The HEV Ventilator

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HEV is a low-cost, versatile, high-quality ventilator, which has been designed in response to the COVID-19 pandemic. The ventilator is intended to be used both in and out of hospital intensive care units, and for both invasive and non-invasive ventilation. The hardware can be complemented with an external turbine for use in regions where compressed air supplies are not reliably available. The standard modes provided include PC–A/C (Pressure Assist Control), PC–A/C–PRVC (Pressure Regulated Volume Control), PC-PSV (Pressure Support Ventilation) and CPAP (Continuous Positive Airway Pressure). HEV is designed to support remote training and post market surveillance via a web interface and data logging to complement the standard touch screen operation, making it suitable for a wide range of geographical deployment. The HEV design places emphasis on the quality of the pressure curves and the reactivity of the trigger, delivering a global performance which will be applicable to ventilator needs beyond the COVID-19 pandemic. This article describes the conceptual design and presents the prototype units together with their performance evaluation.

COVID-19 | Mechanical Ventilator | Biomedical Engineering

The worldwide community currently faces a shortage, especially in low and middle income settings, of medical equipment to address the COVID-19 pandemic (1–4). In particular this is the case for ventilators, which are needed during COVID-19 related treatment both in the acute phase, when invasive fully controlled ventilation is needed, and also in the sub-acute phase during the weaning from mechanical ventilation, which can last for an extended time period. The pandemic has also drawn attention to the lack of ventilation equipment in low and middle income countries. Globally, pneumonia is the most common infectious cause of death (5–7), and the need for adequate respiratory equipment for treatment and management of pneumonia patients will persist even as the COVID-19 pandemic wanes.

A large number of proposals are already circulating for devices which can be quickly manufactured cheaply and on large scale (8). However, the designs of many of these devices limit the ability to reach high quality performance and monitoring. The HEV (High Energy particle physics Ventilator), first proposed here (9) is intended to provide full functionality while being capable of manufacture at relatively low cost. The design is based on regulations and recommendations from MHRA (Medicines and Healthcare products Regulatory Agency), EU, AAMI and WHO (10–12). HEV has been developed by a group of physicists and engineers affiliated to CERN and partner institutes, reinforced by an international advisory body of clinicians, with advice, collaboration and equipment provided from local hospitals. The design and controls are based on concepts routinely used in the context of High Energy Physics

Significance Statement

Pulmonary lung disease has a global impact as a major cause of morbidity. The COVID-19 pandemic presents new challenges for the scientific community that cross the boundaries of scientific expertise and need to be addressed with new interdisciplinary collaborations. In this article, we describe the development of a high-quality, low-cost ventilator to provide artificial support for lung function of patients using technologies developed by the particle physics community for pressure and gas regulation. In addition to providing functionality for COVID-19 management, in the long-term this collaboration provides novel tools for ventilator performance monitoring, remote training, and clinical support, as well as the possibility to develop new algorithms and techniques based on the HEV design.

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research and use functionality which has been developed over decades for this field. The advantage of this cross-disciplinary approach and open collaboration is that the highest quality of ventilator construction can be expected, while being able to incorporate novel ideas during the development.

1. Overview of HEV functionality

Patients affected by COVID-19 face serious issues of lung damage, and the ventilatory equipment must be able to deliver protective pressure controlled ventilation throughout situations of rapidly changing lung compliance as well as potential collapse and consolidation. In light of the prolonged recovery/weaning phases involved in COVID-19 critical care cases, the ventilator must also deliver pressure-assisted ventilation to be efficient for the ventilator weaning process. HEV* delivers as basic modes PC–A/C (Pressure Control – Assist Control) and PC–A/C–PRVC (Pressure Control – Assist Control – Pressure Regulated Volume Controlled), PC-PSV (Pressure Control – Pressure Supported Ventilation), and in addition CPAP (Continuous Positive Airway Pressure). The CPAP mode is included with the HEV modes in order to provide the widest range of support throughout COVID-19 treatment, and may be a crucial option for selection in low resource settings (13). For all modes, PEEP (Positive End-Expiratory Pressure) is provided, to support steady low positive pressure to the lungs to avoid alveolar collapse.

In all modes it is possible to measure the plateau pressure and intrinsic PEEP in order to provide clinical diagnoses and estimation of the patient static lung compliance or to detect AutoPEEP. This is achieved by allowing a manual operation of a pause time at the end of the inhalation phase of a few hundred milliseconds during which the valves are occluded, in order to accurately measure plateau alveolar pressure at zero flow. The intrinsic PEEP at the end of the exhale phase can be measured in the same way during the pre-inhale state.

