Flow Field Analysis in Expanding Healthy and Emphysematous Alveolar Models Using Particle Image Velocimetry

Particulates that deposit in the acinus region of the lung have the potential to migrate through the alveolar wall and into the bloodstream. However, the fluid mechanics governing particle transport to the alveolar wall are not well understood. Many physiological conditions are suspected to influence particle deposition including morphometry of the acinus, expansion and contraction of the alveolar walls, lung heterogeneities, and breathing patterns. Some studies suggest that the recirculation zones trap aerosol particles and enhance particle deposition by increasing their residence time in the region. However, particle trapping could also hinder aerosol particle deposition by moving the aerosol particle further from the wall. Studies that suggest such flow behavior have not been completed on realistic, nonsymmetric, three-dimensional, expanding alveolated geometry using realistic breathing curves. Furthermore, little attention has been paid to emphysema geometries and how pathophysiological alterations effect deposition. In this study, fluid flow was examined in three-dimensional, expanding, healthy, and emphysemic alveolar sac model geometries using particle image velocimetry under realistic breathing conditions. Penetration depth of the tidal air was determined from the experimental fluid pathlines. Aerosol particle deposition was estimated by simple superposition of Brownian diffusion and sedimentation on the convected particle displacement for particles diameters of 100–750 nm. This study (1) confirmed that recirculation does not exist in the most distal alveolar regions of the lung under normal breathing conditions, (2) concluded that air entering the alveolar sac is convected closer to the alveolar wall in healthy compared with emphysematous lungs, and (3) demonstrated that particle deposition is smaller in emphysematous compared with healthy lungs. [DOI: 10.1115/1.4000870]

Keywords: alveolar sac, emphysema, particle image velocimetry, compliant model, deposition

1 Introduction

In the United States approximately \(35 \times 10^6\) Americans have some form of chronic lung disease, which leads to about 400,000 deaths per year [1]. To predict particulate delivery to the lung whether it is in the form of aerosol medication or airborne pathogens, it is crucial to understand the physiological conditions that affect fluid flow and particulate behavior in the pulmonary region. Since disease alters the structure of the lung, it is expected that airflow and mass transport differ in diseased compared with healthy lungs. With emphysema, there is a decrease in the alveolar wall compliance and surface area accompanied by an increase in lung volume. The mechanisms by which these changes influence flow field and deposition in emphysemic patients are not fully understood. Kohlhäuf et al. [2] found an increase in ventilation asymmetry in emphysema, which was suspected to alter particle deposition. Sweeney et al. [3] measured lower particle deposition in emphysemic compared with healthy hamsters. Sturmf and Hofmann [4] found a decrease in alveolar particle deposition in emphysema compared with normal using multiple generation stochastic models with two-dimensional rigid geometries. However, no work has been done to examine the fluid flow mechanisms that may be responsible for the decreased particle deposition in emphysema.

It is widely accepted that the predominant mechanisms by which particles are transported in the pulmonary region is by sedimentation and diffusion since slow moving velocities in the pulmonary region render impaction negligible. However, this understanding stems primarily from analyses of multiple bifurcating tubes with nonmoving boundaries. It is possible that expanding alveolar walls provide additional convective motion, or that flow around alveolar septa induces recirculation zones that could aid in mixing or particle trapping. Animal lung casting experiments have suggested that mixing is present in the respiratory zone [5] and inhaled bolus dispersion experiments have shown that mixing influences particle deposition [6–9]. Several studies have been done to examine the potential effect of these structural and physiological mechanisms on particle transport. Tsuda et al. [10] in a numerical model of torus geometry and Karl et al. [11] in an experimental model of square shaped alveoli, showed that fluid flow is significantly affected by certain features of the alveolus; recirculation occurs with a large alveolus depth (D) to mouth diameter (MD) ratio (see Fig. 1(b)). Szmitan et al. [12] in a three-dimensional numerical model of an alveolus on a duct, Tippe and Tsuda [13] in an experimental alveolated torus model, and Tsuda et al. [10] in a numerical torus geometry, showed that the flow becomes irreversible with a large flow rate ratio (ratio of the flow in the duct to the flow into the alveolus). Haber et al. [14] and Szmitan et al. [15] showed in a numerical model that recircula-
sight into the mechanisms that govern mixing and how alterations in these mechanisms affect particle penetration and deposition in diseased lungs.

