Vapor deposition during cigarette smoke inhalation in a subject-specific human airway model

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Abstract
Validated computer simulation results of vapor deposition from inhaled cigarette smoke are helpful to assess potential health effects of conventional and so-called less-harmful tobacco products. In this paper, the depositions of four critical tobacco-smoke vapors, i.e., acrolein, 1,3-butadiene, acetaldehyde and CO, in a subject-specific human airway model from mouth to generation G9 under different inhalation conditions have been simulated. The results show that vapor deposition is strongly influenced by its property values as well as inhalation waveform, i.e., puffing behavior. As almost insoluble species in the mucus layer, the deposition of butadiene vapor and CO is very low in the upper airways. The remaining vapors may penetrate further and deposit in deeper lung regions. As medium-to-high soluble vapors, acrolein and acetaldehyde have very high deposition values in the human upper airways from mouth to generation G9. The deposition result for steady matching flow (where the average flow rate between mean and peak values was taken) is a good conservative estimate of the actual deposition fraction under transient normal inhalation condition. However, the vapor transport delay may largely reduce the vapor deposition for transient puffing. A correction factor has been proposed, considering vapor transport delay, in order to calculate efficiently actual deposition fraction values under transient puffing condition. Furthermore, the effect of different puffing waveforms for conventional cigarettes and PREPs (potential reduced exposure products) on smoke vapor deposition has been discussed as well. Finally, a set of deposition correlations have been developed to estimate the deposition of acrolein and acetaldehyde vapors in different segments of the human upper airways under both puffing and normal inhalation (i.e., post-puffing) conditions.

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1. Introduction

Tobacco-smoking can be addictive, with potentially detrimental effects and related high health-care cost. So far, more than 60 carcinogens have been detected in mainstream smoke of cigarettes and most of the same carcinogens are present in sidestream smoke. Hecht, (2002, 2003), Burns et al. (2008) and Hecht et al. (2010) summarized the most important carcinogens in cigarette-smoke compounds, i.e., acetaldehyde, acrolein, benzene, benzo[a]pyrene (BaP), 1,3-butadiene, carbon monoxide (CO), ethylene oxide, cadmium, 4-aminobiphenyl, formaldehyde, NNN, and NNK. Some of these toxicants...
(e.g., acetaldehyde, acrolein, 1,3-butadiene, CO) inhaled from cigarettes appear as gas/vapor. Hence, the deposition doses of such vapors in human lungs are directly linked to the harmful effect of tobacco smoking. In addition, the recent appearance of potential reduced exposure products (PREPs) is a step to reduce harm of tobacco products (cigarettes); but, the validity of that claim requires careful testing (Laugesen & Fowles, 2006; Lin et al., 2010; Zhang et al., 2012). In fact, PREPs with tobacco reconstitution and new device designs may also alter a smoker’s puffing behavior, which can also change the lung deposition patterns of smoke vapors when compared to conventional cigarettes. Hence, tracking and computing the intake and deposition of toxic vapors of both PREPs and conventional cigarettes during transient puffing and post-puffing is also helpful to test the “less-harmful-cigarette” claim of PREPs and to provide toxicologists with reliable quantitative data sets. Furthermore, as many inhaled toxic or drug aerosols may appear partially in vapor form, validated computer simulation of local and regional uptake dosage of vapors in the respiratory tract would provide vital information for pharmacokinetic modeling.

As reviewed by Baker & Dixon (2006), very limited information has been published on the retention of vapors from cigarette smoke. Tolman (1973) measured the retention of carbon monoxide as a function of breathing patterns and hold time and found that the total retention of CO increased from 37% to 82% with holding time from 0.3 s to 60 s. Backhurst & Martin (1973) measured a range of smoke vapors in different subjects during puffing. They reported very high total lung retentions of acetaldehyde vapor (> 94%) and acrolein vapor (> 97%). However, local and regional deposition data of smoke vapors in human lungs are not available. More experimental studies on vapor deposition focused on laboratory animals. For example, Morris & Blanchard (1992) and Morris (1996, 1997), using rats and other animals, measured the uptake of inhaled acrolein and acetaldehyde vapor. They detected high-level deposition of these two vapors in the URT (upper respiratory tract) of such rodents. The results also indicated that the average URT acrolein deposition efficiency was significantly dependent on the inspired concentration when such concentrations are higher than 2 m\(\mu\)g/L (0.87 ppm) for acrolein and 1 ppm for acetaldehyde. However, the realistic human exposure level is usually lower (say, < 1 ppm). Hence, the measured dosimetry data for animals under high-exposure scenarios cannot be directly extrapolated to humans.

1-D mathematical modeling and 3-D computational fluid dynamics (CFD) simulations are alternative approaches to obtain deposition data of vapors in human lungs. 1-D mathematical modeling for steady or unsteady diffusion of vapors usually assumes uniform airflow in the airway lumen (see Asgharian et al., 2011) and hence ignores the effects of 3-D airflow primarily in this study. During puffing, the inhalation flow rate is low (say, \(Q_{in} < 80\) mL/s), the maximum Reynolds number in human airways is less than 800 and hence the flow should be laminar. However, during the post-puffing period
and at normal breathing rates, the local Reynolds numbers range from 0 to 10,000; hence, airflow through the oral airway region and first few generations is incipient turbulent, becoming laminar at about the sixth to eighth generation, and remaining so thereafter. In order to capture the airflow structures in the laminar-to-turbulent flow regimes, a modified version of the transitional shear-stress-transport (SST) model was selected (Zhang & Kleinstreuer, 2011b). For the SST transition model two additional transport equations, i.e., one for the intermittency and one for the transition-onset criterion in terms of the momentum-thickness Reynolds number, were introduced for a wide range of transitional flows (Menter et al., 2006a,b). Recently, Tan et al. (2008) demonstrated that a correlation-based transitional version of Menter’s SST-transition model achieved a good overall agreement with experimental data for pulsatile flow in an axisymmetrically restricted tube. Our simulations also demonstrated that the transitional SST-model can predict mean velocity distributions and turbulence kinetic energy profiles accurately for laminar-transitional-turbulent flow (Zhang & Kleinstreuer, 2011b). The corresponding turbulence equations can be found in Menter et al. (2006a,b) as well as in Zhang & Kleinstreuer (2011b).

