

**“In vitro” evaluation of Heat and Moisture Exchangers designed for spontaneous breathing
tracheostomized patients**

Claudia Brusasco¹, Francesco Corradi², Maria Vargas^{1,3}, Margherita Bona¹, Federica Bruno¹,
Maria Marsili¹, Francesca Simonassi¹, Gregorio Santori⁴, Paolo Severgnini⁵, Robert M Kacmarek⁶,
Paolo Pelosi¹.

¹ Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate, Sezione Anestesia e Rianimazione, Università degli Studi di Genova, IRCCS AOU San Martino –IST, Genova, Italy;

² Dipartimento Cardio-Nefro-Polmonare, Sezione Terapia Intensiva Cardiochirurgica, Azienda Ospedaliero Universitaria di Parma, Italy;

³ Dipartimento di Anestesia e Terapia Intensiva , Università di Napoli “Federico II”, Napoli, Italy.

⁴ Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate (DISC), Università degli Studi di Genova, Genova, Italy.

⁵ Dipartimento Scienza ed Alta Tecnologia, Sezione Ambiente Salute Sicurezza Territorio, Università degli Studi dell'Insubria, Varese, Italy.

⁶ Department of Anesthesiology and Critical Care and the Department of Respiratory Care, Massachusetts General Hospital, Boston, Massachusetts

Corresponding Author: Claudia Brusasco, M.D. Dipartimento di Scienze Chirurgiche e Diagnostiche Integrate. Università degli Studi di Genova, Largo Rosanna Benzi 8 16132, Genova, Italy. Phone:+39-010-5554894; Fax: 010-5556309; Email: claudia.brusasco@gmail.com; Personal mobile: +39-3291185009; Secretary email: anestesia@unige.it

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Abstract

BACKGROUND: Heat and moisture exchangers (HMEs) are commonly used in chronically tracheostomized spontaneously breathing patients to condition inhaled air maintaining lower airway functions and minimizing viscosity of secretions. Supplemental oxygen flow can be added to most HMEs designed for spontaneously breathing tracheostomized patients.

AIM OF THE STUDY: To test the efficiency of seven HMEs designed for spontaneously breathing tracheostomized patients in a normothermic model at different minute ventilations (\dot{V}_E) and supplemental oxygen flows.

METHODS: HME efficiency was evaluated using an in vitro lung model at two \dot{V}_E (5 and 15 L/min) and four supplemental O₂ flows (0, 3, 6, and 12 L/min). Wet and dry temperature of the inspiratory flow was measured and absolute humidity was calculated. In addition, HME efficiency at 0, 12, and 24 h use was evaluated as well as resistance to flow at 0 and 24 h.

RESULTS: The progressive increase in O₂ flow from 0 to 12 L/min was associated with a reduction in temperature and absolute humidity. Under the same conditions, this effect was greater at lower \dot{V}_E . The HME with the best performance resulted in an absolute humidity of 26 mgH₂O/L and a temperature of 27.8° C. No significant changes in efficiency or resistance were detected during the 24 h evaluation.

CONCLUSIONS: The efficiency of HMEs in terms of temperature output and absolute humidity is significantly affected by O₂ supplementation and \dot{V}_E .

Key Words: tracheostomized patients, absolute humidity, inspiratory air temperature, air conditioning, heat and moisture exchangers.

