Importance of the Tongue as an Impactor for Orally Inhaled Aerosols from a Pressurised Metered Dose inhaler (pMDI) With and Without a Valved Holding Chamber (VHC)

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BACKGROUND

- Positioning of the tongue during inhaler medication delivery is something that is not thought about by either users or caregivers.
- The tongue acts as an impaction surface for the high initial velocity of the expanding plume emitted from a pMDI.
- An alternative is to use the inhaler with a VHC that by virtue of its internal volume, allows the plume to expand and slow its forward velocity before being inhaled.

OBJECTIVE

- To compare the amount of oropharyngeal impaction by using a series of model adult oropharyngeal cavities (OCs) in which only the tongue size was progressively reduced.

MATERIALS & METHODS

- Measurements undertaken (n = 5 replicates at each condition) using pMDIs delivering a nominal dose/actuation of 90 µg salbutamol ex actuator mouthpiece and assayed drug mass by a validated HPLC method.
- We developed four sintered nylon adult oropharyngeal casts (Figure 1) based on the ADAM-III internal geometry by a 3-D printing process (Materialise, Leuven, Belgium).
- We connected the exit from the model on test directly to an abbreviated Andersen cascade impactor to measure total mass ex inhaler with or without VHC and FPM<4.7µm.
- In the first series of measurements, the primed and shaken pMDI was actuated 5 times into the lips of the OC without a VHC.
- In the second series, we repeated the measurements with the original pMDI, this time adding an antistatic ***AeroChamber Plus**** VHC/ mouthpiece.
- 2 s delay interval between pMDI actuation and starting to sample to simulate use by a poorly coordinated patient.

TONGUE VOLUMES IN THE MODELS

- Model 1: volume of tongue not reduced (reference)
- Model 2: tongue volume 60% of reference
- Model 3: tongue volume 30% of reference
- Model 4: tongue volume 0% of reference

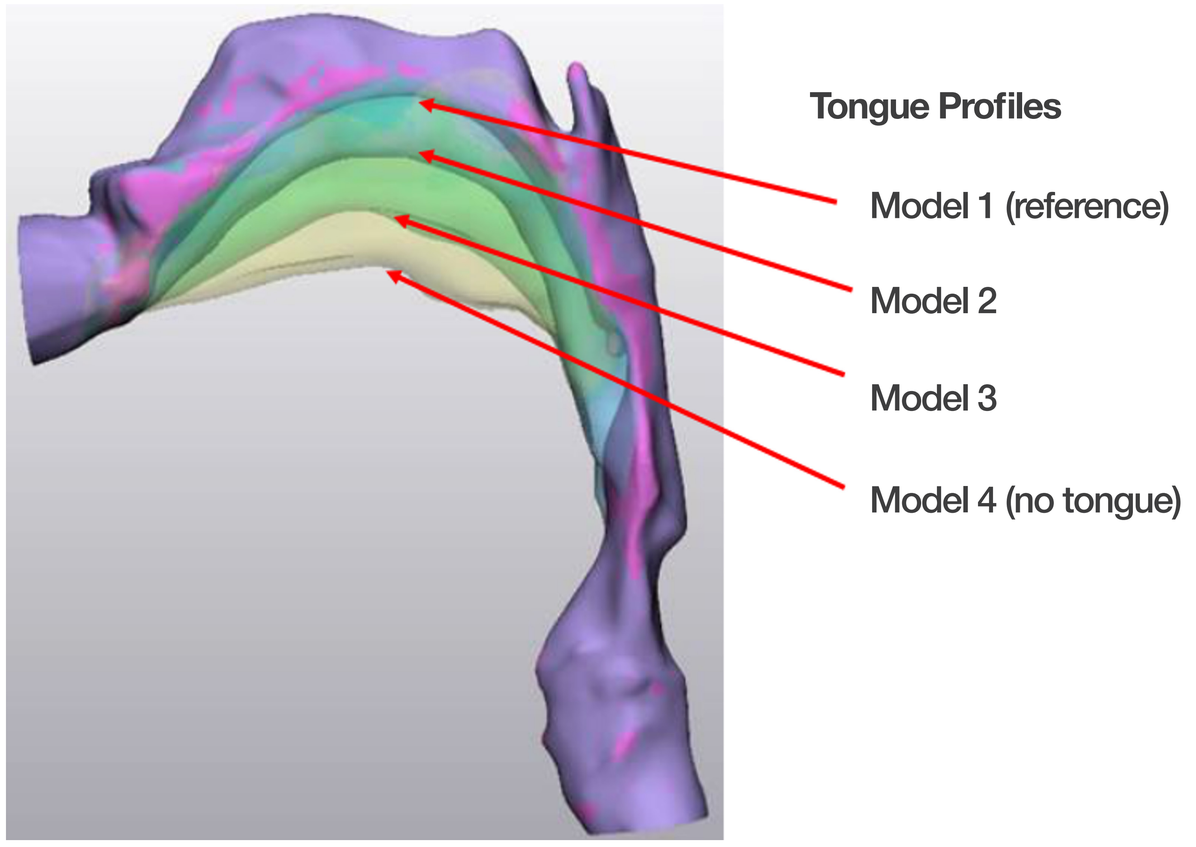


Figure 1: Combined Sagittal View Superimposing the Four Model Adult OCs Having Tongue Volumes of 100% (Model 1), 60% (Model 2), 30% (Model 3), and 0% (Model 4)

RESULTS

- Fine particle mass fraction <4.7 µm aerodynamic diameter ($FPF_{<4.7\mu m}$) and fine particle mass/actuation ($FPM_{<4.7\mu m}$) is illustrated Table 1 for the pMDI alone and in Table 2 for the pMDI with VHC with 2 s delay following actuation before initiating sampling.