In this study, we present the first data that use realistic nonsymmetric healthy and emphysemic geometry with compliant walls and realistic breathing conditions. For both geometries, morphometric data [21–25] were used to create large scale physical models of the alveolar sac. The fluid flow was characterized using particle image velocimetry (PIV). The velocity fields were analyzed to determine whether or not recirculation exits and to quantify the difference in particle penetration depth due to convection in the healthy and emphysemic models. Further analysis was completed to estimate, by simple superposition of convective motion with sedimentation and diffusive motions, the difference in deposition on the alveolar walls between healthy and emphysematous lungs.

2 Methods

2.1 Model Fabrication. Alveolar sac models were created to represent healthy and emphysemic lungs at functional residual capacity (see Fig. 1) using the data available in literature (see Table 1). The healthy and emphysematous models' effective airway diameters (EAD) were within the standard deviation reported by Kohlhäufl et al. [23]. Figure 2 shows the D/MD ratios (D = Alveolar depth, MD = Alveolar mouth diameter) of the models compared with literature. The healthy alveolar sac D/MD ratio was maintained at 0.8, to keep it within the range reported by Mercer et al. [24] and Klingele and Staub [22] by reducing the average number of alveoli from 17 as reported in Weibel 1964 [25] to 13. Although no D/MD ratio could be found in open literature for emphysema, the smaller ratio of 0.4 is consistent with the pathology of the disease state in which the septa break down and several alveoli merge into a single sac. The alveolar sac models were scaled to 75 times in vivo dimensions and manufactured for flow visualization. Rapid prototyping was used to create a four part hollow model, which was used to construct a solid aluminum cast model. The hollow compliant alveolar sac models were created by dipping the aluminum cast into the molten compliant material (Ultraflex, Douglas and Sturgess Inc., CA). Ultraflex is a hyperelastic material and there is currently no models to describe its behavior. The material properties are currently being studied.

2.2 Fluid Scaling. In order to properly represent in vivo flow physics in the scaled up experimental model, the dominant forces present in vivo were maintained. These dominant forces were determined by scaling the Navier–Stokes equations (see Appendix A), which resulted in two nondimensional parameters that govern the fluid regime, Reynolds and Womersley numbers. The Reynolds number was calculated from Re = 8EV/ fDr, where E is the percent expansion, Vf is the initial volume of the alveolar sac, f is

Table 1 In vivo alveolar sac model dimensions compared with morphometric literature: Experimental models were scaled 75 times in vivo size listed in this table

<table>
<thead>
<tr>
<th>Published dimension</th>
<th>Article</th>
<th>Healthy dimension</th>
<th>Emphysemic dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duct diameter (µm)</td>
<td>250</td>
<td>Haeferi-Bluer and Weibel [21]</td>
<td>250</td>
</tr>
<tr>
<td>Alveolus radius (µm)</td>
<td>140</td>
<td>Weibel [25]</td>
<td>122</td>
</tr>
<tr>
<td>Alveolus depth (µm)</td>
<td>230</td>
<td>Weibel [25]</td>
<td>165</td>
</tr>
<tr>
<td>Sac length (µm)</td>
<td>750</td>
<td>Haeferi-Bluer and Weibel [21]</td>
<td>748</td>
</tr>
<tr>
<td>Number of alveoli</td>
<td>17</td>
<td>Weibel [25]</td>
<td>17</td>
</tr>
<tr>
<td>D/MD</td>
<td>0.8–1.2</td>
<td>Klingele and Staub [22] and Mercer et al. [24]</td>
<td>640–870</td>
</tr>
<tr>
<td>EAD (µm)—healthy</td>
<td>250</td>
<td>Haeferi-Bluer and Weibel [21]</td>
<td>312–554</td>
</tr>
<tr>
<td>EAD (µm)—emphysema</td>
<td>280 ± 50</td>
<td>Kohlhäufl et al. [23]</td>
<td>312–554</td>
</tr>
<tr>
<td>EAD (µm)</td>
<td>630 ± 200</td>
<td>Kohlhäufl et al. [23]</td>
<td></td>
</tr>
</tbody>
</table>

*Alveolus radius was scaled to 50% TLC [31].
the breathing frequency, \( D \) is the diameter of the duct, and \( \nu \) is the kinematic viscosity. For normal breathing the average in vivo Reynolds number for the alveolar sacs is approximately \( 4.85 \times 10^3 \) and the in vivo Womersley number is approximately \( 0.037 \). Based on the scaling analysis it was shown that pressure and viscous forces will govern the fluid behavior in the alveolar sac. Therefore experimental conditions will represent in vivo conditions for low Re and Wo.

