

Impact of Humidification and Nebulization during Expiratory Limb Protection: An experimental bench study.

Alexandre Tonnelier, MD ^{1,2,3}, François Lellouche, MD, PhD ⁴, Pierre Alexandre Bouchard, RT ⁴, Erwan L'Her, MD, PhD ^{1,2,3,5,6}

1. Réanimation Médicale et Urgences Adultes, CHRU de la Cavale Blanche, 29609 Brest, Cedex, France
2. Université de Bretagne occidentale, Faculté de Médecine et des Sciences de la Santé, Brest, 29200 France
3. Université Européenne de Bretagne, France
4. Institut de Cardiologie et de Pneumologie de Québec / Université Laval, Québec, Canada
5. LATIM INSERM UMR 1101, CHRU Brest, UBO
6. Chaire de Recherche en Médecine d'Urgence Hôtel-Dieu de Lévis / Université Laval, Québec, Canada

Address for correspondance:

Pr Erwan L'HER, MD, PhD*
Réanimation Médicale
CHRU de la Cavale Blanche, 29609 Brest, France
Tel. 33 2 98 34 71 81 Fax. 33 2 98 34 79 65
Email : erwan.lher@chu-brest.fr

Grants: This study was partly financed by a grant from Maquet SA to the Chaire de Recherche en Médecine d'Urgence HDL/ULaval – Québec

ABSTRACT

BACKGROUND: Different filtering devices are used during mechanical ventilation to avoid dysfunction of flow and pressure transducers or for airborne micro-organisms containment. Water condensates resulting from the use of humidifiers, but also residual nebulization particles, may have a major influence on expiratory limb resistances.

OBJECTIVES: To evaluate the influence of nebulization and active humidification on the resistance of expiratory filters.

METHODS: A respiratory system analog was constructed using a test lung, an ICU ventilator, heated humidifiers, and a piezoelectric nebulizer. Humidifiers were connected to different types of circuits (unheated, monoheated, biheated-new and old generation). Five filter types were evaluated (electrostatic, heat-and-moisture exchangers, standard, specific and internal heated HEPA). Differential pressure measurements were carried out after 24-hrs of continuous in-vitro use for each condition, and after 24hrs of use with an old-generation biheated circuit without nebulization. Baseline characteristics were also obtained from each dry filter.

RESULTS: While using unheated circuits, measures had to be interrupted before 24-hrs for all filtering devices, except the internal heated HEPA. Heat-and-moisture exchangers occluded before H24 with unheated and mono-heated circuits. The circuit type, nebulization practice, or even the duration of use did not influence internal heated HEPA resistances.

CONCLUSION: This bench-study confirms that expiratory limb filtration is likely to induce several major adverse events. Resistance of expiratory filters increase is mainly due to the humidification circuit type, rather than to nebulization itself. If filtration is mandatory while using unheated circuits, a dedicated filter should be used for equal or less than 24-hrs, or a heated HEPA for a longer duration.

Keywords: expiratory limb protection, filters, humidification, mechanical ventilation, nebulization

Abstract word count: 255

Methods word count: 618

Manuscript word count: 2832

INTRODUCTION

When performing nebulization under mechanical ventilation, filtering of expiratory gases is mandatory to prevent dysfunction of flow and pressure transducers [1-3]. Such a problem has already been identified with the administration of Ribavirin during mechanical ventilation back in the 1980's, for pediatric patients with bronchiolitis due to Respiratory syncytial virus [4]. Whereas there have been advances in the humidifier design and efficiency, and the arsenal of aerosolized drugs and indications has expanded, this topic is relevant to intensive care and mechanical ventilation today. Expiratory limb filtration might also be considered to prevent cross contamination in case of airborne contaminants (tuberculosis, flu pandemic, SARS...) [5-9]. Few recommendations exist to help clinicians choosing the filtering devices in such cases [3,8,9]. Moreover, manufacturers usually recommend a daily replacement of the device, thus leading to potential healthcare workers' exposure to aerocontaminants and inducing recurrent depressurization of the circuit and alveolar de-recruitment. Problems related to the use of filters with nebulized drugs are another part of the problem [3, 10].

Performances of filters not only depend on its type, and bacterial or viral filtration efficiency may be inadequate or highly misleading [1,9].