Uniform velocity profiles were prescribed at the mouth inlet (see Fig. 1), and a uniform pressure was assumed at the outlets. Exit tubes were extended a few tube diameters from the terminal bifurcation-ends to reduce the influence of the zero-pressure assumption at the outlet. Based on prescribed flow rates and the impedances of the small airway trees downstream, Ma & Lutchen (2006) reported that pressures at the 13 outlets of an anatomically based G-6 airway model were very close to each other. Moreover, the lobar ventilation rate ratios (i.e., LUL:LLL:RLL:RML:RUL as indicated in Fig. 1) for \( Q = 30 \text{ L/min} \) obtained with the present simulation assuming uniform outlet pressures are 0.183:0.255:0.287:0.095:0.180. These findings are quite close to the values given by Horsfield et al. (1971) for a normal subject, i.e., 0.205:0.249:0.232:0.096:0.217. Zhang & Kleinstreuer (2011c) also investigated the impact of different outlet flow-rate ratios on vapor/nanoparticle deposition in bronchial airways and found that different outlet pressures primarily influence the velocity profiles and vapor/nanoparticle deposition fractions at that particular branch and adjacent bifurcations. In addition, the impact of change in outlet flow-rate ratio on total deposition was confined to all same-level bifurcations and direct upstream-level bifurcations. Lung compliance or lung motion may influence lobar flow, which will be part of future studies.

2.2. Vapor transport and airway wall uptake

The vapor mass transfer equation, including turbulent dispersion, can be written as:

\[
\frac{\partial Y}{\partial t} + \frac{\partial}{\partial x_j} (u_j Y) = \frac{\partial}{\partial x_j} \left[ \left( \hat{D}_s + \frac{\nu_T}{\sigma_Y} \right) \frac{\partial Y}{\partial x_j} \right]
\]

Fig. 1. Configuration of a subject-specific human airway model. Note that LUL to RUL only refer to the corresponding airway branches for deposition calculations.
where $Y$ is the mass fraction of vapor, $\sigma_Y = 0.9$ is the turbulence Schmidt number for $Y$, and $\tilde{D}_a$ is the molecular diffusivity of vapor in air.

Assuming that the airway wall is a perfect sink for aerosols or vapors upon touch, the boundary condition at the wall is $Y_w = 0$. This assumption is reasonable for fast gas-wall reaction kinetics, or vapors of high solubility and reactivity, and also suitable for estimating the maximum deposition of vapors in the airways. For less soluble vapors, the wall concentration would be greater than zero so that transport in tissue and in airways must be considered simultaneously when simulating vapor uptake.

Assuming that the surface of the respiratory epithelium is covered by a mucus layer with uniform thickness and that a lipid layer (tissue) lies below the mucus-tissue interface, representing a transport barrier by the epithelial cell membrane, quasi-steady radial mass transfer in the mucus layer, tissue and blood (capillary) may occur. If the concentration below the lipid layer (tissue) lies below the mucus-tissue interface, representing a transport barrier by the epithelial cell membrane, vapor uptake.

When tissue concentration is greater than the saturable plateau ($Y_t > Y_t^*$), Eq. (3b) becomes:

$$\frac{\partial Y_t}{\partial t} = \tilde{D}_t \frac{\partial^2 Y_t}{\partial n^2} - K_f Y_t - \frac{V_{\text{max}}}{K_m V_t} Y_t$$

(3b)

The analytical solutions of unsteady vapor concentrations in the tissue are also given by Asgharian et al. (2011). For the quasi-steady case, the boundary condition at the air-tissue interface for $Y_t > Y_t^*$ can be still represented by Eq. (2a) when using

$$K = \frac{\tilde{D}_t \sqrt{K_f / \tilde{D}_t}}{\beta \tilde{D}_a \tanh(H_t \sqrt{K_f / \tilde{D}_t})}$$

(4a, b)

However, when $Y_t > Y_t^*$, the boundary condition at air-tissue interface should be

$$\frac{\partial Y}{\partial n} + K Y + K_0 = 0$$

(5a)

where

$$K = \frac{\tilde{D}_t \sqrt{K_f / \tilde{D}_t}}{\beta \tilde{D}_a \tanh(H_t \sqrt{K_f / \tilde{D}_t})}$$

(5b)
and

\[
K_0 = \frac{V_{\text{max}}}{D_s V_1 \sqrt{K_f / D_t}} \left[ \frac{1}{\tanh \left( \frac{H_1}{K_f / D_t} \right)} - \frac{1}{\sinh \left( \frac{H_1}{K_f / D_t} \right)} \right]
\]  

(5c)

It can be expected from the boundary conditions (2a) and (5a) that vapor absorption at the airway surface is greatly influenced by the absorption coefficient \( K \). Clearly, for vapors of different species the absorption coefficient \( K \) should be different as well. Although actual vapor absorption in the mucus-tissue-blood system is transient, the quasi-steady conditions (2a) and (5a) represent conservative, i.e., possibly maximum, vapor depositions at the airway surface. The comparison between the present quasi-steady boundary conditions and more realistic transient absorption as well as the limitation of such somewhat simplified boundary conditions is discussed in Sections 3.7 and 3.8.

2.3. Calculation of vapor deposition

Evaluation of injuries from inhalation exposure to toxic vapors requires a detailed knowledge of the deposited amount and distribution of toxins in the human airways. The inhaled dose of vapors is described by the deposition fraction (DF) or deposition efficiency (DE), which can be calculated by summing up local wall mass fluxes. The local wall mass flux of vapors can be determined as:

\[ \dot{m}_w = -\rho A_i \left[ \frac{\partial Y}{\partial n} \right] \]  

(6)

where \( A_i \) is the area of the local wall cell (j). The local vapor deposition fraction or deposition efficiency, which is defined as the ratio of local wall mass flux to the mass flux at mouth inlet or local inlet of the airway segment, can be expressed as:

\[ DF_{\text{local}} = \frac{A_i \dot{m}_w}{Q_{\text{mouth, in}} Y_{\text{mouth, in}}} \]  

(7a)

\[ DE_{\text{local}} = \frac{A_i \dot{m}_w}{Q_{\text{local, in}} Y_{\text{local, in}}} \]  

(7b)

The regional DF or DE can be determined as:

\[ DF_{\text{region}} = \frac{\sum_{i=1}^n (A_i \dot{m}_w)}{Q_{\text{mouth, in}} Y_{\text{mouth, in}}} \]  

(7c)

\[ DE_{\text{region}} = \frac{\sum_{i=1}^n (A_i \dot{m}_w)}{Q_{\text{local, in}} Y_{\text{local, in}}} \]  

(7d)

where \( n \) is the number of wall cells in one specific airway region, e.g., oral airway, first airway bifurcation, etc. The subscript “mouth, in” refers to mouth inlet, while “local, in” refers to the inlet at the specific airway bifurcation. The local inlet flow rate and particle mass are calculated as the sum of local values of cells at this specific inlet.

