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Mechanical Ventilator Development During COVID-19 Crisis: Preclinical Data Analysis from Porcine Bio-model

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Abstract: This paper describes a mechanical ventilator prototype with preclinical test performed on 10 bioporcine models, where tests were performed for eight hours for each individuals, giving the respective life support on different scenarios inducing stress and evaluating that each subject physiological parameters remain and return swiftly to the normal values. The results have shown the capabilities to maintain physiological parameters for each subject under test and present also the capability of monitoring the pulmonary parameter, compliance (C), computed from the pressure-volume hysteresis loop measured by the prototype, so that this is the unique proposed prototype to present this capability at this extended subject samples. The ventilator prototype was designed following the *Medicine & Healthcare products Regulatory Agency* (MHRA) from United Kingdom (UK), that was the first guidelines for manufactured ventilator system in the pandemic of COVID-19 emergency. Finally the components used in the mechanical ventilator comes from different industrial applications, that its performances were tested for years and its supply were no affected by the surge of the acquisition of critical electro-mechanical components used by the commercial ventilator factories under pandemic situation as COVID-19 pandemic.

Keywords: Compliance, COVID-19, Mechanical Ventilator, Pressure-volume Hysteresis Loop, Porcine bio-model, Preclinical Data

1. Introduction

The COVID-19, at its early stage of propagation, has put in evidence the requirements and necessities of the installed health facility capacities [1, 2]. This situation has became a global health problem [3] attending the incremental number of COVID-19 cases.

The acquired experiences dealing with the COVID-19 infection cases from patients with respiratory distress [4, 5], mechanical ventilation was the first procedure applied [6, 7] and recommended [8].

The COVID-19 effects to the respiratory system were the variation of the normal lungs biophysical parameters such as compliance, resistance and others [9], resulting in a critical respiratory distress. For this reason the use of mechanical ventilation systems was vital at the early stages of this critical conditions, in order to help and support the patients recovery [8]. Thereafter, recommendations were submitted for the use of this medical devices to help the patients with this critical condition [6, 10, 11].

This paper describes a tested device of mechanical ventilator prototype that have passed preclinical test, in order to increase the installed capacity for COVID-19 patients with respiratory distress, in case of shortage of mechanical ventilators, as it was taken place in different countries [12, 13] where the population was affected by the COVID-19.

2. Principal Aspect for an Emergency Mechanical Ventilator

Due to the shortage of mechanical ventilator as consequence of the COVID-19 pandemic, different mechanical ventilator designs were proposed during 2020. It is worthy to highlight the effort of the MHRA from UK [14], to issue guidelines of minimal clinically acceptable ventilator specifications, due to the potential shortage of ventilators supply. For this reason, we have been proposed a prototype, which can be quickly manufactured cheaply and on large scale if it is necessary, highlighting important technical aspects of the patient safety.

The aspects of the developed mechanical ventilator prototype are describes in detail in Table 1.

Table 1. *Aspects of the mechanical ventilator.*

Parameter	Value	Observations
Working Pressure	0 to 50 cmH_2O	
Peak Pressure	40 cmH_2O	Limited by valve protection
Operation Mode	VCV	
Flow	-100 to 100 L/min	
Inhalatory Trigger	2 to 6 L/min	
Respiratory Rate	10 to 30 cycles/min	
Inspiratory:Expiratory ratio (I:E)	1:5 to 5:1	
PEEP	5 to 20 cmH_2O	Regulated with PEEP valve
Tidal Volume	100 mL to 800 mL	Depends on the Ambu®Bag used

3. Designing and Development

3.1. Base Pump System

Due to the emergency at the pandemic situation, the use of disposable resuscitator (AmbuBag) as a pumping container was essential [15, 16], because this devise brings important advantage for a swift mechanical ventilator development process as follow:

a) It is a tested and registered for medical uses device in almost all the countries.
b) It is cheap and easy to acquired.
c) It permits to get a controlled range volume of 100 mL to 1000 mL.
d) The (positive end-expiratory pressure) PEEP valve and exhaust protection valve are easily implemented or its included in some models.
e) It has compatibility with respiratory circuit tubing used in mostly all the hospitals.
f) It has the adaptability to be connected to hospital oxygen outlets.

Implementing this devices into the prototype developing process, in place of a compressor or turbine system, we were able to focus into developing electromechanical and its respective sensor system.

3.2. Electromechanical Pump System

Principally to delivery an oxygen mix volume using a disposable resuscitator, it must be deformed appropriately in a fixed frequency with an appropriate implemented control system. For this pumping process a linear electromechanical actuator was used.