The experimental Reynolds number \( \text{Re}=\frac{4Q}{\pi \nu D} \), where \( Q \) is the volumetric flow rate, was varied for the healthy and emphysemic alveolar sacs in accordance with the tidal breathing curve (variation in flow rate with time) and therefore ranged between approximately 0 and 0.42. The Womersley number was 0.25 for the healthy alveolar sac and 0.21 for the emphysemic alveolar sac. Because these values are less than unity, the pressure and viscous forces will dominate the flow equations (see Appendix A), yielding experimental streamlines and velocity vectors that will represent in vivo conditions.

2.3 Breathing Curve. The expansion and contraction of the alveolar sacs in our experiments was controlled by a realistic unsteady breathing curve. Using a spirometer, the general form of the flow rate curve was acquired from a 21 year old healthy female volunteer during resting breathing conditions. A two part polynomial function was fitted to the flow rate to remove noise induced during measurement (see Fig. 3). Assuming the same transient flow rate behavior throughout each airway branch and acinus of the lung (i.e., homogeneous ventilation), the spirometer data were scaled for the alveolar sac models by applying a desired maximum expansion of 30% change in volume of each model, using an initial volume of 13.3 ml and 18.2 ml for the healthy and emphysemic models. To keep the flow rate the same in each model, the breathing period was scaled to 8 s and 11 s for the healthy and emphysemic models, respectively. Keeping the flow rate constant allowed us to isolate the effects of diseased geometry from the influence of breathing conditions.

2.4 Experimental Setup. The main experimental components included a laser, camera, data acquisition, and control system, pressure expansion chamber, and compliant alveolar sac model (see Fig. 4). The compliant model was attached inside a glycerin filled pressure chamber. Glycerin (kinematic viscosity \( \nu \) for pure glycerin is \( 11.26 \text{ cm}^2/\text{s} \)) was used for the experimental fluid because it has an index of refraction (1.487 ± 0.002) that matched the material (1.481 ± 0.002) used for the compliant alveolar sac models. The glycerin inside the alveolar model was seeded with fluorescent 8 \( \mu \text{m} \) diameter polymer microspheres with a density of 1.05 g/cm\(^3\), peak excitation wavelength of 542 and peak emission wavelength of 612 nm (Duke Scientific Corp, CA). A force balance on the particles, involving buoyancy, drag, and gravitational forces was used to estimate that the particles migrate at a rate of \( 5.3 \times 10^{-7} \) cm/s upward. This corresponds to a negligible
displacement of 0.063 μm from the streamlines in 12 s, the time scale of our experiment. The alveolar sac models were expanded and contracted drawing a negative pressure on the glycerin inside the chamber. Expansion of the model allowed the seeded glycerin in the model inlet tube to be drawn into the sac. The fluorescent microspheres were illuminated by a laser sheet generation (1 mm thick and 48 mm wide) connected to a 20 W copper vapor laser, which produced two wavelengths, 510.6 nm and 578.2 nm.

The motion of the fluid was captured by a monochromatic MotionPro X3 Plus camera (Redlake Inc., FL), which had a 1280 × 1024 pixel² resolution, for a frame rate up to 2000 fps. Each pixel on the array was 12 μm in length and width. A frame rate of 100 fps and a shutter speed of 4996 μs were used for the experimentation. The magnification of the physical object by the sensor array was 0.23 times. Even though the magnification was small, the particle image size was between 2 pixels and 3 pixels because of diffraction limited optics. The glycerin/microsphere mixture was created to allow for approximately 32 pixels per each cross correlation interrogation region.