The local vapor deposition patterns can be quantified in terms of a deposition enhancement factor (DEF), which is defined as the ratio of local to average deposition densities, i.e.,

\[ DEF = \left\{ \left( \frac{\hat{D}}{\frac{\partial Y}{\partial n}} \right) \left[ \sum_{i=1}^n A_i \left( \frac{\partial Y}{\partial n} \right) \right] \right\} / \left\{ \frac{1}{n} \sum_{i=1}^n A_i \right\} \]  

(8)

DEF indicates vapor deposition “hot spots” in a given region.

2.4. Calculation of mass transfer coefficients

Calculation of the respiratory mass transfer coefficient, \( h_m \), is helpful in quantitatively predicting the regional deposition of inhaled vapors (Kleinstreuer & Zhang, 2010). The relationship between the deposition efficiency (DE) in an airway segment and a given \( h_m \) can be described as (Zhang & Kleinstreuer, 2011a):

\[ DE = 1 - \exp \left( -\frac{h_m D_s K}{h_m + D_s R} \frac{A_i}{Q_{\text{local, in}}} \right) \]  

(9a)

Clearly, the DE for \( K = 0 \) is equal to zero, and for \( K \to \infty \), Eq. (9a) reduces to

\[ DE = 1 - \exp \left[ -\frac{h_m A_i}{Q_{\text{local, in}}} \right] \]  

(9b)

With simulated DE-values, the mass transfer coefficient for one airway segment can be determined from Eq. (9) as well. The Sherwood number (Sh), representing the ratio of convective to diffusive mass transport, can be expressed as:

\[ Sh = (h_m D_s) / D_p \]  

(10)
where $D$ is the characteristic diameter of the airway segment. Necessary physical property values for the vapors of interest are listed in Table 1.

### 2.5. Numerical method

The numerical solutions of the governing equations subject to appropriate boundary conditions were carried out with a user-enhanced, commercial finite-volume based program, i.e., CFX12.1 from ANSYS Inc. The computational mesh was generated with Ansys ICEM-CFD. A multi-layer region consisting of dense hybrid tetrahedral/pentahedral elements was generated near the wall surface to fully contain the viscous sub-layers and to resolve any geometric features present there. Such high local mesh resolution is also necessary to accurately calculate near-wall derivative values, such as the deposition fluxes. The mesh topology was determined by refining the mesh until grid independence of the flow field solution and vapor deposition fractions was achieved.

The computations were performed on a local Dell workstation with 12GB RAM and four 3.0 GHz CPUs as well as the multi-processor IBM Blade Center at NCSU HPC (where 32–64 processors were used for this study). The solution of the flow field was assumed to be converged when the dimensionless mass residual was negligible, i.e., $(\text{Total Mass Residual})/(\text{Mass Flow Rate}) < 10^{-4}$. The convergence of other variables was monitored as well. Typical run times for the steady air and vapor flow were approximately 72–96 CPU hours and about 1000–1500 CPU hours for a single puffing period.

### 3. Results and discussion

#### 3.1. Model validations

It is impossible to directly validate the transport and deposition of the selected vapors in the human respiratory tract because there are no relevant measured data available. Instead, the current simulation approach for species-mass deposition due to diffusional transport has been validated via analytical solutions in straight pipes, experimental data for a multi-bifurcation airway model as well as experimental data in the nasal airway model and tracheobronchial airways (see Shi et al., 2008; Zhang et al., 2008; Zhang & Kleinstreuer, 2011b). Fig. 2 depicts another validation example, which is for iodine vapor deposition in a tracheobronchial airway model. Specifically, Li et al. (1998) measured the deposition of iodine

### Table 1

<table>
<thead>
<tr>
<th>Source</th>
<th>Physical properties of selected vapors and gases (at 25 °C and 1 atm).</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D_a$ (cm$^2$ s$^{-1}$)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Acrolein</td>
<td>0.105</td>
</tr>
<tr>
<td>1,3-butadiene</td>
<td>0.1158 $^4$</td>
</tr>
<tr>
<td>Acetaldehyde</td>
<td>0.124$^4$</td>
</tr>
<tr>
<td>CO</td>
<td>0.19</td>
</tr>
</tbody>
</table>

$^a$ The removal of contaminant molecules in the mucus by chemical reaction and the resistance to transport across the lipid barrier are ignored, and the absorption parameter $K$ is approximately calculated as $K = \frac{D_m}{D_a}$ where $H_m = 1 \times 10^{-3}$ cm.

Fig. 2. Comparison of vapor (iodine) deposition fractions based on the present simulation results and experimental measurements in tracheobronchial airways.
vapor in a replicate cast from the trachea (G0) to generation nine (G9) for flow rates between 5 and 30 L/min. It can be seen that simulated depositions based on the present airway configuration from G0 to G9 (i.e., without the oral airway) are in very good agreement with the measurements. Any discrepancies can be attributed to: (i) different airway geometries; and (ii) the lack of an oral airway in the cast model for the experiments.

In summary, the good agreements between independent observations and numerical predictions instill confidence that the present computer simulation model can accurately predict vapor transport and deposition in three-dimensional human airways.

3.2. Vapor deposition under steady puffing and normal inhalation conditions

As indicated via Eqs. (2) and (5), mass transport of vapors in the mucus-tissue system greatly influence vapor deposition form the air stream onto the airway wall. In this study, Sections 3.2–3.6 focus on vapor transport and deposition in the mucus layer under both transient and steady puffing/inhalation, where the relatively simplified boundary conditions (2a) and (2b) were employed. The impact of saturable pathway elimination (i.e., boundary conditions (2a), (4) and (5)) and transient uptake of vapors in the mucus-tissue-blood system are discussed in Sections. 3.7 and 3.8.