Different actuator systems were proposed, such as NEMA standard motor (National Electrical Manufacturers Association) based system among all the diffused mechanical ventilator prototype ideas. It is known that a NEMA standard motor well implemented with a feedback system, it could be very precises in motion and position, however without a validated reduction gearbox and encoder system, the prototype will not withstand at least for a few of continuous functioning hours.

For this propose, an industrial certificated linear actuator was chosen from FESTO, Germany. The principal parameters for an actuator for this application, pumping continuously a full oxygen mix AmbuBag are:

a) To have a position controlled range of 0 to 100 mm.
b) To have a minimum pushing force of 100 N.
c) Long life cycles.
d) Support continuous operation at least 50 days [17].

3.3. Pressure and Flux Sensor System

The pressure must be monitored as close as possible to the breathing circuit outlet. In this case, the pressure is sampled on an outlet port of the filter. By measuring the pressure in real time, its enables us to plot this parameter on screen, visualizing the breathing cycle and setting the pressure range for the alarms: over pressure, under programmed PEEP pressure, breathing circuit leaks and other programming settings that are required. The pressure signal from the subject observation is depicted in Figure 1.

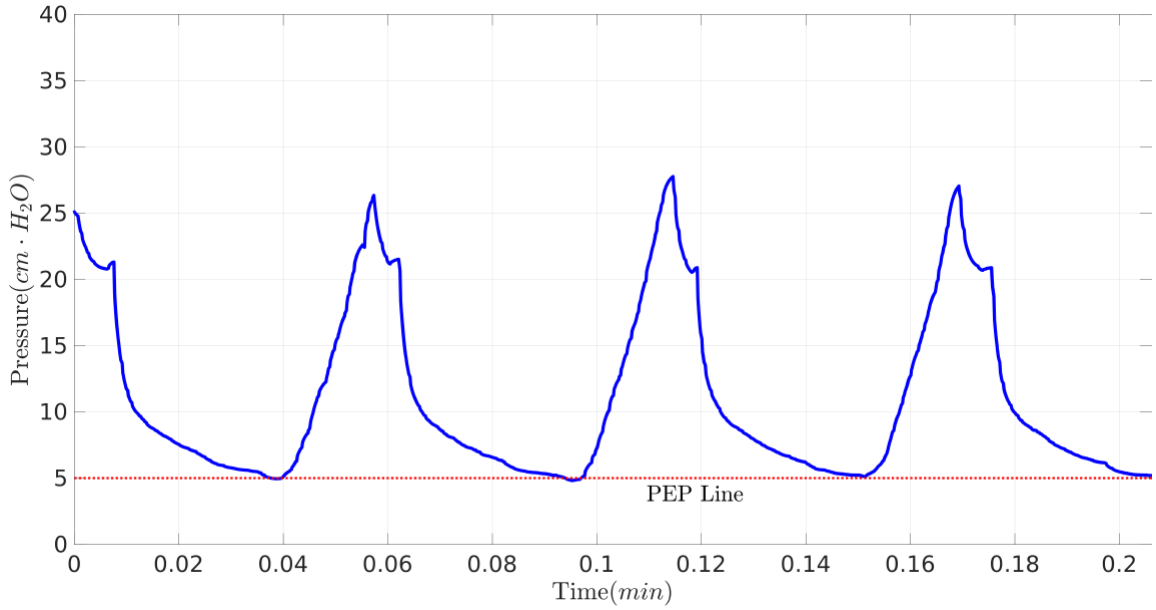

Figure 1. *Prototype pressure signal from subject data analysis where the PEEP line remains constant over the subject intervention.*

The flux is also measurement in real time. The sample rate of the flux measurement must be high as possible and its signal properly filtered in order to compute the delivered volume by performing an adequate integration procedure of the flux signal, as shown in Figure 2.