2. HEV Conceptual Design

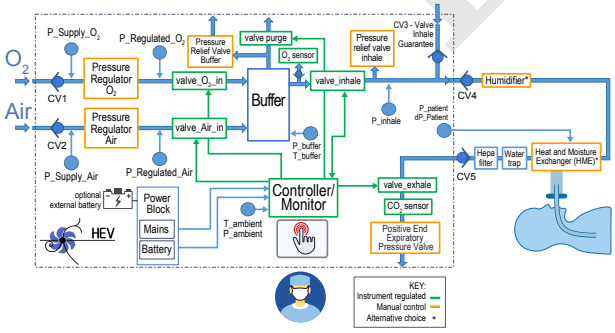

Fig. 1. Conceptual design of the HEV ventilator.

Central Pneumatic Unit. The HEV design, shown conceptually in Fig. 1, is based around a central buffer which pneumatically decouples the ventilator circuit into two independently functioning parts, for filling the buffer and supplying gas to the patient. The air and oxygen are supplied separately and passively mixed inside the buffer, which is filled to a target pressure. Once this has been achieved, the buffer output valve is opened, initiating the respiratory cycle. The inhale valve is controlled by a PID (Proportional–Integral–Derivative) controller, which allows a stable delivery of pressure and a fine tuning of the pressure rise time. After the inhalation phase finishes, the exhale valve is opened for exhalation and the buffer is re-filled for the next breath cycle. For CPAP operation the input valves to the buffer are kept open and the PID valve is regulated to supply a constant level of pressure. The PID algorithm ensures that the system is robust against fluctuations in flow or gas supply pressure.

The buffer concept presents many operational advantages. In general, the separation of the fill and exhale cycle into two separate circuits makes the design, control and component selection more straightforward, and allows less expensive components to be selected. The initial step-down of the pressure between the supply and the patient introduces safety and robustness, and makes precise pressure control on the patient side of the circuit more readily accessible. The buffer volume also avoids that the O_2 and air delivery systems need to be able to handle the peak flow rates of up to 120 L/min needed in the inhale phase, and the patient air supply is protected. The mixing of the gases, which is provided inside the buffer with an turbulent flow mechanism, avoids the need to purchase an external gas blender. In addition the measurement of the O_2 concentration, which can be done by spying on the static gas volume, is an inherently more precise measurement than measuring on a gas stream. Should the design need to be adapted to a more extreme (very hot or very cold) environment, thermal control of the gas in the buffer is straightforward. In addition, the delivered tidal volume can be calculated from the pressure drops in the buffer, providing a precious monitoring cross-check in addition to the standard tidal volume measurement, reinforcing the safety of the design.

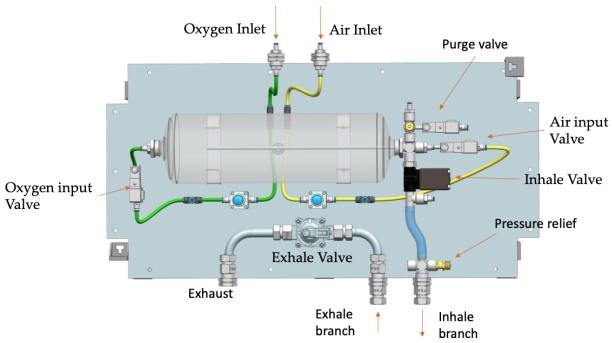

Fig. 2. Schematic of the pneumatic part of the HEV system.

A schematic of the central pneumatic part of the system is shown in Fig. 2. This diagram highlights how pure oxygen and air are injected separately into the buffer by using two different valves. To achieve a good mix via turbulent air flow, a tube is inserted into the tank from the air side, taking air to be injected close to the oxygen injection point. The oxygen levels can be mixed from 21 to 100 percent, and the oxygen fraction is measured with zirconia sensors inserted after the oxygen tank which are reliable, inexpensive and readily available. The sensors are installed after a bypass, which enables them to be independent of the patient supply and to operate with low

*https://hev.web.cern.ch

flow of gas.

Alternative air supply and accessories. The HEV collaboration has designed an alternative to the compressed air supply available in hospitals. The major requirement is that the system should be able to fill the HEV buffer in less than one second. It consists of a small and transportable system, based on miniature turbine blowers installed in series. The air reaches thermal equilibrium with the environment via transport in a corrugated pipe before delivery to the ventilator via a HEPA (high-efficiency particulate air) filter. For increased independence from the hospital setting, an external battery can be included to power the turbine and the HEV together; good performance has been obtained from an option based on the e-bike battery market. The design of the prototype with a photograph of the constructed turbine is shown in Fig. 3.

