Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Original Research Article

CRISIS ventilator: A 3D printed option for ventilator surge in mass respiratory pandemics

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ABSTRACT

Background: The COVID-19 pandemic revealed flaws in the stockpiling and distribution of ventilators. In this study, we assessed the durability, sterilizability, and performance of a 3D-printed ventilator.
Methods: SLS-printed devices were dropped from 1.83 m and autoclaved before evaluation on a COVID-19 simulated patient. The respiratory performance of an extrusion-printed device was studied using a variable compliance model. Ranges of sustainable respiratory rates were evaluated as a function of tidal volume.
Results: Autoclaving and dropping the device did not negatively impact minute ventilation or PIP for sustained ventilation. Equivalence was significant across all measures except for comparing the autoclaved and dropped with $p = 0.06$. Extrusion produced ventilators achieved minute ventilation ranging from 4.1 to 12.2 L/min for all simulated compliances; there was an inverse correlation between tidal volume and respiratory rate.
Conclusion: The CRISIS ventilator is a durable, sterilizable, and reusable 3D-printed ventilator using off-the-shelf materials which could be employed variety of adult lung diseases. Further in-vivo testing is needed.

1. Introduction

During the early 2000's, outbreaks of influenza and Middle-Eastern Respiratory Syndromes (MERS) prompted healthcare workers to reinvestigate strategies for managing surges in ventilator demand and ICU admissions. Lessons learned from mass-casualty events, the influenza pandemic, and the polio epidemic highlighted the need for planning.[1,2] Two main strategies arose: the first to create a tangible stockpile of ventilators; the second to rapidly mobilize new production and allocation of ventilators.[3] In 2015 models of a future influenza-like pandemic estimated the maximum number of critically ill patients in the United States to be 135,000 with 60,000 patients requiring ventilators during the predicted peak. These estimates may have been inadequate with the unexpected rise of the Coronavirus 2019 (COVID-19) pandemic. By April 10th, 2020, the state of New York had reached over 170,000 reported cases[4] with many patients exhibiting profound hypoxemia. Many of these patients had a COVID-19 related Acute Respiratory Distress Syndrome (ARDS) illness with impaired respiratory compliance and prolonged ventilatory support. Initial estimates reported a need for over 120,000 ventilators by week 20 of the pandemic.[5] These models predicted that 46,000 additional ventilators would need to be produced for the United States alone, suggesting that the 2015 models of ventilator surges were only half what was expected in the COVID-19 pandemic.

To account for the difference between available ventilators and the rising numbers of critically ill patients, the US government began to utilize the strategic national stockpile. During the early mobilization of these emergency ventilators, it was discovered that many of them were nonfunctional or broken,[6] which limited the ability to provide essential care to patients with respiratory failure from COVID-19 and other causes. Shortages in supplies related to the production of ventilators, as well as the high cost of completed ventilators which ranged from $6000 to $30,000 per ventilator.[7,8] In addition, there were costs related to the storage, maintenance, and mobilization of these devices. To meet the rising demand for mechanical ventilation, in the setting of severely

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limited supplies during the initial COVID-19 surge, several institutions developed strategies to share ventilators between patients[9–11] allowing two or more patients to receive mechanical ventilation with one ventilator. While these heroic efforts were able to save some lives, they were unreliable and clearly additional solutions are needed to meet emergent ventilator surges in a reliable and equitable manner.

Pandemic responses required out of the box thinking to close the gap between demand and supply. Many groups around the country-and indeed the world-focused on adapting and improving a wide range of cheaper and simpler alternatives to the large, expensive, and unavailable industrially produced ventilators. Some groups developed new ventilators under the Food and Drug Administration, FDA, emergency use authorization. Many of these ventilators utilized adapted bag-mask ventilation systems in addition the 3D printing. Published reviews to the pandemic response highlight the use of alternative industrial and makeshift ventilators[12–15] and have shown that 3D printing has risen among the list of options to rapidly fill in gaps in these critical supplies. Other authors have further shown the use of 3D printers to create PPE, ventilator valves, and emergency ventilation devices.[16] No matter the design, these emergency ventilators must reliably deliver and consistently deliver breaths to patients at an adequate rate, volume, and safe pressures to achieve adequate gas exchange and oxygenation. Here we highlight the initial results in our proposed solution to steep ventilator surges with a 3D printed ventilator.