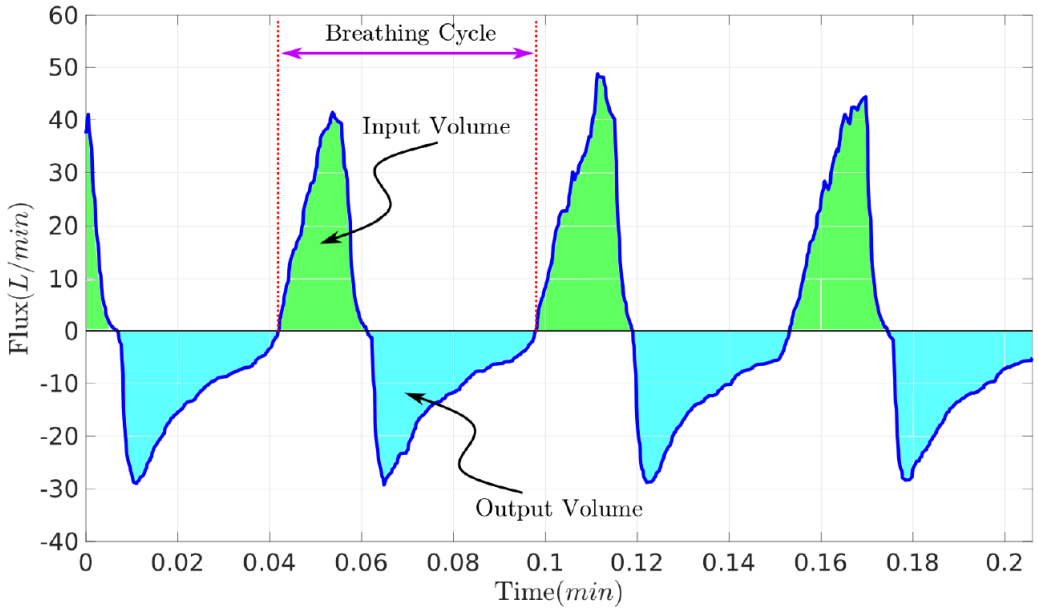

Figure 2. *Prototype flux signal from subject data analysis, the volume can be computed by integration of the signal for each breathing cycle.*

3.4. Intuitive Graphical Interface

As part of the system, described in Figure 4, the graphical interface is an important component for visualizing, controlling and setting the working parameters for a mechanical ventilator. In our case, a touchscreen equipped with an electronic signal processing system was implemented in order to interact with the user and to display the settings, see Figure 3. Furthermore, the touchscreen electronic system must have an Analog to Digital Converter circuit (ADC) with an optimal sample rate to process the flux and pressure signals, performing the volume computation and displaying the signal on the screen. This condition must be revised on this kind of devices that are usually used on industrial applications and cost-effective, because not all the brands have the capability to implement an ADC with a sample rate more than 100 samples per second.