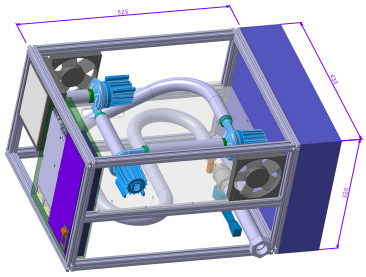

Fig. 3. Turbine system proposed as an alternative to the compressed air supply. The system is divided into two parts; the top part containing the turbines, the bottom containing the corrugated pipe, the thermal and pressure sensors and the outlet connector. Mounted on the left side of the box are the air filter, the power supply and the box containing the controller. The blue box on the right provides an enclosure for the optional battery system.

HEV has been tested with both a concentric tube geometry and a double limb circuit, and can be supplied with an adapter to use either method. The breathing circuit can also be equipped with humidifier or a heat and moisture exchanger (HME) filter by choice, which is necessary to protect the patient, who may be dehydrated, from the dry medical or ambient air.

All equipment that comes in contact with the patient needs to be either changed or disinfected and sterilised after every patient. There are multiple options to do this and currently autoclave cleaning is supported. The entire exhaust block may be easily dismounted and swapped with a spare block, so that the ventilator can continue to be used for the next patient while the block undergoes steam or autoclave sterilisation.

Control system and User Interface. The control software is implemented directly on an embedded controller, which receives signals from the sensors and valves and fully controls the ventilator operation. An ESP32 microcontroller chip has been chosen for this function due to its high availability and low cost. Several alternatives exist and could be used depending on local availability in different geographical locations.

The user interface (UI) is provided via a touchscreen controlled by a Raspberry Pi, which also provides WiFi and Ethernet connection. The Raspberry Pi and embedded controller are hosted on a motherboard which also provides the interfaces to the valves and sensors, embedded sensors, LEDs and buzzers for monitoring, and connectors to allow the powering of the fans and touchscreeen. HEV can run on AC power or an external battery, and includes a UPS which takes over automatically if mains power is lost, allowing autonomous operation.

All of the primary functions corresponding to the breathing function of the patient are controlled by the microcontroller. If the communications are interrupted, the ventilator continues to run normally. A web server is also provided such that display information can be seen remotely.

Following the advice of clinicians, the user interface has been designed based on the following concepts:

- Respect of regulatory guidelines for included quantitities.
- Clear text, symbols and graphs which can be seen from the end of a hospital bed through PPE.
- Neutral colours for normal running; flashing indicators and messages when there are alarms.
- Screen locking/unlocking feature with a timeout to prevent accidental touchscreen presses.
- Confirmation required for all parameter changes (two parameter changes require two separate confirmations).
- Set and read back information clearly displayed.
- Simple navigation: no setting/parameter is more than two clicks away. Normal operation should be separated from calibration/expert testing, to maintain an uncluttered interface.
- Interface is touchscreen friendly: items are placed far enough apart to minimise accidental mis-clicks.
- Familiarity: designed to look familiar to clinicians, similar to already existing ventilator interfaces.
- Language selection is provided to increase regional adaptability.

Two user interfaces are provided: a Native UI and a Web UI. The Native UI runs on the touchscreen integrated into the ventilator unit. Remote access is provided via the Web UI, accessible via WiFi or Ethernet connection to the ventilator on computer screens or mobile devices. In this way the data of one or more patients can be displayed, for example, at the nurses' station. This also opens up the possibility of remote consulting and performance monitoring which can be very useful for training or patient management in remote settings. The web interface can be configured so that full control, partial control, or no control is possible remotely. Access rights are configurable as required and can be disabled for reasons of security.

The Native UI is automatically displayed on power up of the device. At start-up, the mode is selected, with set parameters associated with that mode, which can be revisited at any time during operation. Indicators for the power source (mains or battery) are given on the UI, including residual charge indicators.

Fig. 4. Example page displays from the Native User Interface. On the left, a typical homepage, on the right, two screens showing alarms and settings. Numbers and graphs are indicative.