3.2.1. Typical vapor deposition values

Clearly, the degree of local vapor absorption by the airway wall influences downstream vapor transport and deposition. For most vapors, the absorption parameter $K$ in Eq. (2b) may fall into a very large value range (e.g., $1 \times 10^{-4} < K < 1000 \text{ cm}^{-1}$) because of the variations in mucus-layer thickness and physical species properties. Nevertheless, $K_{\text{acrolein}} = 23.6 \text{ cm}^{-1}$, $K_{\text{butadiene}} = 0.0328 \text{ cm}^{-1}$, $K_{\text{acetaldehyde}} = 35.8$ and $K_{\text{CO}} = 2.33 \times 10^{-3} \text{ cm}^{-1}$ are representative values for the human upper airways (see Table 1).

The total deposition fractions of the selected four vapors in the upper airways, incorporating the representative wall absorption conditions, are shown in Fig. 3a. In this case, steady puffing with inspiratory flow rates of 37.5 mL/s and 60 mL/s, post-puffing with inhalation flow rate of 500 mL/s and two-step inhalation were considered. The inhalation flow rate of $Q = 2.25 \text{ L/min}$ (37.5 mL/s) is the mean value of a typical puffing action of one particular PREP (PMP, 2010), while $Q = 30 \text{ L/min}$ represents the normal inhalation, or post-puffing, flow rate. Inhalation of cigarette-smoke aerosols is usually a two-step process, consisting of puffing followed by normal inhalation (post-puffing), as pointed out by Dickens et al. (2009). During puffing, the soft palate (or glottis) is closed for most smokers; however, some smokers directly inhale the aerosols into the lung (Bernstein, 2004). In this study, steady puffing and normal inhalation refer to the latter (presumably worst) case, so that the aerosols are assumed to be inhaled directly into the lung. The simulations for the combined two-step smoking process were also conducted for comparison. Clearly, the impact of airway wall absorption (or vapor solubility) can be vital for vapor
deposition in human upper airways. As medium-to-high soluble vapors, acrolein and acetaldehyde almost completely deposit in the human upper airways from the mouth to generation G9 under steady puffing conditions (i.e., the total deposition fractions are larger than 98%). In contrast, as almost insoluble species in the mucus layer, the deposition of butadiene vapor and CO is very low in the upper airways, i.e., actually \( DF_{\text{butadiene}} = 0.026 \) and \( DF_{\text{CO}} = 0.0032 \) at \( Q = 60 \text{ mL/s} \). The remaining vapors may penetrate further and deposit in deeper lung regions. In fact, with the reduction of mucus layer thickness \( (H_m) \) in the lower airways and alveolar regions (say, \( H_m \sim 0.1 \mu m \) in the alveolar regions), the increased absorption coefficient \( (K) \) may result in enhanced deposition of butadiene vapor and CO in the deeper lung areas. Still, it can be expected that the butadiene vapor and CO depositions are much lower than those of acrolein and acetaldehyde.

The local deposition fractions (DFs) for acrolein and acetaldehyde vapors are depicted in Fig. 3b. The regional deposition for acrolein and acetaldehyde may gradually decrease from the oral cavity to bifurcation B3 because of the heavy (upstream) deposition, causing lower vapor concentrations at the inlet of each downstream region. The different surface areas of different airway regions also lead to different vapor-deposition values. Usually, an airway region with a relatively large surface area may receive a large portion of absorbed vapors. Influenced by the different airway geometries, surface areas, local flow rates and inlet vapor concentrations, the deposition fractions in individual bifurcations vary as well. For example, in the distal airway branches, RLL receives the highest vapor deposition while LUL has the lowest deposition.

As shown in Fig. 3, the inhalation flow rate and puffing behavior may affect vapor deposition, especially in terms of local depositions. The simulated acrolein vapor deposition fraction (DF = 69%) in the oral airway (from mouth to larynx) during puffing \( (Q = 37.5 \text{ mL/s}) \) is very close to the in vivo measured retention data by Backhurst & Martin (1973) \( (DF = 72\%) \). Backhurst & Martin (1973) also found that almost all acrolein vapor deposits in the human lung (say, \( DF > 97\%) \).

Considering the fact that deposition of CO and butadiene vapor is very low in the airway model from the oral cavity to generation G9, the following analyses will focus on vapors of acrolein and acetaldehyde vapors only.

### 3.2.2. Vapor deposition pattern

Local vapor deposition patterns can be described in terms of distributions of the deposition enhancement factor (DEF, see Eq. (8)). Fig. 4 shows the DEF contours of acrolein vapor in the upper airway model for steady puffing \( (Q_{\text{oral, in}} = 37.5 \text{ mL/s}) \). Clearly, the deposition patterns are somewhat inhomogeneous. Enhanced deposition may occur at the entrance, anterior part of the oral cavity, the outside bend of the pharynx, throat, and carinal ridges of the first bifurcation because of high degrees of mixing, i.e., large concentration gradients and/or complicated airflows in these regions.

![Fig. 4. Vapor deposition (acrolein) pattern in the upper airway model (steady state, \( Q = 37.5 \text{ mL/s} \)).](image-url)
Fig. 5. A typical PREP-puffing waveform (PMP, 2010).

Fig. 6. Transient vapor (acrolein) deposition pattern during puffing period.
3.3. Vapor deposition under transient puffing and inhalation conditions

Realistic inhalation processes during cigarette smoking, including puffing and post-puffing, are transient. The puffing waveforms may vary for different subjects and cigarette brands. As mentioned in the Introduction, the puffing waveforms may change significantly for some PREPs when compared to conventional cigarette smoking. Following the information provided by PMP (2010), Fig. 5 depicts a typical puffing waveform. Thus, possible PREP vapor deposition results under transient puffing and post-puffing (normal inhalation) conditions are discussed next.

Fig. 6 depicts the instantaneous DEF contours of acrolein vapor during the transient PREP-puffing period. As expected, vapor travels and deposits gradually from the mouth inlet to distal branches. The vapor deposition patterns after $t = 2.0$ s are very similar to those under steady flow conditions (see Fig. 4).

