SALBUTAMOL DELIVERY IN AN *IN VITRO* PAEDIATRIC VENTILATOR-LUNG MODEL: COMPARISON OF JET, ULTRASONIC AND MESH NEBULISERS

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Introduction

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- Nebulised salbutamol is often administered to mechanically ventilated children. Comparative studies of the efficacy of nebulisers are still scanty. A number of patient-, delivery system- and ventilator-related factors may prevent a drug to reach its site of action.
- In a first study, we used an *in vitro* model to compare different nebulisers; in an extension of this first study, we now use this model when coupled to mechanical ventilation.

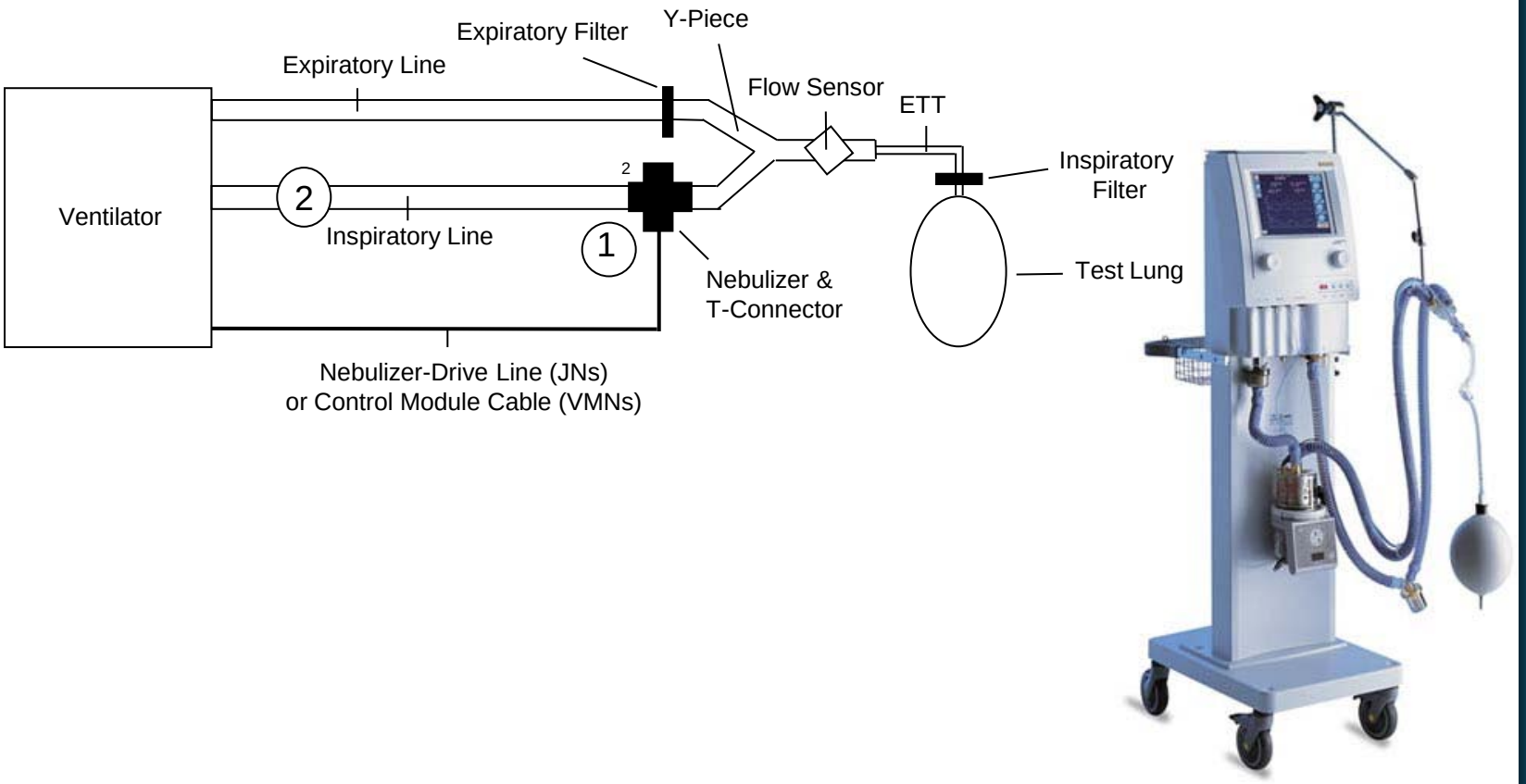
Aim

- To determine the influence of nebuliser types and nebulisation modes on the delivery of aerosolised salbutamol in an *in vitro* paediatric mechanical ventilator-lung model.

