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A compact low-power wireless system for *in vivo* evaluation of heat and moisture exchanger performance

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Abstract

Reliable tools for monitoring heat and moisture exchanger (HME) performance are in high demand by physicians, in order to assess the proper air conditioning delivered to intensive care unit (ICU) patients undergoing mechanical ventilation. To date, there is no system that comprehends all the requirements for clinical applications, in terms of performance and design. In this paper, a compact measurement system is proposed for monitoring HME performance *in vivo*, comparing the results with *in vitro* testing outcomes. The portable system presented is connected to the ventilation circuit close to the HME and assures wide compatibility with the new generation of smart devices because of its embedded Bluetooth low-energy module. Low power consumption ensures long-term monitoring capability of more than 24 h. Laboratory tests performed both in static and dynamic conditions showed rise- and fall-times for humidity measurements between 1 s and 1.8 s, compatible with many common variations in working operative conditions during mechanical ventilation.

Clinical tests performed in the ICU demonstrated the possibility to effectively and continuously monitor *in vivo* HME performance. Furthermore, the comparison of the *in vivo* performances with the *in vitro* standard procedure and the agreement of the parameter ranges monitored allowed us to confirm the reliability of the system, highlighting the usefulness of this approach for proper real time HME monitoring.

Keywords: temperature monitoring, humidity monitoring, low-power system, *in vivo* monitoring, artificial ventilation, critical care

(Some figures may appear in colour only in the online journal)

1. Introduction

Heat moisture exchangers (HME) represent one of the most convenient strategies to gradually vary temperature (T) and humidity of the inhaled air provided to mechanically ventilated patients in intensive care units (ICU), to fit the lungs' needs, emulating the physiological function of the bypassed upper airways. To prevent severe complications possibly caused by inadequate heating and humidification of inhaled gases during mechanical ventilation (e.g. airway obstruction and infection) [1], the use of heaters/humidifiers has become essential in clinical practice [2], especially during surgery and in the ICU [3].

Heaters/humidifiers are usually classified as active or passive, according to their operating principle. HMEs belong to the passive class, since they work without any external power

supply, retaining thermal power and a part of the water content of the exhaled gas (at about 32 °C and 100% relative humidity (RH)), bringing them back through the gas mixture delivered by the ventilator [4, 5]. Additionally, they play a role in the prevention of microbial contamination that may develop in the ventilator circuit as they have a filtering membrane.

Nowadays, HME performances are commonly assessed using *in vitro* procedures (UNI® EN ISO 9360-1 of 2002) under controlled laboratory conditions. Nevertheless, according to the American Association of Respiratory Care (AARC) Clinical Guidelines [6], one of the greatest issues faced by clinicians concerns the realistic monitoring of device accuracy *in vivo*, which is influenced by numerous factors, such as the patient's general condition, the specific clinical condition requiring ICU admission, as well as the volume of gas, inspiratory time, ambient T, patient's body T and the distance from the airways that cannot be controlled under *in vitro* tests [7, 8]. There is an increasing interest in bringing to person-centered care the same metrological accuracy of the physical sciences and engineering [9], with specific examples in the area of mechanical ventilator monitoring [10].

To date, the evaluation of HME performances described in the literature have been performed *in vitro* and *ex vivo* [11, 12] with various methodologies ranging from dew point to optical fiber sensors [13, 14], reaching best accuracies of ±2% RH (range 0%–80% RH) and ±0.3 °C (from −40 °C to 115 °C) [15], and response times down to 0.1–0.2 s for the fastest heated capacitive hygrometer [16, 17]. However, due to the clinical scenario discussed above, accuracy and fast response times should be combined in a portable stand-alone device that could be integrated with all the ICU instrumentation, providing an easily interpretable feedback. Thus, only HME testing *in vivo* can take into consideration all the contour conditions in terms of physiological signal variation and ICU daily routines that can affect HME performance and cannot be reproduced with the standard *in vivo* procedure. Among the literature reporting on *in vivo* monitoring, some interesting examples addressing these requirements can be observed. Zuur *et al* [18] analyzed, *in vivo*, the air sampled from the trachea with an external humidity sensor. The setup presents limitations due to the non-portability and the not-optimal control of the distal end of the catheter, which might affect measurement accuracy (around 5%) due to minimum contact with the trachea. Another approach was presented by Ricard *et al* [19], with a long-term study on HME performance (around 7 d) showing the ability to detect performance decrease during HME lifetime, even if the system did not provide fast responses. Castro *et al* [20] designed an interesting *in vivo* monitoring system, by means of an electronic digital thermo-hygrometer with an accuracy of 2% for RH and 0.5 °C for T, and response times of 1.4 s for 90% RH response and 150 ms for 90% T response. The minimal values averaged over four respiratory cycles of T and absolute humidity (AH) on the patient's side were used to assess the effective humidification of air introduced by HME inside an anesthesia workstation. The main limitation of this study is related to possible bias introduced by the unblinded study, and by the short monitoring time (120 min), which cannot give complete information on HME performance over its lifetime (24 h). Finally, in [21], a method for measuring T and AH within the nasal cavity was proposed, obtaining very good accuracies but with intrinsic difficulties related with the narrow airway passages in the complex nasal geometry, that might have an impact on the measured parameter.

In the discussed literature, it emerges that the design of a proper sensing system for *in vivo* evaluation of HMEs requires a faster humidity sensor as well as the setup of specifications to ensure compatibility with ICU practices. The first requirement is mainly related to the response of each sensor, which should be fast enough to follow the dynamics of the humidity of the single breath (normally occurring in a time window between 2 s and 20 s). The second requirement is strongly related to the system dimensions and to the signal transmission. In this regard, it is estimated that 30% to 70% of patients in ICU may suffer from states of severe agitation and delirium [22, 23]. In such conditions, abrupt movements may damage existing wiring, exposing the patient to serious adverse events. A wireless portable system, with sensors and conditioning electronics properly integrated in a device of limited dimensions, is the preferred solution that leaves much more freedom of movement to both patient and operators, allowing non-invasive long-term *in vivo* monitoring, as recommended for any suitable breathing analyzer [24, 25]. Furthermore, only components able to be sterilized can be used to reduce any risk of infection to the patient.

HME performance can be assessed using specific parameters that can be calculated assuming the temperature and absolute humidity values of exhaled and inhaled gases by the patient as the maximum and the minimum values of T and AH signals of the respiratory cycles, respectively. In light of this, three most relevant parameters (efficiency, efficacy and losses) can be highlighted in the correlated literature. The efficiency is described as the ability of the HME to transfer, to the patient, a part of the heat and humidity of the exhaled air to the inhaled air, limiting the amount of humidity and heat loss [15, 20, 26]. The efficacy is defined as the ability of the HME to properly condition the air to the patient, and it is represented by the T and AH of the air inhaled by the patient, conditioned by the HME [15, 20, 27]. Finally, heat and moisture losses are described as an indicator of the ability of the HME to avoid the dispersion of heat and moisture from the HME [20].

In light of this, we propose here a wireless system with low-power and easy-to-use characteristics that can monitor the conditioning of gases during ventilation with HME *in vivo*, aiming to:

(1) evaluate the effect of the use of a generic HME inside a circuit for mechanical ventilation, owing to the estimation of efficiency and efficacy during its life time (24 h);
(2) increase the accuracy of the quantitative evaluation of the HME parameters by using a faster humidity sensor and setting the right sensor position;
(3) evaluate the accuracy in the calculation of the parameters.

The majority of previous analyses studied the conditioning properties in a laboratory setting [11, 12] or the effects of HMEs on health conditions [19]. Only few studies monitored HME in an ICU real-use setting [18, 20] during mechanical

ventilation. The unique and main novelty of our proposal relies on portability, low weight, a user-friendly interface and low power, which ensure complete integration with the clinical setup for continuous evaluation of HME performance in a real-use setting. Furthermore, these aspects are combined with an evaluation of sensor uncertainty, thus to provide to the clinician an understanding of the measurement accuracy at the different mechanical ventilation parameters. Thus, the proposed compact low-power system allows continuous prolonged monitoring, compatible with ICU practices.

After a proper laboratory evaluation of the system and a critical discussion of the main sources of uncertainty, *in vivo* clinical trials have been performed, demonstrating the possibility for using the proposed system for long-term *in vivo* monitoring of T and RH during mechanical ventilation with an HME.

2. System design

The measurement system topology is shown in figure 1. The system is composed of two main sections, referred to as the measuring module and the display module.