Nebulization and humidification tends to be similar processes in that they are both methods to convert liquid (medication or water) into mist or vapour for humidification and particles that remain suspended within a gas for a period of time for nebulization, that can both be inhaled into the lower respiratory tract. If humidification provides warm water vapour on a continuous process to prevent damage to the airway lining of the tracheobronchial tree, nebulization produces cool mist that is to be administered intermittently. In case of a decrease in temperature, condensation and formation of droplets will occur while using humidifiers. Humidification of the inspiratory gases by a heated humidifier may therefore have a great impact on the mechanical properties of expiratory filters, thus modifying filtration properties and leading to potentially lethal ventilator dysfunctions [10-17]. This effect may be enhanced by temperature variations within the circuit, thus generating condensation. Whatever the device that is used, nebulization particles are usually of higher size than water mist and may thus increase saturation of filters, especially in case of

“sticky” buffer use like colistine or several other pharmaceutical drugs [18]. However, whereas nebulizers are usually delivered intermittently, humidification is provided continuously, it could be hypothesized that humidification may a more prominent effect.

The aims of this experimental bench test study were: 1- to evaluate the consequences of active humidification on the performances of different types of breathing filters considering the type of ventilatory circuit used; 2- to evaluate the impact of nebulization on these devices.

MATERIAL - METHODS

Devices

Artificial respiratory system

(Figure 1)

- ICU ventilator: Evita2 dura[®], Dräger, Lünebeck, Germany for most measurements, and AVEA[®], Viasys Healthcare, Yorba Linda, California for evaluation of internal heated expiratory filter. Respiratory parameters were as follows: assist-control mode; respiratory rate=18breath/min, tidal volume=600mL, inspiratory time=0.8 sec, inspiratory flow=60L/min, oxygen inspiratory fraction=21%, positive end-expiratory pressure (PEEP)=5cmH₂O.
- Heated humidifier (MR850[®], or MR460[®], Fisher Paykel[™], Auckland, New Zealand) for different ventilatory circuits testing.
- Piezoelectric nebulizer (Aeroneb pro[®], Aerogen Ltd, Galway Ireland) after the Y-piece on the expiratory limb, to maximize the impact of nebulized drug (Colimycine 6 million units/24h, in 4 mL saline) on the filters.
- Standard test lung (Test lung 190, Maquet critical care AB, Solna, Sweden; volume=1L; compliance 30 mL/cmH₂O and resistance 20 cm H₂O/L/s).

Expiratory filtering devices

Tested filters were placed on the expiratory limb, at the ventilator input. Five different types were tested:

- Electrostatic: Anest-Guard[®], Gibeck-Teleflex, High Wycombe, England; internal dead space (DS)=50 mL

- Standard High Efficiency Particulate Air filter (HEPA): Iso-Gard® HEPA Light, Gibeck-Teleflex, High Wycombe, England; DS=80mL
- Specific HEPA, conceived for expiratory limb protection: Servo Duo Guard®, Maquet SA ; Solna, Sweden ; DS=170mL
- Heat and Moisture Exchanger (HME-filter): Humid-Vent® Compact, Gibeck-Teleflex, High Wycombe, England; DS=38 mL
- Internal heated HEPA: filter of the AVEA® ventilator, CareFusion, San Diego, CA, USA

Baseline characteristics of these filters are provided within Table 1.

Ventilatory circuits

- Corrugated unheated circuit (used with a MR460 heated humidifier): no heating of either inspiratory and expiratory limbs is provided; due to condensation, a water trap on each limb is mandatory
- Mono-heated circuit (RT212): only the inspiratory limb is heated by a wire; the occurrence of condensation within the expiratory limb requires a water trap
- “Old generation” bi-heated circuit (RT100), no water trap: both inspiratory and expiratory limbs are heated
- “New generation” bi-heated circuit, (EvaquaTM; RT340), no water trap: both inspiratory and expiratory limbs are heated, and it minimises condensate in the expiratory limb by allowing water vapour to diffuse through the tubing wall

In all cases, breathing systems and filters were kept horizontal to avoid drainage of the expiratory limb into the filter, or into the test lung.

Measurements

Filters’ resistances measurement

Resistances were measured ex-vivo using a heated-wire pneumotachograph and a differential pressure transducer (PF302TM, IMT, Buchs SG, Switzerland). Differential pressures were measured before experimental procedures (dry filter) and after 24-hrs under each condition, progressively increasing gas flow through the device from 10 to 100L/min. If consistent, differential pressures measured at 30, 60 and 90 L/min were

computed to calculate filtering devices resistances. Measures were performed at constant room temperature (21°C). Same measurements were also performed using a bi-heated circuit (RT100), but without nebulization. At least 4 different measures were performed for each filter and condition.

Several measurements were performed in-vivo at the bedside, while retrieving filters after clinical use (Table 3).

Hygrometric measurements

Hygrometric measures were performed after 3 hours for each breathing system, in 3 different locations (inspiratory limb before the Y-piece, expiratory limb after the Y-piece and expiratory limb before the ventilator input; figure 1) using the psychrometric method [19,20]. Three measurements were recorded for each circuit. Results are expressed as absolute and relative humidity (AH; RH) of delivered gases.