The CRISIS ventilator is a first-of-its kind resuscitator device which can be made from readily available materials. The ventilator shown in Fig. 1 can be made using on-site extrusion 3D printed materials, a silicone membrane, and a spring which can be bought in bulk and has remained readily available even during the height of the COVID-19 pandemic. The device does not use any electricity for continuous function, functioning purely on compressed gas, and performs for an average of 3 h on a single H tank of compressed oxygen/air. Longer and shorter times can be achieved by chaining together multiple tanks in a field hospital setting in addition to adjusting the supplied gas flow rates. In contrast to other devices, this device does not depend on a bag-valve system and utilizes a modified pressure regulated ventilatory system. The device highlighted here utilizes 3D printed parts in addition to a spring, which could be manufactured using a wire and a drill, and a silicone membrane which can be purchased from hobby shops and modified using a knife or dye to fit our schematic.

When using 3D printed materials there can be concerns regarding the durability, variance between printing/manufacturing techniques on performance, and the ability to provide safe and reliable treatment. In this study we evaluated a collection of 3D printing techniques to create a low-cost and reusable device. Further, internal testing has shown that because the only directly modifiable components of the device's performance are Inhale to Exhale (I:E) ratio and Peak Inspiratory Pressure (PIP). Respiratory rate, Positive End Expiratory Pressure (PEEP), and Tidal Volume are dependent on the patient's compliance, airway resistance, and oxygen flow rates. Thus, it is necessary to determine how these resultant dependent parameters can be achieved for a given lung compliance and desired tidal volume. We present the results of the testing here.

2. Methods

2.1. Resuscitator design and manufacture

The CRISIS device uses a similar mechanism to the GO2Vent resuscitator (Vortran Medical, Sacramento CA) that is part of the United States national emergency ventilator stockpile: which includes the number of physical and theoretical (e.g. in storage or awaiting manufacture) ventilators and resuscitator devices that can be employed at any given moment.[17] The resuscitator provides a continuous flow of blended oxygen until a peak inspiratory pressure is reached and the exhale rate is determined by the user. Because of the interplay between supplied oxygen flow rates, airway resistance, respiratory compliance, and set exhale rate, the device does not allow for individual selection of certain settings. In brief the user sets the inspiratory flow rate, the maximum PIP, and the I:E ratio to achieve a desired respiratory rate, PEEP, and tidal volume which depend on the patient's specific respiratory mechanics.

For the purposes of evaluating a durable and reusable device we 3D printed the design (as highlighted in Fig. 1a) using a selective laser sintering technique, SLS, manufactured at 3D Systems (Wilsonville OR) with Nylon 12. This material was selected for its ability to tolerate temperatures encountered in an autoclave which is key for decontamination and potential reuse. While this technique cannot be employed for low-resource environments, other forms of this device utilizing extrusion techniques are undergoing continued optimization and is reported elsewhere. This was designed in accordance with ISO guidelines for a gas-powered resuscitator 10651-5.[18] Additionally, the device requires a silicone membrane to serve as a pressure relief system. For the purposes of this experiment, we hand-cut a shore D-50 0.1 mm silicone membrane which was purchased from commercial sources (Jiawanshun Dancheng Soukkou, China). As shown in Fig. 1a the device uses a spring, which in

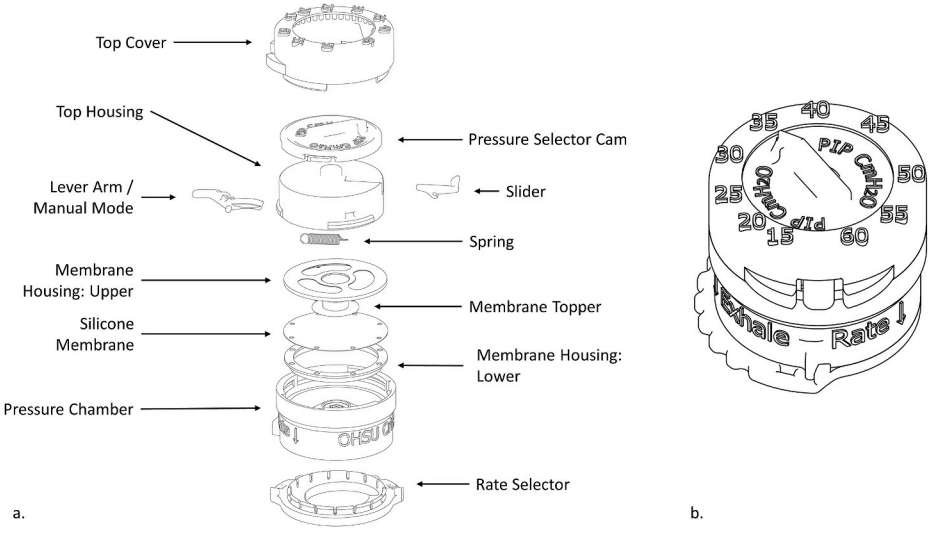

Fig. 1. a. (left) represents the individual components of the ventilator with 12 individually 3D printed parts in addition to an aluminum spring and a silicone membrane. b. (right) shows the ventilator in its assembled state. PIP selection dial on the top and the I:E and respiratory rate selector on the bottom.