A "homepage" is shown for the current ventilation mode with the most important settings, parameters, waveforms and control buttons (Fig. 4). Similar to the locking feature, the Native UI defaults to presenting the homepage after a period of inactivity by the user. A selection is provided for time ranges of the waveforms (i.e., showing the last 5, 15, 30 or 60 seconds). Historical data are recorded for up to 10 days. Encryption is an option for stored patient data. Settings (or target values) and measured values are clearly distinguishable in the UI. The HEV Graphical User Interface is organised to respect the requirements listed in (11, 12, 14), in particular for the available information on the homepage. Alarms are displayed in an intuitive way at the top of the screen at all times. A dedicated alarm page shows a list of the last ten alarms, ordered by alarm priority, and current and historical alarms are easily distinguishable. It is possible to reset or silence alarms (for a period of time). The alarm on-screen visualisation matches the "traffic light" lamps mounted on the unit. Finally, more technical details of the internal operation and calibration of the ventilator are provided on a separate "expert" page. The aim of the prototyping was to put in place all underlying software flexibility to be able to freely implement the desired UI. Before final manufacture a full useability study will be performed in order to optimise the UI.

3. HEV Prototyping

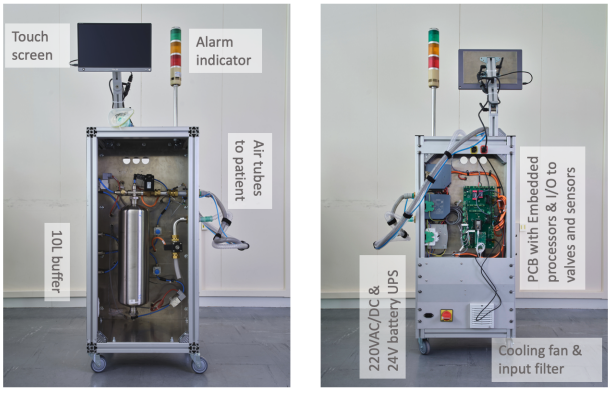

Fig. 5. HEV prototype showing a front (left) and back (right) view.

Three prototypes were constructed with an identical mechanical design in order to allow work in parallel on different aspects of the design implementation. In parallel, a fourth prototype was developed at the Galician Institute of High Energy Physics at the University of Santiago de Compostela (IGFAE/USC) with a two-fold goal. Firstly, we wished to demonstrate that HEV could be reproduced easily in other places than CERN. Secondly, having successfully reproduced the design within a short timescale, we were able to launch additional development and contributions to the control software. In addition, this triggered discussions with local hospitals and physicians, further improving the design of the device.

Functionally, the prototype designs (Fig. 5) follow the concept described above. The resulting cabinet is mounted on wheels, can easily be moved by one person, is very stable, and provides a convenient surface to mount the display at head height. The cabinet is closed with doors, so that easy access for cleaning is possible. For safety, two compartments (front and back) provide complete separation between the pneumatic and electrical parts of the ventilator. The air tubes connect through a standard bulkhead thread connector on the outside, that make it easily replaceable to match hospital connection standards around the world.

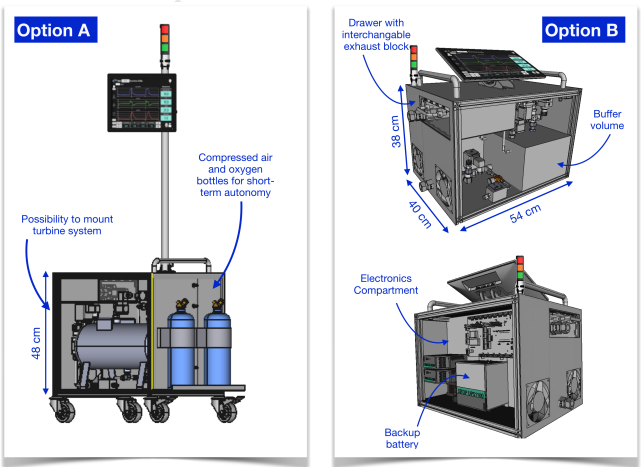

Fig. 6. Potential alternative mechanical designs with an identical functionality to the HEV prototypes.

Alternative mechanical designs. The prototypes were built with a deliberately large form factor to allow rapid development and exchange of parts. The final HEV ergonomics may look quite different depending on the requirements in the region of deployment and the accessories included. The HEV collaboration has provided two different alternative mechanical designs to which the HEV design could be adapted to fulfill different needs, which are illustrated in Fig. 6. Option A is more compact and can be mounted on wheels or a trolley. Space is provided to support oxygen and compressed air bottles, as well as the turbine system, so that the entire system and accessories can be provided as one integrated unit, which can be desirable for certain geographical locations. Option B is a still more compact and light version, for which the weight can be further reduced and the total dimensions are comparable to existing commercial ventilators. The touch screen can be folded away for transport and the ventilator easily mounted on a trolley. Both options are identical in functionality to the HEV prototypes which have been built and tested.