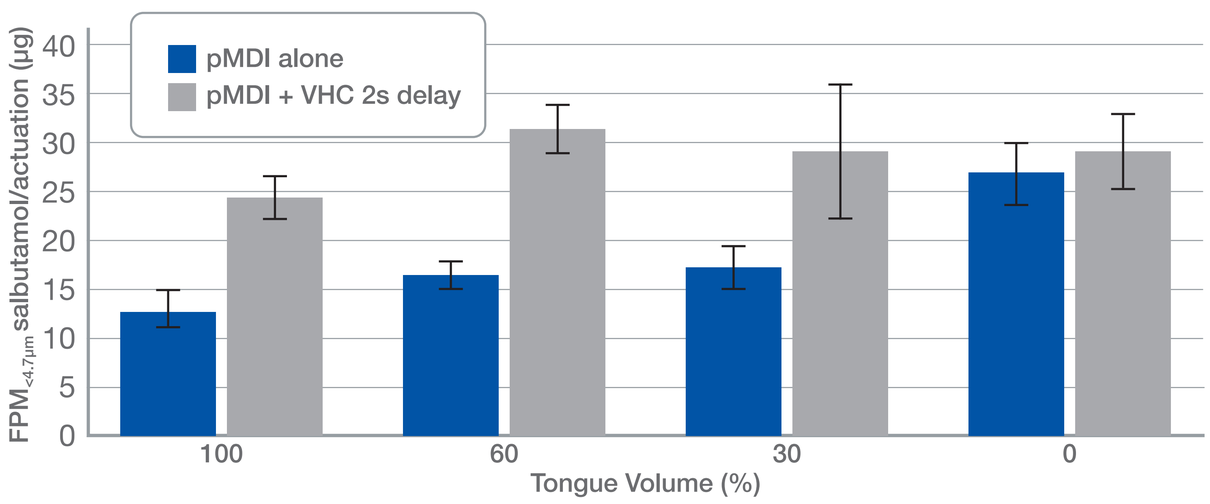
Model	1	2	3	4
% tongue volume	100	60	30	0
$FPF_{<4.7\mu m}$ (%)	26.7 ± 3.6	28.2 ± 3.4	22.6 ± 3.0	38.5 ± 6.5
$FPM_{<4.7\mu m}$ (µg/actuation)	12.9 ± 2.1	16.3 ± 1.6	17.2 ± 2.4	26.5 ± 3.8

Table 1: pMDI-Delivered Salbutamol without VHC (mean ± S.D.) to Four Adult OCs with Differing Tongue Volumes

Model	1	2	3	4
% tongue volume	100	60	30	0
$FPF_{<4.7\mu m}$ (%)	89.1 ± 3.5	89.0 ± 3.0	93.4 ± 1.9	90.5 ± 2.8
$FPM_{<4.7\mu m}$ (µg/actuation)	24.5 ± 2.0	30.7 ± 2.4	29.6 ± 5.9	29.5 ± 3.7

Table 2: pMDI- Delivered Salbutamol with VHC to Four Adult OCs with Differing Tongue Volumes

- $FPF_{<4.7\mu m}$ for the pMDI alone increased significantly with larger OC volumes (1-way ANOVA, p <0.0001) from 16.7 ± 3.6% with the full tongue volume present (model 1) to 38.5 ± 6.5% when the tongue was completely removed (Model 4).
- This change was associated with an increase in $FPM_{<4.7\mu m}$ from 12.9 ± 2.1 µg/actuation to 26.5 ± 3.8 µg/actuation (p <0.0001).
- In contrast, when the VHC was present, with a 2 s delay between actuation and inhalation, $FPF_{<4.7\mu m}$ remained relatively consistent across the different tongue volume conditions and $FPM_{<4.7\mu m}$ changed much less than with the MDI alone.



pMDI Alone and pMDI +VHC with a 2 s Delay Following Actuation

DISCUSSION

- The findings of Xi and Yang (J Drug Delivery Sci Technol. 2019; 49: 674-682.) who found a 6%–25% reduction in medication delivery efficiency caused by the tongue are comparable with the 26% increase in $FPM_{<4.7\mu m}$ observed going from Model 1 to Model 2, in which the volume occupied by the tongue was decreased from 100% to 60% (Table 1).
- This change was also accompanied by a significant increase in $FPF_{<4.7\mu m}$ (unpaired t-test, p <0.001), indicating that the location of the tongue when fully present, could also capture some fine particles <4.7 µm aerodynamic diameter, as well as coarser particles.
- Importantly, the further reductions in tongue volume by 70% (Model 3) and 100% (model 4) are not meant to represent clinical situations, but to serve as a means of demonstrating the progressive changes in these two measures of interest, moving to an extreme situation with no tongue present.

CONCLUSION

- This study confirms the importance of the tongue in controlling the amount of medication as fine particles capable of reaching the airways of the lungs.
- If a VHC is absent, it confirmed that fine particle mass will be reduced compared with the case when a VHC is interposed between inhaler and the mouth of the patient.
- If a VHC is present, it showed consistent fine particle delivery, independent of tongue position, without the need to coordinate actuation with inhalation.
- When assessing inhaler technique a VHC should be recommended, and if not, tongue position should be discussed with the patient.

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