Introduction

The main functions of the upper airways are warming, humidifying and filtering the inspired gases. In patients with tracheostomies the upper airway is bypassed, thus losing conditioning and filtering function. Breathing non-conditioned air for a prolonged time may damage the mucociliary function resulting in a decrease in secretion clearance.^{1, 2} Moreover, breathing cold and dry air results in heat loss and water loss by evaporation.^{1, 2} Several animal and human studies have attempted to determine the “optimal” temperature and absolute humidity of inspired air when the upper respiratory tract is bypassed by an endotracheal tube or a tracheostomy.³⁻⁶ Since 1992 the AARC’s Clinical Practice Guidelines⁷ have recommended that inspired gases be warmed to 30° C and humidified to 30 to 33 mgH₂O/L. Heat and moisture exchangers (HMEs) conserve a portion of the heat and humidity from the exhaled gas, conditioning the subsequently inspired gas.⁸⁻¹⁰ The use of HMEs in chronically tracheostomized spontaneously breathing patients can reduce retained secretions and improve quality of life.^{11, 12} HMEs can also provide supplemental oxygen flow through a direct connection to an oxygen deliver system. However, a dry and cold gas flow directly on the HME’s membrane might reduce the amount of water and heat retained and transferred by the HME. In addition, a loss of HME efficiency during mechanical ventilation has been reported at high minute ventilation.^{13, 14} Our hypothesis was that additional oxygen flow and different minute ventilation (\dot{V}_E) will affect the efficiency of HMEs designed for tracheostomized spontaneously breathing patients.

The aims of this study were: 1) to evaluate the effects of oxygen flow at 3, 6 or 12 L/min and different \dot{V}_E (5 L/min and 15 L/min) on the performance (temperature and absolute humidity) of various commercially available HMEs; and 2) to test the efficiency of HMEs during a 24 h period.

Material and methods:

Experimental protocol and hygrometric measurements

The experimental lung model used in this study consisted of a piston pump that was connected to one end of a breathing circuit to simulate a spontaneously breathing patient (Figure 1). The expiratory gas flow was heated and humidified (DAR HC 2000 HWH, Mallinckrodt DAR, Mirandola, Italy) to mimic normothermic conditions (34°C).^{13, 15} The HME was connected to the opposite end of the circuit and to oxygen flow. A breathing circuit with four unidirectional valves to separate inspiratory and expiratory flows was inserted between the HME and the lung model. Two temperature probes, one dry and one wet (coated with cotton soaked with sterile water) were placed at both the inspiratory and expiratory sides of the circuit. The dry probe measured the actual gas temperature, while the wet one the temperature as lowered by evaporation. Since the wet probe measured a temperature proportional to gas dryness, absolute humidity of inspired and expired gases could be calculated from the difference in temperature between probes, according to specific formula previously reported.^{16, 17} Temperatures were measured electronically, displayed on a screen and printed on a chart recorder (436004 uR 1000, Yokogawa, Tokyo, Japan). This psychrometric method is commonly used by clinicians and researchers interested in valuation of humidity.^{15, 16} The system was considered stabilized after 1 h of ventilation without HME. The expiratory gas was maintained saturated at a temperature of temperature of 34°C. Once the lung model was stabilized, the HMEs were tested in a random order. Temperature and humidity output of the lung model were checked before each measurement.

Evaluation of effects of O₂ flow and \dot{V}_E

Each HME was tested at two different \dot{V}_E (5 and 15 L/min; 500 ml tidal volume and rates of 10 and 30 breaths/min) and four O₂ flows (0, 3, 6 and 12 L/min). For each combination of \dot{V}_E and O₂ flow, 15 minutes after stabilization, three consecutive temperature measurements were taken and

averaged. Room temperature and relative humidity were measured before each experiment and maintained constant throughout the experiment. Each pair of probes was calibrated by measuring room temperature and differences were always $<0.3^{\circ}$ C. This value was used to correct all measurements. All HMEs were tested on four different study-days (a different HME was used each day) for assessment of reproducibility.

Evaluation after 24-h of use

Each HME was studied for 24 consecutive hours with the piston pump set at a \dot{V}_E of 10 L/min. A \dot{V}_E of 10 L/min was chosen since it was midway between the 2 minute ventilations tested short term and represents a typical minute ventilation in critically ill patients. Temperature measurements were recorded at 0, 6, 12 and 24 h, resistance and weight of the HME were recorded at 0 and 24 h. Flow resistance was estimated from the pressure drop across the HME at 60 L/min flow. HME weight was measured by a precision balance and the absolute change for each HME was determined.