4. Prototype test results

Setup. The HEV prototype is tested by connecting it to a lung simulator through a coaxial breathing circuit set. The coaxial breathing circuit set[†] has a differential pressure based flow sensor[‡] whose readout is embedded in HEV (`dP_patient`). Alternatives to this sensor are available with other manufacturers[§], and a specific breathing circut for HEV in order to decrease reliance on the existing supply chain can also be an option. The lung simulator is a TestChest light[¶](15), which allows mechanical parameters of the lung to be changed (e.g. resistance of the airways, compliance of the lung) as well as generating adjustable spontaneous breathing and effects such as patient heartbeat. The setup is equivalent to the MHRA (14) and ISO 80601-2-12 Fig. 201.102 (16).

Target Pressure Performance. As discussed in Section 2, when the inhale starts, the proportional valve `valve_inhale` opens in a controlled way in order to reach the target pressure in a given time. This is done through a PID controller that monitors the `P_inhale` pressure measurement as input for the inhale valve opening control. As illustrated in Fig. 7, any pressure level within the setting range can be reached and the system stays stably locked to this value with an uncertainty below 3% in most of the cases.

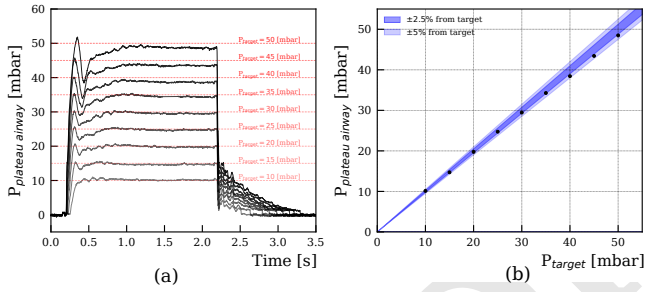

Fig. 7. (a) Pressurisation of a 20 $\mathrm{cm\,H_2O}$/ml compliance, 5 $\mathrm{cm\,H_2O/l/sec}$ resistance patient with various target pressures. The inhalation time is set to 1.5 seconds, and is followed by a pause of 0.5 seconds. (b) Deviation of the inhale pressure from the target as computed during the pause.

The performance was checked using the leak settings available with TestChest and even with the highest leak setting, no difference in the pressure profile is visible.

Thanks to the flexibility provided by the PID control, the time needed to reach the maximum of pressurisation can be tuned between the fastest setting of about 50 ms up to about 300 ms, as illustrated in Fig. 8. This gives the clinician the possibility to use the fastest response of the ventilator, typically for intubated, sedated patients, through to slower rise times which may be useful at other periods of recovery.

The response of the HEV ventilator to lungs with compliance varying from 10 to 100 ml/ $\mathrm{cm\,H_2O}$ and with resistance from 5 to 50 $\mathrm{cm\,H_2O/l/s}$ has been studied. The PEEP values range from 5 to 15 $\mathrm{cm\,H_2O}$ and target pressure up to 45 $\mathrm{cm\,H_2O}$ were tested. A sub-sample of the pressure, flow and volume curves are reported in Fig. 9.

[†] Hamilton PN 260128.
[‡] Hamilton PN 281637.
[§] Intersurgical P/N 2072000
[¶] Organis GMBH, Landquart, www.organis-gmbh.com

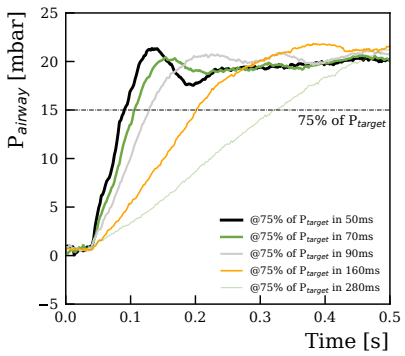

Fig. 8. Rising edge of the inhalation for various rise time settings. The lung compliance here is 50 ml/ $\mathrm{cm\,H_2O}$ for a resistance of 5 $\mathrm{cm\,H_2O/l/s}$.

