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The effects of geometry on airflow in the acinar region of the human lung

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Abstract

Understanding flow phenomena in the pulmonary acinus is important for predicting particle transport and deposition and hence, in designing effective drug delivery strategies for the lung. In the current study, a three-dimensional honeycomb-like geometry involving a central airspace and surrounding alveoli is used to represent an alveolar duct and sacs. Numerical results predict that flow in the presence of wall motion is characterized by the presence of a developing recirculation region within the cavity and by a flow entrainment region indicative of the weak nature of interaction between duct and cavity. Under the normal breathing condition (2.5 seconds) and volumetric expansion (~25%) considered here, recirculation disappears for $Re < 0.6$. Alveolar flow in higher generations (at lower Reynolds number) results from significantly higher entrainment of the ductal flow, and does not exhibit any recirculation. In an asymmetric arrangement of the alveolar cluster, topological differences in cavity result in significant differences in the size of recirculation and the size of entrainment region within the alveoli of the same acinar generation, indicative of a non-uniform alveolar ventilation. The flow in the terminal alveolar sac is non-recirculating and not affected by variation in geometrical features.

Keywords

Acinar fluid dynamics; Low Reynolds number flow; Finite Element; Open cavity flow; Recirculation

1. Introduction

The human airway architecture is categorized into conducting and respiratory airways; dichotomously branching an average of twenty-three generations starting from the trachea. Alveoli are the air pockets that occupy a part of, or completely cover the walls of respiratory

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Conflict of Interest

There is no conflict of interest for the authors of the manuscript titled “The effects of geometry on airflow in the acinar region of the human lung”.

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airways. An acinus consists of the entire region of alveoli and alveolated ducts that are distal to a single terminal bronchus, on average beyond the fifteenth generation (Haefeli-Bleuer & Weibel, 1988; Finlay, 2001). The acinus is therefore comprised of respiratory airways and forms the functional tissue of the lung, or, the lung parenchyma. Understanding transport of particles in the acinar region is useful in designing effective pharmaceutical aerosol or other drug delivery strategies, as well as treating disease with compromised lung function (Dailey & Ghadiali, 2007). The deposition of particles is dependent on the flow by which they are transported, and the flow is dependent on alveolar geometries and ventilation conditions. Thus, faithful portrayal of close-to-reality geometry *in silico*, and solving for air flow using realistic breathing conditions are two crucial elements in understanding alveolar flow phenomena. In contrast to the progress achieved in upper airway reconstruction, the success in three-dimensional (3D) imaging of lung parenchyma has been limited by its size and accessibility (Tsuda et al., 2008). Recent studies have attempted to reconstruct the 3D image-based alveolar structure (Namati et al., 2007, Popp et al., 2007 and Tsuda et al., 2008), and define the dynamics of alveolar mechanics (Carney et al., 2005).

In their classical paper, Davidson & Fitz-Gerald (1972) studied flow patterns in spherical, cylindrical and ellipsoidal sections as representative of lung units. Tsuda et al. (1995) performed simulations on simplified torus surrounding a central channel. They observed a saddle point associated with the recirculating flow within the alveoli. Later, Henry et al. (2002) expanded this axi-symmetric model to 9-cell geometry and postulated the series of vortices and associated saddle points as the source of flow-enhanced mixing.

Unsteady 3D simulation efforts of fluid flow in the alveolated ducts and sacs in the past decade have been scarce. Darquenne and Paiva (1996) adopted a simplified model of the alveolated duct using sections of an annular ring around a central channel. Harrington et al. (2006) used a similar representation, but compared the effect of acinar branching using bifurcation models. Haber et al. (2000) performed analytical investigation using a spherical cap to represent a single alveolus. The acinar flow was observed to induce mixing when there was phase lag between the ductal and acinar flows. Some of the later works also used self-similar breathing motion although using 3D cavity to represent an alveolus (Haber et al., 2003; Sznitman et al., 2007a). A recent effort towards simulation in the acinar tree was carried out by Sznitman et al. (2007b, 2009) who followed Fung (1988) to create an assemblage with 190 polyhedral units.

Given the limitations and challenges posed in view of modeling and assumption of alveolar dynamics, earlier efforts have relied on either axi-symmetric geometry or complex branching structure in two-dimensions under static loading. Although technologies are emerging for acquiring alveolar geometries and constructing image-based alveolar models (Tsuda et al., 2008), challenges arise in deforming these models and imposing boundary conditions for computation due to lack of knowledge and data on alveolar mechanics. To bridge the gap between image-based and simplified alveolar models, it is imperative to understand the transport phenomena using idealized, but more realistic, controlled geometries that account for the asymmetric feature of alveolar geometry. The present study aims to examine fluid flow in the acinar region using realistic, honeycomb-like polygonal geometries under imposed rhythmic breathing at varying Reynolds number. Specific effort is made to highlight the details and the role of the geometry chosen in view of fluid exchange to investigate duct-cavity interaction.