The following commercially available HMEs were tested: A) HCH-6V (Mediflux, ICOR, AB, Sweden) B) HCH-6F (Mediflux, ICOR, AB, Sweden); C) Hydro-trach T (Intersurgical Ltd, Woingham, Berkshire); D) Edith Trach (GE Healthcare, Finland); E) TracheolifeTMII (Mallinckrodt DAR, Mirandola, Italy); F) Tracheal HME 9500/01S (Air Safety Limited, NFC House, Lancashire, United Kingdom); G) HMED6 (DEAS S.r.l., Castelbolognese (RA), Italy). Their main characteristics, according to manufacturer, are described in Table 1.

Statistical Analysis

Descriptive statistics were expressed as mean \pm standard deviation (SD), median, minimum/maximum values, 95% confidence interval (CI), and/or percentages. The coefficient of variation (CV) was calculated for both temperature and absolute humidity related-measurements. Normal distribution was evaluated with the Shapiro-Wilk normality test. Pearson correlation was

performed to determine the degree of correlation between continuous variables. HMEs were compared as means of repeated measures by two-way ANOVA with HSD Tukey post-hoc test. Homogeneity of variance was evaluated with the Flinger-Killeen test. Statistical significance was assumed by a two-sided p value <0.05 . Statistical analysis was performed using the R software/environment (2012 The R Foundation for Statistical Computing, ISBN 3-900051-07-0). At the time of this writing, R-2.15.2 was available.

Results

Effects of O₂ flow and \dot{V}_E

Mean and medium data for temperature and absolute humidity of each HME device are presented respectively in Table 2 and Table 3. In all HMEs, the progressive increase in O₂ flow from 0 to 12 L/min was associated with a reduction in the temperature ($p = 0.0003$) and absolute humidity ($p < 0.0001$). Under the same conditions, this effect was greater at lower \dot{V}_E (5 versus 15 L/min) ($p < 0.0001$) (Figure 2). Comparing the average performance of all HMEs across all experimental settings, the minimum performance was a temperature of 24.6° C and an absolute humidity of 18.2 mg/L at \dot{V}_E 5 L/min and O₂ flow 12L/min, while the best performance was a temperature of 26.6° C and an absolute humidity of 23.4 mg/L at \dot{V}_E 15 L/min and O₂ flow 0L/min.

Effects of different HMEs on Temperature and Absolute Humidity

All HMEs showed a variable degree of O₂ flow-dependency with increasing differences between measured and expected performance in terms of temperature and absolute humidity as O₂ flow increased and \dot{V}_E decreased ($p < 0.001$). The overall performance of all HMEs tested is presented in Table 4 and 5 and Figure 3. Tracheolife™II showed the best performance, absolute humidity 26 mgH₂O/L and temperature 27.8°C.

Effects of 24-h use on performance, airflow resistance and weight

No significant drop in absolute humidity was detected over the 24 h evaluation of any HME ($p=0.99$). No significant changes in flow resistance and pressure drop were observed between baseline and 24 h for any HMEs, except for Tracheolife™II (pressure drop at 60 L/min increased from 0.2 cmH₂O at baseline to 0.8 cmH₂O at 24 h, $p<0.05$). The increase in weight at 24 h were 1.46 gm for HCH-6V, 0.39 gm for HCH-6F, 0.22 gm for Hydro-trach T, 2.05 gm for Edith-trach, 0.47 gm for Tracheolife™II, 0.37 gm for Tracheal HME 9500/01S and 0.47 for HMED6, without any significant correlation with flow resistance at 60 L/min ($r^2=0.33$, $p=0.46$).

Between the four study days room temperature was $24^{\circ}\text{C} \pm 0.5$, whereas relative humidity was $13\% \pm 11$. The dynamics of daily room temperature and relative humidity did not significantly affect the results ($p = 0.58$).

