Computational Fluid Dynamics simulations and in vitro testing on the importance of expiratory valves for spacers

Emeline Furon[1], Faustine Vanel[1], Thierry Porée[1], Jean-Christophe Dubus[2]

[1]Laboratoire Protec'Som; [2]Service de pneumologie pédiatrique, Unité de Médecine Infantile, CHU de Marseille - Hôpital de la Timone

Introduction

A valved holding chamber (VHC) is more than a spacer extending the distance between the mouth of the patient and the pressurized metered dose inhaler (pMDI). Fitted with one-way inspiratory valves, preventing exhalation into the device, some also present an expiratory valve[1].

Drug delivery from holding chambers is dependent on multiple factors, including the efficacy of the valve system[2]. Using computational fluid dynamics (CFD) modelling and *in vitro* experimentation, the influence of 2 small apertures (3*3mm) situated before the inspiratory valve, as a mean of expiratory valve, was tested.

CFD modelling

A simple 3D geometry (figure 1) of a pMDI coupled to a VHC with a volume of 200 mL and comprising 2 opposite apertures (3 mm diameter) was created with SOLIDWORKS (DassaultSystèmes).

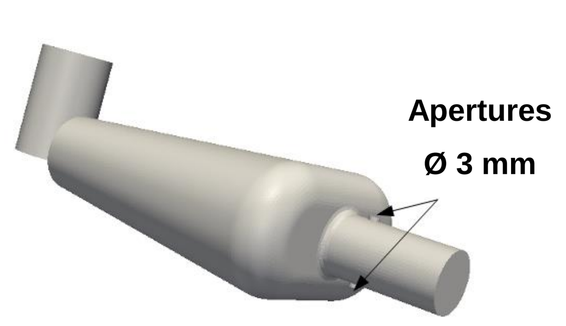

Figure 1 : Model VHC 3D geometry.

An automatic mesh generator (Protec'Som) for spacers was used to create a tridimensional mesh of the spacer. CFD modelling using a laminar flow was performed with the open source OpenFOAM software (OpenCFD Ltd) and the SimpleFOAM Solver.

CFD modelling predicted that, with a constant inspiratory flow of 15L/min, 69.3% of the air going through the mouthpiece would come from the side apertures, leaving only 4.6 L/min of the flow coming from the back of the spacer.

