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Parametric study on mouth–throat geometrical factors on deposition of orally inhaled aerosols

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ABSTRACT

There is a growing need to select a realistic mouth–throat (MT) model to replace the USP induction port (IP) which underestimates MT deposition of inhaled particles. Even though there are many image-based MT models in literature, substantial inconsistencies exist regarding the critical geometrical factors that affect the MT deposition. The objective of this study was to systematically evaluate the relative importance of MT geometrical factors that affect the deposition of orally inhaled aerosols, which include the oral cavity volume, glottis area, airway curvature, and MT airway volume. Four existing MT models with different level of complexities were implemented. HyperWorks was used to vary the dimensions of the geometrical factors. For each factor, five variants were studied in each airway model. A well-validated fluid–particle transport model was used to simulate the airflow and particle deposition. The geometrical-factor-induced deposition variations were analyzed using ANOVA to determine the relative influence of each factor on particle deposition in the MT airway. Results showed that the realism of airway models significantly affected the MT deposition, and the USP IP under-estimated the realistic model by up to 55%. The glottis area and total airway volume were found to be the two most predominant factors (both p values < 0.01). Replacing the USP IP 90° elbow with curved bends significantly reduced the deposition. However, the MT airway curvature in the other three models had insignificant effects. The effect of the oral cavity volume was also found to be insignificant. Results of this study can provide guidance in developing or selecting a representative MT model to replace the conventional USP IP. A realistic glottis area should be retained in future computational and *in vitro* deposition studies.

1. Introduction

There is a need to develop a realistic mouth–throat (MT) model to replace the United States Pharmacopeia (USP) induction port (IP) to account for the oral deposition of inhaled drugs. A USP IP was intended to provide a common standard

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to compare different formulations of inhalers (Pharmacopeia, 2005). It collects most of the large, fast moving particles, which likely deposit in the oropharynx region. However, deposition predictions using the USP IP are not satisfactory. One major issue is that drugs deposited in the USP IP generally underestimate the deposition obtained from *in vivo* measurements (Clark, Newman, & Dasovich, 1998; Newman, 1998; Zhou, Sun, & Cheng, 2011). For pressurized metered dose inhalers (pMDIs) and dry powder inhaler (DPIs), MT deposition comprises the majority of the deposited dose (Ali, Mazumder, & Martonen, 2009; Longest, Tian, Walenga, & Hindle, 2012). The simple geometry of the USP IP (a 90° bend with uniform circular cross-sections) does not resemble complex morphologies of the human mouth–throat, which have highly irregular cross-sectional areas along the airway.

More realistic human MT models have been developed based on either measurements or medical images of human subjects (Burnell et al., 2007; Cheng, Cheng, Yeh, & Swift, 1997a; DeHaan & Finlay, 2004; Grgic, Finlay, Burnell, & Heenan, 2004; Stapleton, Guentsch, Hoskinson, & Finlay, 2000; Xi & Longest, 2008; Zhou et al., 2011). For *in vitro* tests, Cheng et al. (1997a) considered deposition of micron particles in an *in vitro* cast model of the mouth–throat geometry. The oral cavity of the cast was modeled using a dental impression of the mouth from a human volunteer, while the throat was made from a cadaver. The cross sectional area and perimeter as a function of the airway axial distance were reported in Cheng, Zhou, and Chen (1999). This model has also been used to study delivery efficiencies of the pressurized metered dose inhaler (pMDI) (Cheng, Fu, Yazzie, & Zhou, 2001) and dry powder inhaler (DPI) (Cheng et al., 2003). Stapleton et al. (2000) developed a simplified MT model while retaining basic anatomical features based on averaged data from computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, as well as direct observations of living subjects. Using this cast model, Heenan, Finlay, Grgic, Pollard, and Burnell (2004) measured the flow field and regional deposition for 3–5 μm diameter aerosol particles, which revealed a strong correlation between regional deposition patterns and local flow features. Grgic et al., (2004) measured aerosol deposition in seven MRI-Based MT geometries and showed large inter-subject variations in both total and regional deposition fractions. More recently, Golshahi, Noga, and Finlay (2012) measured the deposition in MT replicas based on CT images of children 6–14 years old, aiming to minimize the inter-subject variances in deposition correlations.

A number of numerical studies have investigated particle transport and deposition in realistic and idealized MT models. Kleinstreuer and Zhang (2003) considered particle dynamics in an approximate MT model characterized by a 180° bend and circular cross-sections that are comparable to the hydraulic diameters of human airways specified by Cheng et al. (1999). They demonstrated the importance of transitional and turbulent flows on particle deposition throughout the oral airway

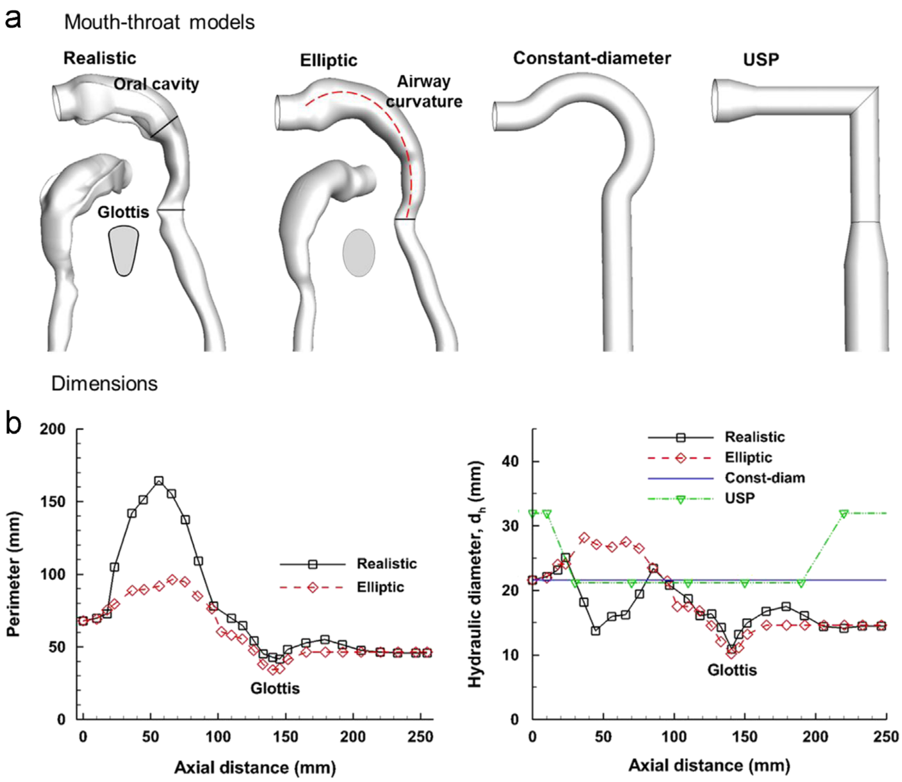

Fig. 1. Mouth–throat (MT) models and their dimensions. (a) Four MT models with decreasing physical realism were used: realistic, elliptic, constant-diameter, and USP induction port. The perimeter and hydraulic diameter of the realistic and elliptic models were compared in (b) as a function of the axial distance from the mouth inlet. The hydraulic diameters for the constant-diameter and USP IP models are superimposed for comparison purposes. The minimum perimeter and hydraulic diameter represent the glottis.

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