2.5 PIV Analysis. The fluid displacement vectors were calculated by cross correlation of the light intensity within small interrogation regions in successive images with the use of the TSI product, Insight 3G (TSI Inc., MN). A fast Fourier transform based [26] multiple step recursive Nyquist grid cross correlation method was used to allow for good detection of displacement vectors at high spatial resolution (32 pixels²). The initial displacement vectors used an interrogation size of 64 pixels² with a 50% window overlap and were used to determine the best overlap for the interrogation region of 32 pixels². To allow for subpixel accuracy in determination of the location of the cross correlation peak a Gaussian curve fit was used [27]. Only measurements with a signal to noise ratio, defined as the ratio between the highest and second highest correlation peak, greater than 2 were accepted. The pixel size of 2–3 pixels and 32 pixel² interrogation region has been shown to have a displacement error less than 0.1 pixels [27] for the cross correlation analysis.

Tecplot 360 (Tecplot Inc., WA) was used to visualize the flow field. Streamlines plotted tangent to the velocity vector were used to analyze the instantaneous flow. Lagrangian pathlines (location of the particle at each point in time) were used to visualize the flow over a breathing cycle. Details of the pathline analysis and error estimation are in Appendix B. We showed that the PIV analysis error may be reduced by increasing the time separating frames Δτ but there is a limit to how large Δτ can be; if Δτ was too large, the PIV particles may leave the interrogation region, and there would be an increased PIV analysis error e.

The alveolar sac was photographed at the middle cross-section, which allowed for analysis of the duct and several alveoli. The model was divided vertically in two sections since the laser light sheet was not large enough to illuminate the entire model. Streamlines and pathlines were plotted to evaluate the presence of recirculation and reversible flow. The differences between healthy and emphysemic models were analyzed relative to the measurement error (Eq. (B3)).

2.6 Transport and Deposition Approximations. Fluid pathlines were used to evaluate the difference in bulk fluid motion and particle transport between the healthy and emphysemic models. Specifically, penetration depth for the bulk fluid and aerosol particles was estimated as well as the number of breaths to achieve 100% particle deposition efficiency. These analyses were completed on pathlines scaled to in vivo lengths (divided by 75) so that particle motion calculations would be relevant to an alveolar sac in vivo.

One measure of the penetration depth utilized was the distance that the bulk fluid (inhaled tidal air) travels into the expanding alveolar sac during inhalation due to the expansion of the alveolar walls. The difference in tidal air penetration depth was estimated by comparing the average pathline lengths at the end of inhalation for the healthy and emphysemic models. Another metric of penetration depth utilized was the remaining distance that an aerosol particle must travel to reach the alveolar wall, after being carried into the alveolar sac by the bulk fluid motion of the tidal air. As a first approximation, it was assumed that the aerosol particles traveled along the tidal air pathlines with minimum drift flux by diffusion or sedimentation, until the end of inhalation. The particle size range having a 20% drift flux was calculated to quantify the validity of this assumption. The shortest distance of travel (in any direction) to reach the wall from the location at the end of inhalation was measured for particles traveling on each pathline. We assumed reversible flow and therefore particles were assumed to not defer from tidal flow during exhalation. The distances to reach the wall for the healthy and emphysemic models were averaged and compared.

To determine the relative significance of tidal air penetration depth on aerosol particle deposition, the time for an aerosol particle to travel from the inhaled position to the alveolar wall was estimated by superimposing a calculated diffusive and gravitational settling distance [28] on top of the initial penetration depth. Again, the particle size range examined was limited to particles having less than 20% drift flux off the inhalation pathline. Specifically, the analysis was limited to particle sizes whose migration from the tidal air pathline during inhalation (due to combination sedimentation or diffusion) would be less than 20% of the measured inhalation pathline lengths for a 2 s inhalation. This particle size range was calculated for a combination of sedimentation and diffusion [28] using the settling velocity of a unit density sphere in air and the diffusion coefficient (D = K_Tc / 3 μd, where K is the Boltzmann constant, T = 98.6 deg F, C is the Cunningham slip correction factor, d is particle diameter), respectively. At the end of inhalation, particles will diffuse in the direction of the concentration gradient. The travel distance is different for each pathline and for each direction from that pathline to the wall. The pathline that brought the particles furthest from the alveolar wall at the end of inhalation, and the longest distance from this point to the alveolar wall was chosen for this analysis; so that, 100% deposition efficiency could be implied if particles on the chosen pathline were able to travel the additional distance to reach the wall in the given amount of time. The differences between healthy and emphysemic distances were evaluated relative to a reasonable range of inhalation times.

