

# Using Computer Modelling to Investigate the Effect of Inhaler Design, and Patient Variation in the Deposition of Particles in the Upper Airway of Paediatric Patients

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## Summary

Data from studies conducted on adults cannot be extrapolated to children due to differences in physiology, anatomy, pathology and breathing patterns. This paper presents the development of appropriate mouth throat geometries that can be used to assess the flow through the paediatric airway, and could be used to improve inhaler design for children. Using the geometries developed, combined with the flow and usage data, a series of computational studies were undertaken, and the deposition patterns observed. It was found that there is increased deposition on the tongue, and a reduction in deposition at the back of the mouth. It was also found that for the smallest child geometry the amount of drug particles passing through to the lung was significantly reduced.

## Introduction

Data from studies conducted on adults cannot be extrapolated to children due to differences in physiology, anatomy, pathology and breathing patterns. Furthermore, for ethical reasons most countries forbid deposition studies using radio-labelled imaging in young children [1]. Therefore in the design of a dry powder inhaler for use by children, computational modelling can give us a unique insight into the deposition patterns of drug in the upper airway.

One of the challenges faced when modelling the deposition of drug particles in the upper airway is the selection of a suitable anatomical model. For studies into adults, an idealised mouth-throat geometry has been developed at the Aerosol Research laboratory of Alberta [2]. For paediatric studies, the Sophia Anatomical Infant Nose-Throat model (SAINT) [3], model has been developed based on scans of a patient aged 9 months. However, neither of these geometries represents the anatomy of children who are of an age where they are able to handle an inhaler. This study discusses the approaches that have been used to produce computational models of the human airway and details the development of appropriate mouth-throat geometries for a paediatric study.

Using the geometries developed, combined with flow and usage data, a series of computational studies will be presented for a range of inhaler designs. The details of the computational methods used to model the particles as they travel through the inhaler, mouth and throat region will be discussed and images produced showing the flow characteristics. Conclusions will be drawn discussing the relative merits of each design with regard to patient independence in consistency of drug deposition in the upper airway.

## Geometry Creation

A broad range of approaches have been undertaken to build suitable geometries for both computational and experimental studies. Broadly these can be split into two groups; models which are based on scans of real patients, and models which attempt to approximate the geometric features. This section will discuss the approaches taken, and detail the models used in this study.

Perhaps the most well known model of a paediatric airway is the Sophia Anatomical Infant Nose-Throat model (SAINT) [2], which was developed based on computerised tomography (CT) scans of a healthy 9 month old child. This model has been used in a number of computational [20] and experimental studies [3][4]. Children aged 9 months are primarily nasal breathers, and certainly unable to handle an inhaler. Hence the SAINT model is inappropriate when looking at inhaler design and interaction.

Computational fluids dynamic (CFD) modelling was used to model the effect of airway geometry on the internal pressure in the upper airway of three children with obstructive sleep apnea syndrome (OSAS) [5]. Here the model geometry was reconstructed from Magnetic Resonance Imaging (MRI) scans of three children aged 3-5 years with OSAS. Another study was found where geometry was constructed from MRI scans of a 5 year old child [6], and the flow was modelled computationally and compared with a validated computational study of an adult geometry.

In each of the approaches referenced above it was emphasised that the anatomy of a child's airway is not simply a scaled down version of an adults. A few of the key differences are listed below:

- At birth the larynx is different in form and position of that of an adult, and although most of the descent of the larynx is complete by the age of 2, the final position is not reached until age 15.

- The position of the larynx is influenced by the length of the pharynx which is proportionally shorter than in adults.
- The trachea is smaller and shorter in children, and the smallest diameter is at the cricoid ring below the vocal chords, rather than the chords themselves.
- The tongue is proportionally larger in relation to the size of the oral cavity.

Although models based on scans on real patients are able to capture the precise (limited to the scan resolution) details of a patient's anatomy, they fail to be generally applicable when looking to design a device that is suitable for a range of patients. It is inadvisable to design a device to the nuances of a particular patient, and furthermore scans are limited when looking at the interaction of a patient with a number of inhalers. The only solution to these limitations would be to take a large number of scans of a range of patients coupled with the device designs of interest.