Fig. 7 shows the variation of momentary deposition fraction (i.e., fraction of deposited mass) during one puffing cycle, which is defined as the ratio of deposited mass at each time interval (0.02 s) to total inhaled mass at the mouth inlet over the entire cycle. As expected, the variation of momentary deposition fraction has a similar trend as the flow rate; because, the inhaled vapor mass at each time level is proportional to the flow rate. However, apparent delays can be observed between deposition and airflow because vapors cannot transport instantaneously into the deeper lung airways, especially

![Graphs showing variations of momentary deposition fraction during one PREP-puffing cycle.](image)

Fig. 7. Variations of momentary deposition fraction during one PREP-puffing cycle: (a) Acrolein vapor deposition in different airway regions; and (b) acetaldehyde vapor deposition in different airway regions.
during puffing at a relatively low flow rate. The delay time into a specific airway segment can be estimated, using the traveling speed and travel distance, as:

\[ \int_0^{t_{\text{delay}}} u(t) \, dt = L \]

where \( t_{\text{delay}} \) is the delay time of vapor transport into the specific airway segment, \( u(t) \) is instantaneous cross-sectionally averaged velocity, and \( L \) is the distance starting from the inlet. As shown in Fig. 7, the deeper the extent into the lung, the longer the delay time is. The delay time at different airway regions is given in Table 2, being almost the same for acrolein and acetaldehyde.

### Table 2
Transport delay time of vapors in different airway regions.

<table>
<thead>
<tr>
<th>Region</th>
<th>Oral</th>
<th>Oropharynx</th>
<th>Larynx</th>
<th>Trachea</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>B4–B9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delay time (s)</td>
<td>0.06</td>
<td>0.1</td>
<td>0.2</td>
<td>0.32</td>
<td>0.64</td>
<td>0.76</td>
<td>1.02</td>
<td>1.04</td>
</tr>
</tbody>
</table>

Fig. 7. Variations of momentary deposition fraction during one post-puffing cycle: (a) Acrolein vapor deposition in different airway regions; and (b) acetaldehyde vapor deposition in different airway regions.
Fig. 7 also indicates that the flow rate near the end of inspiration rapidly decreases to zero, but the fraction of deposited mass drops only slightly. This is because of the continuous deposition of lingering vapors occurring over the previous time intervals.

Fig. 8 depicts the variation of momentary deposition fraction during one post-puffing cycle. A sine-wave is assumed for post-puffing (being close to a normal inhalation waveform), i.e.,

$$Q(t) = Q_{\text{max}} \sin\left(\frac{\pi t}{2}\right)$$  \hspace{1cm} (12)
Clearly, at the much higher velocities the delay times for vapors in various segments are much shorter when compared to just puffing, especially in the oral airways.

3.4. Deposition comparisons between steady and transient conditions

The total and regional deposition fractions of acrolein and acetaldehyde vapors in the upper airway model for transient puffing are compared with those for steady inhalation in Fig. 9. The matching flow rate is defined as the average between the mean and maximum flow rates, i.e., \( Q_{\text{match}} = C(Q_{\text{mean}} + Q_{\text{max}}) \) and \( C = 0.5 \) (see Zhang and Kleinstreuer 2004). The values of different steady flow rates for different transient inhalation modes are given in Table 3.

As shown in Fig. 9, the total deposition fractions at three steady flow rates related to puffing are quite similar for two vapors, i.e., around 95% to 99%. But the deposition fractions under transient puffing are lower than those under steady inhalation conditions with three different flow rates, which are about 79% for acrolein vapor, and 83% for acetaldehyde. This is mainly due to the time delay for vapors penetrating deeper into the lung. This phenomenon can be further observed for regional deposition, as shown in Fig. 9b and c. Clearly, with larger time delay in the deeper lung region, the regional deposition fractions for transient puffing are much lower than those under corresponding steady flow conditions.

A deposition correction factor \( C_{DF} \) is proposed to account for the reduced deposition at each airway region during transient puffing. Specifically, when assuming equivalent steady flow per cycle, the delay of vapor transport during transient flow results in the reduction of inhaled vapors in various regions. So, a correction factor can be employed to represent the reduced vapor concentration at the inlet for the specific region with transport delay, i.e.,

\[
C_{DF} = 1 - \frac{\int_0^{t_{\text{delay}}} Q(t)Y_{\text{in}}(t)dt}{\int_0^T Q(t)Y_{\text{in}}(t)dt} \tag{13}
\]

and

\[
DF_{\text{transient}} = C_{DF} \cdot DF_{\text{steady,match}} \tag{14}
\]

where \( t_{\text{delay}} \) is the delay time of vapors to the specific region (see Table 2) and \( T \) is the cycle period. Obviously, it is computationally very advantageous to run steady-state simulations, rather than transient ones, and obtain very similar vapor-deposition results. The correction factor and modified regional deposition fractions for two PREP vapors are given in Table 4. As expected, the modified deposition values based on the correction factor for the matching (steady) flow-rate case are very close to those under realistic transient puffing for most parts of the tract as well as the entire region.
A relatively large difference still can be observed in the lower region B4 to B9, because a unique delay time and correction factor are employed for all individual bifurcations in the entire region of B4 to B9.

As shown in Fig. 10, the total and regional deposition fractions of acrolein and acetaldehyde vapors in the upper airway model for transient post-puffing (normal inhalation) are compared with those for steady inhalation as well. The situation differs measurably, depending on the mode of puffing. During normal transient inhalation, high flow velocities largely reduce the transport delay time of vapors into the deeper airways. The effect of transport delay is minor on both regional and total deposition in the upper airways from oral cavity to B9. Hence, both total and regional deposition fractions of vapors for cyclic inspiratory flow are very close to those for constant flow with the matching flow rate. As previously stated, vapor transport and deposition during transient inhalation are not synchronized with the variations in flow rate.

Fig. 10. Comparisons of deposition fractions for transient normal inhalation and constant flow with different flow rates: (a) Vapor deposition in the entire upper airway model; (b) acrolein vapor deposition in different airway regions; and (c) acetaldehyde vapor deposition in different airway regions.
For example, lingering vapors near the end of the inspiration cycle still deposit while the flow rate approaches zero (see Fig. 8). Such unsynchronized behavior causes the deposition fraction for transient inhalation to be different from the constant flow and vapor transport/deposition at the corresponding mean flow rate. It can also be seen from Fig. 10 that vapor deposition fractions for transient inhalation are lower than those for constant flow (at the mean flow rate) and higher at the maximum flow rate. However, the vapor deposition fractions for transient inhalation can be reasonably approximated when employing the matching flow rate approach. This is also consistent with previous studies for vapor deposition in the human nasal cavity (Shi et al., 2006), in an idealized human oral airway model (Zhang et al., 2004), and in nasal cavities of rats (Jiang & Zhao, 2010).