The particles that do not have enough time to reach the alveolar wall during the first breath may migrate by diffusion or sedimentation to another pathline. With each inhalation and exhalation cycle, the sequence of convective and drift motion (which actually occur simultaneously, although described here as sequential for illustrative purposes) moves the particle closer to the wall. To estimate the number of breaths required for particles to travel the distance in this idealized manner, we assumed reversible tidal air flow and zero particle drift flux during exhalation. The maximum number of 3 s breaths required for 100% deposition efficiency was estimated and compared for each model.

3 Results

Observation of the seeded flow over several breathing cycles in multiple image planes indicated that there were no obvious recirculation regions in either the healthy (H) or emphysemic (E) model, even during high flow rate portions of the breathing cycle. Furthermore, it was confirmed that the flow was reversible. Streamlines and pathlines calculations further confirm that the flow was behaving reversibly. Figure 5 shows a plot of five streamlines in the top left alveolus, of the H model at maximum flow rate (7.13 m/s at 1.43 s). These streamlines confirmed that there were no low pressure zones around the alveolar walls that would result in recirculation. Similar streamline plots were created for the E model (not shown), indicating no low pressure zones. Figure 6 shows the experimental velocity magnitude vector
plots for maximum flow rate for \( H \) (a) and \( E \) (b) for the top portion of the models only. The velocity in the lower region (not shown) is close to zero. It was observed that throughout the inhalation portion of the breathing cycle, the direction of the vectors was consistent. The magnitude of the vectors is proportional to the flow rate at the inlet and can be related to in vivo velocity magnitude by multiplying by the ratio of the in vivo flow rate to the experimental flow rate. Figure 7 shows a plot of eleven pathlines for one complete breathing cycle of the \( H \) and \( E \) models. The pathlines show that the fluid particles trace the same path during inhalation and exhalation with an estimated uncertainty of 0.195 mm, indicating reversible flow for both \( E \) and \( H \) models.

The fluid pathlines were further evaluated to estimate the difference in penetration depth of the bulk fluid (inhaled tidal air) between the \( H \) and \( E \) models. Pathlines were longer in the \( E \) model compared with the \( H \) model for all but pathline 11. However, for most pathlines the difference was very small (see Table 2). Tidal air in the \( E \) model penetrated on average only 9% further (range of 0–46%) than the \( H \) model, even though the volume intake was 37% larger in the \( E \) model compared with the \( H \) model (both were expanded 30% of their initial volume).

The remaining distance that an aerosol particle must travel to reach the alveolar wall, after being carried into the alveolar sac by the bulk fluid motion of the tidal air is also shown in Table 2. Assuming the particles have not drifted off the streamline by gravitational or diffusive drift flux, inhaled aerosol particles would need to travel on average 71 \( \mu \text{m} \) (71%) further to reach the alveolar wall in the \( E \) model compared with the \( H \) model. The increase in distance ranged from 35 \( \mu \text{m} \) (43%) to 138 \( \mu \text{m} \) (96%).

The analysis of time for an aerosol particle to travel from the inhaled position to the alveolar wall was limited to particles within the 20% drift flux range \( 100–750 \text{ nm} \). Since particles above and below this range, would have migration distances greater than 20% of the inhalation pathlines by sedimentation and diffusion, respectively. Pathline 6 was chosen for the \( H \) model and
4 Discussion

The alveolar sac model geometry used in this study represents incremental improvement over the experimental models that have already been presented in the literature. Prior to this work, no results were available to accurately assess the flow field in both a healthy and emphysema alveolar sac. This study provides further convincing evidence that recirculation is not likely present in the alveolar sacs of the human lung. Although unique geometric models analyzed in this study, the conclusion that flow is reversible is consistent with Sznitman et al. [12], Tsuda et al. [10], Tippe and Tsuda [13], Haber et al. [14], Sznitman et al. [15], Cinkotai [16], and Davidson and Fitz-Gerald [17], when one considers similar generation numbers, flow rate ratios, and D/MD ratios, respectively. Inconsistencies between our results and reports of recirculation over rigid walls from Karl et al. [11], for similar flow rate and D/MD ratios, can be explained by the nature of the flow when