this study a stainless-steel type 316 spring (Lee Spring Brooklyn, NY). These materials were chosen for the durability assessment as they have a heat tolerance that would allow them to be autoclaved. A second version of the device was created using a commercially available extrusion printer (Prusa MK3 Pusa Research Prague, CZ) using Polyethylene Terephthalate. This version of the device is not autoclavable; however, it can demonstrate the performance of the device should production of the resuscitator be necessary from an entry-level device in the setting of overwhelming surge, as opposed to commercial production techniques. The average print time for this extrusion printer was about 5 h. While this form of the device does not offer as wide of a range of tidal volumes and peak inspiratory pressures as our previous version of the device, it does allow for more fine-tuning of the device to produce tidal volumes in healthy lung compliance range. As noted above while the main components of the device are created from 3D printed parts, two components do require procurement from off the shelf sources. Even during the initial peak of the pandemic our group did not have any difficulty obtaining the silicon membrane from consumer sources and note that the springs could be manufactured by hand although this would require more calibration and may hinder performance at more extreme settings.

2.2. Respiratory simulation and measurements

The ventilator was connected to a standard hospital wall-pressure blended oxygen source, ventilator tubing, and a FLUKE VT 650 flow analyzer (FLUKE Biomedical, Cleveland OH) to measure gas flow rates, volumes, and pressures over time. Tubing was then connected the Michigan Test Lung Simulator (Michigan Instruments, Grand Rapids MI) to simulate the respiratory system over a wide range of clinical conditions.

Respiratory system compliance and airflow resistance were established to simulate patients with healthy lungs, moderate, or severely decreased respiratory system compliance, as would be typically seen in a patient with severe respiratory failure secondary to COVID-19 and acute respiratory distress syndrome based on established parameters and manufacturer recommended settings.[19–23] A summary of the lung models, compliances, and resistances are shown in Table 1. The ventilator is connected to a Y-connector and oxygen source with in-line flow measurements using the FLUKE as shown in Fig. 2D.

2.3. Respiratory performance testing

Using the extrusion printed devices, which have increased porosity and assumed variances in inter-device performance, each ventilator was connected to the lung testing apparatus as shown in Fig. 2D. The compliance was set using the measured compliance from the FLUKE device to each of the 'healthy adult', 'moderately decreased compliance', and 'severely decreased compliance' settings. For each simulated condition, gas flow rates of 20 L/min and 30 L/min were established. Due to the demonstrated importance of achieving a targeted tidal volume as demonstrated in the ARDSnet trial,[23] the supplied PIP from the device was adjusted to achieve continuous performance with inspiratory tidal volumes of 250 mL, 350 mL, 450 mL, 550 mL, and 650 mL. The PIP and exhale time was adjusted to achieve a minimum and maximum respiratory rate for a given target tidal volume without stalls in the device to establish a range of sustainable respiratory parameters for a patient's given compliance state. This range was chosen as a cross-section of lung protective tidal volumes for patients with predicted body weights from 30 to 80 kg. Once the device was confirmed to be functioning without stalling or any significant changes in the respiratory dynamics respiratory rate, tidal volumes, PIP, and Peak End Expiratory Pressure were measured continuously for 1 min. Example airway volume, flow, and pressure tracings across a 10 s window are shown in Fig. 2A–C.

2.4. Durability and autoclaving testing

The study was designed to assess whether minute-ventilation (the product of respiratory rate and tidal volume) and peak inspiratory pressure would be affected by different scenarios that could stress a 3D printed system. SLS printed ventilators were selected due to their high resolution and diminished pore size that would make them sterilizable in an autoclave as they would not create isolated areas refractory to steam sterilization techniques. 27 devices were produced and assigned to this experiment to create a balanced statistical model as detailed below. Accounting for the possibility that autoclaving may somehow adversely affect the durability, devices were assigned to one of three treatment orders with a combination of sham, dropping, and autoclaving. A sham durability test was created where the device was disassembled in its entirety and reassembled. Drop testing was performed by dropping the assembled device in a different orientation from a height of 1.83 m three times per device. Autoclave testing was performed by placing the device in for a steam-based sterilizer for 30 min with a temperature of 121 °C and 15 p.s.i with a 5-min dry time. After their assigned treatment, the devices were connected to the durability model lung and ventilation was established with a Peak Inspiratory Pressure, PIP, of 26cmH_2O and a respiratory rate of 16 breaths per minute. This was chosen as it is a feasible and potentially safe peak inspiratory pressure providing tidal volumes around 450 cc in a patient with severe ARDS.[22] Oxygen flow rate was set to 30 L/min at 40% FIO_2.