3.5. Deposition comparisons between PREP and CC vapors

There are two major differences for some PREP vapors and conventional cigarette (CC) vapors during transient puffing. The first is that the initial and inlet concentrations at the mouth inlet are different for PREPs and CCs. The second difference is the puffing waveform. The different inlet and initial vapor concentrations naturally influence actual vapor mass deposition.

![Fig. 11. Variations of momentary deposition fraction during one CC puffing cycle: (a) Acrolein vapor deposition in different airway regions; and (b) acetaldehyde vapor deposition in different airway regions.](image-url)
depositing on airway wall surfaces; however, they may not affect the vapor deposition fractions. In this section the effects of puffing waveforms on total and regional vapor deposition fractions in the upper airway model are discussed.

Fig. 11 depicts a typical CC-puffing waveform (see Dickens et al., 2009) and the variation of momentary deposition fractions of acrolein and acetaldehyde vapors during one puffing cycle. Clearly, the relationship between the momentary deposition fraction and flow rate is similar for PREPs and CCs. However, the transport delay times (cf. Tables 5 vs. 2) are different because of different mean and maximum flow rates (see Table 3) as well as the puffing-time period. Clearly, CC vapors cannot reach deeper airway regions, i.e., beyond B3.

The deposition correction factors for CC-vapor deposition are given in Table 5 as well. Again, CC-vapor deposition fractions for transient puffing can be represented by the modified deposition values with correction factors for constant flow at the corresponding matching flow rate (see Table 6).

Fig. 12 compares regional deposition fractions of acrolein and acetaldehyde vapors under transient PREP- and CC-puffing conditions. Of interest is that the deposition fractions in the oral and oropharynx are close; although, the inhalation waveforms are quite different. This is because the deposition decrease, due to longer vapor transport delay, offsets the deposition increase due to a lower flow rate (i.e., longer residence time). However, beyond the larynx the vapor deposition fraction for CC puffing becomes lower and lower than for PREP puffing because the travel delay effect becomes more and more dominant. So, the total deposition fraction in the upper airways for transient PREP puffing ($DF_{acrolein} = 79\%$, $DF_{acetaldehyde} = 83\%$) is higher than for transient CC puffing ($DF_{acrolein} = 68\%$, $DF_{acetaldehyde} = 74\%$). In summary, compared with CC puffing, PREP puffing implies a higher flow rate and longer period. Hence, the vapor can penetrate and deposit more in the deeper lung airways under transient PREP-puffing conditions.

**Table 5**
Transport delay time of CC vapors in different airway regions.

<table>
<thead>
<tr>
<th>Region</th>
<th>Oral</th>
<th>Oropharynx</th>
<th>Larynx</th>
<th>Trachea</th>
<th>B1</th>
<th>B2</th>
<th>B3</th>
<th>B4–B9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delay time (s)</td>
<td>0.21</td>
<td>0.31</td>
<td>0.39</td>
<td>0.55</td>
<td>0.95</td>
<td>1.11</td>
<td>1.35</td>
<td>&gt; 1.7</td>
</tr>
<tr>
<td>Correction factor</td>
<td>0.943</td>
<td>0.873</td>
<td>0.804</td>
<td>0.644</td>
<td>0.253</td>
<td>0.15</td>
<td>0.05</td>
<td>0</td>
</tr>
</tbody>
</table>

**Table 6**
Regional deposition of CC vapors under transient puffing and steady matching flows.

<table>
<thead>
<tr>
<th>Region</th>
<th>Acrolein vapor deposition</th>
<th>Acetaldehyde vapor deposition</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Steady matching flow</td>
<td>Steady matching flow corrected</td>
</tr>
<tr>
<td>Oral</td>
<td>0.2411</td>
<td>0.2274</td>
</tr>
<tr>
<td>Oropharynx</td>
<td>0.2219</td>
<td>0.1937</td>
</tr>
<tr>
<td>Larynx</td>
<td>0.2041</td>
<td>0.1641</td>
</tr>
<tr>
<td>Trachea</td>
<td>0.1163</td>
<td>0.0749</td>
</tr>
<tr>
<td>B1</td>
<td>0.0493</td>
<td>0.0125</td>
</tr>
<tr>
<td>B2</td>
<td>0.0416</td>
<td>0.0062</td>
</tr>
<tr>
<td>B3</td>
<td>0.0268</td>
<td>0.0013</td>
</tr>
<tr>
<td>B4–B9</td>
<td>0.0748</td>
<td>0.0000</td>
</tr>
<tr>
<td>Total</td>
<td>0.9758</td>
<td>0.6801</td>
</tr>
</tbody>
</table>

**Fig. 12.** Comparisons of regional vapor deposition fractions for transient PREP puffing and CC puffing.
3.6. Vapor deposition correlations

As given in Eq. (9), the vapor deposition efficiency \( (DE) \) in a given airway segment can be calculated as a function of species diffusivity in air, airway wall absorption coefficient, mass transfer coefficient, airway wall surface area, and local inlet flow rate. Hence, obtaining the respiratory mass transfer coefficient, \( h_m \), is critical in quantitatively predicting the regional deposition of vapors. Traditionally, the mass transfer coefficient in terms of non-dimensional Sherwood number \( (Sh) \) is a function of Reynolds number \( (Re) \) and Schmidt number \( (Sc) \). Zhang & Kleinstreuer (2011a) developed a set of generalized \( Sh = fct.(Re, Sc) \) equations based on a combined nasal-oral-tracheobronchial airway model for normal inspiratory flow rates. However, the oral and tracheobronchial airways in that study are not subject-specific, i.e., they were relatively idealized. Furthermore, the flow rates considered in Zhang & Kleinstreuer (2011a) are not in the puffing flow regimes. Hence, based on the present computer simulation data, the Sherwood-number for vapors of acrolein and acetaldehyde in different segments of subject-specific upper airways are also correlated as a function of local Reynolds numbers during puffing to post-puffing (see Tables 7 and 8). It should be noted that these correlations are for constant flows, and that the realistic deposition values can be inferred based on constant matching flows with time delay corrections.