pathline 5 was chosen for the $E$ model since particles traveling on this pathline would be further from the wall at the end of inhalation (325 $\mu$m for the $H$ model and 425 $\mu$m for the $E$ model) than particles traveling on any other pathline. The calculations predicted that none of the particle sizes would migrate to the alveolar wall after inhalation (see Fig. 8). Furthermore, an additional breath hold of 5 s, for a total residence time of 8 s was not sufficient time. Figure 8 also shows the number of 3 s breaths that would be required for particles in the 20% maximum drift flux range to reach the wall with 100% deposition efficiency. A 750 nm particle, which is dominated by sedimentation in the alveolar sac, will reach the wall in at most five breaths for $H$ and seven breaths for $E$. A larger discrepancy between $H$ and $E$ was found for the smallest particles in the size range considered, which are diffusion dominated while traveling in the alveolar sac. At most 23 breaths for $H$ and 42 breaths for $E$ were required to achieve 100% deposition of 100 nm particles.

Table 2 In vivo tidal pathline lengths for tidal air entering the top of the model and the minimum remaining distance (in any direction) a particle must travel to reach the alveolar wall after inhalation

<table>
<thead>
<tr>
<th>Pathline</th>
<th>Healthy ($H$) model $\mu$m</th>
<th>Emphysema ($E$) Mm</th>
<th>Increase for $E$ model compared with $H$ model $\mu$m %</th>
<th>Pathline</th>
<th>Healthy ($H$) model $\mu$m</th>
<th>Emphysema ($E$) model $\mu$m</th>
<th>Increase for $E$ model compared with $H$ model $\mu$m %</th>
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<tbody>
<tr>
<td>1</td>
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<td>11</td>
<td>106</td>
<td>83</td>
<td>$\sim$ 23 $\pm$ 2</td>
</tr>
</tbody>
</table>

Average 9 ± 4 Average 71 ± 5

*Experimentally derived distances were scaled to obtain in vivo lengths (divided by 75). The error was based on the 0.195 mm experimental error converted to 2.60 $\mu$m representing the in vivo length scales.*
induced by the slowly expanding alveolar walls. Negative pressure created by the wall motion draws the fluid toward the alveolar wall in an orderly fashion. By contrast, flow over a rigid backward facing step, creates separation points, low pressure zones, and induces recirculation.

Further evidence that acinus morphometry and wall motion play an important role in particle transport through convective motion was found when analyzing particle penetration into the alveolar sac. Even though the E model tidal air penetrated the alveolar sac deeper than the H model, the difference was very small, and would not likely enhance particle deposition because the E model did not bring the aerosol particles closer to the wall compared with the H model. The larger travel distance required for aerosol particles to reach the wall after inhalation, for the E model compared with H model can be attributed to a larger effective airway diameters and slower moving fluid in the E model. Specifically, the velocity gradient between the alveolar wall and the center of the sac was larger for the healthy model compared with the emphysemic model, so that more particles were traveling slower, and therefore not as deep into the emphysemic model compared with the healthy model for the same breathing period. Our experimental model geometry was based on average morphometric data from the literature, however, accuracy could be improved by considering the inhomogeneous nature of alveolar size and shape. Furthermore, slightly larger D/M ratios than used in the current study have been reported, however it is unlikely that the subtle changes in shape would create recirculation zones that were not observed in the present model nor change the conclusion from this study that alveolar sac flow is reversible. A healthy breathing curve was utilized in this study for both from this study that alveolar sac flow is reversible. A healthy breathing curve was utilized in this study for both from this study that alveolar sac flow is reversible.

The significance in the fluid flow results, specifically how close the tidal fluid travels to the alveolar wall, was amplified by linking the results to particle transport and deposition. Although a simple superposition of convective displacement with diffusive displacement and sedimentation was employed, the results are appealing in that they qualitatively agree with animal studies reporting lower particle deposition in emphysemic compared with healthy hamsters [3]. Certainly, a more complex analysis in which the convective-diffusion equation is solved in a transient flow field, is the next step to better quantify the particle deposition differences in healthy and emphysematous lungs.