The measuring module represents the core of the project since it executes the main operations by reading the sensors, building the data block and managing the Bluetooth low-energy (BLE) connection. It presents two subsections (machine and patient side), before and after the HME filter, thus two different measurement points can be observed, considering the direction of the ventilator air flux; the machine side of the HME measures T and RH, while the patient side only measures T. On the patient side, only T measurement is required since the air is almost saturated by water content (RH 100%) during expiration and it is about RH 98% during inspiration [28, 29].

The display module reads the data sent by the measuring module and calculates AH and the relevant parameters, providing an easy-to-understand set of data for the user. The following provides a detailed description of the two sections, shown in figure 1.

2.1. Measuring module

The measuring module acquires the signals from the sensors and transmits them to the display module via a BLE communication channel. The wireless link between the measuring module and the display module is created with a couple of Bluetooth modules (RN4020). The RN4020 is an easy-to-use component with integrated antenna, a serial interface (UART) and a command interpreter. To reduce the data flow and minimize the power consumption we use a private profile defined by Microchip called MLDP (microchip low-energy data profile) which provides an asynchronous serial data connection between two RN4020 devices.

A block diagram of the measuring module is shown in figure 2. The sensors block contains one resistance T detector (Pt1000) and a T-RH sensor (IST HYT 271) [30], which includes the sensitive element and optimized support electronics for local processing of the obtained data. The IST HYT 271 integrates a capacitive polymer humidity sensor with ultra-fast response times, if compared with the majority of RH sensors [31–33], and it can automatically compensate the thermal drift by exploiting an onboard T sensor. The operating ranges are −40 °C to +125 °C and 0% RH to 100% RH, with linearity errors less than ±1% RH. The accuracies are ±2% RH at +23 °C (0% RH to 90% RH) and ±0.2 °C (0 °C to +60 °C), and the reproducibility is ±0.2% RH and ±0.1 °C.

The measuring block is based on two different integrated circuits, one for the Pt1000 (MAX 31865) and one integrated in the IST HYT 271. The MAX31865 (Maxim) is an easy-to-use resistance-to-digital converter, optimized for platinum resistance T detectors. For managing the whole board, a PIC24 microcontroller unit (MCU, Microchip) has been chosen.

The board is powered by a Li–Po battery pack (850 mAh) and includes a DS2745 battery monitor (Maxim Integrated), which monitors the remaining power, and a TPS7133 Low Drop Out (LDO) voltage regulator (TI), assuring a reference voltage of 3.3 V. In figure 3, the fabricated measuring module is shown. The two different sections are visible; a main board on which resides the majority of the electronics (placed machine side—dimensions 60 mm × 45 mm × 27 mm), and a daughter card for T measurement (placed patient side—dimensions 40 mm × 20 mm × 10 mm) containing the conversion device MAX 31865 and the Pt1000. The two sections are connected via a 10-pole flat cable. The weight of the measuring module is about 80 g. The circuit board was manufactured in printed circuit board (PCB) technology, and its dimensions are 55 mm × 35 mm.

The measured power consumption during active mode (measurement and transmission every 180 ms) is about 12.5 mA with a voltage of 3.3 V. We carried out a battery discharge test to analyze the autonomy and the result demonstrated an autonomy of about 70 h. Lower bitrate has a negligible impact on the power required by the Bluetooth module.

The firmware is divided into two distinct macro sections (figure 4): the initialization phase and the measurement phase. During the initialization phase, the microcontroller is programmed to sequentially interrogate all the devices and assess the operation. During this phase, a self-test is carried out to verify that all the sensors and the integrated circuits (ICs) are connected and in working status. If a problem is revealed a physical red LED indicator will turn on. After a successful initialization phase, the measuring phase starts; the sensors are cyclically interrogated to obtain T and RH.

2.2. Display module

Due to the wide compatibility of the BLE protocol, the data should be displayed on every smartphone, using a proper app. In order to reduce the development time, in this project, data are shown on a personal computer, acting as a human machine interface (HMI). The HMI is written in LabVIEW and it receives the data from a custom-made USB-to-BLE dongle, as shown in figure 5. The LabVIEW virtual instrument (VI) is written from scratch and it manages the BLE

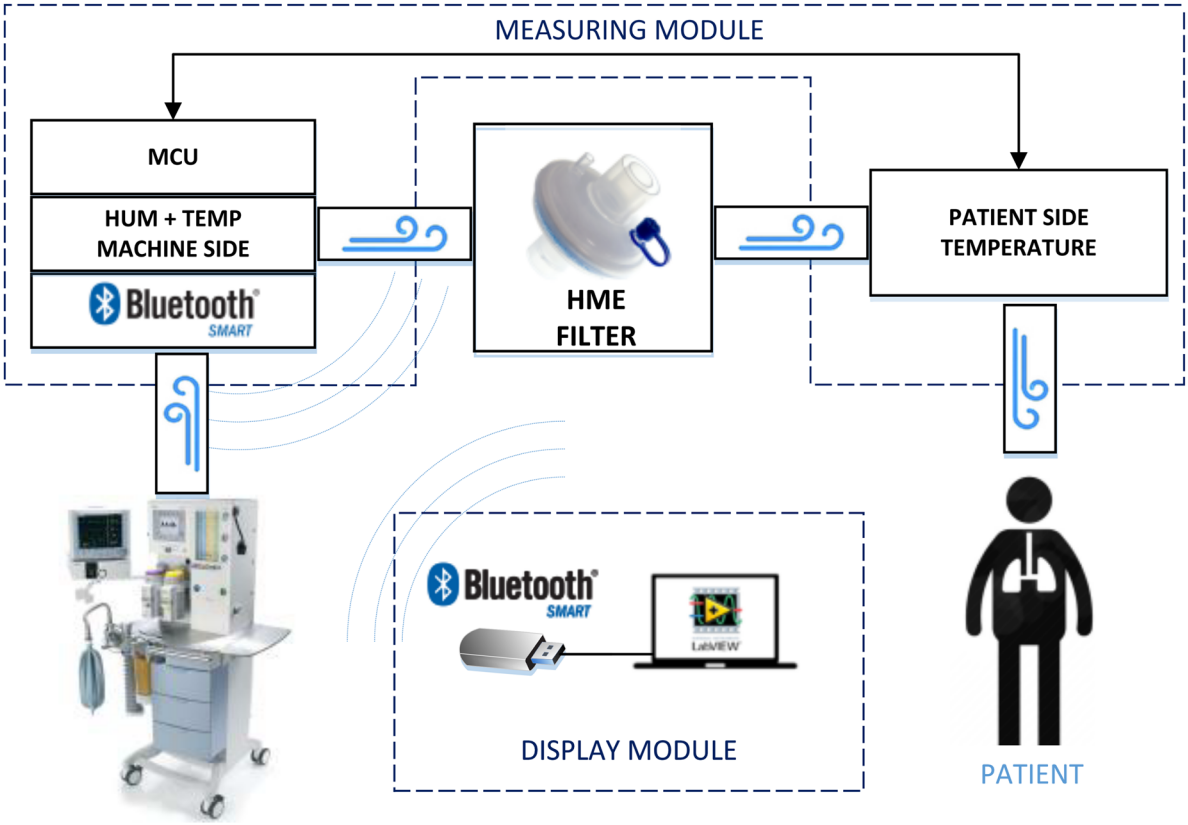

Figure 1. A schematic system representation.

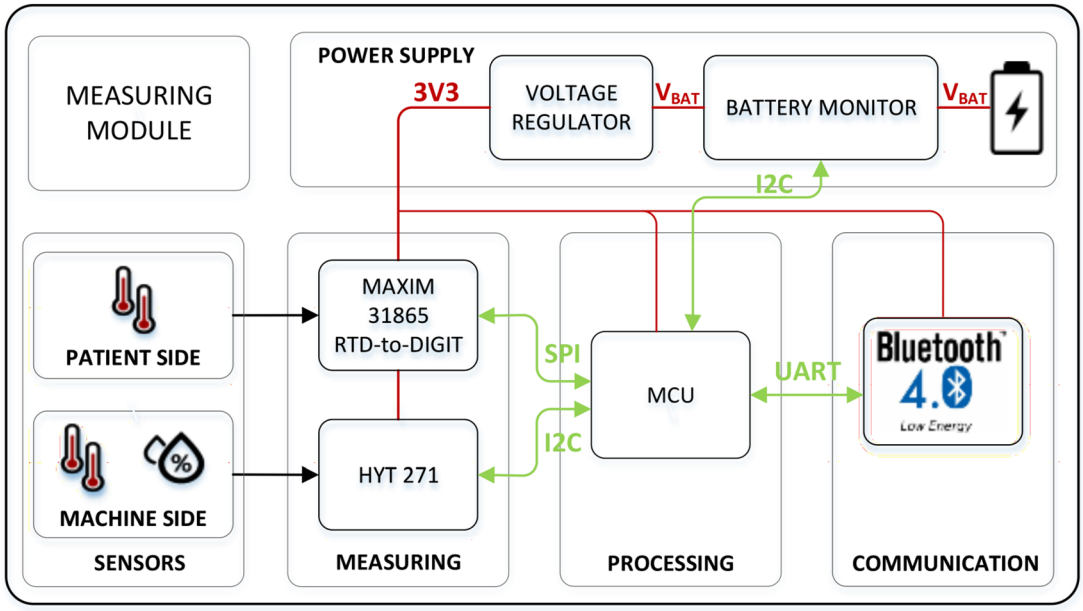

Figure 2. A block diagram of the measuring section.

communication and the data conversion. The main HMI view is shown in figure 6.