Minute ventilation was chosen as the primary outcome as any degradation of the device with treatment would be reflected in changes in tidal volume for a given set respiratory rate and PIP (or driving pressure). Any changes in the minute ventilation would therefor denote a failure in the device to obtain a given PIP, and I:E ratio. Respiratory dynamics, including tidal volumes and respiratory rate, were measured breath-to-breath utilizing the FLUKE device and minute ventilation was calculated from these measurements. To increase the robustness of the testing each ventilator was evaluated with all three treatments with the order in which the treatments were performed randomly assigned to each of the 27 devices.

2.5. Statistics and data handling

Data was collected and placed into a spreadsheet using Microsoft Excel (Microsoft Corporation Redmond, WA). This was parsed, sorted, and averaged using a custom designed script in MATLAB (MathWorks Natick, MA). To establish a balanced data set for durability testing, each ventilator device was randomly assigned to one of three possible treatment orders using a Latin-squares design with a sample size to achieve a statistical power of 80%. The performance across the 10 min was averaged and then compared pairwise using a Two One-Sided Test of Equivalence (TOST) with a set Cohen d of 0.7. Significance was defined as $p < 0.05$ and equivalence was determined when both the upper and

Table 1
Table Respiratory system compliances and airway resistances range for crisis ventilator testing.

Model	Compliance (mL/cmH_2O)	Airway Resistance	Equivalent Model
Healthy Adult	100	RP20	Intubated Healthy Adult
Moderately Decreased Compliance	60	RP20	Intubated Adult with Moderate ARDS
Severely Decreased Compliance	30	RP20	Intubated Adult with Severe ARDS
Durability Model	50	RP5	Adult with COVID-19

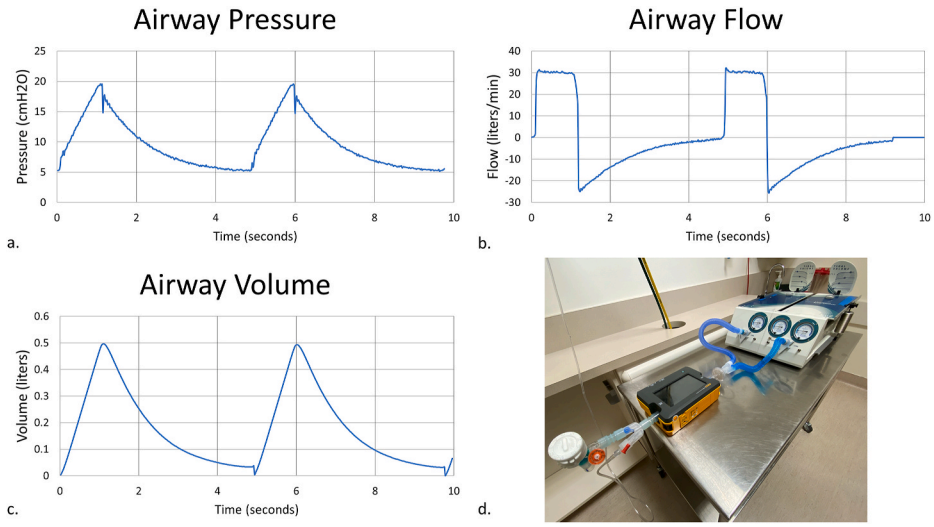

Fig. 2. a. (top left) shows a high resolution airway pressure over time tracing for two delivered breaths. b. (top right) shows a high resolution airway flow over time tracing for two delivered breaths. C. (bottom left) shows a high resolution airway volume over time tracing for two delivered breaths. d. (bottom right) shows the CRISIS ventilator in-line with a gas-flow analyzer in-line with the calibrated test lung experimental apparatus.

lower bounds had a $p < 0.05$. This was done using an available package[24] in R (R Foundation for Statistical Computing Vienna, Austria) Due to the high sample rate of the FLUKE device, any parameter which was more than three standard deviations beyond each 10 min performances average was not included in the final data set for analysis.

3. Results

3.1. Respiratory performance testing

Table 2 shows the performance for a severely decreased compliance lung on an intubated patient simulating severe ARDS while Tables 3 and 4 show same for moderately decreased and normal lung compliances, respectively. Measurements were recorded at each tidal volume for three devices were averaged and are represented in the tables below. As shown in Tables 2–4 the device was able to achieve a consistent tidal volume of 250 mL over a range of 16–38 breaths per minute with a minute ventilation range of 4.1–9.5 L/min, PIP of 7.8–18.6 cmH_2O, and a PEEP of 3.0–7.1 cmH_2O depending on the supplied oxygen flow rate and lung compliance. For volumes of 650 mL respiratory rates ranged from 8 to 18 with a minute ventilation range of 5.2–11.7 L/min, a PIP of 12.0–40.0 cmH_2O, and PEEP of 3.5–13.7cmH_2O. For all tidal volumes, supplied oxygen rates, and lung disease models the PEEP ranged from 3.0 to 14.1 cmH_2ORespiratory rates were directly dependent on the supplied oxygen rate. Tidal volumes had an inverse relationship with respiratory rates. The oxygen flow rate and respiratory rate were also directly proportional to PEEP.