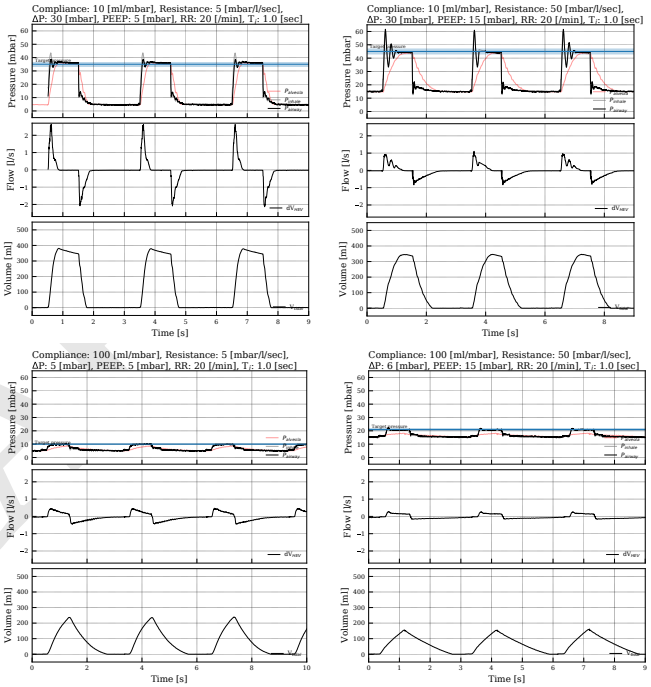

Fig. 9. Pressure, flow and volume registered for four different patient configurations to illustrate the performance of the ventilator with the lowest and highest lung compliance, together with the lowest and highest airway resistance. The ventilator copes correctly with all conditions, showing, as expected, a more peaked flow, as the complicance and resistance is reduced.

When the patients show no airway resistance or when their lung compliance is low enough, the flow can fully develop during the allocated inhalation time so that the tidal volume can be computed from the product of the compliance and the differential pressure. As expected, higher resistances naturally slow down the rise of the inspiratory pressure (at the airways). Lung compliances lower than 10 $\mathrm{cm\,H_2O/ml}$ could not be tested with this lung simulator but will be the subject of a dedicated test later; extrapolating from the current results we expect a consistently good performance.

Inhale Trigger Peformance. The inhale and exhale triggers are essential to guarantee the comfort of the patients and to ensure fast recovery time. The trigger functionalities were developed with this aspect in mind and particular effort was made to qualify them.

Inhale trigger algorithm description. Whenever the patient initiates a breath, the proximal flow sensor detects an increased flow and a drop in pressure. The increase in flow is used as a trigger for the inhale sequence. The inhale trigger algorithm works in the following way. Whenever the flow reaches 10% of the maximum exhale flow, the window allowing for an inhale trigger is opened. This condition is by definition always met when the patient initiates an inhalation. The expected flow at a given instant is computed by a linear regression from a given time window before that point. It provides the baseline, to which the measured flow is compared. If the measured flow, corrected for the baseline, is above a threshold that can range from 0.2 l/min to 20 l/min, then the inhalation starts. Lower thresholds are sensitive to noise, in particular that induced by the heart-lung interactions. This threshold is set by the clinician. Other means of triggering such as a pressure-based trigger can be easily incorporated using the modular software design.

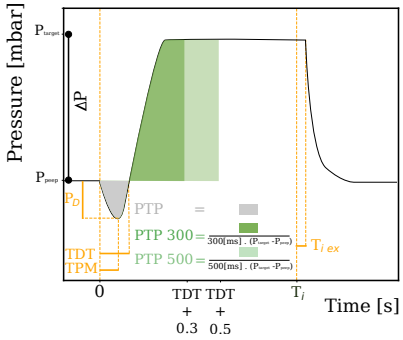

Fig. 10. Measured parameters to qualify the inhalation trigger. The variables used in this work are based on the work presented in (17) and (18).

Inhale trigger qualification. To qualify the performance of the inhale trigger, the variables defined in (17) are used. Figure 10 illustrates those variables: the Time to Minimum Pressure (TPM) is defined as the time between the beginning of the inhalation effort and the minimum value measured by `P_patient`, and the Trigger Delay Time (TDT) is defined as the time between the beginning of the inhalation effort and the moment the pressure returns to zero. Values of TPM in commercial ventilators typically vary between 50 and 150 ms depending on the inhalation effort, see for example (17), while TDT, which should ideally be below 150 ms so as not to be felt by the patient, varies for commercial ventilators in practice between 90 and 250 ms (17). The pressure-time product during trigger (PTP) is represented in Fig. 10 by the grey area and represents the effort until the pressure is effective. It ranges from 0.02 to 0.3 cm H_2O.s in commercial ventilators (17). The ideal PTP300 (PTP500) percentage is the ratio of the pressure integral over the 300 ms (500 ms) following the trigger delay (the area of the green regions in Fig. 10) and the ideal PTP at 300 (500) ms. It should be as large as possible, with typical commercial ventilators exhibiting values between 10 and 50% (20 and 75%) for PTP300 (PTP500) depending on the inhalation effort (17).