Method

- A 10-kg mechanically ventilated patient was simulated using a Galileo® ventilator (Hamilton Medical, Rhäzuns, Switzerland).

Pediatric ventilator lung model



Method

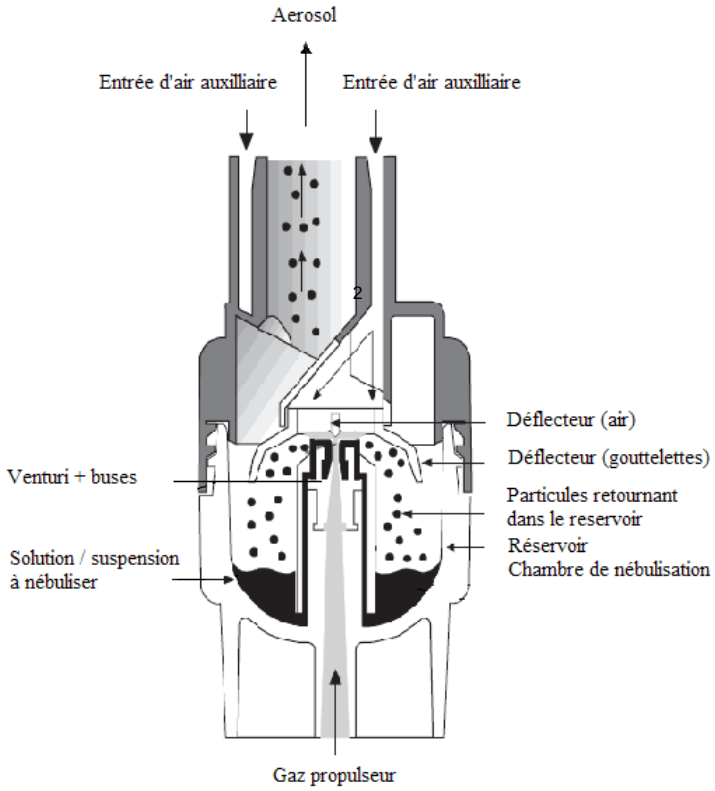
- A 10-kg mechanically ventilated patient was simulated using a Galileo® ventilator (Hamilton Medical, Rhäzuns, Switzerland).
- Three different nebulisation modes were tested:
  - Intermittent nebulisation during the inspiratory phase: “Intermittent/Inspiratory” mode
  - Continuous nebulisation :"Continuous" mode
  - Intermittent nebulisation during the expiratory phase: "Intermittent/Expiratory" mode

Method

- A 10-kg mechanically ventilated patient was simulated using a Galileo® ventilator (Hamilton Medical, Rhäzuns, Switzerland).
- Three different nebulisation modes were tested.
- Three nebuliser types were tested:
  - Jet Nebuliser

Jet Nebuliser[5] (JN)

Sidestream® (Profile Therapeutics, UK)