The remainder of the article is divided into three sections. Section 2 briefly provides the numerical methodology. Section 3 presents results of computed flow for three cases. Section 4 discusses and summarizes the results.

2. Methodology

The problem of alveolar flow is solved using the incompressible Navier-Stokes equations in a moving Arbitrary-Lagrangian Eulerian (ALE) grid setting (Sung et al., 2000; Quarteroni et al., 2000; Xia and Lin, 2008) as given below in index form.

$$\frac{\partial u_i}{\partial x_i} = 0$$

$$\frac{\partial u_i}{\partial t} + (u_j - \tilde{u}_j) \frac{\partial u_i}{\partial x_j} = -\frac{1}{\rho} \frac{\partial P}{\partial x_i} + \frac{\partial}{\partial x_j} \left(\nu \frac{\partial u_i}{\partial x_j} \right)$$

Here, u_i is the i -component fluid velocity, $\tilde{u}_i$ is the i -component mesh velocity, P is the fluid pressure, ν is the kinematic viscosity of air, and $(x_1, x_2, x_3) = (x, y, z)$. The system of equations is split using a fractional four-step method (Choi et al., 1997; Yue et al., 2003; Lin et al., 2005) and then discretized spatially using an equal-order finite element method. The domain is discretized using tetrahedral elements with a smallest element having side of $5\mu\text{m}$. A single alveolar unit consists of $\sim 40,000$ elements. The Reynolds number is measured at peak

inspiration: $\text{Re} = UD/\nu$ where U is the peak inspiration speed, $D = \sqrt{4A/\pi}$ is the effective diameter of the duct and A is the duct cross-sectional area. One may also define a RMS-Reynolds number $\text{Re}_{\text{RMS}} = \bar{U} \bar{D}/\nu$, where $\bar{U} = U/\sqrt{2}$ and $\bar{D} = (D_{\text{max}} + D_{\text{min}})/2$ are time averaged values of velocity and diameter, respectively. The max min Womersley number,

$W_o = \bar{D} \sqrt{\omega/\nu}$ (where $f = \omega/2\pi = 1/T$ is the frequency and T is the breathing period) is 0.22 for Cases I and II, and is 0.12 for Case III. The breathing period chosen here, of 2.5 seconds (at 24 breaths/minute) is similar to earlier alveolar studies (Tsuda et al., 1995; Henry et al., 2002). The equations are normalized using the alveolus mouth dimension L_A as shown in the isolated model alveolus of Fig. 1, peak velocity U , and ρU^2 for pressure. At $\text{Re}=1$, for example, $U=3.21$ cm/s corresponds to tracheal flow rate $Q_0=0.25$ liters/second by assuming that flow rate varies with generation number, n , as $Q(n)=Q_0/2^n$, based on an idealized dichotomous lung.

The longitudinal path length of the acinar region from an average 16th to 23rd generation may vary between 5,000–12,000 μm depending on the generation in which it terminates (Haefeli-Bleuer & Weibel, 1988). Although during respiratory ventilation the airflow has a single unobstructed path, the problem is dealt with using geometrical structures representative of regions along the acinar tree (Fig. 1). The flow rate at the duct entrance is denoted by Q_D , the flow rate associated with cyclic expansion and contraction of the walls of a single alveolus is Q_A , and the flow rate associated with wall motion of the duct is Q_B . If the volume of an alveolar model is $\forall$, the total flow rate caused by alveolar wall motion is $\dot{\forall} = M Q_A + Q_B$, where M is the number of alveolar sacs in the model. The relationship between Q_D and $\dot{\forall}$ along the acinar tree is illustrated in Fig. 1(a–c). Tsuda et. al. (1995) used Q_A/Q_D as a measure of the fractional loss of inhaled volume. Due to alveolar expansion, this amount is displaced from the lumen and is unavailable to latter generations (Sarangapani and Wexler, 2000). Case I corresponds to respiratory bronchioles which have occasional alveolar units. The model for Case II is an alveolar duct lined completely with alveoli asymmetrically and represents the lung units in generation 18–22. Case III represent closed-end alveolar sacs. The current treatment uses a cluster of truncated octahedron to obtain a nearly space filling polyhedra (Tawhai & Burrowes, 2003; Burrowes, 2005). Fig. 2(a) shows a micrograph image cross-section of alveoli surrounding an alveolar duct with demarcated boundaries of septa. As shown by the 3D schematic in Fig 2(b), the structured arrangement of alveolar wall around the axial channel rationalizes the choice of the honeycomb-like polygonal model.