Discussion

The main results of the present study are: 1) the addition of O₂ to an HME inversely affects the HME's efficiency; 2) the efficiency of all HMEs is better at higher \dot{V}_E ; and 3) Tracheolife™II was best able to maintain temperature and absolute humidity of inspired gases.

To the best of our knowledge this is the first study evaluating the effects of the addition of O₂, various minute volumes and 24 h use on the efficiency of HMEs for tracheostomized spontaneously breathing patients. It is important to stress that none of the HME's tested met the AARC Clinical Practice Guideline standards for humidification: 30-33 mg/L and 30°C.⁷

Effect of O₂ flow and \dot{V}_E

Absolute humidity and temperature of inspired gases were significantly, inversely affected by the addition of O₂ flow. The drop in efficiency from 0 to 12 L/min of O₂ flow was higher for absolute humidity than for temperature and these results were consistent for all HMEs. We found that Tracheolife™II maintained an acceptable performance up to 6 L/min O₂ flow then demonstrating a fall at 12 L/min, while the others HMEs presented a more gradual reduction in

efficiency as O₂ flow increased. Most HMEs commercially available have the capability of adding supplement O₂ flow to increase FiO₂. However, to our knowledge, there is no information in the manufacturers literature discussing the effect of adding O₂ on the efficiency of the HME. The decrease in efficiency of HMEs at increasing O₂ flow should be considered by physicians trying to optimize the clinical condition of their patients. The interdependence of HME's performance and supplemental O₂ flow should be expected since HMEs are characterized by a hygroscopic membrane that retains water and heat from the exhaled air and then returns it to inspired air. The addition of supplement O₂ dries and lowers the temperature of the hygroscopic material, thus negatively affecting HME performance. The method of oxygen delivery may be one of the reasons for the different behavior of each HME to increasing oxygen flows, since some HMEs allow O₂ to travel to the patient without traversing the hygroscopic membrane while others direct the added O₂ flow through the hygroscopic membrane.

In general, considering all HMEs tested at the two different \dot{V}_E conditions, they provided better temperature and humidity output at higher \dot{V}_E . Previous studies, reported contradictory results on the effects of \dot{V}_E on HMEs performance, during mechanical ventilation.¹³⁻¹⁵ In fact, Unal et al¹⁴ found better performance at lower \dot{V}_E , while Pelosi et al¹⁵ demonstrated better performance at higher \dot{V}_E , and Chiumello et al¹³ found the best performance at 10 L/min with a decrease in performance both at higher and lower \dot{V}_E . However, contrary to our study, these Authors did not test HMEs designed for tracheostomized patients during spontaneous breathing. Our results can be explained by the fact that at lower \dot{V}_E the hygroscopic membrane receives less conditioned exhaled air per minute allowing more time to cool down, thus losing more water molecules and being less efficient in the subsequent inspiration. Moreover the HMEs were tested at two different \dot{V}_E (5 versus 15 L/min) by modifying only the respiratory frequency (10 versus 30 breaths/minute). The differences in efficiency may be a direct result of the fact that with a higher respiratory frequency

there is less time for the hygroscopic membrane to cool down. This finding may be minimized by increasing tidal volume to increase \dot{V}_E instead of rate.