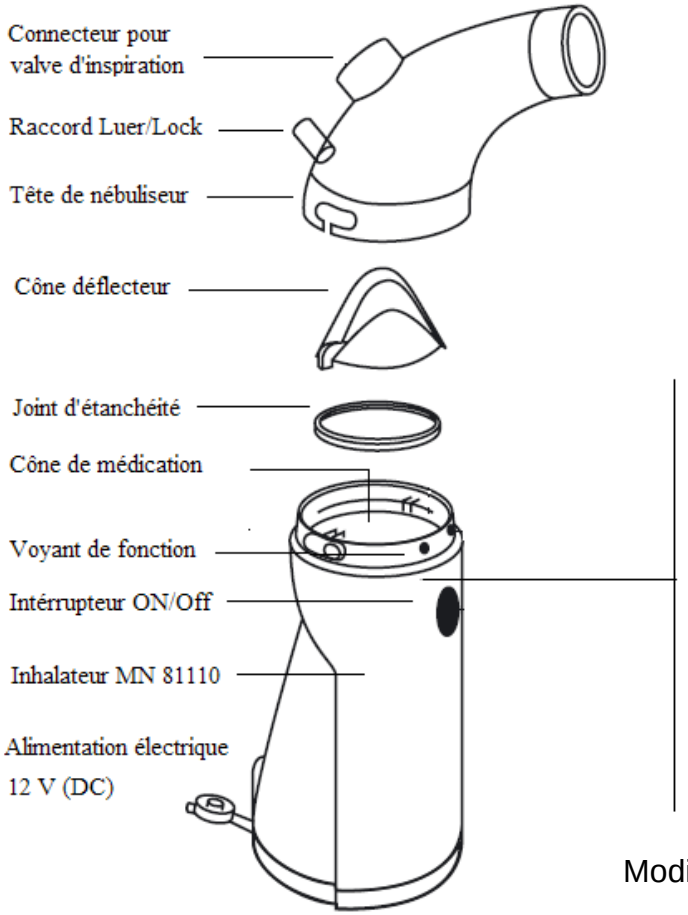
Modified from : O'Callaghan, C., Barry, P. W., The science of nebulised drug delivery. *Thorax* **52 Suppl 2**, S31 (1997)

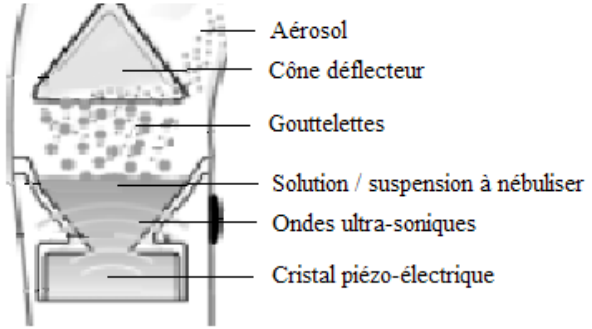
Method

- A 10-kg mechanically ventilated patient was simulated using a Galileo® ventilator (Hamilton Medical, Rhäzuns, Switzerland).
- Three different nebulisation modes were tested.
- Three nebuliser types were tested:
  - Jet Nebuliser
  - Ultrasonic Nebuliser

Ultrasonic Nebuliser[6] (USN)

Multisonic InfraControl® MN 81100, (Schill GmbH, Germ





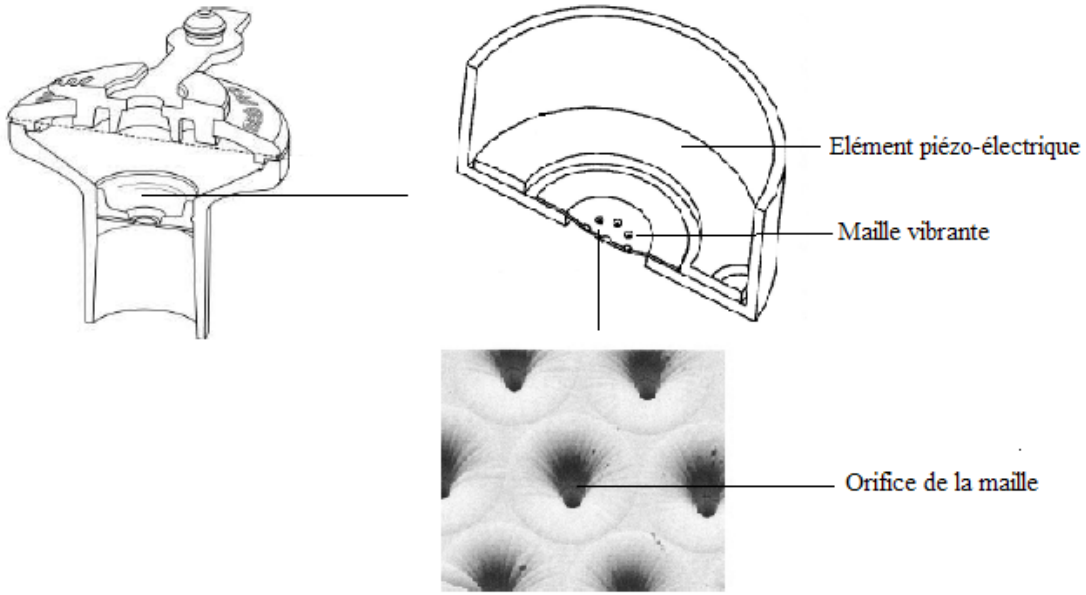
Modified from Multisonic Infra Contrôl, manual