**Table 7**

Correlation of \( Sh \)-number of acrolein vapor \( (\bar{D}_a = 0.105 \text{ cm}^2/\text{s}) \) as a function of local inlet Reynolds number \( (Re) \) in segments of human upper airways.

<table>
<thead>
<tr>
<th>Airway segment</th>
<th>Correlation equation * ( a )</th>
<th>( r^2 )</th>
<th>Parameter range ( (Re) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity and oropharynx</td>
<td>( Sh = 0.155Re^{0.7} )</td>
<td>0.992</td>
<td>100–3500</td>
</tr>
<tr>
<td>Larynx</td>
<td>( Sh = 0.221Re^{0.647} )</td>
<td>0.998</td>
<td>100–3500</td>
</tr>
<tr>
<td>Trachea</td>
<td>( Sh = 0.0768Re^{0.744} )</td>
<td>0.990</td>
<td>100–3500</td>
</tr>
<tr>
<td>B1</td>
<td>( Sh = 0.479Re^{0.536} )</td>
<td>0.993</td>
<td>100–3200</td>
</tr>
<tr>
<td>B2</td>
<td>( Sh = 0.521Re^{0.522} )</td>
<td>0.935</td>
<td>60–2500</td>
</tr>
<tr>
<td>B3</td>
<td>( Sh = 0.751Re^{0.473} )</td>
<td>0.918</td>
<td>30–2300</td>
</tr>
<tr>
<td>B4–9</td>
<td>( Sh = 0.577Re^{0.401} )</td>
<td>0.988</td>
<td>20–800</td>
</tr>
</tbody>
</table>

* Trachea diameter is considered as the characteristic length for segments of oral cavity, oropharynx, larynx and trachea; while diameter of parent tube is the taken as the characteristic length of the bronchial airway bifurcation.

**Table 8**

Correlation of \( Sh \)-number of acetaldehyde vapor \( (\bar{D}_a = 0.124 \text{ cm}^2/\text{s}) \) as a function of local inlet Reynolds number \( (Re) \) in segments of human upper airways.

<table>
<thead>
<tr>
<th>Airway segment</th>
<th>Correlation equation * ( a )</th>
<th>( r^2 )</th>
<th>Parameter range ( (Re) )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral cavity and oropharynx</td>
<td>( Sh = 0.150Re^{0.7} )</td>
<td>0.995</td>
<td>100–3500</td>
</tr>
<tr>
<td>Larynx</td>
<td>( Sh = 0.203Re^{0.653} )</td>
<td>0.998</td>
<td>100–3500</td>
</tr>
<tr>
<td>Trachea</td>
<td>( Sh = 0.069Re^{0.747} )</td>
<td>0.988</td>
<td>100–3500</td>
</tr>
<tr>
<td>B1</td>
<td>( Sh = 0.470Re^{0.531} )</td>
<td>0.993</td>
<td>100–3200</td>
</tr>
<tr>
<td>B2</td>
<td>( Sh = 0.486Re^{0.523} )</td>
<td>0.939</td>
<td>60–2500</td>
</tr>
<tr>
<td>B3</td>
<td>( Sh = 0.725Re^{0.470} )</td>
<td>0.912</td>
<td>30–2300</td>
</tr>
<tr>
<td>B4–9</td>
<td>( Sh = 0.480Re^{0.517} )</td>
<td>0.992</td>
<td>20–800</td>
</tr>
</tbody>
</table>

Fig. 13. Calculated Sherwood-number of acrolein vapor and correlation curves as a function of local Reynolds number in segments of human upper airways.
Fig. 13 depicts the $Sh - Re_{local}$ correlation curves and the simulated data points for acrolein vapor. The contribution of convection (i.e., Re-number) on mass transfer can also be observed from these graphs. Clearly, the stronger the convection (higher Re-numbers), the higher is the mass transfer. The flow structures and airway geometric features also have an important effect on vapor mass transport. Specially, the $Sh = Sh(Re)$-relationship may be different at various airway regions because of the interactions among local geometric features, flow turbulence (starting typically after the throat), and upstream deposition.

3.7. Effect of saturable pathway elimination

As mentioned in Section 2.2, the saturable pathway elimination can influence vapor absorption in the mucus and tissue layers. As described by the boundary conditions (2a), (4), and (5), vapor deposition with the saturable pathway elimination is dependent on the reaction and metabolism properties (e.g., $K_f$ and $K_m$) of vapors in the tissue. Hence, the accurate simulation of vapor absorption with reaction and metabolism must be based on reliable properties. However, there are only a very few reaction/metabolism property data sets available for vapors of acteldehyde and acrolein, especially for humans. In fact, the Michaelis-Menten parameters for the same vapor vary a lot in different publications. For example, Schroeter et al. (2008) argued that the best $K_m$-value for acrolein vapor in humans and rats is 0.5 mg/m$^3$, based on the match between their mass transfer simulations and measured deposition in rats. However, Mitchell & Petersen (1989) measured a $K_m$-value of acrolein vapor in rats being about 4600 mg/m$^3$.

Fig. 14 depicts the total deposition fraction of acetaldehyde vapor in the human upper airway model from mouth to generation G9 at a steady puffing rate of $Q = 37.5$ mL/s. The reaction/metabolism properties used in these simulations are given in Table 9. As the inlet concentration increases, the tissue concentration increases as well. After the local/regional tissue concentrations reach the saturable plateau, the uptake of vapor at this region decreases. For acetaldehyde vapor under a puffing flow rate of 37.5 mL/s, the vapor deposition fraction drops about 13% when the inlet concentration increases from zero to 200 ppm. After that, the deposition hardly changes with the inlet concentration.

In the transient absorption process, the tissue concentration may not reach the saturable plateau as rapidly as in the quasi-steady case and the tissue concentration can also be depleted somewhat during exhalation and pausing (Asgharian et al., 2011). In this case, the effect of inlet vapor concentration on vapor deposition can decrease.