Effect of different HMEs on Temperature and Absolute Humidity

The present study has shown significant differences in efficiency among the seven HMEs evaluated. Comparing the temperature output and absolute humidity of the HMEs at 15 L/min \dot{V}_E and 0 L/min O₂ flow, the best performance was by Tracheolife™II with 28.4 mgH₂O/L and 29.2° C respectively, while the worst performance was by HME6 with 18.4 mgH₂O/L and 25.3° C respectively. Optimal levels of inspired air conditioning in tracheostomized patients are still debatable. To the best of our knowledge there are no specific guidelines on the levels of absolute humidity and temperature in spontaneously breathing tracheostomized patients. Some studies on tracheostomized dogs have defined the optimal range of humidity to be 100% saturation at between 25 and 30° C, i.e. 23.1-30.5 mgH₂O/L absolute humidity.^{18, 19} In addition, excessive heating and humidification are recognized as harmful to the airway mucosa.²⁰⁻²² In normal conditions the temperature of expired gases ranges between 28 and 32° C with an absolute humidity of 27-33 mgH₂O/L, and thus a temperature of inspired gases ranging between 29-33° C with an absolute humidity of 28-35 mgH₂O/L should be adequate.²³ These guidelines⁷ might also apply to tracheostomized patients even if the portion of the artificial airway above the carina is shorter than with an endotracheal tube. We found that, only Tracheolife™II reached the levels recommended in all conditions except for low \dot{V}_E with 6 or 12 L/min O₂ flow and high \dot{V}_E with 12 L/min. The structure of Tracheolife™II is very different from that of the other HMEs. In fact Tracheolife™II is not composed by a spongy material like the others, but is composed of an embossed and pleated membrane which allow a significant increase of hygroscopic surface and consequently a greater entrapment of water particles.

We found that the performance of HMEs designed for tracheostomied patients during spontaneous breathing was poorer than that reported for HMEs for mechanically ventilated patients

under similar experimental conditions.^{13, 15, 24} HMEs for spontaneously breathing patients are inserted into an open breathing circuit, drawing air from the room; whereas HME's for mechanically ventilated patients are used in a closed ventilatory circuit, thus the heat and moisture are kept within the system. Furthermore, HMEs for spontaneous breathing patients, except for Tracheolife™II, are hollow in the middle and the membrane is displaced to the periphery allowing the collection of secretions and minimizing the increase of airway resistance, while all HMEs for mechanically ventilated patients have the membrane throughout the device promoting efficiency but increasing resistance.

Effects of 24 h use on performance, airflow resistance and weight

Absolute humidity and temperature output was not affected during the 24 h study period. Several investigations of HMEs for mechanical ventilation demonstrated that changing HMEs after 48 h²⁵⁻²⁷ or even 96 h²⁸ did not influence efficiency nor incidence of nosocomial pneumonia. HMEs for spontaneously breathing patients have not been tested for longer than 24 h use and are marketed with directions to replace them every 24 h. They do not have an antibacterial filter and are hollow in the middle avoiding an increase of airway resistance. Our “in vitro” data suggest that HMEs could be used for longer periods, but the safety of this procedure should be demonstrated in a large clinical trial.

The efficiency of the HMEs evaluated was independent of room temperature and relative humidity, at least within the conditions during the present study. Room temperature was similar throughout the four study days ($24 \pm 0,5^{\circ}\text{C}$), however, room relative humidity was quite different depending on outside temperature ($13 \pm 11\%$). Room dryness may play an important role in absolute humidity output at different \dot{V}_E .

Our study has some limitations which need to be addressed. First, the model we used only partially reproduced clinical conditions. Thus our results cannot be directly extrapolated to the

clinical scenario. However since all devices were evaluated under the same conditions the comparative efficiency of the devices is accurate. Second, all of the HMEs commercially available worldwide were not evaluated. Thus other devices may demonstrate different performances. Third, the performance at different O₂ flows and \dot{V}_E was not evaluated during the entire 24-hour period. Forth, \dot{V}_E variations were only obtained by changing respiratory rate. Differences in performance between lower and higher \dot{V}_E may be a direct result of altering respiratory rate.

In conclusion, the performance of different commercially available HMEs used in tracheostomized patients during spontaneous breathing is significantly affected by O₂ flow and minute ventilation. The minimal O₂ flow required according to the patient's clinical condition should always be administered. Especially if a tracheostomized patient needs O₂ flows higher than 3 L/min, the clinician should be aware of the negative effect oxygen flow has on HME performance. Most importantly, the performance differences among the evaluated devices should be considered when making the choice of HME in tracheostomized spontaneous breathing patients. Finally, none of the HME's tested met the AARC Clinical Practice Guideline standards for humidification: 30-33 mg/L and 30°C.⁷

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Figure legend

Figure 1: The experimental in vitro lung model used to test heat and moisture exchangers (HME).