A sinusoidal flow rate is specified at one end of the duct while a Neumann boundary condition is employed at the other. Homothetic wall motion, where corresponding sides of the duct and

alveolar wall remain parallel in a geometric expansion or contraction (Gatto et al., 2004), is prescribed. The wall motion is determined by the prescribed temporal variation of the volume of the alveolar model $\forall$. The time histories of normalized flow rate (Q_D/Q_{Dmax}) and model volume ($\forall/\forall_{min}$) are shown in Fig. 3 to produce a 25% volumetric expansion ratio, i.e. $\forall/\forall_{min} = 1.25$ (Henry et al., 2002). Note that Q_D and $\forall$ are temporally synchronized. Table I provides a list of input parameters for all the simulation cases considered here. The computations were performed and tested for dependence on mesh and timestep.

3. Results

3.1 Validation

Cellular flows are a classical problem in the literature (Pozrikidis, 1994; Shen & Floryan, 1985; Pozrikidis, 2000; Horner et al., 2002). The alveolar cavity poses a disturbance to the outer steady (or oscillating) shear flow. The problem of steady unbounded shear flow over a cavity (opening angle of $\pi/2$ with mouth twice the cavity depth) was studied by Pozrikidis (1994). The geometry demonstrates the characteristics of recirculating flows in the presence of a cavity. The 3D flow structure (Fig. 4(a)) and the location of the recirculation center at $\sim 45\%$ of the cavity depth (Fig. 4(b)) match well with literature. The velocity field is extracted onto a chosen plane resulting in a two-dimensional (2D) streamline plot. Wall shear stress (Fig. 4(c)) is plotted along the wall trace with the origin of arclength set at the entrance of the plane containing the cavity. The wall shear stress, in Fig. 4(c) at the corner (which is a singularity point) is under-predicted because of the limitation in resolution of the singularity of the flow, although the flow profiles far away remain unaffected.

3.2 Case I

In geometry involving smooth or sudden expansions in a main channel, separation may occur due to net effect of pressure gradients in the outer flow and due to the sudden expansion. When the flow is steady, two flow regions appear: one within the cavity and the other as bulk flow, separated by a distinct 'separatrix' which attaches itself to parabolic points on the wall (Horner et al., 2002).

Fig. 5(a) presents the geometry considered (Case I in Fig. 1) that represents the respiratory bronchiole. The mean diameter of the air carrying duct is $\sim 500 \mu\text{m}$ (Haefeli-Bleuer & Weibel, 1988). The length of the duct is $\sim 500 \mu\text{m}$ on either side of the alveolus. In the presence of prescribed wall motion and oscillating shear flow, the flow structure is different from that of steady flow. Figs. 5(b–d) show the flow structures for $Re=2, 1$ and 0.52 , respectively. For $Re=2$ and 1 , the combined effects of oscillating ductal flow and rhythmic motion of the wall cause the fluid to recirculate (see 3D and 2D structures in Figs. 5(b) and (c), respectively) near the proximal wall (the wall closest to the mouth during inspiration) of the cavity. The size of the recirculation is dependent on the Reynolds number. For $Re=0.52$, there is no re-circulating flow formed inside the alveolus (Figs. 5(b) and (c)). The inclusion of alveolar wall motion weakens the wall attachment point allowing convective interaction between the cavity and duct in the form of an entrainment region, denoted by "E" in Fig. 5(c) between the bold solid streamline and the ductal wall. The time rate of entrainment is Q_A . In a Lagrangian sense, a fluid parcel/tracer placed within the entrainment region will be drawn into the cavity. The width of the entrainment region changes during breathing; the extent of its unsteadiness is characterized by the Womersley number. As $Wo < 1$, the unsteadiness is not pronounced except at times when the flow rate is small, for example, at the start of inhalation (Finlay, 2001). The entrainment region is a function of Re : for example, it is confined to $\sim 4\text{--}7 \mu\text{m}$ for $Re=2$, $\sim 9\text{--}14 \mu\text{m}$ for $Re=1$, and $\sim 19\text{--}26 \mu\text{m}$ for $Re=0.52$ near the end of inspiration.