To guarantee correct operation an automatic check is done at every measurement cycle and, if a problem is revealed, a physical red LED on the measuring module and/or on the measuring monitor is turned on. The battery level data is obtained through the DS2745 battery monitor. The integrated coulomb counter tracks the battery charge–discharge cycle and provides information on the battery life. These data are converted onboard to a percentage value that is sent to the display module. The firmware is set to send this data every 30 s, in the same packet information about the battery voltage and the current consumption.

Furthermore, the LabVIEW VI converts the raw data to T and RH measurement values. The ISO 9360-2 2002 legislation, which regulates the use of HME in the anesthesia

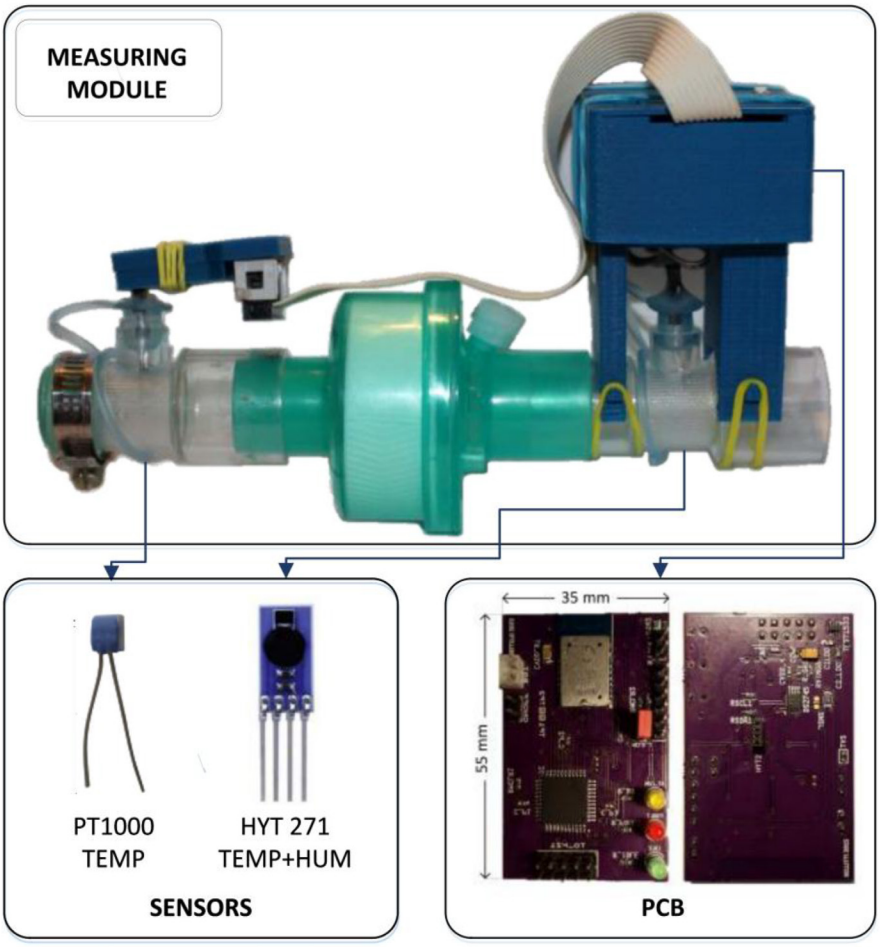

Figure 3. A picture of the manufactured measuring module.

and respiratory field in humans, requires the expressing of humidity measurements in terms of AH, for completeness and transparency. The conversion starting from the RH value is possible due to some mathematical manipulations.

The adopted conversion formulas are reported in [34] and are summarized in equation (1).

$$H_A = \frac{C}{T + 273.15} * \%\mathrm{RH} * \left(A * 10^{\left(\frac{m*T}{T+Tn}\right)}\right). \qquad (1)$$

Where %RH is the relative humidity; T is the temperature in °C; C is a physical constant with 2.166 79 g K J^{-1} value; and A, m, Tn are tabulated for a range of T ($A = 6.116\,441$, $m = 7.591\,386$, $T_n = 240.7263$).

In addition to the functionalities presented in [35], the LabVIEW program can compute T and AH parameters in accordance with ISO legislation permitting a clear analysis of the visualized data by physicians. In detail, the efficiencies are calculated for AH as the ratio between the minimum and the maximum value of the AH signal measured on the patient side, and for T as the difference between the maximum and the minimum value of the T signal measured on the patient side. The efficacy is indicated as the minimum of the measured signals on the patient side (AH min patient and T min patient). The losses are indicated as the maximum of the measured signals on the machine side (AH max machine and T max machine).

3. Laboratory tests

The complete system, which includes the measuring module (sensors and electronics) and the display module, was validated in the laboratory before clinical trials. After an evaluation in the climatic chamber, a specific analysis of the dynamic behavior of the humidity sensor has been performed, including a comparison of the measured data to typical clinical humidity variation to assess the error in the evaluation of the humidity value.

3.1. System evaluation under static conditions

An initial evaluation of the system is performed under static conditions inside a climatic chamber (Perani UC 150/70) able to set specific T and RH conditions with a precision of 0.1 °C and an accuracy of ±0.5 °C for T and of ±3% for RH, by using the setup shown in figure 7.

Parameter values measured by the measuring module (accuracy of the Pt1000 ± 0.35 °C and of the IST HYT 27 ± 1.8% for RH and ±0.2 °C for T) are compared to the measurements from two reference sensors, linked to two digital multimeters (Tektronix DM2510G). The two reference sensors are a Pt1000 for T measurements and the HIH-3610 polymer capacitive sensor (Honeywell) for RH measurements, which has the following technical characteristics: accuracy ±2% RH

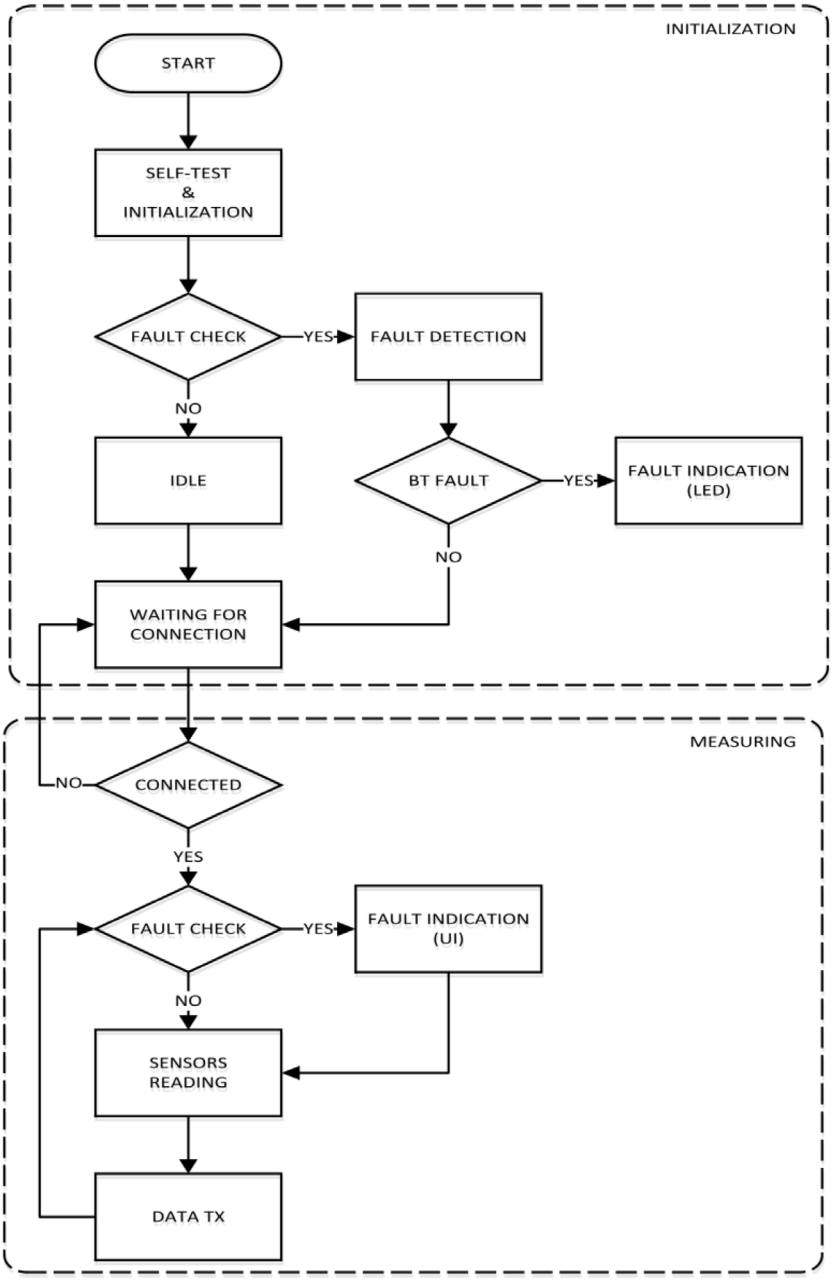

Figure 4. A flow chart for the firmware.