These results were performed to ensure appropriateness of the experimental model.

Statistical analysis

Analysis was performed using StatView v5.0 for Windows (SAS Institute, NC, USA). Values are given as individual values and/or mean \pm SD. A Box and Whiskers Plot figure was used to compare the overall resistance values for each filter, assuming a 20cmH₂O/L/s resistance value when occlusion occurred. Data were compared using non-parametric Kruskal-Wallis and Mann-Whitney tests for independent variables. A $p < 0.05$ was considered statistically significant.

RESULTS

Resistance to flow

(Tables 2 and 3)

Differential pressures of the devices are depicted within Table 2. Measures were performed prematurely because of occlusion for 3 filters with unheated circuits (at 6 hours [H6] for HME-filter, H10 for electrostatic, and H19 for standard HEPA). Measures had to be performed at H19 while using the specific HEPA filter with unheated circuit, because of water level exceeding the tolerated limit, but without occlusion signs. HME-filter was responsible for occlusion prior to H24 with both unheated, monoheated and the “old generation” bi-heated circuit.

With the “new generation” biheated circuits, no significant resistance increase was observed at H24, whatever the filter type.

In-Vivo measurements are depicted within Table 3. No significant resistance increase was observed in these cases. However, no unheated circuits nor electrostatic or HME-filter were used within units. Internal heated HEPA depicted no significant resistance increase, even after a long duration use (more than 3 months).

Figure 2 illustrates the median differential pressure values for each filter type at three different gas flows.

Impact of nebulization

Nebulization does not seem to have a great impact on resistance to flow, except for HME-filter (occlusion prior to H24 with nebulization).

Hygrometry

(Table 4)

Main differences between circuits were observed at the ventilator expiratory input (location of the filter). RH tended to differ when considering circuits with unheated expiratory limbs and those with heated expiratory limbs.

DISCUSSION

This experimental bench-study confirms that expiratory limb filtration may induce several major adverse events, such as experienced in previous clinical studies [10,21]. The increase in the resistance of expiratory filters over time is mainly due to the humidification circuit type, rather than to nebulization. If expiratory limb filtration is mandatory during mechanical ventilation, it may require the use of specifically dedicated filtering devices, and/or heated expiratory limbs. HME-filter should never be used for such purpose as obstruction is predictable and expected. If expiratory filter obstruction related to nebulization may be less common and predictable, clinicians should however stay aware of such a dangerous hazard.

When using expiratory filters to protect healthcare workers from airborne contaminants, it is mandatory to consider devices' efficiency. Depending on the device type and the specific particles size, several devices might be inefficient [1]. In fact, filtration efficiency is extremely variable and manufacturers' tests are often misleading [1,11,22]. Guidelines that were produced after the SARS outbreak recommended the use of "*submicron filters*" [7,9]. Within the Canadian guidelines, the authors recommended the constant use of heated expiratory HEPA filter [8]. Taking into account our results and routine practice, internal heated HEPA filter use seems to be adequate, whereas it allows prolonged ventilation without any increase of the expiratory circuit resistance and thus does not require routine daily changes. However, internal HEPA filter are standards in only half the critical care ventilators on the North American market [9]. Moreover, the addition of external heated HEPA filter may not be adequate, whereas such a fitting is not standardized and may expose to condensation within the final part of ventilators circuits, given the lack of heating of the final part of the circuit. *A contrario*, most unheated HEPA filter will have to be changed daily, thus resulting in potential healthcare workers exposure to contaminants.

An increase of the expiratory circuit resistance might induce intrinsic PEEP and dynamic hyperinflation. This potential adverse event is similar to what has been previously described when using HME-filter on the inspiratory limb [23,24], and it is presumed to be directly proportional to resistance increase. Those changes in

ventilator mechanics might have dramatic consequences in protective ventilation strategies mandatory in severe ARDS as those encountered during the SARS outbreak or the recent H1N1 flu pandemic [5,25-30].

In a recent clinical trial investigating the potential interest of antibiotics nebulization, obstruction of the expiratory filters were observed in 3 patients from a 20 patients cohort, resulting in cardiac arrest for 1 patient [21]. Assuming our results, the increase in expiratory resistances is mainly due to filter saturation by water condensates. Such findings are relevant with hygrometric measurements at the distal end of the expiratory limb. In ventilatory circuits with unheated expiratory limb, RH value is close to 100%, thus resulting in high condensation within the filter. Such high RH value is related to the low gas temperature at that location, and therefore the use of heated filter may thus prevent water condensation. Maintaining high expiratory gases temperature with bi-heated circuits results in lower RH rates and therefore in less water condensation and a lower differential pressure increase through the filters. The AH value observed at the distal expiratory end of “old-generation” bi-heated circuit was higher than that observed in the “new generation” ones. This AH value in the circuits with an unheated expiratory limb reduces as it enters a cooler circuit, which may be responsible for condensation. In this specific case, the extent of condensation will vary with ambient temperature, so that units will observe variations in the levels of condensation occurring.