Figure 2: Comparisons of progressive increase in O₂ flow (from 0 to 12 L/min) on median (25-75%) temperature and absolute humidity for all HMEs at 5 and 15 L \dot{V}_E .

Figure 3: Comparisons of medium (25-75%) temperature and absolute humidity output for each HME at all conditions tested.

Type of HME	HCH-6V	HCH-6F	Hydro-trach T	Edith-trach	Tracheolife™ II	Tracheal HME 9500/01	HME-D6
Moisture output (mgH ₂ O/L) at 0.5 L tidal volume	25.5	20.5	26	24	27.1	27.4	30.8
Weight (g)	5	2.9	8	6	8.5	4.5	5
Tidal Volume range (ml)	50-1000	50-1000	>50	60-1000	-	>25	50-1000
Dead space (ml)	12	9.5	19	16	16	8	12
Pressure drop at 60 L/min at 0 h (cmH ₂ O)	0.25	-	1.3	0.02	2.2	0.76	0.16

Table 1. Characteristics of each HME as described by manufacturers.

Table 2. Descriptive statistics of temperature for each HME

Temperature (°C)								
HME	Mean	SD	Median	Minimum	Maximum	95%CI low	95% CI up	CV
HME-A	25.81	0.73	25.90	24.4	27.5	25.54	26.07	0.028
HME-B	24.55	0.75	24.40	22.8	26.0	24.28	24.82	0.030
HME-C	26.24	1.01	26.40	24.1	28.0	25.88	26.60	0.038
HME-D	25.83	0.99	26.05	24.0	27.7	25.47	26.12	0.038
HME-E	27.81	1.01	28.05	25.6	29.2	27.44	28.17	0.036
HME-F	26.08	0.91	26.05	24.5	27.5	25.75	26.40	0.035
HME-G	24.30	0.67	24.35	22.7	25.3	24.06	24.54	0.027

SD standard deviation; CI confidence interval; CV coefficient of variation

Table 3. Descriptive statistics of absolute humidity for each HME

Absolute humidity (mgH ₂ O/L)								
HME	Mean	SD	Median	Minimum	Maximum	95%CI low	95% CI up	CV
HME-A	23.15	1.62	23.45	19.8	25.6	22.56	23.73	0.070
HME-B	20.68	1.55	20.90	17.5	22.9	20.12	21.24	0.075
HME-C	21.36	2.30	21.80	16.8	25.1	20.52	22.19	0.11
HME-D	20.89	1.67	21.05	16.0	22.9	20.28	21.49	0.08
HME-E	25.98	2.45	27.20	19.9	28.6	25.09	26.86	0.09
HME-F	21.91	2.37	22.30	16.4	25.3	21.06	22.76	0.11
HME-G	16.86	1.57	16.90	14.0	19.8	16.29	17.42	0.09