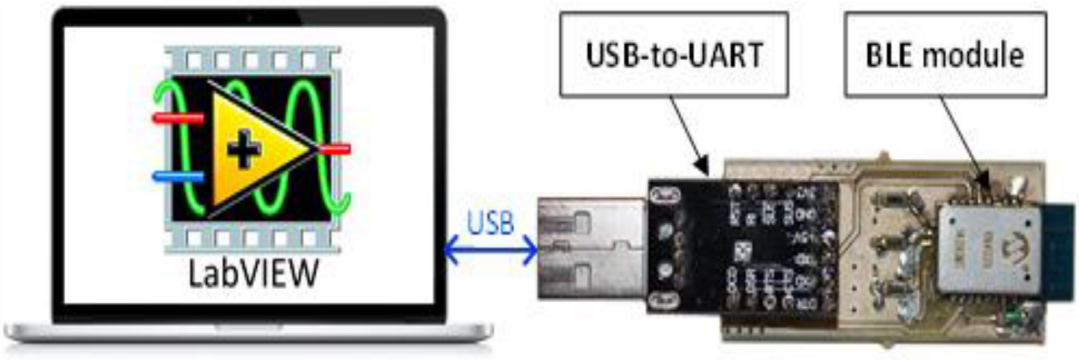

Figure 5. A picture of the manufactured USB-to-BLE module.

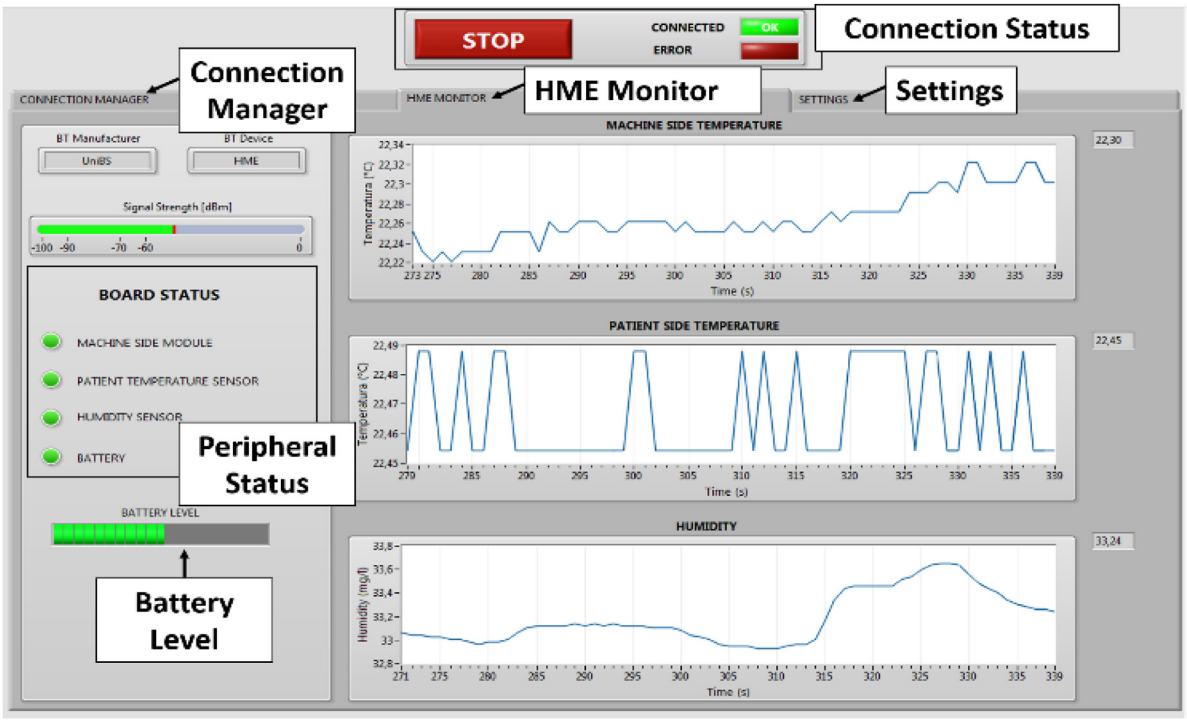

Figure 6. The LabVIEW measuring monitor.

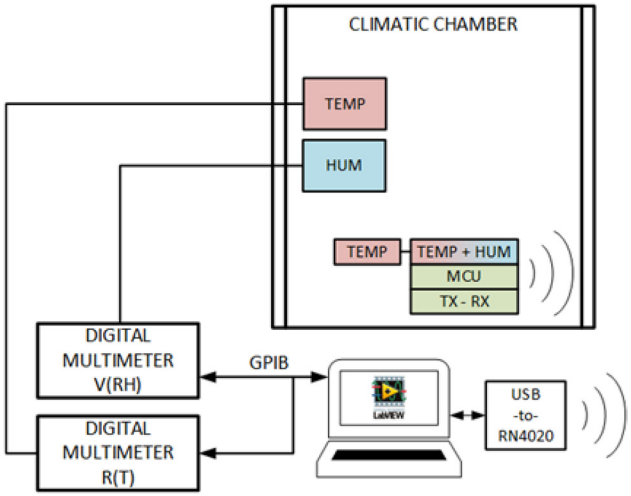

Figure 7. The climatic chamber test setup.

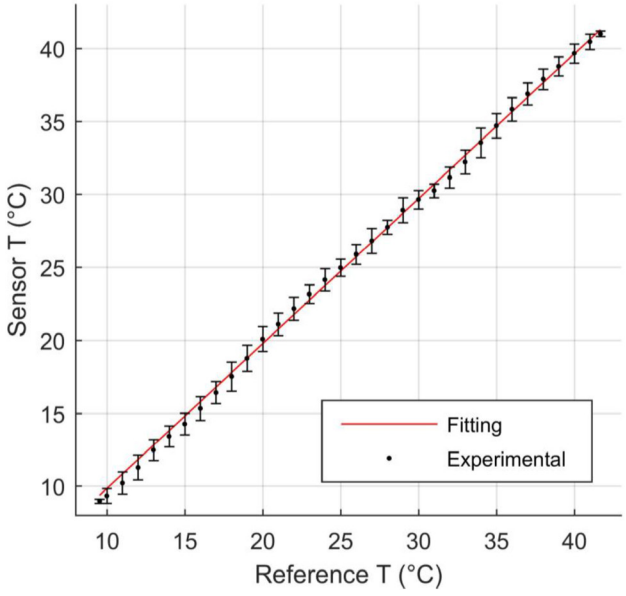

Figure 8. The laboratory test of machine side temperature; the experimental data is represented with a confidence interval of 99%.

(0%–100% RH), linearity ±0.5% RH, repeatability ±0.5% RH and stability of ±1% RH typical over five years [36].

A general-purpose interface bus (GPIB, IEEE 488) connects these multimeters to a PC. An own-written LabVIEW VI controls the whole measurement procedure. In these experimental tests, we used a T and RH range in accordance with the proposed application. The T range is from 9 °C to 45 °C with about a 1 °C step between each measurement. The RH range is from about 7% to 70% with about a 1% step between each measurement.