Method

- A 10-kg mechanically ventilated patient was simulated using a Galileo® ventilator (Hamilton Medical, Rhäzuns, Switzerland).
- Three different nebulisation modes were tested.
- Three nebuliser types were tested:
  - Jet Nebuliser
  - Ultrasonic Nebuliser
  - Vibrating Mesh Nebuliser

Vibrating Mesh Nebuliser (MN)

Aeroneb® Pro (Galway, Ireland)



Modified from Fink, J.B., Power J.,Comparison of a Novel Aerosol Generator with standard Ultrasonic Nebulizer Designed for use During Mechanical Ventilation. *Am. J. Respir. Crit. Care Med* **163**, A127 (2001)

Method

- A flow generator was used with a Galileo Ventilator (Hamilton Medical) in order to simulate a 10-kg child.
- Three different nebulisation modes were tested.
- Three nebuliser types were tested.
- The nebulisation duration: 30’ or until the residual of solution was reached.
- The nebulised solution: 4 mL of 0.05% salbutamol in 0.9% NaCl.
- The amount of salbutamol deposited on the inspiratory and expiratory filters and remained in the ventilator circuit was quantified.

Results

Nebulised albuterol delivery

Nebulisers	Nebulisation Mode	Inspiratory Filter Retention (%) [1]	Expiratory Filter Retention (%) [1]	Nebuliser Retention (%) [1]	Ventilator Circuit Deposition (%) [1]
Sidestream (JN)	Intermittent/Inspiratory	2.8 ± 0.5	37.8 ± 5.8	52.7 ± 5.1	6.7 ± 2.2
	Continuous	3.7 ± 0.3	38.0 ± 3.0	48.8 ± 3.2	9.5 ± 1.3
	Intermittent/Expiratory	6.4 ± 0.9	27.4 ± 5.3	46.1 ± 12.4	20.1 ± 2.2
Multisonic (USN)	Intermittent/Inspiratory	10.5 ± 2.3	46.7 ± 2.8	32.1 ± 1.5	10.7 ± 1.6
	Continuous	5.1 ± 2.0	58.4 ± 2.2	31.4 ± 1.6	5.1 ± 0.8
	Intermittent/Expiratory	**Not Possible**			
Aeroneb Pro (VMN)	Intermittent/Inspiratory	5.4 ± 2.7	62.1 ± 10.1	3.9 ± 0.4	28.6 ± 4.7
	Continuous	13.3 ± 4.6	50.5 ± 2.4	3.4 ± 0.5	32.8 ± 6.5
	Intermittent/Expiratory	8.0 ± 3.0	21.9 ± 4.0	4.1 ± 0.6	66.0 ± 8.9

[1] Mean ± SD (n = 5), expressed as % of the initial dose of salbutamol sulphate.

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Multisonic (USN)	Intermittent/Inspiratory	10.5%	46.7%	32.1 ± 1.5	10.7 ± 1.6
	Continuous	5.1 ± 2.0	58.4 ± 2.2	31.4 ± 1.6	5.1 ± 0.8
	Intermittent/Expiratory	Not Possible			
Aeroneb Pro (VMN)	Intermittent/Inspiratory	5.4 ± 2.7	62.1%	3.9 ± 0.4	28.6 ± 4.7
	Continuous	13.3 ± 4.6	36.9 ± 2.4	3.4 ± 0.5	32.8 ± 6.5
	Intermittent/Expiratory	8.0 ± 3.0	21.9 ± 4.0	4.1 ± 0.6	66.0 ± 8.9

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	Intermittent/Expiratory		Not Possible		
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	Continuous	13.3%	50.5 ± 2.4	3.4 ± 0.5	32.8 ± 6.5
	Intermittent/Expiratory		21.9 ± 4.0	4.1 ± 0.6	66.0 ± 8.9

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	Intermittent/Expiratory	8.0%	21.9 ± 4.0	4.1 ± 0.6	66.0%

[1] Mean ± SD (n = 5), expressed as % of the initial dose of salbutamol sulphate.