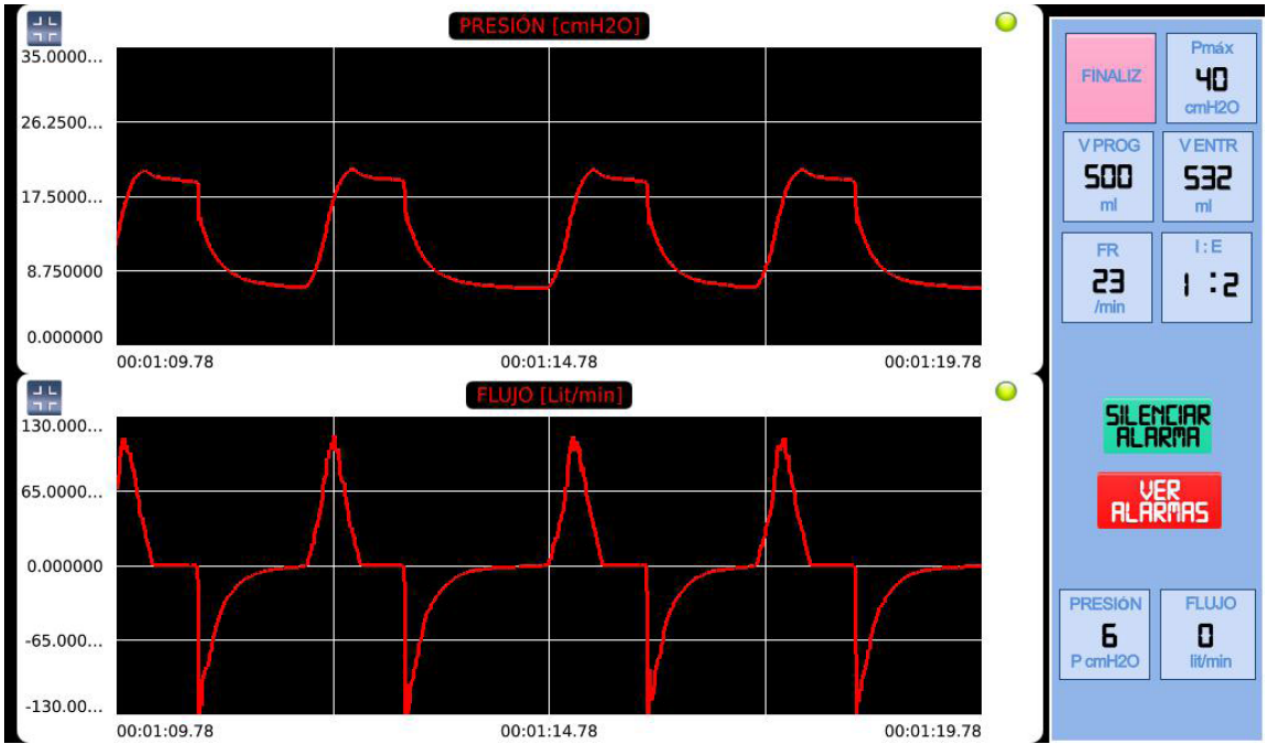

Figure 3. *Mechanical ventilator screenshot of the touchscreen interface, where the pressure and tidal volume timeline is displayed and the setting parameter can be accessed.*

For this reason, all the brands available on the market in Costa Rica, the US10-B10-TR22 touchscreen from UNITRONICS was implemented and its ADC is 12 bits of resolution with a sample rate of 100. This enable us to get a smooth signal flux to compute the tidal volume accurately and an appropriated resolved pressure signal for constant monitoring in order to set the alarm triggers properly.

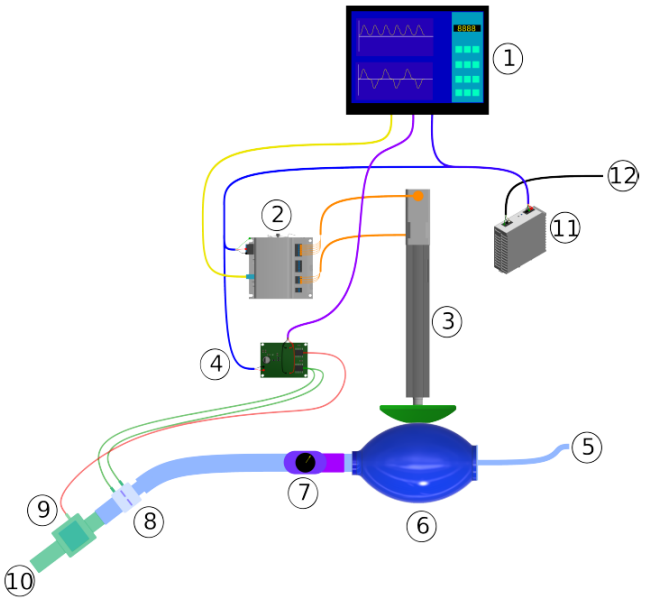

Figure 4. *General scheme of the mechanical ventilator system, for numeric labels refer to Table 2.*

Table 2. *Description of the Figure 4.*

Label	Description
1	Touchscreen
2	Linear Actuator Controller
3	Linear Actuator
4	Sensor Board
5	O_2 Mix Inlet
6	AmbuBag®
7	PEEP and Relief Valve
8	Flux Pitot Sensor and Check Valve
9	Filter and Outlet Port for pressure measurement
10	Breathing Circuit Output
11	Power Supply 24 V DC @ 5.0 Amp
12	To Main 220/110 V AC

4. Pre-clinical Test on Porcine Bio-model and Results

The porcine bio-model has been the milestone stage in biomedical research for many years. In medical respiratory research field, the size and biophysical characteristics of porcine lungs are similar to human lungs system, giving the best condition, as a bio-model, for testing and optimizing a mechanical ventilation device [18].

For this research project, a genetic line pigs of low predisposition of respiratory illness were used, from an animal lot with sanitary traceability profile, in order to assuring subjects free from any respiratory problems. The animal lot

was composed by seven females from Topig genetic line, three months age old, mass range between 25 and 30 kilogram, risen and moved to laboratory under the highest animal welfare conditions.

The subjects were placed in vivarium 72 hours before clinical procedure, where an Objective Structured Clinical Examination (OSCE) procedure was applied to verify and validate the optimal health conditions. The management of the subjects in vivarium was performed in agreement with international welfare animal compliance for this specie from the National Research Council (NRC) [19], such procedure was verified and approved by Institutional Animal Care and Use Committee (IACUC) of the Universidad de Costa Rica.

At the beginning of clinical procedure, the subject were anesthetized using Total Intravenous Anaesthesia procedure (TIVA) with midazolam and ketamine for initial procedural sedation, in combination with midazolam-ketamine-propofol sedation during the interventional procedure. The rocuronium was used for neuromuscular blocking of the subject into the interventional procedure.

The tracheal intubation procedure was applied for every subject, following real time monitoring of O_2 saturation, electrocardiogram, heart rate, breath rate, non invasive arterial pressure and corporeal temperature. These parameters were evaluated and recorded every 10 minutes. The subjects were hydrated properly and keeping warmed with electric blanket as shown in Figure 5.