The AH drop at the distal end of the expiratory limb with new generation biheated circuit is explained by the specific design of the circuit, allowing water vapour to diffuse through the tubing wall. Therefore, such AH drop may not generate condensation due to such design.

Water condensates with unheated circuit resulted in a major and rapid resistance increase with most filtering devices, except with the internal heated HEPA filter. Differential pressure gradient with the specific unheated HEPA filter did not exceed the 5cm H₂O/L/s limit at 60 L/min, however measurements had to be performed after 19-hrs of use due to a water level above the tolerated limit.

Such 5cm H₂O/L/s pressure limit was chosen whereas it has been advocated in the 1992 international standard for HME-filters (International Standard Organisation [ISO] Draft International Standards 9360-1) [31,32], even if it did no longer appear in the

second edition [33]. Whereas expiratory limb heating is not a standard with all humidifiers, such condition may render heated expiratory filtration mandatory.

With “new generation” bi-heated circuit (allowing humidity perspiration through the expiratory limb), humidification tended to increase expiratory limb resistances, at least while using HME-filter, but none of the encountered values exceeded the 5cmH₂O/L/s limit. Such technical consideration could be interesting if expiratory limb filtration is mandatory and if no ventilator with internal heated filters are available.

Intermittent occlusions signs were observed in most conditions with the electrostatic filter, except new-generation biheated circuits, due to water flush. The lower filtration properties of such filters, associated to such potential adverse event, should make the clinician avoid its use, at least when airborne contaminant filtration is mandatory. If no internal heated filters are available and if no “new generation” circuits are used, the specific unheated HEPA filter seems to be indicated since its design minimizes the risk of sudden increase in expiratory resistance by water flush. In no condition should HME-filter be used, due to the potential risk of major resistance increase with most circuits.

As depicted within Table 1, we may also consider that occlusion may be correlated to the effective filtration surface that varies greatly from one device to the other (depending at least of the filter internal volume): the greater the filtration surface, the lower the occlusion risk.

Nebulized Colimycine is used as an alternative antibacterial measure in some ICU units. It was chosen in our study to test the impact of nebulization on expiratory resistances, whereas it is probably one of the products most likely to induce ventilator transducers dysfunction when unprotected, given its “stickiness” when nebulized. Moreover, this drug specifically needs to be nebulized using an ultrasonic or piezoelectric nebulizer, thus also increasing expiratory particles fraction. In our experimental setting, the nebulizer was placed immediately after the Y-piece on the expiratory limb to artificially maximize filter deposition. However, while comparing expiratory resistance values on the “old generation” biheated circuit, no direct consequence of nebulization was assessed in most cases, except when using HME-filter. If one could consider that the use of Colimycine just adds another variable to the system, we conclude that in such condition, the major determinant of expiratory

filter resistance is the humidification system, rather than nebulization itself. HME-filter should never be used for expiratory limb protection.

Like all experimental bench-test study, this one suffers several limitations. First, it could be considered that results that were obtained with such an experimental setting may not reproduce what is observed in the “real-life” situation. Such limitation is accurate, especially because we enhanced particles deposition on the expiratory limb and because the test lung may by itself modify expiratory humidity values. However, i-the few in-vivo measures that were performed within this study seemed to corroborate our main findings; ii- psychometric values tended to fit values that were previously observed within several clinical trials [19]; iii- we tried to standardize climatic conditions within the experimental room. Second, if filters that were used represented the main available filter types, one may also consider that filters from different manufacturers may behave differently [19,31]. Different ventilatory circuits or humidifiers technologies may also lead to different results. Our results however seemed to fairly depict the different clinical situations that may be encountered when associating expiratory filtration to active heated humidification. Third, our experimental settings did not allow the test lung to “expire” water vapour, to mimic a real patient. If this point may be considered as a major limitation, psychometric measurements performed just before the filter however reproduced standard humidification values, which limits such a criticism. Fourth, given the difficulty of standardization and length of the experimental measurements, only one set of four values is reported for each filter type and condition. Several measurements were however performed under the same conditions to ensure the internal validity and reproducibility of the model. Due to the fact that measurements were highly time-consuming, such multiple measurements were not performed in all cases. Last, our suggestion that nebulization plays a lesser role in obstruction of the expiratory filter may be limited to the substance and dose evaluated in the study.