Experimental results obtained from the characterization in the climatic chamber are shown in figures 8 and 9, respectively, for T on the machine and patient side (T_{MC} and T_{PZ}) and in figure 10 for RH on the machine side (RH_{MC}). The maximum variation between the sensor and the reference was 0.55 °C for T and 2.5% RH for humidity. The maximum standard variation between the sensor and the reference was 0.55 °C for T and 2.5% RH for humidity. Starting from these values and also taking into consideration other sources of uncertainty (the climatic chamber and the reference sensor), it was possible to compute the combined standard uncertainty (CU) obtaining a maximum CU of 0.82 °C and 4.7%, respectively, for T and RH. The results reported in figures 8–10 were then further elaborated to extract the coefficient of linearity and the average difference between the sensor and the reference, for temperatures measured at patient and machine side (T_{MC} and

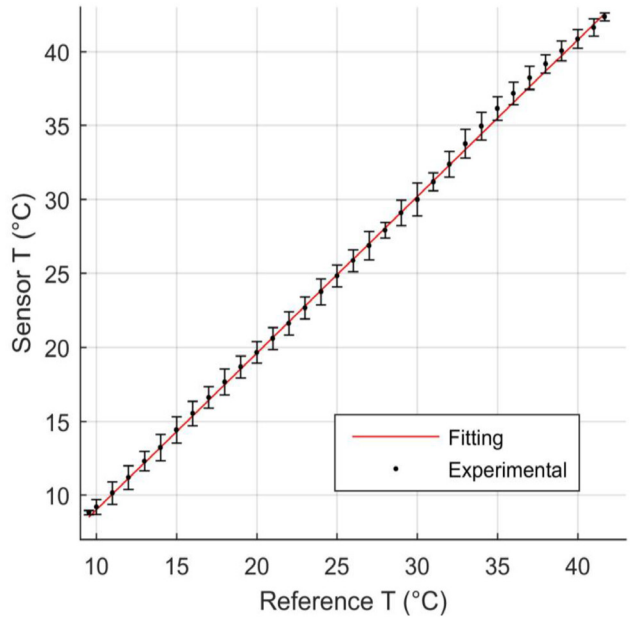

Figure 9. The laboratory test of patient side temperature; the experimental data is represented with a confidence interval of 99%.

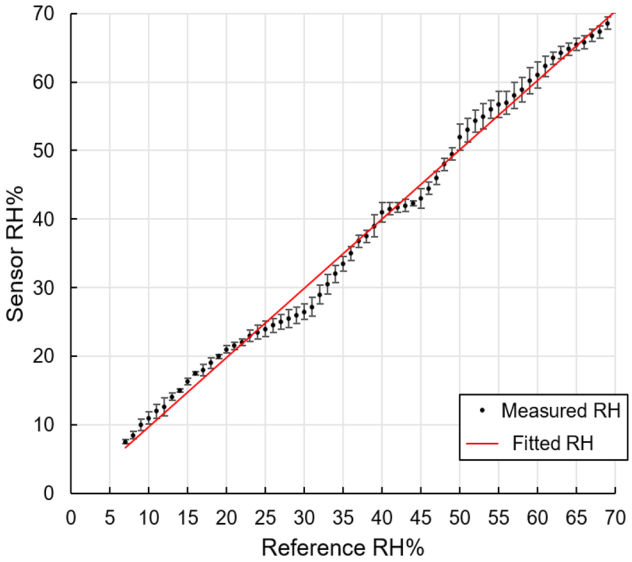

Figure 10. The laboratory test of machine side RH; the experimental data is represented with a confidence interval of 99%.

T_{PZ}), obtaining the results reported in table 1. Regarding the RH average deviation, the corresponding variation in terms of AH (more often used in the clinical environment) has been calculated as $\Delta AH(T = 34.5\ °C) = 0.578\ mg\ l^{-1}$.

These results are in accordance with the graphs obtained in a preliminary version of the system, described in [35]. This behavior was expected and it represents an improvement with respect to the device in [35], since the new module permits us to compensate for drifts and linearity errors.

3.2. System evaluation under dynamic conditions

The HYT 271 component installed on the device, due to its longer time response compared to Pt1000 (<1 s), has been further investigated under dynamic conditions to assess the real response times and compare them with typical variation in clinics.

Table 1. The linearity and deviation of the sensor's static evaluation.

	T_{MC}	T_{PZ}	RH_{MC}
Linearity (R^2)	0.9981	0.9992	0.9907
Average deviation from mean (Δ)	0.33 °C	0.36 °C	1.5%

3.2.1. Humidity variation measurements. A small pneumatic system that allows exposing the sensor to different values of humidity was designed and fabricated to perform sensor dynamic testing.

The system, shown in figure 11, is connected to the input (a) of a compressor, by means of a pressure regulator, to create a pressure-controlled airflow. The two solenoid valves (VXD232) (c) and (d), alternately opened and closed, allow the selection of the path that the flow must follow. The open and close times are less than 10 ms. By opening the valve indicated by (d), the air reaches the tube end unconditioned, whereas, by opening the valve (c) the flow is forced through a bubbling humidifier (b) that is able to raise the moisture by increasing the water vapor content in dry air. At the end of the system, there is a tube section (e) that is suitably sensorized. The installed sensors are the HIH 3610 humidity sensor (Honeywell) used only to measure the humidity value once the transition time is ended, and the TESTO-405-V1 hot-wire anemometer (f) for the evaluation of the flow velocity. The control signals of the two valves are connected to a National Instrument DAQ that, through LabVIEW, allows controlling of the valves and acquiring of the signals coming from the sensors. The tests allow evaluation of the behavior of the module as a function of many different factors, such as different flow values and orientations of the sensitive element with respect to the flow direction. Therefore, three test cycles, one for each flow rate value, are repeated by placing the HYT 271 module with different orientations: parallel to the flow, perpendicular with the sensitive part facing in the same direction of the flow and perpendicular with the sensitive side directed in the direction opposite to the flow. For each of the sensor positions, five tests were performed for flow values of 15, 22, 30, 37 and 45 l min^{-1}, which is a consistent interval in mechanical ventilation tests. After assessing the steady state value of dry air keeping only valve (d) open and of saturated air keeping valve (c) opened, the rise- and the fall-time has been measured by creating steps of an increasing and a decreasing humidity, respectively, by switching valve position. Each step was then repeated 18 times to assess variability. An RH of 10% and of 70% was applied and verified using the experimental setup reported before and these two values were considered, respectively, as dry and humidified air. Thus, RH variation for every test was fixed at about 60%, from 10% to 70%.

Figure 12 shows the time intervals measured for different flow values and for three sensor orientations when the humidity changes from 10% to 70%. As expected, by increasing the flow rate, there is a decrease in rise-time values. Two orientations

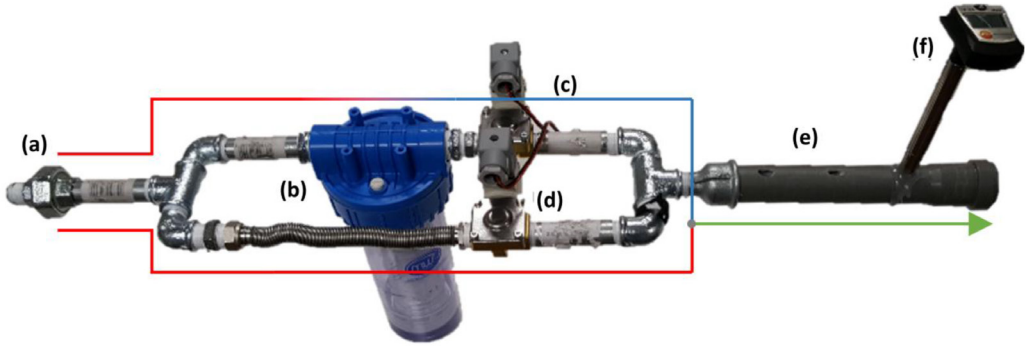

Figure 11. The dynamic test setup.

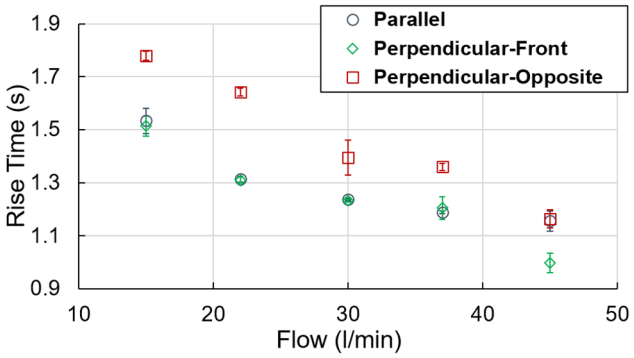

Figure 12. The rise-time for humidity from 10% RH to 70% RH.