Computational Fluid Dynamics modelling

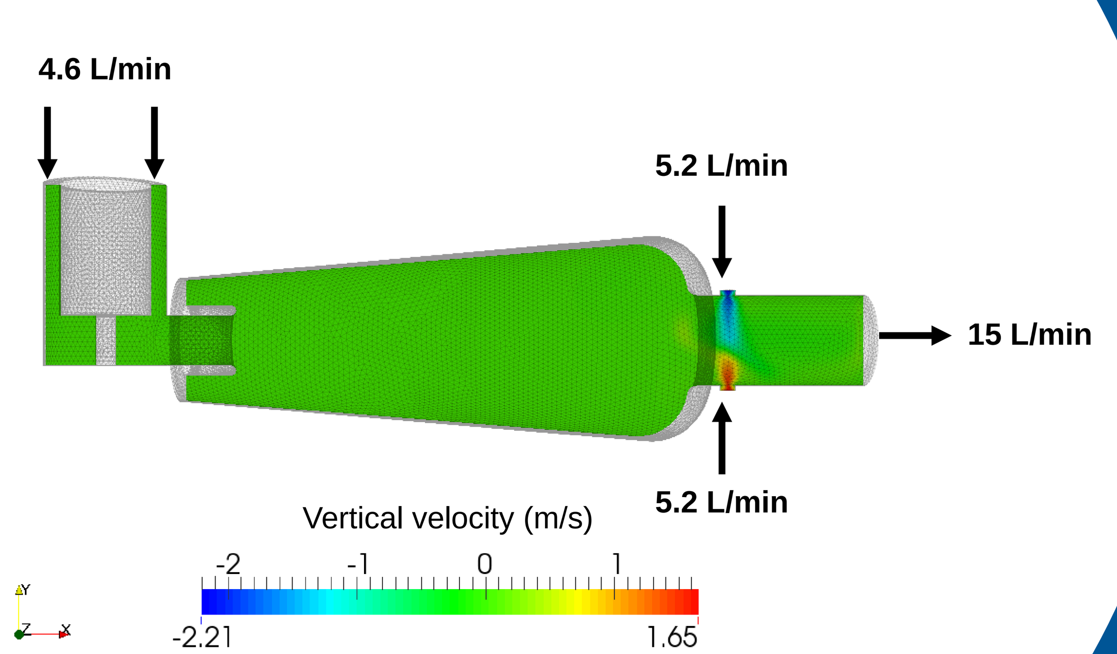

Figure 2 : Side view of the model spacer and MDI: vertical velocity.

VHC Seal

Chamber seal and aperture influence was determined by placing the model spacer (with or without apertures plugged) in line between 2 flow meters and connecting to a pump (figure 3) delivering a constant flow (15 or 50mL/min). CFD modelling data were confirmed *in vitro*, where 66.8% of the airflow came from the apertures so only 33.2% coming from the back of the spacer. That proportion of air traversing the VHC increased to 53% when using a 50L/min flow.

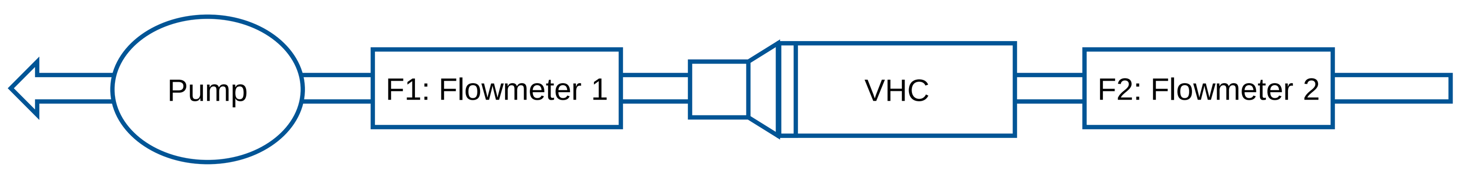

Figure 3 : VHC seal testing experimental set up.

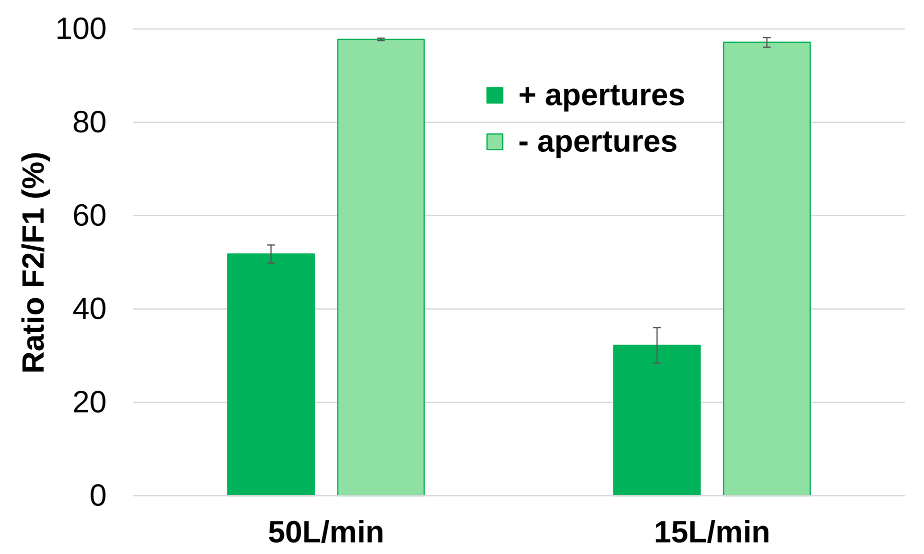

Figure 4 : VHC seal was determined by measuring the flow ratio at 15 and 50 L/min.