In conclusion, this study confirms the major impact of active humidification on the resistance on unheated expiratory filters. Nebulization by itself does not seem to be the primary determinant in expiratory limb resistance increase, except maybe while using HME-filter and specific types of circuits. Such deleterious consequences may however be limited when using bi-heated (especially “new generation”) circuits, thus

allowing maintaining filtering devices for at least 24-hours. With unheated circuits, only internal heated HEPA filters shall be used, in order to avoid circuit occlusion. HME-filter should never be used for expiratory limb protection, given their rapid occlusion rate and the impact of nebulization particles on their resistance level.

Acknowledgments

Alexandre Tonnelier performed the measurements and wrote the manuscript.

François Lellouche helped designing the study, monitored the psychrometric measurements and corrected proofs.

Pierre-Alexandre Bouchard helped designing the study and performed the psychrometric measurements.

Erwan L'Her had the original idea, designed and monitored the study, and wrote the manuscript.

REFERENCES

1. Demers RR. Bacterial/viral filtration: let the breather beware! *Chest* 2001;120(4):1377-1389.
2. Palmer LB, Smaldone GC, Simon SR, O'Riordan TG, Cuccia A. Aerosolized antibiotics in mechanically ventilated patients: delivery and response. *Crit Care Med* 1998;26(1):31-39.
3. Wilkes AR. Heat and moisture exchangers and breathing system filters: their use in anaesthesia and intensive care. Part 2 – practical use, including problems, and their use with paediatric patients. *Anaesthesia* 2011;66(1):40-51.
4. American Academy of Pediatrics Committee on Infectious Diseases. Ribavirin therapy of respiratory syncytial virus. *Pediatrics* 1987;79(3):475-478.
5. Recommandations des experts de la Société de réanimation de langue française. Prévention de la transmission croisée en réanimation. *Réanimation* 2002;11(4):250-256.
6. A. Mercat, J-C. Richard, A. Combes, J Chastre, JD Ricard, D Dreyfuss et al. on behalf of the REVA group. Syndrome de Détresse Respiratoire Aiguë lié à la grippe A (H1N1): Recommandations pour l'assistance respiratoire ; http://www.sante.gouv.fr/IMG/pdf/AREC-ECMO_fiche_DGS_LC.pdf. Accessed July 27, 2012.
7. Levy MM, Baylour MS, Bernard GR, Fowler R, Franks TJ, Hayden FG, et al. Clinical issues and research in respiratory failure from severe acute respiratory syndrome. *Am J Respir Crit Care Med* 2005;171(5):518-526.
8. McKeon S. Vancouver Coastal Health Guidelines for the use of Respiratory Equipment for Patients on Airborne or Enhanced Droplet Precautions in Acute Care Facilities; 2009 <http://www.csrt.com/en/professional/pdf/Vancouver-Guidelines.pdf>. Accessed on October 27th, 2012.
9. Thiessen RJ. The impact of severe acute respiratory syndrome on the use of and requirements for filters in Canada. *Respir Care Clin N Am* 2006;12(2):287-306.
10. Lawes EG. Hidden hazards and dangers associated with the use of HME/filters in breathing circuits. Their effect on toxic metabolite production, pulse oximetry and airway resistance. *Br J Anaesth* 2003;91(2):249-264.
11. Thiessen RJ. Filtration of respired gases: theoretical aspects. *Respir Care Clin N Am* 2006;12(2):183-201.
12. Barton RM. Detection of expiratory antibacterial filter occlusion. *Anesth Analg* 1993;77(1):197.
13. Buckley PM. Increase in resistance of in-line breathing filters in humidified air. *Br J Anaesth* 1984;56(6):637-643.
14. Prados W. A dangerous defect in a heat and moisture exchanger. *Anesthesiology* 1989;71(5):804.
15. Prasad KK, Chen L. Complications related to the use of a heat and moisture exchanger. *Anesthesiology* 1990;72(5):958.
16. Schummer W, Schummer C, Fuchs J, Voigt R. Sudden upper airway obstruction due to invisible rain-out in the heat and moisture exchange filter. *Br J Anaesth* 2002;89(2):335-336.
17. Stacey MR, Asai T, Wilkes A, Hodzovic I. Obstruction of a breathing system filter. *Can J Anaesth* 1996;43(12):1276.
18. Davies JBS, Bromilow J. Bacterial filter obstruction with the use of ultrasonic nebulisation. *Anaesthesia* 2011;66(5):394-395.
19. Lellouche F, Taille S, Lefrancois F, Deye N, Maggiore SM, Juvet P et al. Humidification performance of 48 passive airway humidifiers: comparison with manufacturer data. *Chest* 2009;135(2):276-286.
20. Ricard JD, Le Miere E, Markowicz P, Lasry S, Saumon G, Djedaini K, et al. Efficiency and safety of mechanical ventilation with a heat and moisture exchanger changed only once a week. *Am J Respir Crit Care Med* 2000;161(1):104-109.
21. Lu Q, Yang J, Liu Z, Gutierrez C, Aymard G, Rouby JJ, on behalf of the Nebulized Antibiotics Study Group. Nebulized Ceftazidime and Amikacin in ventilator-associated pneumonia caused by *Pseudomonas aeruginosa*. *Am J Respir Crit Care Med* 2011;184(1):106-115.
22. Medicines and Healthcare products Regulatory Agency. An assessment of 104 breathing system filters. Evaluation 04005. 2004. London
23. Iotti GA, Olivei MC, Braschi A. Mechanical effects of heat-moisture exchangers in ventilated patients. *Crit Care* 1999;3(5):R77-R82.
24. Iotti GA, Olivei MC, Palo A, Galbusera C, Veronesi R, Comelli A, et al. Unfavorable mechanical effects of heat and moisture exchangers in ventilated patients. *Intensive Care Med* 1997;23(4):399-405.