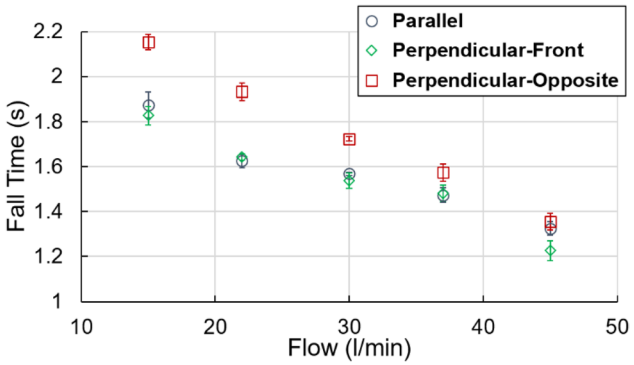

Figure 13. The fall-time for humidity from 70% RH to 10% RH.

(parallel and perpendicular-front) have rise-time values shorter than the perpendicular-opposite orientation.

Figure 13 shows the fall-times measured for different flow values and for three sensor orientations when the humidity changes from 70% RH to 10% RH. The behavior observed is coherent with what is reported on the datasheet of the sensor, which means that the fall-time values (figure 13) are slower than the rise-time values (figure 12).

Considering the perpendicular-front orientation, the obtained experimental results show that, for all the five tested conditions, the measured time values are the lowest for each value of flow. Therefore, in the implementation, the perpendicular-front orientation was chosen. The measured rise- and fall-times at perpendicular-front orientation for the analyzed flow values permit us to indicate the working operative conditions at which the system can correctly monitor humidity variations.

3.3. Accuracy of the measuring system

The system behavior is analyzed considering its operation in the clinical environment. On the machine side, the interest of clinicians relies on measuring the long-term variation of the maximum values of T and AH to quantify heat and moisture loss. Therefore, considering the longer response time of the humidity sensor compared to the temperature sensor, which was verified experimentally in the previous section, an analysis on the uncertainty introduced by the purposed system while measuring the maximum of the humidity signal has been performed.

In mechanical ventilation, considering a classical volume-controlled ventilation, the operative conditions for each patient depend on the rates at which breaths occur, and on the ratios of the duration of inspiration to the duration of expiration (I:E). In light of this, starting from the experimental values of the rise/fall times and fixing the flow value to 30 l min^{-1}, a software-based analysis using Matlab has been performed to estimate the response of the system to typical humidity variations, considering as variables the number of acts per minute (between 9 and 27) and four different I:E ratios (1.2:1, 1:1, 1:1.2 and 1:1.5). Modelling the sensor as a first order system [37], typical clinical humidity signals have been transformed in the frequency domain, filtered, and then re-constructed back in the time domain, in order to compare the humidity input signal with the output after the sensor. The same process has been repeated for each different respiratory rate and I:E ratio, quantifying the percentage of error of the maximum value of the humidity output with respect to the real input value (figure 14). The error trend is linear with the increase in the frequency rate, and is inversely proportional to the I:E ratio. Furthermore, time domain reconstruction of the humidity signal confirmed the possibility of following the transient of the humidity signal, allowing physicians to have some additional information on the shape of the signal.

The results obtained from the analysis in terms of percentage errors with respect to the input maximum value have been plotted in figure 15. They provide an estimation of the uncertainty of the system useful to evaluate a realistic HME performance, in terms of humidity loss.

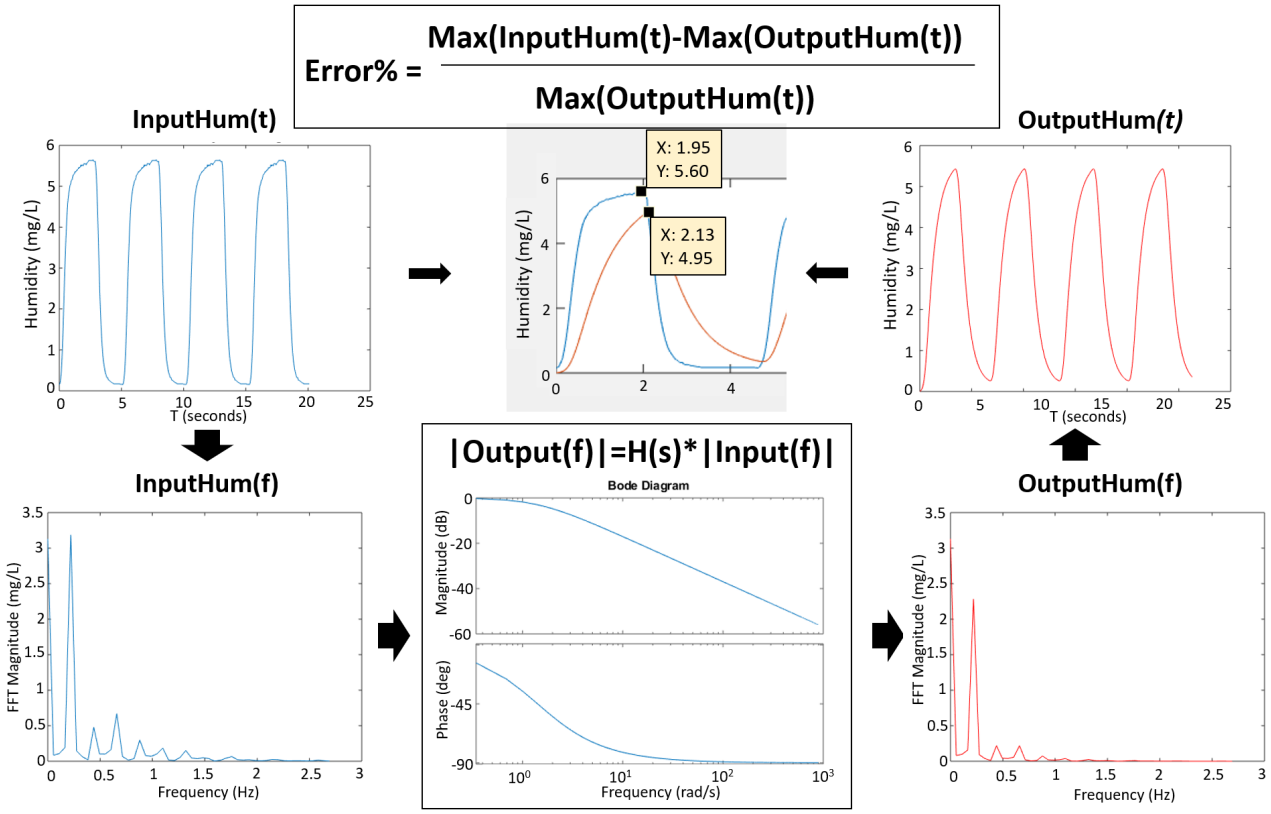

Figure 14. Analysis of the sensor response to a typical humidity signal.

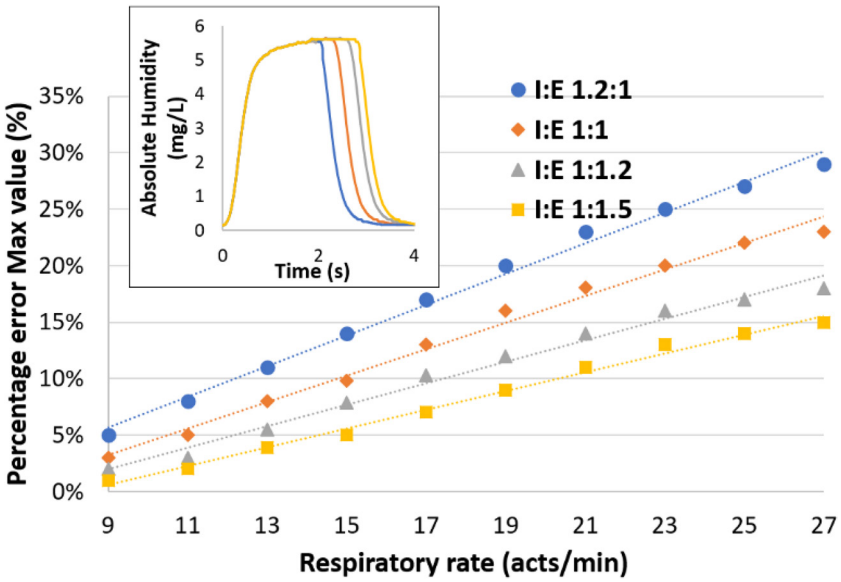

Figure 15. Estimation of the percentage error of the measured maximum humidity value compared to the real signal.

4. Clinical trials

4.1. Setup and methods

The study was approved by the Ethics Committee of the University of Brescia at Spedali Civili (protocol number 2440, June 20, 2016). After the laboratory evaluation, the system was properly integrated in a mechanical ventilation system of ICU patients to evaluate HME performance *in vivo*. The specific model evaluated is the DARTM HygrobacTM S (Tyco Healthcare), produced in Italy by Mallinckrodt Dar S.r.l. Figure 16 shows the measuring module in a clinical environment, attached to a subject, positioned on the tracheal tube, closer to the HME and, therefore, closer to the subject's mouth.