3.2. Device durability

As shown in Table 5, the minute ventilation, which reflect changes in both RR and tidal volume, and PIP were not significantly affected when comparing the autoclaved and dropped devices. PIP was noted to be statistically equivalent for performance regardless of sham treatment, autoclaving, or dropping the device multiple times. Minute ventilation was noted to be equivalent between the sham and dropped/autoclaved groups. The autoclaved and dropped groups were notably similar but failed to achieve statistical equivalence ($p = 0.06$). One device was

Table 2
Performance of the CRISIS Ventilator with a set Respiratory System compliance of 30mL/cmH_2O. Here the tolerances with an adult lung with severely decreased compliance for a given inflow rate is demonstrated. Listed resultant values represent Mean ± the standard deviations.

Set Flow Rate (L/min)	Goal Tidal Volume (mL)	Goal Respiratory Rate	Measured Tidal Volume (mL)	Measured Respiratory Rate	PIP (cmH2O)	PEEP (cmH2O)
20	250	Low	254.1 ± 8.3	19.2 ± 1.8	12.25 ± 0.2	2.96 ± 0.2
		High	250.7 ± 2.1	31.2 ± 3.2	18.63 ± 2.3	7.28 ± 1.5
	350	Low	347.6 ± 2.9	14.6 ± 1.7	15.73 ± 0.4	3.38 ± 0.4
		High	351.1 ± 3.3	22.4 ± 3.5	27.32 ± 4.4	10.40 ± 2.7
	450	Low	449.4 ± 3.8	12.1 ± 1.0	19.60 ± 0.2	3.98 ± 0.6
		High	447.7 ± 5.6	19.5 ± 3.5	28.72 ± 4.0	9.59 ± 2.3
	550	Low	550.1 ± 2.6	10.1 ± 0.2	23.41 ± 0.6	4.73 ± 1.1
		High	547.0 ± 2.7	16.1 ± 4.0	32.82 ± 2.8	10.49 ± 1.7
	650	Low	649.6 ± 0.9	9.9 ± 0.4	28.45 ± 2.5	5.34 ± 1.1
		High	646.7 ± 2.1	13.7 ± 2.4	35.42 ± 5.8	11.24 ± 2.0
30	250	Low	247.0 ± 4.7	24.0 ± 2.0	13.80 ± 0.5	3.98 ± 0.5
		High	248.2 ± 8.8	38.0 ± 2.3	17.03 ± 1.2	7.05 ± 0.9
	350	Low	350.9 ± 1.3	17.5 ± 1.2	17.79 ± 0.8	4.40 ± 0.8
		High	344.2 ± 6.7	30.4 ± 1.9	28.30 ± 5.1	12.17 ± 3.4
	450	Low	448.0 ± 5.1	16.6 ± 2.3	26.08 ± 6.1	5.04 ± 0.7
		High	448.3 ± 6.7	26.9 ± 2.7	31.43 ± 3.3	13.23 ± 2.6
	550	Low	554.9 ± 3.2	12.0 ± 0.4	25.43 ± 0.8	5.70 ± 0.9
		High	551.2 ± 4.4	20.9 ± 2.9	37.71 ± 1.7	14.05 ± 1.6
	650	Low	649.6 ± 1.6	11.3 ± 0.6	28.95 ± 0.9	6.30 ± 1.0
		High	655.7 ± 3.4	18.4 ± 2.1	40.17 ± 3.9	13.72 ± 2.2

Table 3
Performance of the CRISIS ventilator with a set respiratory system compliance of 60mL/cmH_2O. Here the tolerances at a moderately decreased compliance for a given inflow rate is demonstrated. Listed resultant values represent MEAN ± the standard deviations.