25. Chiumello D, Marino A, Lazzerini M, Caspani ML, Gattinoni L. Lung recruitability in ARDS H1N1 patients. *Intensive Care Med* 2010;36(10): 1791-1792.
26. Jaber S, Conseil M, Coisel Y, Jung B, Chanques G. [ARDS and influenza A (H1N1): patients' characteristics and management in intensive care unit. A literature review]. *Ann Fr Anesth Reanim* 2009;29(2):117-125.
27. Davies A, Jones D, Bailey M, Beca J, Bellomo R, Blackwell N, et al. on behalf of the Australia and New Zealand Extracorporeal Membrane Oxygenation (ANZ ECMO) Influenza Investigators. Extracorporeal Membrane Oxygenation for 2009 Influenza A(H1N1) Acute Respiratory Distress Syndrome. *JAMA* 2009;302(17):1888-1895.
28. Hui DS, Lee N, Chan PK. Clinical management of pandemic 2009 influenza A (H1N1) infection. *Chest* 2010;137(4):916-925.
29. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med* 2000 ;342(18):1301-1308.
30. J.C. Richard, C. Girault, S. Leteurtre, F. Leclerc, on behalf of the SRLF. Prise en charge ventilatoire du syndrome de détresse respiratoire aiguë de l'adulte et de l'enfant (nouveau-né exclu) - Recommandations d'Experts de la Société de Réanimation de Langue Française. *Réanimation* 2005;14:10.
31. Lucato JJ, Tucci MR, Schettino GP, Adams AB, Fu C, Forti G Jr, et al. Evaluation of resistance in 8 different heat-and-moisture exchangers: effects of saturation and flow rate/profile. *Respir Care* 50(5):636-643.
32. Morgan-Hughes NJ, Mills GH, Northwood D. Air flow resistance of three heat and moisture exchanging filter designs under wet conditions: implications for patient safety. *Br J Anaesth* 2001;87(2):289-291.
33. BS EN ISO 9360-1:2009. Anaesthetic and respiratory equipment - Heat and moisture exchangers (HMEs) for humidifying respired gases in humans-part I: HME for use with minimum tidal volume of 250 ml. BSI editor

Figures Legend:

Figure 1: Experimental bench-test

An Evita 2 dura was used for most measurements, except for the internal heated filter testing. Nebulization was performed on the expiratory limb to enhance particles deposition on the filter. Hygrometric measurements were performed on 3 different locations:

- 1 : inspiratory limb, immediately before the Y-piece
- 2 : expiratory limb, immediately after the Y-piece (expiratory 1)
- 3 : expiratory limb, immediately before the ventilator input (expiratory 2)

Breathing systems and filters were kept horizontal to avoid drainage of the expiratory limb into the filter, or into the test lung.

Figure 2: Box and Whiskers Plot for differential pressure assessments at three different gas flow

A p value equal or below 0.05 was considered statistically significant. Red line depicts the safety limit under each flow condition. A resistance to gas flow of 5 cm H₂O/L/s implies a pressure difference of 5 cm H₂O at a flow of 60 L/min, and may be considered as a safety limit. Given the presumed linear relationship between pressure and flow, the differential pressure limit at 30 L/min and 90 L/min can be assumed as 2.5 and 7.5 cm H₂O respectively.

By convention, a 20cmH₂O value was considered when occlusion was experienced.

At all gas flows, a statistical difference was observed for HME-filter and internal HEPA devices, as compared to the other filter types. In all cases, differential pressure values crossed the safety limit with HME-filter.