To test the inhalation trigger, the same lung parameters, pressurisation parameters and inhalatory effort as in (17) were used. TestChest was set with a compliance of 50 cm H_2O/ml and a resistance of 5 cm H_2O/l/s, breath cycles at 12 respirations per minute consisted in a 1 s inhalation with a constant inhalation flow giving an occlusion pressure at 100 ms ($P_{0.1}$) of 2 cm H_2O (low effort) and 4 cm H_2O (high effort) and several pressurisation parameters: ΔP of 10, 15 and 20 cm H_2O with a PEEP of 0 and 5 cm H_2O. The inhale trigger threshold was set to 0.5 L/min.

	Small effort $P_{0.1}$=2[cm H_2O]			Large Effort $P_{0.1}$=4[cm H_2O]		
ΔP [cm H_2O]	10	15	20	10	15	20
TPM [ms] ±5ms	110	101	76	106	82	73
TDT [ms] ±5ms	134	108	99	142	106	97
PD [cm H_2O] ±0.2 cm H_2O	1.9	1.9	1.6	4.4	3.8	3.3
PTP [cm H_2O.s] ±0.01 cm H_2O.s	0.11	0.06	0.05	0.26	0.18	0.15
PTP300 [%] ±2%	29	40	45	27	37	42
PTP500 [%] ±1%	41	52	57	36	44	51

Table 1. Results of the inhale trigger characterisation. The results of the two PEEP settings (0 and 5 cm H_2O) are averaged in the table. The typical measurement error of each variable is reported next to the variable name.

Table 1 summarises the results of the inhale trigger qualification. The results of the two PEEP values are within errors such that they are averaged in the table. Comparing the results to the ventilator studied in (17), the HEV inhale trigger appears to perform very well.

The trigger response is studied again in the presence of leaks. Only one set of pressurisation is used, with PEEP at 0 cm H_2O and ΔP=20 cm H_2O. Four settings are examined: no leaks, weak, medium and strong leaks as set by TestChest. All results are well within 10%.

Exhale trigger algorithm description. The implementation of the exhale trigger is more straightforward. When the inhale flow decreases down to a fraction of the maximum inhale flow, the exhale phase is triggered.

Exhale trigger qualification. In order to qualify the performance of the exhale trigger, the time $T_{I_{ex}}$ defined as the duration of pressurisation by the ventilator in excess with respect to T_I, which represents the true duration of inhalation by the patient, is measured as in (18). This is illustrated in Fig. 10. It is not a property of the ventilator per se, but by appropriate tuning of the exhale trigger it should be possible to bring it down to below 100 ms. Values of $T_{I_{ex}}$ below 10 ms are achieved.

Oxygen mixing test. Because the mixing is performed in the buffer in a phase which is physically uncorrelated to the patient breath cycle (i.e. during patient exhalation when the buffer is disconnected from the patient), we perform the mixing test independently from the test of the ventilator modes.

The O_2 concentration in the buffer is controlled by changing the relative opening time of `valve_O2_in` and `valve_Air_in`. For a given O_2 concentration setting, the opening times can be computed. After stabilisation of the measured O_2 concentration (FIO_2) in the lung simulator, the FIO_2 is compared to the set value. Further control will be introduced in the future by regulating the opening time from a feedback of the measured O_2 concentration in the buffer.

The measured FIO_2 as function of the expected O_2 percentage as calculated from the relative time opening of

valve_O2_in and valve_Air_in is shown in Fig. 11. The measured FIO_2 in the lung is within 5% of the set value, which is an acceptable performance. Further tuning to the valve opening time can be done in order to correct for the small non-linearity in the response.

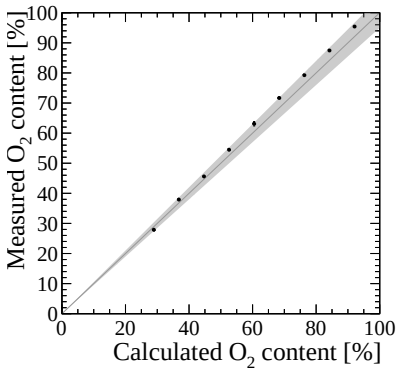

Fig. 11. Measured FIO_2 as function of the expected O_2 percentage as calculated from the relative time opening of valve_O2_in and valve_Air_in. The grey band represents the region within $\pm 5\%$ of the set value.