Set Flow Rate (L/min)	Goal Tidal Volume (mL)	Goal Respiratory Rate	Measured Tidal Volume (mL)	Measured Respiratory Rate	PIP (cmH2O)	PEEP (cmH2O)
20	250	Low	243.2 ± 8.0	16.6 ± 2.5	8.5 ± 1.8	3.5 ± 1.6
		High	243.4 ± 9.4	21.8 ± 3.4	8.8 ± 0.8	3.8 ± 0.7
	350	Low	343.3 ± 3.5	13.2 ± 2.3	9.3 ± 0.4	2.8 ± 0.3
		High	353.7 ± 5.7	18.7 ± 2.1	12.9 ± 1.6	5.3 ± 1.3
	450	Low	449.8 ± 6.7	9.9 ± 1.4	11.1 ± 0.4	2.9 ± 0.3
		High	447.1 ± 6.0	15.5 ± 2.4	16.7 ± 3.1	6.5 ± 2.2
	550	Low	549.0 ± 6.8	9.4 ± 0.1	12.8 ± 0.3	3.1 ± 0.2
		High	544.8 ± 6.2	14.1 ± 2.4	17.6 ± 2.8	6.3 ± 1.8
	650	Low	648.0 ± 2.6	8.5 ± 0.8	14.8 ± 0.4	3.5 ± 0.7
		High	652.4 ± 10.4	12.8 ± 2.7	19.9 ± 1.8	6.9 ± 0.9
30	250	Low	239.6 ± 8.8	19.5 ± 2.0	9.1 ± 0.6	3.8 ± 0.4
		High	242.7 ± 8.8	28.3 ± 2.4	12.0 ± 0.5	6.5 ± 0.2
	350	Low	340.5 ± 9.7	12.8 ± 2.5	11.1 ± 0.3	3.8 ± 0.2
		High	351.9 ± 9.1	23.1 ± 2.4	14.5 ± 2.0	6.8 ± 1.6
	450	Low	455.4 ± 3.7	11.8 ± 1.5	12.9 ± 0.4	4.0 ± 0.2
		High	449.1 ± 5.4	20.0 ± 2.1	17.7 ± 7.9	7.9 ± 1.4
	550	Low	543.4 ± 2.8	9.4 ± 1.5	14.6 ± 0.5	4.1 ± 0.3
		High	557.9 ± 5.7	17.2 ± 2.8	22.3 ± 2.2	9.8 ± 1.3
	650	Low	652.2 ± 4.9	8.8 ± 0.4	16.6 ± 0.5	4.4 ± 0.5
		High	645.6 ± 6.9	15.7 ± 3.2	25.8 ± 2.9	11.0 ± 1.7

Table 4
Performance of the CRISIS ventilator with a set respiratory system compliance of 100mL/cmH2O (Healthy Lung). Here the tolerances for a healthy adult lung for a given inflow rate is demonstrated. Listed resultant values represent MEAN ± the standard deviations.

Set Flow Rate (L/min)	Goal Tidal Volume (mL)	Goal Respiratory Rate	Measured Tidal Volume (mL)	Measured Respiratory Rate	PIP (cmH2O)	PEEP (cmH2O)
20	250	Low	257.0 ± 13.2	16.2 ± 1.1	8.3 ± 1.7	4.5 ± 1.3
		High	250.8 ± 7.1	18.7 ± 1.6	7.8 ± 1.6	4.2 ± 1.5
	350	Low	342.6 ± 24.1	14.4 ± 1.0	8.5 ± 0.7	4.0 ± 0.8
		High	350.3 ± 10.6	15.8 ± 0.8	10.9 ± 1.0	5.6 ± 0.6
	450	Low	446.9 ± 18.0	10.5 ± 1.7	8.4 ± 0.3	3.1 ± 0.1
		High	447.2 ± 4.5	12.3 ± 2.0	13.0 ± 1.2	6.2 ± 0.6
	550	Low	545.4 ± 15.9	8.6 ± 1.3	9.6 ± 0.5	3.2 ± 0.4
		High	553.3 ± 2.9	11.2 ± 2.0	14.7 ± 1.7	6.5 ± 0.8
	650	Low	658.4 ± 15.7	7.9 ± 2.0	12.0 ± 2.8	4.2 ± 1.8
		High	664.6 ± 5.5	10.0 ± 1.8	14.4 ± 2.8	5.8 ± 1.6
30	250	Low	269.2 ± 24.1	19.5 ± 3.4	9.4 ± 1.3	5.7 ± 1.3
		High	253.9 ± 21.4	23.2 ± 2.5	8.7 ± 0.2	5.0 ± 0.1
	350	Low	348.6 ± 7.3	15.0 ± 4.0	10.4 ± 3.2	4.9 ± 2.5
		High	339.5 ± 11.4	20.5 ± 1.5	10.4 ± 0.3	5.6 ± 0.4
	450	Low	445.5 ± 5.5	11.8 ± 4.0	10.3 ± 0.3	4.2 ± 0.5
		High	446.4 ± 7.4	16.8 ± 1.0	13.2 ± 1.7	6.8 ± 1.1
	550	Low	555.8 ± 8.3	9.3 ± 1.3	11.0 ± 0.6	3.9 ± 0.5
		High	541.1 ± 15.5	15.1 ± 1.3	15.3 ± 2.2	7.5 ± 1.4
	650	Low	646.5 ± 3.7	8.3 ± 0.7	12.0 ± 0.6	3.9 ± 0.3
		High	641.9 ± 10.8	14.0 ± 1.7	17.5 ± 1.5	8.2 ± 1.1

Table 5
Performance of the CRISIS ventilator after various durability tests. *two-one sided test of equivalence is equal with $p<0.05$. [a]Tests of equivalence for all pairs equivalent $p<0.05$ EXCEPT THE DROPPED VS AUTOCLAVED GROUPS WHICH HAD A LOWER MINUTE VENTILATION PERFORMANCE AT $p=0.06$.