Table 1: Filters characteristics (manufacturers data)

Name	Filter type	Internal volume	Flow resistance at 60 L/min	Pore size
Anest-Guard®	Electrostatic (hydrophobic polypropylene)	50 mL	1.1 cmH ₂ O/L/s	> 0.3 µm
Iso-Gard® HEPA light	HEPA Mechanic (hydrophobic glass fibers)	80 mL	2.0 cmH ₂ O/L/s/L/s	< 0.3 µm
ServoDuo Guard®	HEPA Mechanic and Electrostatic (hydrophobic glass fibers)	170 mL	1.5 cmH ₂ O/L/s	< 0.3 µm
Humid-Vent® Filter Compact	HME and Electrostatic (hydrophobic polypropylene and hygroscopic condensing paper media)	38 mL	1.8 cmH ₂ O/L/s	> 0.3 µm
Avea® Internal Heated HEPA	HEPA Mechanic	> 200 mL	1.75 cmH ₂ O/L/s	< 0.3 µm

Filters' pore size is imprecise and not always provided by the manufacturer; the value proposed within the table is an estimation (except for the internal heated one). Despite this imprecision, all the filters included in this bench-test have the ability to stop most pharmaceutical drugs provided by nebulization under mechanical ventilation (particles mean diameter usually ranging from 2 to 5 µm). However, effective filtration surface varies greatly from one device to the other, depending at least of the filter internal volume.

Table 2: Ex-Vivo resistance measurements at H24

	Tested Filter	Resistance to Flow (cm H ₂ O/L/s)
Baseline	Electrostatic (<i>Anest-Guard®</i>)	1.3 ± 0.1
	HME (<i>Humid-Vent®</i>)	2.3 ± 0.1
	Standard HEPA (<i>Iso-Gard®</i>)	2.3 ± 0.1
	Specific unheated HEPA (<i>Servo Duo Guard®</i>)	1.4 ± 0.1
	Internal Heated HEPA (<i>Avea®</i>)	0.6 ± 0.1
Unheated (MR 460)	Electrostatic (H10)	NA
	HME-filter (H6)	NA
	Standard HEPA (H19)	NA
	Specific HEPA (H19)	NA
	Internal Heated HEPA	0.7 ± 0.1
Monoheated (RT 212)	Electrostatic	2.4 ± 0.1
	HME-filter (H20)	NA
	Standard HEPA	3.1 ± 0.1
	Specific HEPA	1.7 ± 0.1
	Internal Heated HEPA	0.5 ± 0.1
« Old » biheated (RT 100)	Electrostatic	1.3 ± 0.1
	HME-filter (H24)	NA
	Standard HEPA	2.6 ± 0.1
	Specific HEPA	1.5 ± 0.1
	Internal Heated HEPA	0.6 ± 0.1
« New » biheated (RT 340)	Electrostatic	1.3 ± 0.1
	HME-filter	2.3 ± 0.1
	Standard HEPA	2.1 ± 0.1
	Specific HEPA	1.5 ± 0.1
	Internal Heated HEPA	0.7 ± 0.1
RT 100 without nebulization	Electrostatic	1.2 ± 0.1
	HME-filter	2.2 ± 0.1
	Standard HEPA	1.9 ± 0.1
	Specific HEPA	0.9 ± 0.1
	Internal Heated HEPA	0.6 ± 0.1

MR460 : unheated circuit ; RT212 : mono-heated circuit ; RT 100 : old generation bi-heated circuit ; RT340 : new generation bi-heated circuit .

In bold types, sequences interrupted before H24 because of occlusion; between brackets is provided the hour of occlusion.

Table 3 : In-Vivo differential pressure measurements (cm H₂O)

	Tested Filter	Flow (L/min)		
		30	60	90
RT 100	Specific HEPA H24	0,60	1,00	1,64
	Specific HEPA H48	0,61	1,29	2,19
	Specific HEPA H72	0,57	1,21	2,07
	Standard HEPA H24	0,93	1,94	2,98
	Standard HEPA H48	0,92	1,87	3,43
	Standard HEPA H72	0,87	1,94	3,41
RT340	Specific HEPA H24	0,70	1,48	2,46
	HME-filter H24	0,99	2,10	3,52
	Electrostatic H24	0,61	1,29	2,1
	Internal Heated HEPA J86	0,16	0,41	0,74
	Internal Heated HEPA J5	0,46	0,92	1,53
	+ coli 6M x 5			

RT 100 : old generation bi-heated circuit ; RT340 : new generation bi-heated circuit

A differential pressure below 2.5 cm H₂O at 30 L/min, 5 cm H₂O at 60 L/min, and 7.5 cmH₂O at 90 L/min is considered as the safety limit.