During exhalation, the flow reverses in direction, but the motion of the alveolar wall is reversed, causing contraction of the geometry. Counter-intuitively, the fluid still recirculates in the proximal region within the cavity; although, the sense of flow about the recirculation is opposite to that during inspiration, being consistent with Tsuda et al. (1995). The presence or absence of recirculation is an important determinant of the nature of mixing of fluid particles. It is known that, even in Stokes flows, the presence of recirculation can result in considerable stretching and folding of material interfaces (Ottino, 1989; Anderson et al., 1999).

Fig. 5(d) shows the contours of velocity magnitude in the yz-plane near the end of inspiration. The flow in the cavity is an order of magnitude smaller than the bulk flow, being similar to the observations by Sznitman et al. (2007a). Within the cavity, the flow near the proximal wall is slower corresponding to flow recirculation.

3.4 Case II

Fig. 6(a) is a model of an alveolar duct. Fig. 6(b) shows 3D flow structure near the end of inspiration, and an enlarged view is also displayed to show the 3D recirculation inside an alveolar sac. Fig. 6(c) plots selected streamline patterns projected onto the yz-plane for alveolar compartments, placed asymmetrically on opposite sides of the central air-carrying duct. The sizes of the entrainment region on the left and right asymmetric units vary $\sim 13\text{--}18\mu\text{m}$ and $\sim 27\text{--}32\mu\text{m}$, respectively resulting in different sizes of recirculation regions, although the alveolar mouth area and Re are the same. The differences in ventilation pattern arising out of asymmetry in the model geometry are clearly evident here. Fig. 6(c) illustrates this difference at $Re=1$ and 0.6 . Note that the recirculatory flow is absent in some alveoli in Fig. 6(c) at $Re=0.6$ with an accompanying larger entrainment region. That is, recirculation occurs in only 9 of the 18 alveoli. As mentioned earlier, the differences in entrainment and the presence (or absence) of recirculation translate to non-uniform transport and mixing of particles within the alveoli. With subsequent inhalation cycles and the added role of gravity, the effect on estimations of dispersion and deposition may be different from computations based on simplified (e.g., axisymmetric) models.

3.5 Case III

Alveolar sacs are the blind-ending terminal units of alveolar ducts. In contrast to the alveolar ducts they are covered with alveoli even on their terminal surface (Fig. 7(a)). Fig. 7(b) shows 3D flow structure near the end of inspiration. The flow within the alveoli does not recirculate during inhalation and exhalation. The flow is radial and a significant portion of the flow from the duct entrains the alveoli. Thus, the Q_A/Q_D ratio for case III is much larger than those of cases I and II (see Table 1). The entrainment region from the outer airway lumen into the alveoli in the first stack is $\sim 45\mu\text{m}$ and $\sim 53\mu\text{m}$ on the left and right asymmetric units, respectively. Hence, unlike case II asymmetry did not contribute significantly to any variation in flow ventilation pattern across the entire acinus in the last generation.

4. Discussions and Conclusions

Simulating flow in the eight peripheral generations of the human airway tree helps understand the mechanisms of mixing, transport and deposition. This effort aims to investigate transport in the acinar region using honeycomb-like polygonal geometries under imposed rhythmic breathing. Simulations were performed in the range, $0.05 \leq Re \leq 2$. It is observed that for $0.6 \leq Re \leq 2$ the flow structure is chiefly characterized by the presence of a developing recirculation region within the cavity as also noted earlier by Tsuda et al. (1995) and Henry et al. (2002) and others. Velocity magnitude inside the alveoli is an order of magnitude smaller than that in the duct. Net transport is the result of interaction between the entraining flow in the distal regions and the slowly recirculating flow near the proximal wall. For $Re < 0.6$,

recirculation disappears. The size of recirculation becomes a function of the peak Re and decreases in size with Re . Fig. 8 compares the Reynolds number in the current study and the observed recirculatory flow regime. The Reynolds numbers used by Tsuda et al. (1995) and Henry et al. (2002) have also been plotted for comparison although these references did not mention the corresponding generation for which the results are applicable. The Re_{RMS} correlation with presence of recirculation in our model roughly agrees with predictions of Tsuda et al. (1995) and Henry et al. (2002). Our model predicts that the recirculatory flow regime extends only upto the third acinar generation. The study of recirculation near the proximal corner at higher Reynolds number ($Re \geq 0.6$) is relevant only in the respiratory bronchioles. In the adult human lung, a significant percentage of the alveoli originate from alveolar ducts and sacs in the later generations of the respiratory airways where Re is lower and recirculation is absent. The net transport of particles from the particle-laden tidal air to the residual air occurs as a result of irreversible transfer processes, referred to as convective mixing (Heyder et al., 1988; Sarangapani and Wexler, 2000). The nature and origin of convective acinar mixing remain unclear (Darquenne and Prisk, 2005), but convective mixing is found to have an independent effect on particle deposition. The recirculation within the alveoli and its associated flow are believed to have a significant effect on convective mixing (Tsuda et al., 1995; Henry et al., 2002; Anderson et al., 1999), but may be restricted to the first three acinar generations.