The overall time taken for the preclinical test for each subject was 7 hours, applied to 10 subjects.

Figure 5. *Subject under care during the preclinical ventilator test. The mechanical ventilator was connected to a PC for recording data in real time for further analysis.*

The mechanical ventilators were consecutive submitted to several tests on the subjects for a determined period of time, following a designed experimental clinical procedure, simulating all possible situations that could be shown in a human patience needed of this medical devices. For each test, the subjects were exposed to a different degree of breathing restrictions, in order to verify the performance of the mechanical ventilator to restore and maintain the breathing parameters.

Specifically, the performed test were: mechanical ventilation without breathing restriction, with neuromuscular blocking, neuromuscular blocking with hyperoxygenation, neuromuscular blocking with hyperventilation, induced moderated respiratory distress and induced severe respiratory distress. At the final stage of the clinical procedure, each subject were humanely euthanized and a necropsy procedure were performed to verify any injury due to external factors.

An induced severe respiratory distress by removing the pulmonary surfactant was the final stage of the preclinical test. The recorded data from the mechanical ventilator was possible to verify the behavior of the lungs by plotting Volume-Pressure Loop, as seen in Figure 6.

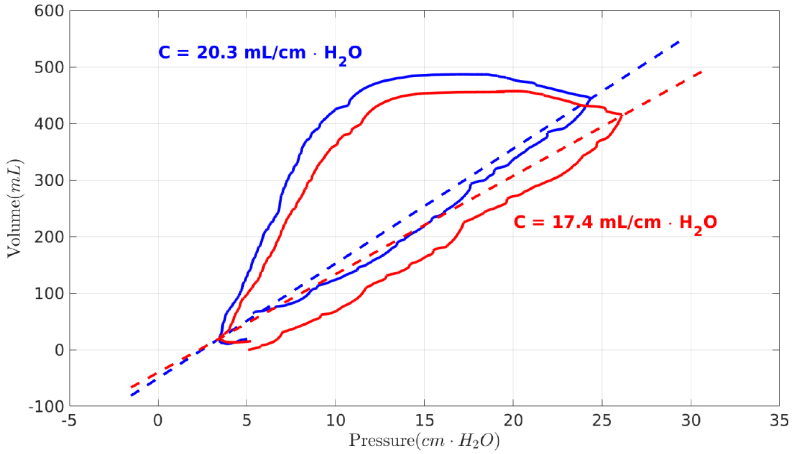

Figure 6. *Pressure-Volume hysteresis loop from subject data before (- - -) and after (- - -) removing pulmonary surfactant.*

Finally, the results computed from plotted data in Figure 6 are described in Table 3, where the evolution of pulmonary parameters of the subject, under those two detailed conditions, are quantified.

Table 3. *Pulmonary parameters computed from Pressure-Volume hysteresis loop data recorded by the mechanical ventilator under test.*

	Parameter	Values	Units
Initial State	Compliance	20.3	mL/cmH_2O
	Hysteresis Loop Area	4463.44	$mL{\cdot}cmH_2O$
Final State	Compliance	17.4	mL/cmH_2O
	Hysteresis Loop Area	4933.73	$mL{\cdot}cmH_2O$
Relative Variations	Δ Compliance	-14.3	%
	ΔHysteresis Loop Area	10.5	%

Here we can see, in Table 3, the pulmonary compliance dV/dP decreases 14.3% due to removing procedure of the pulmonary surfactant at the last stage of induce severe respiratory distress procedure. All the subject, at this stage of the preclinical procedure, were supported efficiently by the mechanical ventilator prototype. The Figure 7 shown the final prototype with the designed requirements to be implemented in an intensive care unit (ICU) or primary care facility in case of a shortage situation of mechanical ventilation units.

Figure 7. *Prototype under demonstration with the final-designed case, ready to be implemented in an ICU or primal care facility in case of shortage of mechanical ventilation units.*

5. Conclusions

The preclinical analysis was applied to 10 subjects, where the performance of the prototype was verified by evaluating each subject physiological parameter, that remains and returns swiftly to the normal values for each induced stress, regarding the preclinical protocol.

One remarkable result was the prototype is capable to produce data for evaluating the evolution of pulmonary parameters of the subject under test, as is shown in Figure 6, where this is the unique proposed prototype to present this capability.

At the final stage of the preclinical protocol, where induced stress by removing pulmonary surfactant, the prototype was successful to support the subject under test in this induced state, close to a critical respiratory distress.

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Conflicts of Interest

The authors declare no conflicts of interest.

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