SD standard deviation; CI confidence interval; CV coefficient of variation

Table 4 – HME comparisons for temperature

Fligner-Killeen test of homogeneity of variances - P = 0.1166

Overall ANOVA model - F value = 56.03; P <0.0001

Multiple comparisons of means * – Tukey contrasts

HME	Estimate	95% CI**	95% CI	P value
HCH-6F vs HCH-6V	-1.2594	-1.9131	-0.6057	<0.001
Hydro-trachT vs HCH-6V	0.4344	-0.2193	1.0881	0.432
Edith-trach vs HCH-6V	0.0250	-0.6287	0.6787	1.000
Tracheolife™II vs HCH-6V	2.0000	1.3463	2.6537	<0.001
Tracheal HME vs HCH-6V	0.2719	-0.3818	0.9256	0.879
HME-D6 vs HCH-6V	-1.5031	-2.1568	-0.8494	<0.001
Hydro-trachT vs HCH-6F	1.6938	1.0401	2.3474	<0.001
Edith-trach vs HCH-6F	1.2844	0.6307	1.9381	<0.001
Tracheolife™II vs HCH-6F	3.2594	2.6057	3.9131	<0.001
Tracheal HME vs HCH-6F	1.5312	0.8776	2.1849	<0.001
HME-D6 vs HCH-6F	-0.2438	-0.8974	0.4099	0.925
Edith-trach vs Hydro-trachT	-0.4094	-1.0631	0.2443	0.506
Tracheolife™IIE vs Hydro-trachT	1.5656	0.9119	2.2193	<0.001
Tracheal HME vs Hydro-trachT	-0.1625	-0.8162	0.4912	0.990
HME-D6 vs Hydro-trachT	-1.9375	-2.5912	-1.2838	<0.001
Tracheolife™II vs Edith-trach	1.9750	1.3213	2.6287	<0.001
Tracheal HME vs Edith-trach	0.2469	-0.4068	0.9006	0.920
HME-D6 vs Edith-trach	-1.5281	-2.1818	-0.8744	<0.001
Tracheal HME vs Tracheolife™II	-1.7281	-2.3818	-1.0744	<0.001
HME-D6 vs Tracheolife™II	-3.5031	-4.1568	-2.8494	<0.001
HME-D6 vs Tracheal HME	-1.7750	-2.4287	-1.1213	<0.001

* See Table 2 for row values of each HME device. ** CI: confidence interval

Table 5 – HME comparisons for absolute humidity

Fligner-Killeen test of homogeneity of variances - P = 0.1787

Overall ANOVA model - F value = 62.47; P <0.0001

Multiple comparisons of means * – Tukey contrasts

HME	Estimate	95% CI**	95% CI	P value
HCH-6F vs HCH-6V	-2.4719	-3.9385	-1.0053	<0.001
Hydro-trachT vs HCH-6V	-1.7937	-3.2604	-0.3271	0.006
Edith-trach vs HCH-6V	-2.2625	-3.7291	-0.7959	<0.001
Tracheolife™II vs HCH-6V	2.8281	1.3615	4.2947	<0.001
Tracheal HME vs HCH-6V	-1.2406	-2.7072	0.2260	0.158
HME-D6 vs HCH-6V	-6.2906	-7.7572	-4.8240	<0.001
Hydro-trachT vs HCH-6F	0.6781	-0.7885	2.1447	0.814
Edith-trach vs HCH-6F	0.2094	-1.2572	1.6760	0.999
Tracheolife™II vs HCH-6F	5.3000	3.8334	6.7666	<0.001
Tracheal HME vs HCH-6F	1.2312	-0.2354	2.6979	0.165
HME-D6 vs HCH-6F	-3.8188	-5.2754	-2.3521	<0.001
Edith-trach vs Hydro-trachT	-0.4688	-1.9354	0.9979	0.964
Tracheolife™IIE vs Hydro-trachT	4.6219	3.1553	6.0885	<0.001
Tracheal HME vs Hydro-trachT	0.5531	-0.9135	2.0197	0.921
HME-D6 vs Hydro-trachT	-4.4969	-5.9635	-3.0303	<0.001
Tracheolife™II vs Edith-trach	5.0906	3.6240	6.5572	<0.001
Tracheal HME vs Edith-trach	1.0219	-0.4447	2.4885	0.372
HME-D6 vs Edith-trach	-4.0281	-5.4947	-2.5615	<0.001
Tracheal HME vs Tracheolife™II	-4.0688	-5.5354	-2.6021	<0.001
HME-D6 vs Tracheolife™II	-9.1188	-10.5854	-7.6521	<0.001
HME-D6 vs Tracheal HME	-5.0500	-6.5166	-3.5834	<0.001