In vitro deposition

Lung deposition of fluticasone (Flixotide 50µg/dose, GSK) was assessed *in vitro* by connecting the model spacer to a model trachea and collecting filter (figure 5) coupled to a breathing simulator (Copley scientific) generating a child breathing profile (155mL/5 breaths). The presence of those apertures reduced the lung dose deposition *in vitro* by 38% (3.54±0.27 vs 5.71±1.46 µg/puff, $p<0.005$) when compared to the spacer with plugged apertures.

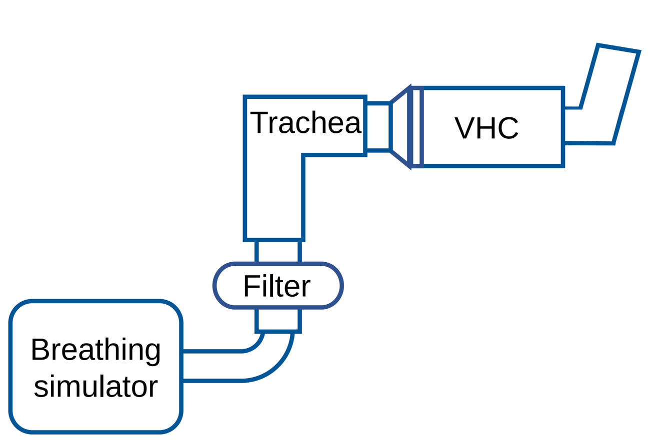

Figure 5 : *In vitro* filter deposition experimental set up.

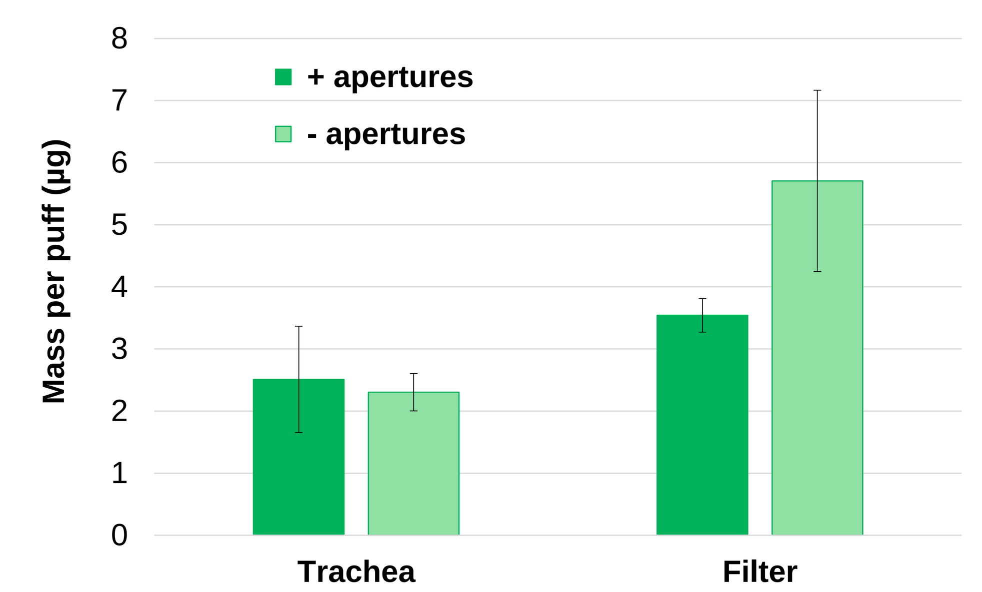

Figure 6 : Lung and throat deposition *in vitro* estimation

Conclusion

The *in vitro* validation of the computational modelling simulation of flow through a model VHC, confirms the pertinence of our in silico models.

Effective seal between the patient and inspiratory valve is essential, therefore an efficient valve system is required, especially for children with lower inspiratory flow.

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References

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2. Mitchell, J. P. & Nagel, M. W. Valved holding chambers (VHCs) for use with pressurised metered-dose inhalers (pMDIs): a review of causes of inconsistent medication delivery. Primary Care Respiratory Journal 16, 207–214 (2007).