FDA Emergency Use Authorization-Approved Novel Coronavirus Disease 2019, Pressure-Regulated, Mechanical Ventilator Splitter That Enables Differential Compliance Multiplexing

Michael J. Paulsen,* Yuanjia Zhu,*,† Matthew H. Park,*,‡ Annabel M. Imbrie-Moore,*,‡ Sam Baker,§ David Walter Edmonston,¶ Tyler Dawson,¶ Evan Ly,¶ Shannon Martin Bell,¶ Nick A. Tran,* Jinsuh Jung,* Jordan Cedarleaf-Pavy,¶ K. R. Sridhar,¶ Venkat Venkataraman,¶ and Y. Joseph Woo*,†

Infection with the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), may cause viral pneumonia and acute respiratory distress syndrome (ARDS). Treatment of ARDS often requires mechanical ventilation and may take weeks for resolution. In areas with a large outbreaks, there may be shortages of ventilators available. While rudimentary methods for ventilator splitting have been described, given the range of independent ventilatory settings required for each patient, this solution is suboptimal. Here, we describe a device that can split a ventilator among up to four patients while allowing for individualized settings. The device has been validated *in vitro* and *in vivo*. *ASAIO Journal* 2022; 68;1228–1231

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Infection with SARS-CoV-2 often causes severe illness termed coronavirus disease 2019 (COVID-19). While COVID-19 has wide-ranging effects on nearly every organ system,[1–7] severe cases cause pneumonia and ARDS, characterized by diffuse inflammatory lung injury. Mechanical ventilation is the mainstay treatment for ARDS, which typically takes weeks to resolve on a ventilator.[8,9]

In areas with surges of COVID-19, there may not be enough ventilators to support all patients.[10,11] Ideally additional ventilators can be procured; however, this requires significant lead time and expense. To avoid immediate loss of life, a bridging strategy is necessary. Ventilator multiplexing is a potential solution, whereby two or more patients are sustained by a single ventilator. Methods for splitting ventilators have been described using Y-connectors and other common parts.[13,14] However, these rudimentary solutions pose challenges when treating patients with ARDS, due to the requirements of individualized settings for each patient, such as peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), and tidal volume (V_T).

Here, we describe a device that can split one ventilator among four patients. Our device, the ventilator sharing and monitoring system (VSMS), allows titration of PIP, V_T, and PEEP for individual, simultaneously ventilated patients. Excluding the monitoring system, the device is entirely mechanical, low cost, and scalable, making it well-suited for resource-limited settings. We hope this device can temporarily bridge ventilator capacity during shortages, helping to avoid unnecessary loss of life due to resource limitations.

The VSMS, developed with industry partners from Bloom Energy (San Jose, CA), achieves individualized multiplexing via independent flow regulation and monitoring (Figure 1A). Each of the four circuit limbs consists of: 1) an adjustable valve to individually regulate flow, controlling PIP, and V_T; 2) one-way valves on inspiratory and expiratory lines, isolating patients from the system and reducing cross-contamination risk; and 3) independent monitoring of PIP, PEEP, inspiratory V_T, expiratory V_T, average V_T, and continuous pressure, flow, and volume, with individually adjustable alarms (Figure 1B). The system is reusable with disposable components and safeguards in place to limit cross-contamination. The VSMS also includes circuitry and software to monitor each patient's ventilatory parameters in real time.

To verify safety and efficacy, we first evaluated parameter accuracy and alarming, measuring PIP, PEEP, and V_T over a range of volumes, pressures, and compliances. Using an *in vitro* artificial lung on a single ventilator, we compared the monitored results of the VSMS with that of a gas flow analyzer (VT650, Fluke Inc., Everett, WA). The in-line monitoring system of the VSMS accurately reported V_T across a range of PIP using both compressed air and oxygen (Supplemental Table 1A, http://links.lww.com/ASAIO/A818). Cross-dependence of V_T over a range of PIP when other variables such as respiratory rate, PEEP, resistance, and compliance are held constant were also measured. Additional tests are reported in the Supplementary information, http://links.lww.com/ASAIO/A818.

To demonstrate that the VSMS can independently manipulate V_T, PIP, and PEEP for each patient without influencing others, we examined the effects of adding and subtracting patients from the circuit *in vitro* using four different elastomeric lungs.

*From the Department of Cardiothoracic Surgery, Stanford University, Stanford, California; †Department of Bioengineering, Stanford University, Stanford, California; ‡Department of Mechanical Engineering, Stanford University, Stanford, California; §Department of Comparative Medicine, Stanford University, Stanford, California; and ¶Bloom Energy, San Jose, California.