The system has been tested with 35 different subjects admitted to the ICU of the Unità Operativa Anestesia e Rianimazione 2 of the Spedali Civili of Brescia.

The results obtained from HME parameter monitoring have been analyzed using two strategies. The first analysis

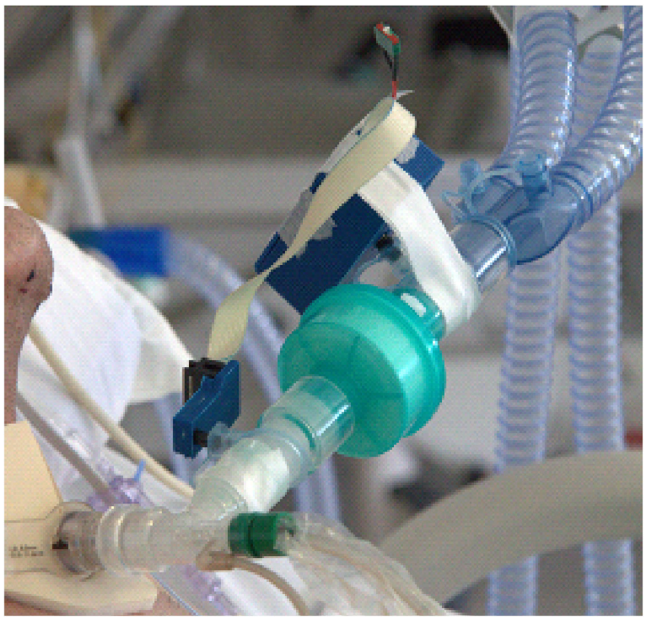

Figure 16. The measuring systems applied to a subject.

was performed considering a time window of a few respiratory acts. This aimed to assess the ability of the system to follow the variation of T and AH during the single breath, discriminating between the inspiratory and the expiratory phases. Following this, a long-term analysis (24 h) was performed, evaluating the HME compatibility with the ICU routine and its performance during the overall lifetime declared by the producer that corresponds to precisely 24 h.

HME efficiency, efficacy and losses have been calculated as described in [15, 20] at three discrete time points ($t0$, $t1$ and $t2$), corresponding to 0, 12 and 24 h from HME positioning.

Regarding the comparison performed with the *in vitro* procedure the efficacy and efficiency values taken as a reference were the outputs obtained using the standard *in vitro* procedure EN ISO 9360-1:2009 [38] and declared on the HME DARTM HygrobacTM S datasheet. Values obtained using a tidal volume of 500 ml were selected, since this represents the condition closer to the *in vivo* conditions.

To perform the comparison among the different time points and between *in vivo* and *in vitro* procedures Student *t*-tests have been performed with a statistical significance for p-value <0.5 and a clinical significance for a difference of $T > 1$ °C and of AH > 1 mg l^{-1}.

Regarding the ethical approval, all the patients involved (or their legal representatives) declared their informed consent to participate in the study, with respect to the laws of the Italian Republic. The research has received the approval of the ethical committee of Brescia (NP 2440) and authorization from the Direction of the Spedali Civili University Hospital, Brescia, where the study has been performed.

4.2. Results

The results from the tests performed in the clinical environment confirmed the less invasiveness of the system, with

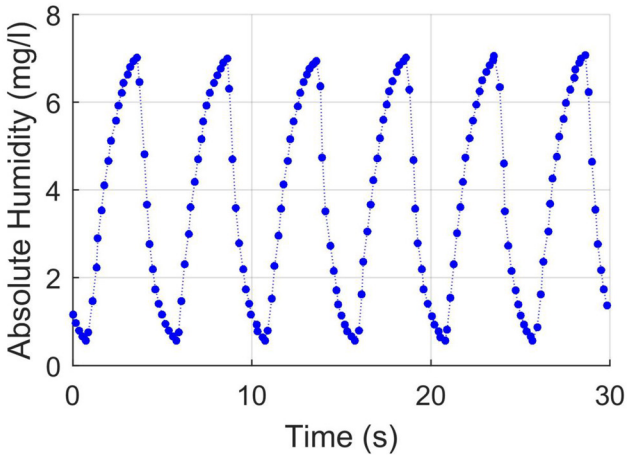

Figure 17. The AH signal (from the machine side).

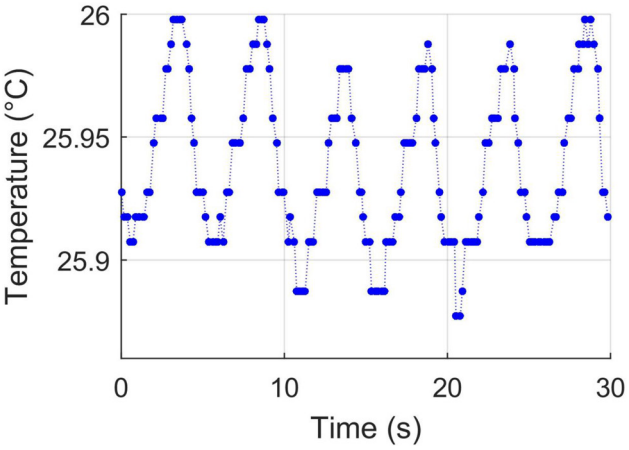

Figure 18. The temperature signal (from the machine side).

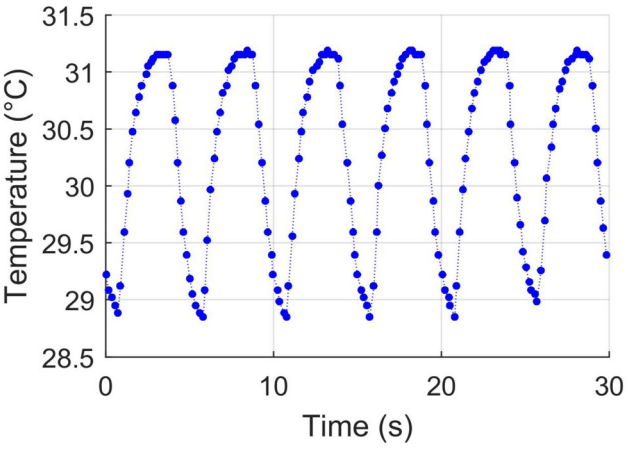

Figure 19. The temperature signal (from the patient side).

no interference with the patient's management, or safety concerns.

Regarding the analysis performed in a short time window, figures 17–19 show 30 s of the recorded dataset, respectively, with respect to AH, machine side temperature and patient side temperature.

The results obtained highlight the dynamics of the different sensors inserted in the measuring module. On the machine