Discussion

		% Dose deposit on pulmonary filter	
Nebuliser	Nebulisation mode	Study results	Literature results
Sidestream (JN)	Continuous	3.7 ± 0.3	5.0 ± 0.6 (1)
	Intermittent/Inspiratory	2.8 ± 0.5	2.7 ± 0.6 (1)
	Intermittent/Expiratory	6.4 ± 0.8	8.9 ± 1.8 (1)
Multisonic (USN)	Continuous	5.1 ± 2.0	-
	Intermittent/Inspiratory	10.5 ± 2.3	-
	Intermittent/Expiratory	Not possible	-
Aeroneb Pro (VMN)	Continuous	13.4 ± 4.6	13 (2)
	Intermittent/Inspiratory	5.4 ± 2.7	-
	Intermittent/Expiratory	8.0 ± 3.0	-

(1) Di Paolo E., Pannatier A., Cotting J. In vitro evaluation of bronchodilator drug delivery by jet nebulization during pediatric ventialtion, Pediatr Crit Care Med, Vol. 6 N°4, 2005

(2) Fink J.B. New technology offers new opportunities: Continuous bronchodilator therapy durig mechanical ventilation. Respiratory therapy, Vol. 2, N°4, 2007

Discussion

Work's limitations:

- It's only an *in vitro* model which mimics the breathing pattern on a 10-kg infant.
- The drug was entirely captured by the inspiratory filter at the end of the endotracheal tube.
- This type of model does not take into account the state of health of the patient.

Conclusion

- The quantity of inhaled drug was less than 14% of the initial dose of salbutamol.
- Important differences between nebuliser types and nebulisation modes in an *in vitro* pediatric ventilator lung model.
- New devices such as USNs and VMNs delivered more aerosols as compared with traditional JNs.
- Aeroneb Pro was the most efficient nebuliser in continuous mode.