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Correspondence: Y. Joseph Woo, Department of Cardiothoracic Surgery, Department of Bioengineering, Stanford University, Falk Cardiovascular Research Building CV-235, 300 Pasteur Drive, Stanford, CA 94305-5407. Email: joswoo@stanford.edu.

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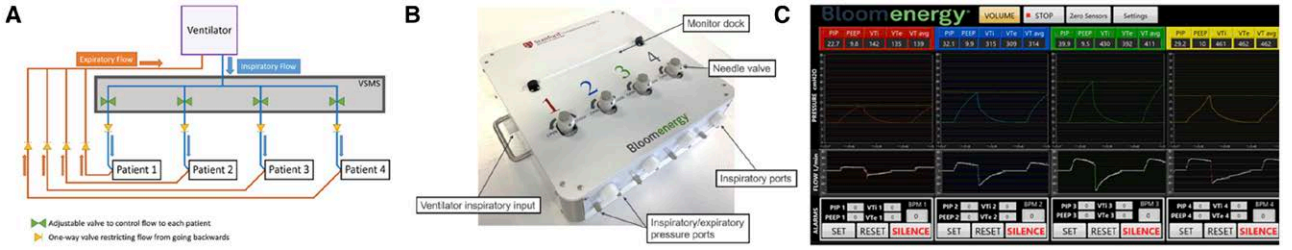

Figure 1. The ventilator sharing and monitoring system (VSMS). **A**: System airflow circuit diagram of the VSMS. Each ventilation line is equipped with adjustable flow and check valves allowing for independent regulation of a wide variety of ventilation settings and isolated air circuits, reducing the risk of cross contamination. **B**: Prototype VSMS device with callouts to relevant external components. **C**: Device monitoring display with graphical user interface. full color online

Patients were sequentially added or removed while fluctuations in PIP, PEEP, and V_T were recorded. Addition had minimal effects on ventilatory parameters of remaining patients. Subtraction resulted in temporary fluctuation of the patient with lowest pressure and volume requirements, which resolved within 8 seconds (Supplemental Table 1B, http://links.lww.com/ASAIO/A818). Temporary disconnect or suctioning events had minimal effects on remaining patients (Supplementary Information, http://links.lww.com/ASAIO/A818).

To validate feasibility and efficacy of the VSMS, we conducted *in vivo* testing using two sheep of different weights (Figure 2A). Recordings of V_T and airway pressure from each sheep are shown in Figure 2, B and C, which showed differential lung ventilation between the two sheep. Arterial blood gas analyses performed at baseline and every 10 minutes are shown in Supplemental Table 2, http://links.lww.com/ASAIO/A818, demonstrating that the VSMS adequately ventilates both sheep simultaneously. Post-VSMS chest x-rays compared with