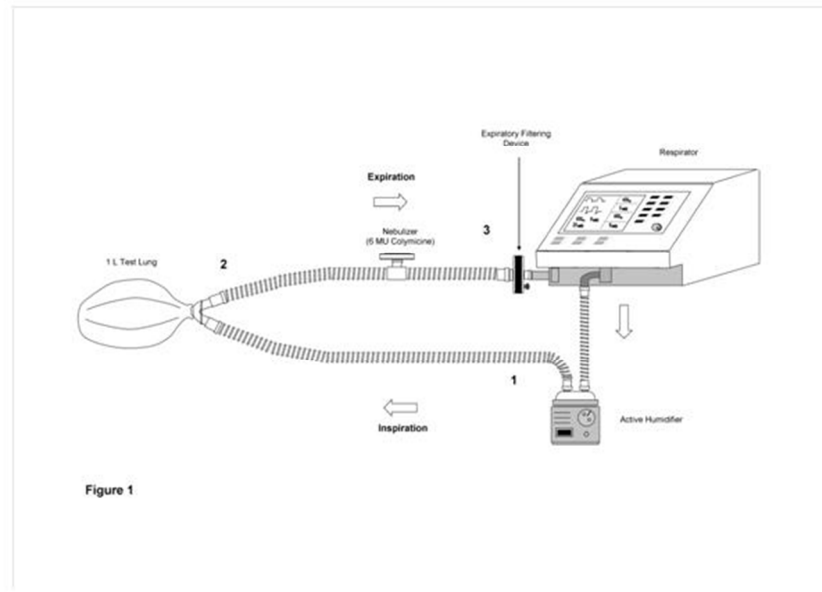
In-Vivo measurements were performed in two different ICUs, while such expiratory limb protection was performed for clinical purpose; in no cases, measurements did cross the safety limit.

Table 4 : Hygrometric measures

	<i>Inspiratory</i>				<i>Expiratory 1</i>				<i>Expiratory 2</i>			
	UH	MH	BH1	BH2	UH	MH	BH1	BH2	UH	MH	BH1	BH2
Absolute Humidity (mg H ₂ O/L)	44.6 ± 1.4	39.3 ± 0.1	39.0 ± 0.6	39.3 ± 0.1	33.5 ± 1.4	33.3 ± 0.4	32.7 ± 1.1	33.0 ± 0.8	22.2 ± 1.4	21.9 ± 0.3	33.8 ± 1.0	24.1 ± 0.6
Relative Humidity (%)	86.5 ± 1.1	100 ± 2.6	83.2 ± 4.5	86.7 ± 2.1	99.1 ± 1.6	97.5 ± 2.0	96.8 ± 1.0	99.1 ± 1.1	100 ± 1.4	95.3 ± 2.7	54.6 ± 3.8	71.1 ± 1.7

Values are given as mean ± STD. No statistical difference was evidenced between measurements.

Inspiratory: hygrometric measurements on the inspiratory limb, immediately before the Y-piece (1; Figure 1); Expiratory 1: measurements on the expiratory limb, immediately after the Y-piece (2; Figure 1); Expiratory 2: measurements on the expiratory limb, immediately before the ventilator input (3; Figure 1). UH: unheated circuit (MR 460); MH: mono-heated circuit (RT 212); BH1: bi-heated circuit "old generation" (RT 100); BH2: bi-heated circuit "new generation" (RT 340).



Experimental bench-test
254x190mm (72 x 72 DPI)

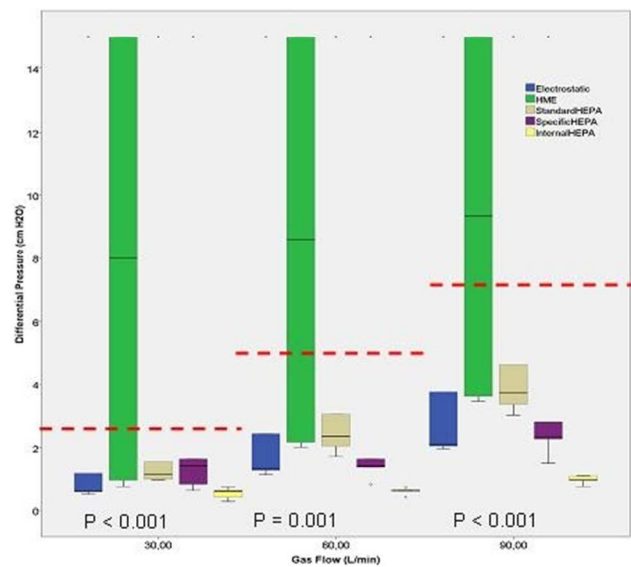


Figure 2

Box and Whiskers Plot for differential pressure assessments at three different gas flow
254x190mm (72 x 72 DPI)