The second approach taken in both experimental and computational studies is to create a simplified geometric representation of the anatomy of the upper airway. The simplest representation is the USP mouth-throat model, which is defined by a 90° elbow consisting of two straight tubes. A more representative geometry which has gained popularity is the Alberta mouth-throat geometry [9]. This geometry was constructed from a series of MRI scans of healthy adult patients taking the key features to create a geometry which is particularly suited to computational modelling. A simplified model taking into account the geometric features of a paediatric airway was not found.

Simplified models are limited by the fact that they are a simplification of reality. They do not contain all of the possible geometric features that could be present in real patients. However, they do allow designers to quickly test a range of device parameters without the expense or limitations of individual patient scans.

In order to conduct this study, the dimensions of the Alberta mouth-throat geometry were altered to take into account the key features of the paediatric airway. Dimensions were taken from a range of studies detailing scans of children of different ages [10][11][12][13][14][15][16][17][18][19]. Children grow at different speeds, so it would be unrealistic to state that geometry represents a specific age. To this end three airway geometries were constructed, the first representing a child aged 4-6 years, the second representing a child aged 7-9 years and the last representing a child aged 10 – 12 years.

A simple tube shaped inhaler was modelled, with three different diameters 15mm, 20mm and 25mm. The positioning of the inhaler was consistently in line with the angle of the mouth. This makes the assumption that the child is able to position the inhaler correctly in their mouth.

## Methodology

The boundary conditions that feed into this study are the result of a user interaction study conducted by Team Consulting [21]. As a result of this work, typical inhalation profiles were established for children of a range of ages, and for two different device resistances. In general it was found that children do not produce the flow rates seen by adults, and that younger children produce a shorter and faster flow profile, whereas older children are able to inhale for longer but at a lower flow rate.

The drug was modelled as spherical particles 4µm in diameter, and with a density of 1500 kg/m<sup>3</sup>. Due to the low flow rates observed, it would be unwise to assume that children could produce the velocities required to deagglomerate a drug in a passive device. Therefore for this study the drug powder was modelled as a stationary cloud at the entrance to the inhaler tube.

The study was undertaken using the commercial CFD code Star CCM+. The computational domain was meshed with predominantly polyhedral elements 1mm size. In order to capture the high velocity gradients close to the wall, the mesh was refined on all surfaces with prism layers allowing a low Reynolds turbulence model to be employed. A mesh sensitivity study was undertaken to check the suitability of the mesh size used.

The flow through the inhaler and oral cavity is turbulent in nature. Accurate turbulence modelling is important because it influences the mixing and dispersion of the particles. Direct Numerical Simulation (DNS) and Large Eddy Simulation (LES) models give reliable predictions of the flow and particle deposition [7][8] but they are computationally prohibitive for the increased accuracy that they offer. The Shear Stress Transport (SST) k-omega turbulence model was shown to represent a good trade between accuracy and computational time [8] and was the chosen turbulence model in this study.

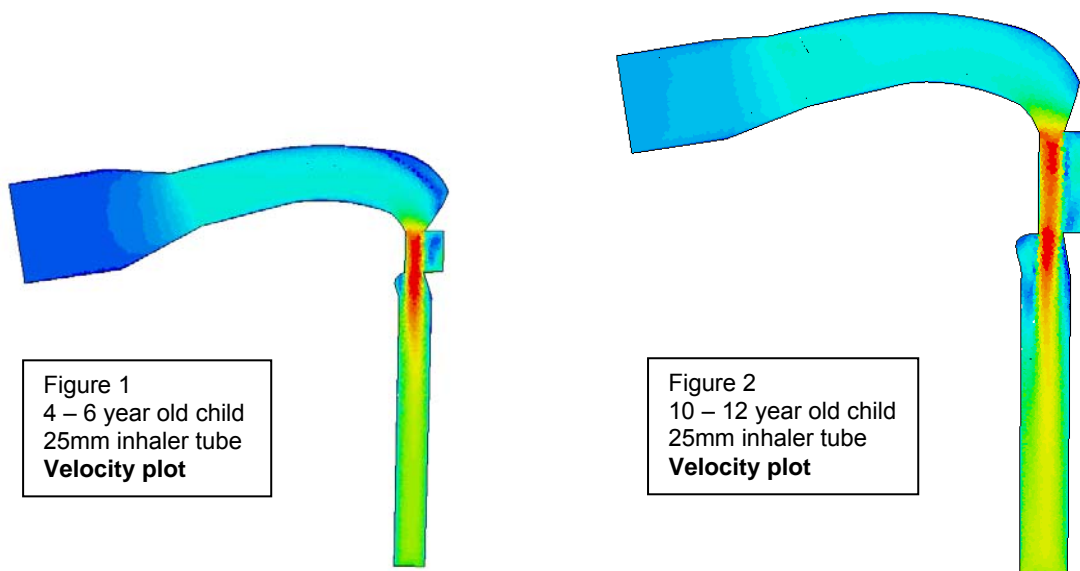
Within the model it was assumed that all particles that impact the walls leave the computational domain. In reality the lining of the mouth and throat contains mucus, and is wet and so it can be expected that particles that impact the walls would stick. Within the inhaler it could be expected that some particles would bounce off the walls, but over time a build up of powder would be seen, altering the geometry and surface properties of the wall.