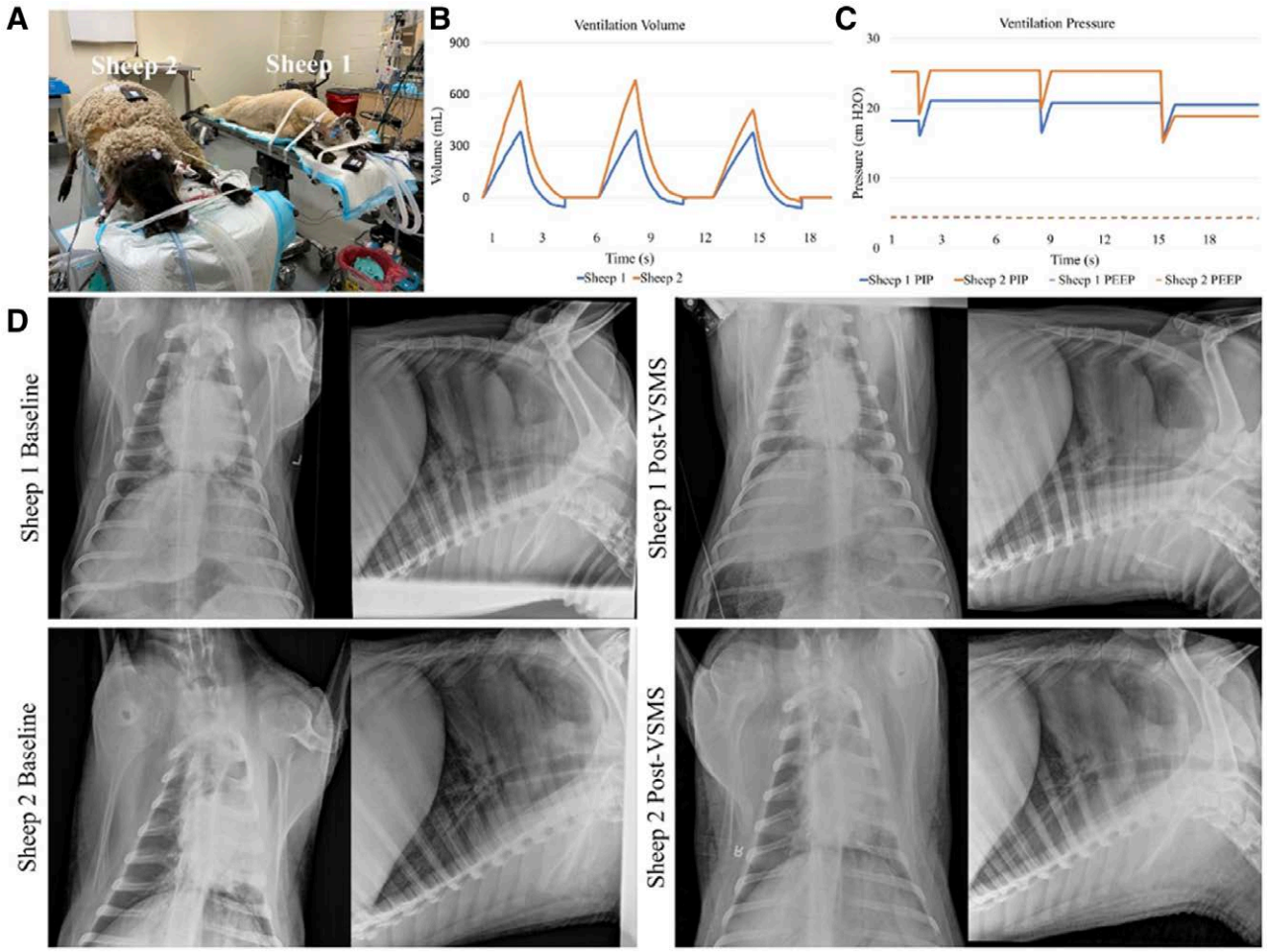

Figure 2. *In vivo* testing of VSMS using two sheep with different weights. **A**: Two sheep tested using the VSMS system. **B**: Ventilation volume changes over time. **C**: Pressure changes over time. **D**: Anteroposterior and lateral chest x-rays of both sheep pre- and post-VSMS testings. PIP, peak inspiratory pressure; PEEP, positive end-expiratory pressure; VSMS, ventilator sharing and monitoring system. full color online

baseline images demonstrated clear lung fields without pneumothorax (Figure 2D).

The goal of ventilating patients with ARDS is to facilitate gas exchange of damaged and inflamed lungs. Issues specific to ventilator splitting in ARDS are variable lung compliance and gas exchange ability between patients. A set volume in one patient may result in an adequate breath with acceptable pressures, whereas in another patient, this volume may be insufficient to overcome the stiffness of the diseased lungs or excessive, resulting in barotrauma. The VSMS eliminates this pitfall through the monitoring component of the multiplexer, allowing safe and effective use of pressure-control ventilation among multiple patients with the ability to individually titrate PIP, V_T, and PEEP. Not all parameters can be individually controlled, however. Since the splitter and ventilator share a common fresh gas input, FiO_2 cannot be individualized, nor can respiratory rate. As such, we envision the VSMS to be used primarily during the long maintenance phase many patients require on a ventilator while recovering from ARDS, and the ability to titrate PIP, PEEP, and V_T would increase the utility of ventilator splitting. In theory, one could add triggering devices or separate gas bleed valves to separately modulate respiratory rate and FiO_2 between patients; however, we chose not to investigate these possibilities in our initial device iteration. In terms of cost-effectiveness, the VSMS device can be built at a fraction (less than 10%) of the cost of a new ventilator. Units can be rapidly manufactured from easily sourced parts with limited tools, making the device particularly attractive for limited resource or emergency settings.

Despite challenges, we have shown that ventilator multiplexing is a viable strategy for patients with moderate-to-severe disease. We have designed and developed a multiplexer that can accurately and independently control and monitor a wide range of ventilator settings for up to four patients with differing ventilatory parameters, which has been given FDA Emergency Use Authorization. Additionally, we have thoroughly analyzed and tested the output metrics of this device both *in vitro* and *in vivo* in an ovine model. In situations where ventilator demand exceeds supply, ventilator multiplexing could be a very effective immediate, temporary measure to prevent substantial loss of life particularly in resource-limited areas.

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