3.8. Limitations of the present study

As mentioned, in this study quasi-steady radial mass transfer in the mucus layer was employed, assuming the concentration below the mucus layer to be zero with rapid removal of vapor molecules by the underlying tissue. Recently, Tian & Longest (2010a,b,c) developed an air-mucus-tissue-blood (AMTB) boundary condition, which can predict different

![Fig. 14. Effect of inlet concentration on the total deposition of acetaldehyde vapor in the entire upper airway model (steady state, $Q = 37.5$ mL/s).](image)

Table 9

<table>
<thead>
<tr>
<th>$K_f$ ($s^{-1}$)</th>
<th>$K_m$ (mg/m$^3$)</th>
<th>$V_{max}/V_t$ (mg/m$^3$/s)</th>
<th>$H_t$ ($\mu$m)</th>
<th>$D_t$ (cm$^2$/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.03573 $^a$</td>
<td>1320 $^b$</td>
<td>$1.214 \times 10^{4b}$</td>
<td>60 $^c$</td>
<td>$0.47 \times 10^{-5}^d$</td>
</tr>
</tbody>
</table>

$^a$ Asgharian et al. (2012).
$^b$ Teeguarden et al. (2008).
$^c$ ICRP (1994).
$^d$ Calculated as one-third value of mucus (Tian & Longest, 2010b).
absorption concentrations in each layer for realistic transient flux conditions. In their first paper they also stressed that what is absorbed by the mucus may not be a good representation of tissue and blood exposures to the compound. In the follow-up paper, Tian & Longest (2010b) simulated the deposition of acetaldehyde vapor in an oral airway model from mouth to trachea. Their simulation results showed that the deposition fractions in the oral airway (under steady inhalation of 30 L/min) were 29.87% considering transient absorption conditions in mucus-tissue-blood layers. It has to be noted that they had used a rather low diffusivity of 0.08 cm²/s. With the same diffusivity (0.08 cm²/s) and air-mucus partition coefficient (320) as employed by Tian & Longest (2010b), the deposition from the mouth to the trachea in the present airway model with the present airway wall boundary condition is 28.22%. Clearly, this deposition value is very close to theirs for transient absorption in both mucus and tissue layers (29.87%); although, the geometries of the two studies were different. It implies that the present quasi-steady mucus absorption boundary condition is a good approximation of transient mucus-tissue boundary conditions in modeling vapor deposition in the mucus layer. In addition, Tian & Longest (2010b,c) also demonstrated that for a steady wall flux model, vapor absorptions in mucus, tissue and blood are all the same, which are dramatically different when transient flux is considered. It should be noted that for the steady multi-layer model of Tian & Longest (2010b,c), the airway wall absorption parameter K in the mucus layer was defined as $K = \frac{D_m}{\bar{D}_a} \beta H_m (1 - \bar{C}_m)$ with $\bar{C}_m = H_t D_m/\bar{D}_a \alpha_m H_m + H_t \bar{D}_m$ and $\bar{C}_m = 0.9448$ for acetaldehyde vapor. However, in the present single mucus-layer model the absorption parameter $K$ is $K = \frac{D_m}{\bar{D}_a} \beta H_m$, which is much larger than that in the multi-layer model of Tian & Longest (2010b,c). The quite different K-values for steady flux conditions in these two studies result in a large difference of deposition in the mucus layer. However, to consider transient absorption of vapors during both inhalation and exhalation (Tian & Longest, 2010c) is helpful to more accurately predict the vapor deposition in air-mucus-tissue-blood system.

As discussed in Section 3.7, the airway wall absorption presented in Sections 3.2–3.6 can be reduced for cases of high inlet concentrations due to saturable pathway elimination. However, as indicated in Eqs. (2), (4) and (5), the vapor deposition with saturable pathway elimination is still a function of the airway wall absorption parameters K; but, the K-values change with the vapor reaction/metabolism properties in the tissue. As reported by Zhang & Kleinstreuer (2011a), the effects of K-values on respiratory mass transfer coefficients in the airways are minor. Hence, the correlations given in Tables 7 and 8 are still effective for estimating vapor deposition, considering saturable pathway elimination with reliable properties. In addition, this study focuses on the comparison of vapor deposition in the airway wall between steady and transient inhalation. The transient boundary conditions with or without saturable pathway elimination should not change the relationship between steady and transient vapor transport in the air and deposition from airway lumen to the wall. However, further studies are still required to investigate the interaction among patient-specific airway geometries, transient inhalation/exhalation of inhaled vapor, and transient absorption in patient-specific mucus-tissue-blood layer with reaction/metabolisms.

The limitations of this study include rigid airway walls and uniform pressure outlet conditions. Hence, effects of moving lung airways and more physiologically corrected outlet conditions will be considered in future studies.

4. Conclusions

The deposition of four selected tobacco-smoke vapors, i.e., acrolein, 1,3-butadiene, acetaldehyde and CO, in a subject-specific airway model under both transient puffing and post-puffing as well as constant flow conditions have been analyzed, employing a realistic and accurate computer simulation model. Both conventional cigarettes (CCs) and potential reduced exposure products (PREPs) with associated inhalation waveforms were considered. The following conclusions can be drawn:

Vapor deposition is strongly influenced by its property values. As almost insoluble species in the mucus layer, the deposition of butadiene vapor and CO is very low in the upper airways. The remaining vapors may penetrate further and deposit in deeper lung regions. As medium-to-high soluble vapors, acrolein and acetaldehyde have very large deposition values in the human upper airways, i.e., from mouth to generation G9. Specifically, the total deposition fractions in the upper airway model during single transient PREP puffing are about 79% for acrolein vapor and 83% for acetaldehyde vapor, ignoring the effect of saturable pathway elimination.

The deposition result for steady matching flow is a computationally efficient and good conservative estimate when compared to the actual deposition fraction under transient normal inhalation condition. However, the vapor transport delay may largely reduce vapor deposition for transient puffing. A correction factor has been proposed to incorporate vapor transport delay, in order to calculate efficiently actual deposition fraction values under transient puffing condition.

Compared to CC puffing, PREP puffing behavior may exhibit a higher flow rate and longer inhalation period. Hence, the vapor can penetrate and deposit more in the deeper lung airways during transient PREP puffing. Specifically, the total deposition fraction in the upper airways for a single transient PREP-puffing action (i.e., $D_{\text{acrolein}} = 79\%$, $D_{\text{acetaldehyde}} = 83\%$) is higher than for transient CC puffing ($D_{\text{acrolein}} = 68\%$, $D_{\text{acetaldehyde}} = 74\%$). It clearly implies that the puffing waveform can alter the local and regional vapor depositions.

A set of deposition correlations have been developed to estimate the deposition of acrolein and acetaldehyde vapors in different segments of the human upper airways under both puffing and normal inhalation (i.e., post-puffing) conditions.
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