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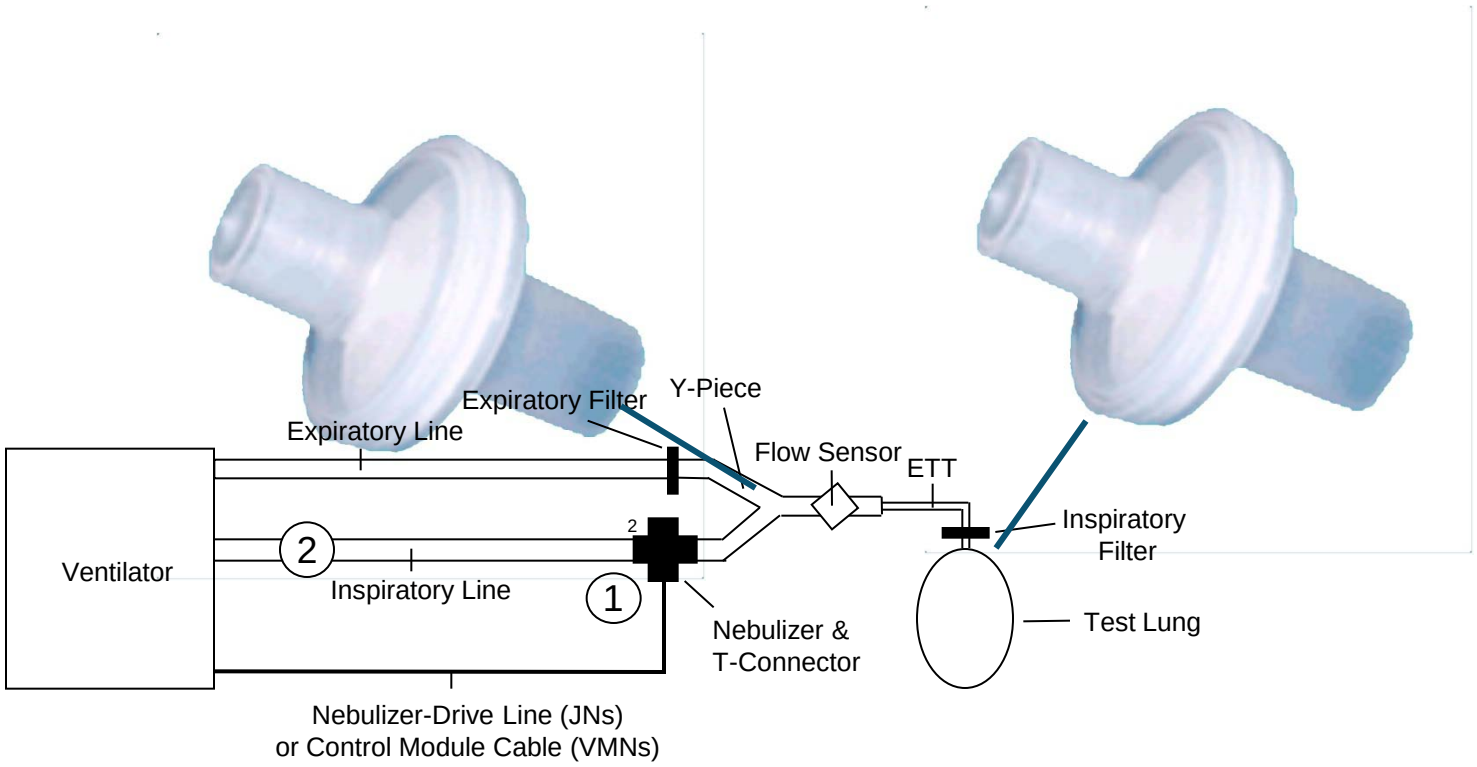
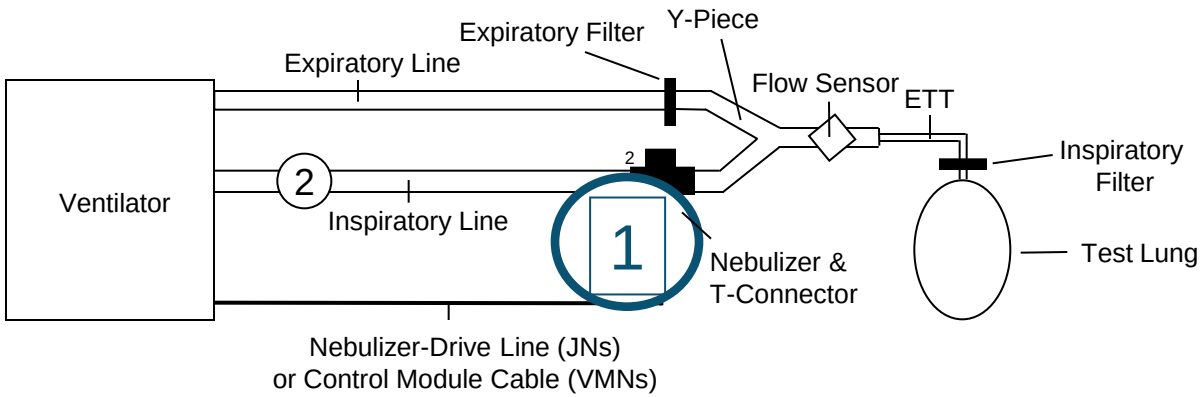
Albuterol deposition