* See Table 3 for row values of each HME device. ** CI: confidence interval

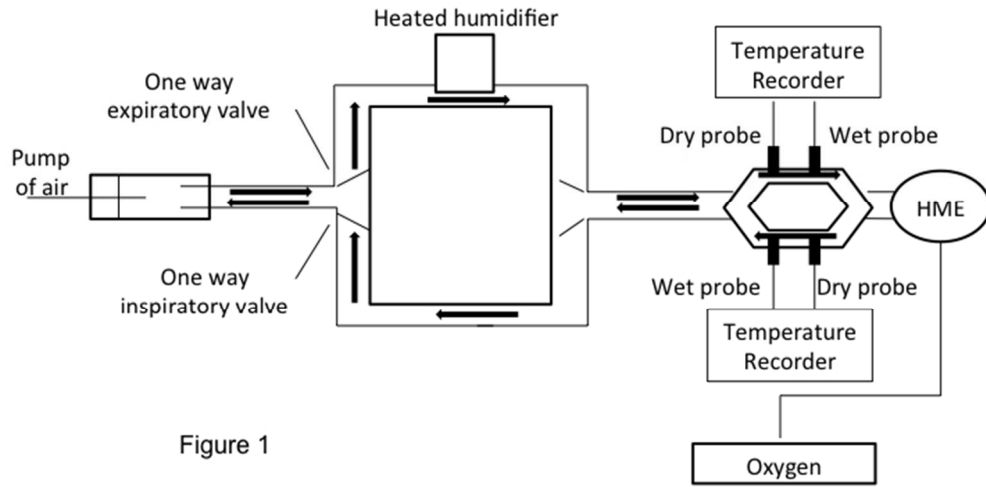


Figure 1

254x190mm (72 x 72 DPI)

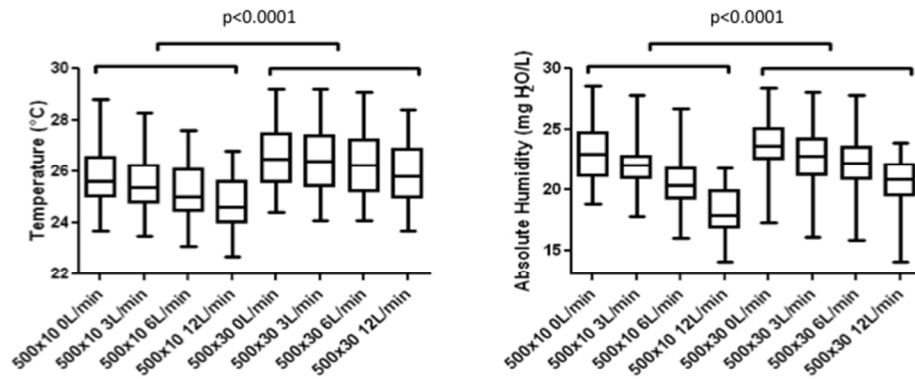


Figure 2

254x190mm (72 x 72 DPI)

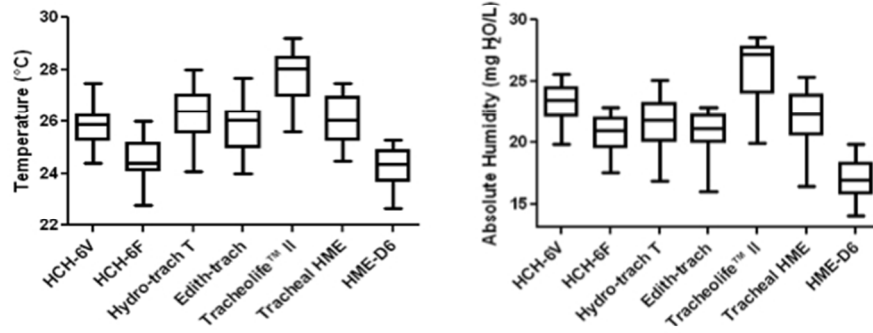


Figure 3

254x190mm (72 x 72 DPI)