## Results

In total 18 cases were modelled looking at three parameters; child age, and hence upper airway geometry, inhalation speed (based on flow resistance) and the inhaler tube diameter.

Figures 1 and 2 show the velocity profiles through the 4-6 year old geometry and the 10 – 12 year old geometry. The two images help to highlight the similarities and differences in flow through the paediatric airway, as well as giving an indication of the relative scales of the two geometries

- Although the depth of the oral cavity does not vary significantly, the height of the mouth away from the tongue increases with age, providing a reduction in resistance to the flow with age.
- A recirculation zone can be seen at the back of the mouth of the smaller geometry. This is less prominent in the large geometry. This may be due to the high, short flow rate produced by the smaller children combined with acceleration due to the smaller oral cavity diameter.
- Due to the shortened pharynx in smaller children, there is only one jet from the throat through to the trachea, as opposed to the two seen in the larger child geometry. The recirculation zone in the pharynx is also much more pronounced for the smaller child geometry, this is due to its shortened length.
- There is a stronger jet from the larynx into the trachea for the larger geometry, causing a large amount of mixing towards the bottom of the trachea.



*Note, the velocity profiles in the two images are not shown over the same range; rather they are scaled to highlight key flow features.*

Between 30% and 60% of the drug powder was seen to pass through the model, and can be assumed to have reached the lung region. The amount of drug passing through the model increases with the child age, which is in agreement with observations [22] that the dose received by a child is scaled with the patient weight, which is proportional to age. The total deposition seen in this study appears to be within the ranges that Wildhaber [22] observed in his study looking at the deposition of radio labelled particle deposition in real patients.

Across the cases as much as 30% of the drug powder is lost to the inhaler walls. It was found that the slower the inhalation speed, and the smaller the inhaler size, the greater the amount of deposition. This is partly due to sedimentation of the drug powder during the time it takes the user to increase the speed of the inhalation. In general active devices such as the Exubera device, eject the powder into a large chamber, where there is less opportunity for the drug powder to deposit due to sedimentation.

Due to the slow flow rates, and proportionally large inhaler diameters, very little powder deposition was seen on the back of the throat. This is due to the absence of a strong oral jet into the mouth which is often seen in studies with higher flow rates. As much as 10% of the drug was seen to deposit on the lips, which act to converge the flow because the inhaler is proportionally large in size in comparison with the oral anatomy.

As much as 10% of the drug was seen to deposit on the tongue, with greater deposition seen for the smaller child. As discussed above, the oral cavity is proportionally smaller, and the tongue large size explaining the increased deposition in this region.

## Conclusions

This study has demonstrated an approach that can be used to develop a generally applicable geometry appropriate for paediatric studies. The modelling has shown the key differences in flow features, and particle deposition for children of different ages, and this along with further studies could be used to aid device design.

It can be concluded that the particular features of the paediatric airway, and the low flow rates produced by children show particular flow characteristics that need to be taken into account when designing a paediatric inhaler. In particular, the deposition seen at the back of the throat in adult studies due to the proportionally small mouthpieces and high flow rates are not seen in children. Similarly the smaller mouth cavity produces higher deposition on the tongue. Other distinct flow features of the paediatric airway were identified such as the pharyngeal jet. These features cannot be influenced directly by inhaler design, however deposition could be reduced through a choice of inhalation instructions or drug particle size.

The conclusions from this study show the potential to use computational modelling to investigate the effect of changes in the geometry of the human airway. Further studies could look into the effect on the airflow and drug deposition of particular illness, or age related features in order to improve the design of inhalers that offer patient independence as far as possible.

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