	Autoclaved	Dropped	Sham
Minute Ventilation[A] (Liters)	11.1±1.0	11.3±0.9	11.2±0.7
PIP* (cmH_2O)	26.1±0.4	26.1±0.3	26.1±0.4

incompletely disassembled during the autoclaving process and did require replacement of a subcomponent (the slider arm as denoted in Fig. 1a) with another device assigned to the same treatment group.

4. Discussion

The increase of consumer grade 3D printing systems has made rapid prototyping and design easier and cheaper than ever. Due to the widespread availability of these at-home production systems many hospitals have been able to fill in gaps during significant shortages of supplies and PPE, including face-shield adapters and facemasks.[12] Though high-resolution 3D printers may be prohibitively expensive for low-resource areas, the ability to rapidly distribute blueprints without using traditional injection molded techniques is desirable when demands for equipment are unpredictable. The device detailed here, adapted from the in-use Vortran ventilator design, has undergone multiple rounds of iterative testing to improve its design. Electronic databases where designs can be shared freely make utilization of 3D printing may be an important way to manage supply-side shortages. With the relative abundance of printing materials, this allows hundreds of devices to be made locally within hours using available resources in a worst-case-scenario. They may even be durable enough to ship and reuse after sterilization. The intent of designing the CRISIS device is to provide a cheap, locally produced alternative to traditional ventilators and fill in gaps in supply, particularly in low resource situations where electricity may not be reliable.

When setting up this device we propose this step-by-step protocol. First, the patient's respiratory compliance and ventilation requirements must be estimated. If a higher peep and respiratory rate are desired a blended oxygen supply should be connected to the device. In adults this

can range from 15 to 35 L/min in general. FIO2 will be dependent on, and consistent with, the supplied blended oxygen source. As the device does not have any electric components, an inline gas flow analyzer should be connected. The PIP dial should be set to provide the desired tidal volume. Next, the rate selector dial should be adjusted until the chosen respiratory rate and Inhale to exhale ratios are observed. In order to prevent CO2 rebreathing, the gas flow analyzer should be removed to keep the patient close to the resuscitator. Since this is an open-air device, a filter should be placed between the patient and the ventilator to reduce the risk of airborne transmission. The tidal volume, respiratory rate, and PEEP should be monitored routinely by a separate device to ensure patient safety and assess for changes in respiratory dynamics. Previous work by our group has investigated how rapid changes in compliance and airway resistance can affect the devices performance.[25]

While volume-control ventilation strategies aimed at delivering lower tidal volumes may mitigate potential barotrauma and volutrauma in a wide range of patients, there is data supporting the use of pressure control ventilation as well.[26] This ventilator may be best suited to provide ventilation to the critically ill patient with relatively normal lung physiology, rather than the patient with severe ARDS. Even in lung-injured patients, such as those with ARDS where lower tidal volumes are required to prevent harm, our ventilator may be set up to provide no more than a set maximum tidal volume.

As the concept of open-lung ventilation in ARDS has evolved, so has our understanding of barotrauma and respiratory mechanics.[27] Pressure regulated ventilation is the primary driving force of respiration in our device and protective tidal volumes can be obtained as is highlighted in Tables 2–4 Additionally, preliminary testing has shown that the device can also be used with a biphasic positive airway pressure mask and spontaneously breathing patients as a form of non-invasive positive pressure ventilation (NIPPV). Benchtop testing has suggested the CRISIS device can functioncontinuously for days at a time without manipulation of the device or significant drift in the set ventilator parameters.