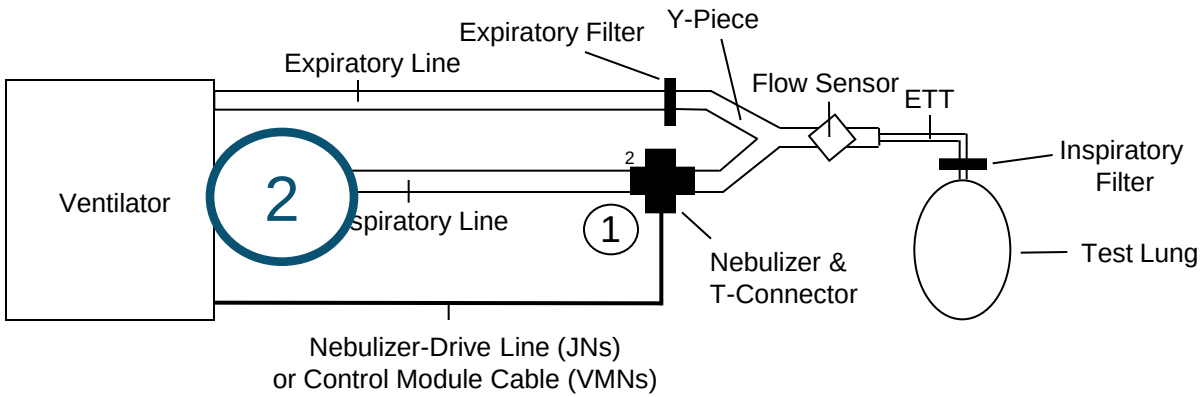


Pediatric ventilator lung model



Pediatric ventilator lung model with the nebulizers placed at a distance of 10 cm from the Y-piece (position 1) for "Intermittent/Inspiratory" and "Continuous" modes).

Pediatric ventilator lung model



Pediatric ventilator lung model with the nebulizers placed at a distance of 160 cm (position 2) for "Intermittent/Expiratory" mode).

% of initial dose of albuterol inhaled

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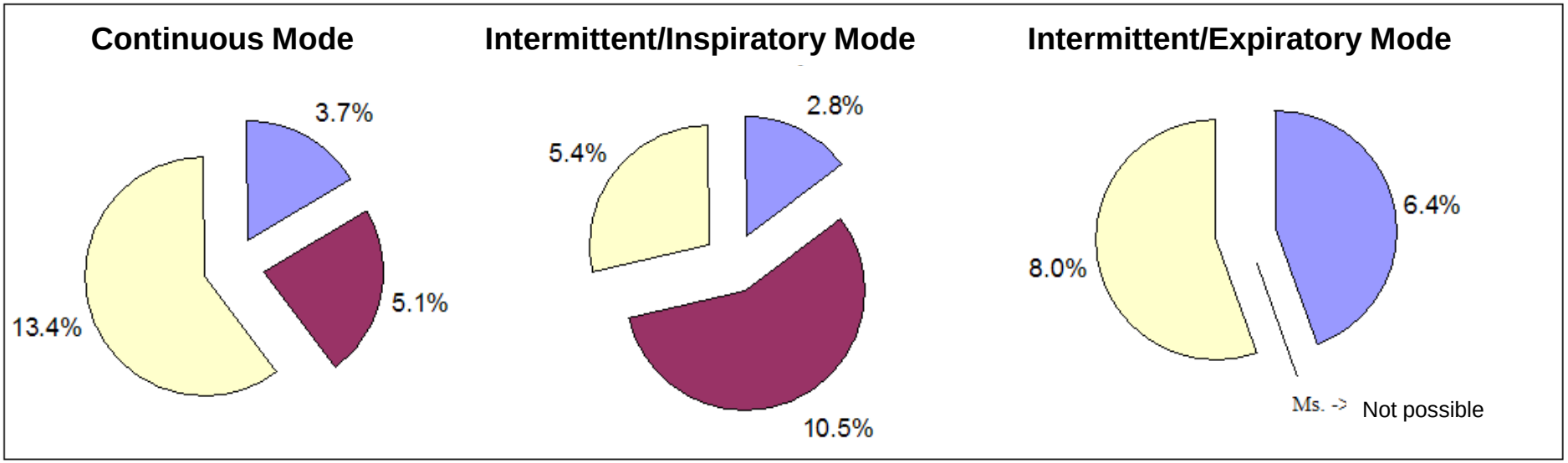

Sidestream **Multisonic** **Aeroneb Pro**

	Continu		Inspirium		Expirium 160cm	
	p	différence	p	différence	p	différence
S. vs. Ms.	>0.05	ns	<0.001	s	-	-
S. vs. A.P.	<0.001	s	>0.05	ns	0.0253	s
Ms. vs A.P.	<0.01	s	<0.01	s	-	-