5. Conclusions

HEV has been developed to be a high-quality, low-cost ventilator, suitable for use in a hospital setting. The design is intended for easy and fast manufacturing that can be performed in a decentralised way with affordable and readily available parts. The central concept of the design with a gas accumulator gives many advantages in terms of robustness, safety, affordability and precise ventilation behaviour. The electrical design is conceived in a modular way for quick prototyping and deployment, which facilitates mass production. The design is intended to be robust and adaptable for a wide range of geographical deployment, including in regions where compressed air may not be readily available and a turbine alternative can be used. Three prototypes have been manufactured and have been tested in situ under clinical supervision with the full range of simulated patients defined in the MHRA specifications and the results are presented in this paper. HEV has also been tested at the ETH Zurich Chair of Product Development and Engineering Design Ventilator test rig. In pressure control mode HEV accurately achieves the target pressures, with fast rise time which is tuneable to slower times on clinician request. Special attention has been paid to the inhale and exhale triggers to optimise patient comfort. The inhale trigger, based on the flow measurement, accurately reacts to the patient effort, with short rise times and excellent PTP values. The system displays and monitoring use concepts familiar to particle physics such as the possibility for remote monitoring from screens or mobile devices, data logging for quality control and performance monitoring, and remote training.

As far as production is concerned, it is foreseen, on the one hand, to enable this through providing partner academic institutions with the detailed design for these institutions to follow up in accordance with local possibilities and standards; on the other hand, directly through industry, non-governmental, governmental and international organizations, such as the World Health Organisation (WHO), for which purpose discussions are ongoing and contacts have been established with potential partners. Every effort is being made to finalise the design of the HEV in accordance with the state-of-the-art best practices and standards, but the formal certification process should of course be initiated by the parties that decide to place this device on the market. The hardware and software design has been done in a flexible way which allows the development of different modes of operation, for instance volume control modes which in principle can be developed and applied as a firmware update. In addition, the HEV prototypes can be used as a testbench to quickly implement and test novel algorithms or hardware updates, and in this way could provide a fresh avenue for medical research.

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1. L Rosenbaum, Facing Covid-19 in Italy – Ethics, Logistics, and Therapeutics on the Epidemic's Front Line. *New Engl. J. Medicine* **382**, 1873–1875 (2020) PMID: 32187459.
2. ML Ranney, V Griffeth, AK Jha, Critical Supply Shortages – The Need for Ventilators and Personal Protective Equipment during the Covid-19 Pandemic. *New Engl. J. Medicine* **382**, e41 (2020).
3. M Malta, AW Rimoin, NA Hoff, SA Strathdee, The 2019-ncov pandemic in the global south: A tsunami ahead. *EClinicalMedicine* **23**, 100384 (2020).
4. EJ Emanuel, et al., Fair allocation of scarce medical resources in the time of covid-19. *New Engl. J. Medicine* **382**, 2049–2055 (2020).
5. JustActions, The Missing Piece. Why Continued Neglect of Pneumonia Threatens the Achievement of Health Goals., Technical report (2018).
6. HJ Zar, SA Madhi, SJ Aston, SB Gordon, Pneumonia in low and middle income countries: progress and challenges. *Thorax* **68**, 1052–1056 (2013).
7. SJ Aston, Pneumonia in the developing world: Characteristic features and approach to management. *Respirology* **22**, 1276–1287 (2017).
8. J Pearce, A review of open source ventilators for covid-19 and future pandemics. *F1000Research 2020* **9**, P218 (2020).
9. J Buytaert, , et al., The HEV Ventilator Proposal. arXiv:2004.00534 (1 April 2020).
10. EU, Guidance on medical devices, active implantable medical devices and in vitro diagnostic medical devices in the COVID-19 context (2020).
11. Association for the Advancement of Medical Instrumentation, Emergency use ventilator (EUV) design guidance, revision 1.2 (2020).
12. World Health Organization, Technical specifications for invasive and non-invasive ventilators for COVID-19: Interim guidance, 15 April 2020 (2020).
13. R Inglis, E Ayebale, MJ Schultz, Optimizing respiratory management in resource-limited settings (2019).

14. UK Medicines and Healthcare products Regulatory Agency, MHRA Specification for Rapidly Manufactured Ventilator System (RMVS), version 4.0 (2020).
15. J Brunner, *TestChest Physiological Model.* (2017).
16. International Organization for Standardization, Medical electrical equipment — Part 2-12: Particular requirements for basic safety and essential performance of critical care ventilators (2020).
17. C Delgado, et al., Performance of the new turbine mid-level critical care ventilators. *Respir. Care* **62**, 34–41 (2017).
18. L Vignaux, D Tassaux, P Jolliet, Performance of noninvasive ventilation modes on icu ventilators during pressure support: A bench model study. *Intensive care medicine* **33**, 1444–51 (2007).