Furthermore, when evaluating the performance of such a device, it is important to acknowledge there are limitations intrinsic to manufacturing. Many materials used in hobby-level 3D printed devices are not amenable to autoclaving techniques due to the larger pore-size creating areas isolated from steam. Chemical autoclaving may be possible, but this has not been investigated by our group. While the average performance after steam autoclaving failed to achieve significance when evaluating for equivalence between the dropped and autoclaved tests, this may be attributable to a greater than expected inter-device variances due to the hand-cut silicone membrane. Using consumer grade laser cutters, CNC machines, or die cutting tools would eliminate the issues with membrane induced variance and increase production capabilities. Additionally, performing the analysis utilizing the repeated measurements across 10 min of ventilation for the target parameters as noted above did achieve significance even when using a Cohen d of 0.2 to detect exceedingly small differences for equivalence. This suggest that ultimately, the device can function as expected after autoclaving. It is also worth noting that while the tidal volumes above were chosen to represent a cross-section of tidal volumes for adult patients, this device can produce tidal volumes as low as 150 mL and more than 1 L if required. Previous versions of our device do have a wider range of peak inspiratory pressures (in excess of 40cmH_2O) which can provide a larger range of tidal volumes in excess of 2 L for a healthy lung compliance. While this prior version of the device did meet the stricter guidelines for a resuscitator in accordance with ISO 10651-5, utilizing this form of the device for an adult's healthy lung compliance routinely created tidal volumes in excess of 600 mL suggested it would become more difficult to utilize in healthy adults. The current device allows for users to adjust the peak inspiratory pressure and I:E ratio with a resultant tidal volume, peep, and respiratory rate which depend on the mechanics of the intubated subject and the oxygen flow rate. Thus, for initial set-up and fine tuning a flow-dynamic monitoring device such as the one utilized here with the FLUKE system is required. Work is ongoing to refine versions for which the ventilator can be adopted to a pediatric and neonate lung in addition to the potential for adjustable provided PEEP. Preliminary studies using this iteration of the device are promising; however, it may not be ideal to use broadly in healthy adult lungs due to potential difference in compliances and thus delivered tidal volumes. Further in vivo work will be completed; as animal trials are ongoing to evaluate any hemodynamic and ventilatory safety.

It is worth noting that other authors have also evaluated the use of resuscitator devices in COVID.[28] In this work the authors evaluated resuscitators and noted how other employed gas-powered resuscitators require a higher oxygen flow rate for their routine use when compared to traditional ventilators. Indeed, this is an ongoing issue with any resuscitator and given the purpose of the device highlighted here is to manufacture a resuscitator on-site to fill in rapid changes in the need for respiratory support, there will be inherent variability depending on the materials and manufacturing techniques. It is because of the uncertainty provided during massive pandemics that a device like this would unfortunately become a necessity. The use of calibration devices, such as the FLUKE system demonstrated here, is essential to establish ventilator parameters for each patient when utilizing our device.

While partnerships between the FDA and the National Additive Manufacturing Innovative Institute have expanded as part of the pandemic response to fill in supply gaps using on-site additive manufacturing, the FDA has issued several guidance statements regarding their use.[29] Most devices employed in the field are related to PPE and are not approved for regular use. As with any other medical device, several safety practices must be employed to ensure that all regulatory benchmarks are met. In the case of decentralized on-site ventilator production, the ability to achieve and maintain government standards would not be feasible except in the direst situation. If this would become necessary, our group plans to make the necessary files and instructions for onsite production utilizing established means of distribution.[30]

5. Conclusion

During a global respiratory pandemic, a surge in patients requiring respiratory support can put a large strain on the global healthcare system. Reliance on a strategic stockpile and rapid international production of basic resuscitators and ventilators has been demonstrated to not be feasible as was experienced early in the pandemic. Using 3D printing and readily available supplies, our group has created a system which utilizes a modified pressure regulated ventilatory support that is durable, potentially reusable, and can provide ventilatory support in a variety of modeled respiratory disease states including the ARDS seen in COVID-19 patients. In addition, the device functions autonomously without dependence on electricity. Clearly as a gas-powered resuscitator the device is nearly designed for nor has it been validated to meet criteria for long-term ventilation in critically ill patients. It does meet several desirable parameters set forth by the WHO[31] but as a resuscitator is clearly not designed to be the go-to device in patients with complex ventilator needs. Preliminary data is promising, further research is required to ensure that the device can be used safely before adoption.

Contributorship

Mr. Menzel, Mr. Fontaine, Dr. Nonas, and Dr. Chi were all directly involved in the development of the device itself. Dr. El Haddi crafted the article and performed the majority of experiments along with analysis. Ms. Kenny performed a great deal of editing and formatting of the article. Dr. Han and Dr. Brito were heavily involved in the formatting, phrasing, and subject matter of the publication.

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Mr. Menzel, Mr. Fontaine, Mr. Child, Dr. Nonas, and Dr. Chi were directly involved with the development of the open-source CRISIS

ventilator. This device has been patented by Oregon Health & Science University. The remaining authors have disclosed that they do not have any potential conflicts of interest.

Data sharing/data availability

The raw data obtained from the experiments detailed here are immediately available upon request to the corresponding authors.

Declaration of competing interest

Mr. Menzel, Mr. Fontaine, Mr. Child, Dr. Nonas, and Dr. Chi were directly involved with the development of the open-source CRISIS ventilator. This device has been patented by Oregon Health & Science University. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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