The motion of the alveolar wall results in net transport into and out of the alveoli and the dynamics transport can be explained by the entrainment regions. The entraining flow characteristics are observed to be dependent on cavity topology and the asymmetry in arrangement of alveolus around the central duct. The entrainment region increases with decreasing Re , as we move deeper into the lung. The flow analysis using honeycomb-like alveolar structures captures the asymmetry in acinar airways in a given generation and the resulting non-homogeneous alveolar ventilation.

The differences in predicted alveolar ventilation and hence the variation in size of alveolar entrainment due to longitudinal asymmetry could be important determinants of particle transport, mixing and the resulting deposition, and hence calls for an accurate modeling of the alveolar structure and dynamics. Also in reality, the alveolated ducts consist of many generations of branching structure. While the use of accurate alveolar dynamics is not immediately realizable, the results presented here will inspire better representative models of the pulmonary acinus in future fluid and solid mechanics analysis of the acinus.

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Respiratory Bronchiole and Alveolar Ducts, $Re=0.1-2$

Alveolar Sac, $Re=0.01$

Figure 1.

(a–c) Representative geometry for the acinar region. Q_D is the input flow rate at inlet and Q_{De} is the exit flow rate. (d) A typical alveolus represented as a truncated octahedron - consisting of 3 hexahedral faces and 5 square faces. 'abcdefa' is the non-coplanar alveolar mouth. Segment length: $L_{seg} = 171 \mu m$, entrance length: $L_A = 416 \mu m$.

Figure 2.

(a) Scanning electron micrograph of cross-section of an alveolar duct (D) showing densely packed alveoli (A) surrounding the duct. (b) Schematic of mechanical structure of basic acinar unit showing the septa and its arrangement around the axial channel of the airways (reprinted from Weibel et al., 2005 with permissions from author and Elsevier, License Numbers 2146610913729 and 214665015932)

Figure 3. Temporal evolution of normalized inlet flow rate (Q_D/Q_{Dmax}) and normalized volume (V/V_{min}) employed in our simulation

Figure 4.

(a) 3D flow structure for $Re=0.01$; (b) extracted flow streamlines in xy -plane; (c) shear stress along trace of the wall in the xy -plane. The zero shear stress line is shown dashed. τ_0 is the unperturbed value corresponding to flow over the plane wall to which the cavity is attached.

Figure 5.

(a) 3D model; (b) 3D flow structure in the alveolar sac below the duct; (c) streamline pattern in the yz-plane near end of inspiration; (d) normalized velocity magnitude in the yz-plane near end of inspiration for $Re=2$, 1 and 0.52. "E" denotes the entrainment region.

Figure 6.

(a) 3D geometry of honey-comb like alveolar duct; (b) 3D flow structure near end of inspiration for $Re=1.0$; (c) streamline pattern in the yz-plane near end of inspiration for $Re=1.0$ and $Re=0.6$. "R" denotes the recirculation region.

Figure 7.
 (a) 3D alveolar sac geometry with a single entrance; (b) 3D flow structure near end of inspiration for case III.

Figure 8.

(a) Reynolds number (Re_{RMS}) and flow rate ratio (Q_A/Q_D) variation with acinar generation number; Generation 15 is marked as 0 and hence generation 23 as 8 (corresponding to Case III in the results of the present study).

Table 1

Input parameters and flow conditions

	T (s)	Re	Re _{RMS}	Volumetric deformation	Maximum flow rate Q_{Dmax} (m ³ /s)	∇/Q_D	Q_A/Q_D
Case I	2.5	2.0	1.334	25%	7.50×10^{-9}	0.041	0.0024
Case I	2.5	1.0	0.710	25%	3.75×10^{-9}	0.082	0.0047
Case I	2.5	0.52	0.355	25%	2.00×10^{-9}	0.164	0.0095
Case II	2.5	1.0	0.710	25%	3.75×10^{-9}	0.122	0.0047
Case II	2.5	0.6	0.390	25%	2.3×10^{-9}	0.200	0.0080
Case III	2.5	0.03	0.019	25%	3×10^{-11}	1.000	0.0570