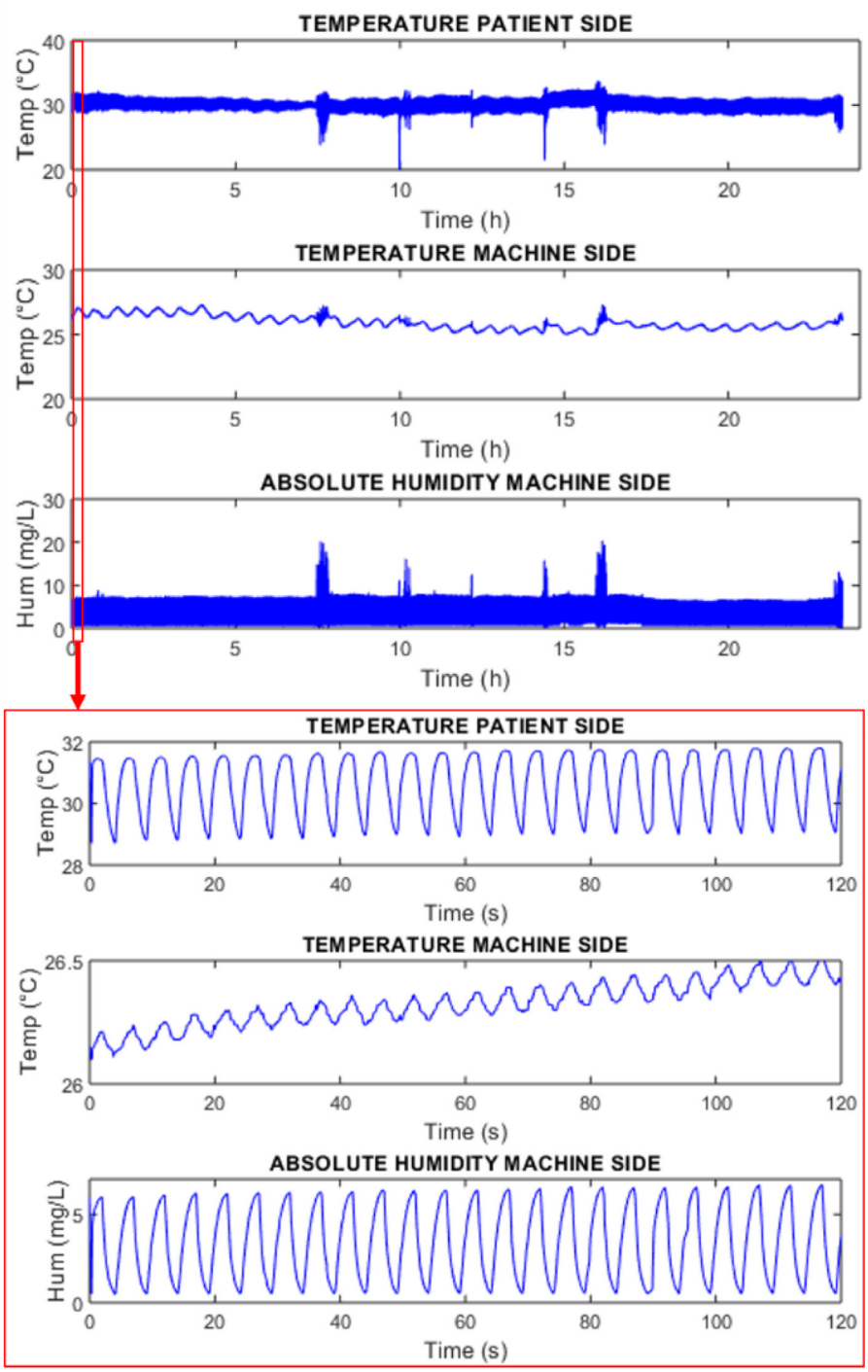

Figure 20. An example of the measured values in a clinical test of 24 h, with a zoom on the specific pattern of variation.

Table 2. Variation of the parameters during the 24 h measurements.

	*t*0		*t*1		*t*2	
	T	AH	T	AH	T	AH
Efficacy	31.47 ±0.44 °C	32.27 ±0.74 mg l^{-1}	31.12 ±0.45 °C	31.65 ±0.75 mg l^{-1}	30.99 ±0.43 °C	31.42 ±0.76 mg l^{-1}
Efficiency	7.63 ±0.46 °C	0.83 ±0.01	8.07 ±0.49 °C	0.81 ±0.02	7.74 ±0.53 °C	0.82 ±0.02
Losses	25.01 ±0.22 °C	6.95 ±0.39 mg l^{-1}	25.29 ±0.24 °C	7.57 ±0.65 mg l^{-1}	25.53 ±0.30 °C	7.28 ±0.86 mg l^{-1}

Table 3. A comparison between parameters obtained *in vitro* and *in vivo*.

	In vitro testing (ISO 9360-1:2002)	*In vivo* testing (portable system)
Efficacy	33.6 mg l^{-1} at 32.3 °C	30.99 ± 0.43 mg l^{-1} at 31.42 ± 0.76 °C
Moisture losses	6 mg l^{-1}	7.28 ± 0.86 mg l^{-1}

side, the absence of a plateau separating the exhalation from the inhalation suggests the impossibility of the IST HYT 271 sensor to reach the maximum value of both RH and T (figures 17 and 18). This issue can however be overcome by taking into consideration the uncertainty calculated in the software-based analysis of the sensor dynamic response (figure 15). Regarding the AH, low values are due to the air conditioned by the mechanical ventilation and the HME filtration effect. Furthermore, regarding the machine side temperature, a low variation during inhalation and exhalation can be observed with a different pattern with respect to the patient's side, due to the air conditioned by the mechanical ventilation. In contrast, patient side T patterns, in accordance with the literature [27], show a plateau discriminating inhalation from exhalation, and the maximum value appears to be correctly measured, owing to the shorter response time of the sensor.

The continuous monitoring over all the HME lifetime, in a time window of 24 h (figure 20), confirmed the possibility for integrating the proposed measuring system in the ICU instrumentation, without affecting patient ventilation. The T trend from the measuring module is consistent with the patient's T values measured by the nurses during the same period. The spikes in the plot are due to temporary disconnection of the measuring module corresponding to routine assistance to the patient carried out by the ICU staff. Despite the fact that the spikes cannot be considered in the performance evaluation, the fact that the acquisition was promptly restored after the operation ensures the compatibility of our system with this type of ICU routine.

During the 24 h measurements, considering the different trial performed, the slight decrease in the average value of the efficacy of both T and AH does not appear to be statistically significant. Similarly, the efficiency of the HME was kept at around an average value of 7.8 °C ± 0.23 °C over the 24 h period tested, with an average increase of 0.5 °C; this is not clinically significant since it is less than 1 °C.

Finally, T (around 25 °C–26 °C) and AH (6–7 mg l^{-1}) averaged among the different 24 h measurements showed a slight increase, which however does not appear statistically or clinically significant, neither for T nor AH (table 2). This finding suggests that, in agreement with the standard *in vitro* procedure, our system is able to confirm the maintenance of a proper air conditioning over all the HME lifetime.

When comparing the *in vivo* measured parameters with the values obtained using the standard UNI EN ISO 9360-1:2002 *in vitro* procedure a substantial agreement could be observed for all the parameters investigated, confirming the ability of the purposed system to reproduce a reliable monitoring of all the required parameters for assessing proper HME functioning, even *in vivo*. Interestingly, possibly due to factors not reproducible *in vitro*, the HME tested *in vivo* with the purposed system showed inferior conditioning performances regarding AH evaluation, both in terms of efficacy and efficiency compared with those obtained *in vitro* (table 3). This suggests the need for further investigation in terms of HME *in vivo* monitoring, to better assess the influence of clinical environment factors on HME performance.

Regarding the temporal variation of the parameters during the 24 h measurements, it is interesting to notice that the efficacy is declining (even if slightly) while the efficiency is maintained quite constant. This result is in complete agreement with the standard maximum window guarantee by the producer and might suggest as a possible improvement the fact that, using the present system, this time window could be extended (always keeping in consideration the limits due to microbial filtration effectiveness), possibly bringing cost savings to the hospital, but without affecting the patient's care.

5. Conclusions

A measurement system for *in vivo* T and RH measurements during artificial ventilation with an HME was developed. This system measures ventilation parameters and transmits the data wirelessly to a reading unit connected to a PC. The embedded BLE module permits low-power consumption, assuring long-time monitoring and wide compatibility with the new generation smart devices. A specific virtual instrument interface was developed to permit user-friendly operations.

Laboratory testing of the overall device, both from a static and a dynamic perspective, allows us to highlight system accuracy, in order to later perform a conscious evaluation of the results from the clinical trials.

More precisely, the dynamic characterization of the humidity sensor through an ad hoc pneumatic system ensured the calculation of rise- and fall-time values, between 1 s and 1.8 s, for the most common flow conditions observed in mechanical ventilation. Starting from these experimental values, the response of the device to realistic humidity variation has been evaluated, performing a software-based analysis to estimate the difference between the maximum value measured and the real maximum value for each condition, with variable respiratory rates and the I:E ratio. The computed error ranges from 3% to 30%, increasing with the increase in respiratory rate, and with the shortening of expiratory phases. These results suggested the need to take into account this limitation when evaluating all the parameters, which were different from the real values due to the inertia of the sensor itself.

After this evaluation, clinical tests performed on 35 patients demonstrated the reliability of the device and its compatibility with the ICU routine. The measuring module connected to the mechanical ventilation circuit monitoring the machine-assisted airflow, owing to its lightness, compactness and to

the wireless transmission, ensured the possibility for properly monitoring HME performance without interference with the patient's management, or safety concerns. Furthermore, the tests permitted monitoring the HME behavior for the entire duration of its lifetime allowing us to evaluate the HME performance *in vivo*.

The comparison performed with the *in vitro* standard procedure allows us to strengthen the reliability of our system due to the agreement of the T and AH ranges monitored. However, the differences observed between the HME performances monitored *in vivo* and *in vitro*, especially regarding AH, suggest an influence of the contour factors of the clinical environment that are not reproducible *in vitro*, and thus demonstrates the usefulness of *in vivo* monitoring to better assess real HME performance. Furthermore, the system allowed us to assess the proper air conditioning of the HME during all of the 24 h, suggesting the potential to apply the system for a longer time with correlated cost savings.

Future studies could evaluate the possible correlations between HME performance decay and clinically relevant disease appearance, helping in the prevention of lung diseases induced by inadequate humidification of inhaled gases during mechanical ventilation.

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