AW} (B) from 107 to 1659 $cmH_2O \cdot L^{-1} \cdot s^{-1}$ and W_R (C) from 62 to 1177 $g \cdot cm \cdot kg^{-1}$.

D. In vivo experiments

Pulmonary lavage during gas ventilation produced a significant decrease of arterial pH and oxygenation, and an increase in P_{aCO2} levels (Figure 3). Tachycardia (increased heart rate) and pulmonary hypertension were associated with the lavage procedure, but no effects were observed on either cardiac output or systemic arterial pressure. The procedure, however, compromised the elastic properties of the lung decreasing C_{dyn} (1.7±0.5 vs. 0.4±0.2 $mL \cdot cmH_2O^{-1} \cdot kg^{-1}$,

$p<0.05$) and increasing in R_{AW} (28±10 vs. 50±11 $cmH_2O \cdot L^{-1} \cdot s^{-1}$, $p<0.05$) and $\overline{P_{AW}}$.

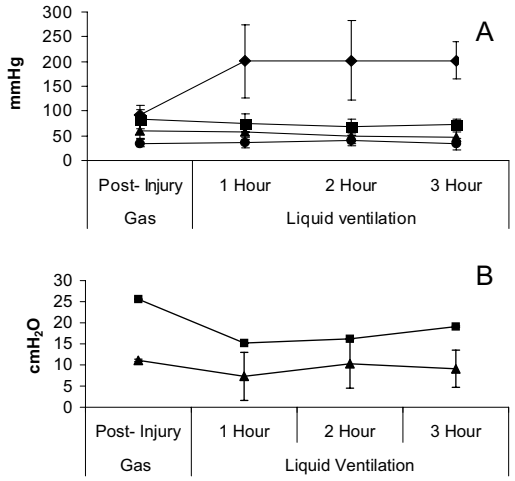

Fig. 3 Mean pulmonary gas exchange parameters during gas and liquid ventilation. Data are shown as mean ± SD. (#) ANOVA, $p<0.05$ vs. baseline; (*) ANOVA *post hoc* treatment, $p<0.05$ all values versus post-injury level. (A) P_{aO2} (♦),P_{aCO2} (■), Systemic arterial pressure (▲) and Pulmonary arterial pressure (●). (B) Quasi-static PIP (■) and mean airway pressure (▲).

After the start of total liquid ventilation, a 2-fold increase in arterial oxygenation and an improvement of ventilation with a significant reduction in carbon dioxide were observed. In addition, arterial pH demonstrated an upward trend while heart rate, pulmonary and systemic arterial pressures, and cardiac output did not change significantly. After one hour, a 4-fold improvement of C_{dyn} (2.0±0.5 $mL \cdot cmH_2O^{-1} \cdot kg^{-1}$) with lower $\overline{P_{AW}}$ and $\dot{V}_E$ was observed with a large increase in R_{AW} (667±525 $cmH_2O \cdot L^{-1} \cdot s^{-1}$). This later finding is related to the high dynamic viscosity and density of perfluorocarbon that flows through the upper airways. During experiments, ventilatory settings were adjusted as needed and physiological data remained stable thereafter.

IV. DISCUSSION

Ventilatory management is generally performed at frequencies of 4 to 8 $cycles \cdot min^{-1}$, I:E ratios of 1:1 to 1:3, tidal volumes of 15 to 25 $mL \cdot kg^{-1}$, inspiratory pressures of 70 to 30 cmH_2O and PEEP's of -10 to 100 cmH_2O [5], [6], [19]. Our system readily handles these ventilatory settings. In addition, in each case, the system can perform well beyond these ranges in order to handle pathophysiological situations. In order to determine the accuracy of our ventilator, we performed an extensive check of errors introduced by each component (volume-delivered linear actuator, pressure transducer, temperature sensor, etc.). This is the first time such quality controls have been reported in the development of total liquid ventilators. In summary, we observe a low mean error in all calibrated signals (pressure: -1.0%, delivered volume: 0.9%, temperature: 0%, T_I: -1.66%, T_E: 2.56%, f: 1.38%). The low error in raw signals suggests that computed pulmonary parameters (compliance, resistance, work of breathing, etc.) accurately represent the physiological state of the lungs. In most cases, errors can be considered negligible. In all cases, measurement errors are sufficiently low that they should not significantly alter the selection of appropriate ventilatory therapies.

Computerized respirator systems with on-line displays have been developed to test lung function during spontaneous and/or conventional mechanical ventilation [3]. A primary goal using these techniques is to develop optimum ventilatory therapies for patients under different conditions [4], [14]. Total liquid ventilation is an active ventilatory technique using forced inspiration and expiration cycles that require continuous monitoring on a breath-by-breath basis. Liquid ventilation must be performed using a dedicated, computerized system in order to obtain reliable measurements without extensive training (beyond that available in a typical clinical setting) and real-time calculations of lung mechanics [20]. Changes in our ventilatory strategy (e.g. frequency, tidal volume, I:E ratio, etc.) produced immediate alterations in lung function (compliance, resistance, work of breathing, etc.), which suggest that the system accurately reflects physiological conditions in the lungs. This finding is also corroborated by the low variance of calculated values (Figure 2).

Some of the analysis protocols during total liquid ventilation utilize the assumption that liquids are relatively incompressible. Under this condition, volume changes in the cylinder-piston produce an equivalent displacement of volume through a closed circuit to the lungs. A way to test the validity of this assumption is to determine whether $C_{circuit}$ is negligible compared to the measured minimum C_{dyn}. If $C_{circuit}$ were in the same range as C_{dyn}, then the accurate measurement of lung compliance becomes much more difficult. In our ventilator, C_{dyn} was 570 times higher than $C_{circuit}$, suggesting that an accurate measure of lung compliance can be obtained.

Our ventilator prototype was able, in lung injured newborn lambs, to maintain precise control of delivered tidal volume for at least 3 hours. The depletion of the surfactant by lung lavage induced an acute respiratory failure, characterized by severe hypoxia and acidosis, low lung compliance and high airway resistance [21]. These findings closely simulate those found in respiratory distress syndrome, a serious problem in preterm babies. Total liquid ventilation has proven its efficacy in the treatment of preterm (rabbit, lamb) [10], [22] and lung injured animals [11], [23].

The gas exchange data during liquid ventilation in our study demonstrate an improvement in gas exchange parameters similar to those described by others. We observed a 200 % increase in oxygenation and a significant decrease in hypercarbia (carbon dioxide levels) and acidosis (pH) that was maintained throughout the total liquid ventilation period (3 hours). Moreover, some animals were sustained for up to 6 hours and cardiopulmonary status were maintain (n=3; P_{aO2}: 202±6 mmHg; Pa_{CO2}: 45±4 mmHg; systemic arterial pressure: 71±14 mmHg; cardiac output: 347±78 $mL \cdot min^{-1} \cdot kg^{-1}$), without

the appearance of adverse clinical symptoms (i.e. incidence of perfluorothoraces, cardiovascular instability, etc…). Also, our measurements of lung mechanics are closely similar to those previously described during total liquid ventilation [6], [24], [25].

In summary, the use of a multiple piston-driven liquid ventilator in animals with acute lung injury induced by repeated lung lavage produced an adequate gas exchange without compromising cardiovascular function. Specifically, our systems have the following advantages: 1) precise control of delivered liquid tidal volume, 2) high accuracy of acquired signals (mean error < 3%), 3) introduction of three nested feedback loops (safety servocontrol limits) for time, volume and pressure, 4) real time display of measured and calculated pulmonary parameters, and 5) PFC's isolation in the respiratory circuit from the mechanical components that could be disposable.

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