5 Conclusion

Our experiments confirmed that irreversible flow is not present in the alveolar sac of either healthy or emphysemic lungs. The pathlines for particle motion in the healthy alveoli terminate closer to the walls then in the emphysemic alveolar sac by approximately 71%. Consequently, the rate of particle diffusion and sedimentation is postulated to be greater in healthy then emphysemic lungs, and this, in turn means particle deposition will occur more quickly when lungs are healthy. This study illustrates the influence of the increased presence of dead space in emphysema on fluid flow into the alveolar sac. We have confirmed that recirculation does not occur in the alveolar sac, therefore future flow and particle analysis should include alveoli in more proximal generations that do have irreversible flow behavior. We showed that expanding walls is necessary in accurately representing acinar flow, therefore the presence of moving walls in experimental and theoretical models is required to adequately model acinar flow. Finally, it is proposed that a more accurate lung deposition model may be developed by incorporating a convective-diffusion model for particle deposition coupled with a realistic moving alveolar geometry.

Acknowledgment

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Nomenclature

\[ D = \text{diameter} \]
\[ E = \text{error of calculating the pathlines} \]
\[ H = \text{location of the alveolar sac with respect to the superior most lobe} \]
\[ P = \text{pressure} \]
\[ P_{alv} = \text{pressure in the alveolar sac} \]
\[ P_{el} = \text{elastic recoil pressure} \]
\[ P_{pl} = \text{pleural pressure} \]
\[ P_{s} = \text{pressure scale} \]
\[ R_m = \text{mean radius of curvature} \]
\[ Re = \text{Reynolds Number} \]
\[ T = \text{membrane tension} \]
\[ U = \text{average velocity at the entrance of the alveolar sac} \]
\[ Wo = \text{Womersley Number} \]
\[ d = \text{interpolated displacement of the velocity vector} \]
\[ e = \text{RMS PIV analysis error} \]
\[ f = \text{frequency} \]
\[ g = \text{gravity vector} \]
\[ k = \text{numerical time step} \]
\[ t = \text{time} \]
\[ f_{int} = \text{integration time} \]
\[ u = \text{velocity vector} \]
\[ x = \text{pathline position} \]
\[ z = \text{local sac height} \]
\[ \Delta t = \text{time separating PIV picture frames} \]
\[ \gamma = \text{lungs specific gravity} \]
\[ \mu = \text{dynamic viscosity} \]
\[ v = \text{kinematic viscosity} \]
\[ \rho = \text{fluid density} \]
\[ \omega = \text{angular frequency} \]

Appendix A

Fluid scaling and nondimensional analysis was performed for the alveolar sac. The momentum equation is given by

\[\rho \frac{\partial u}{\partial t} + u \nabla u = -\nabla P + \mu \nabla^2 u + \rho g \]  \hspace{1cm} (A1)\]

where \( \rho \) is the density of the fluid, \( u \) is the velocity vector, \( t \) is time, \( P \) is the pressure, \( \mu \) is the dynamic viscosity and \( g \) is the gravitational vector. The effect of the gravitational term in Eq. (A1) is to adjust the shape of the alveolar sac through the balance of forces across the alveolar membrane. Specifically, if we assume a simple membrane model for the alveolar septa, the balance of forces across the alveolar membrane is given by

\[ P_{pl} = P_{alv} - [\gamma(H+z) + P_{el}] \]  \hspace{1cm} (A2)\]

where \( P_{alv} \) is the pressure in the alveolar sac, the second term in brackets represents the external forces on the alveolar sac, which are comprised of the lung’s weight per unit area \( \gamma(H+z) \), where \( \gamma \) is the lung’s specific gravity, \( H \) is the location of sac with respect to the superior most lobe, and \( z \) is the local sac height and the pleural pressure \( P_{pl} \). \( P_{el} \) is the elastic recoil pressure of the alveolar septa and can be defined as the membrane tension \( T \) divided by the local mean radius of curvature \( R_m \). [29]. It is clear from Eq. (A2) that gravity has little effect on the local deformation of the alveoli in vivo since \( z \) is much smaller than \( H \). Apart from this, gravity does not impart motion to the air in vivo, as can be demonstrated by the introduction of the stream functions into the
Navier–Stokes equations in which gravity is eliminated [30]. Since our experiments involve using fluids whose properties are the same on both sides of the sac, the boundary conditions across the membrane are also gravity-independent. Thus, for both in vivo conditions and model experiments, the effect of gravity on the fluid motion can be neglected.

The remaining terms in Eq. (A1) were scaled as follows: \( u \sim U \), where \( U \) is the average velocity at the entrance of the sac \( t = t_0 \), \( \omega = 2 \pi f \) and \( f \) is the frequency (Hz), \( \nabla = 1 / D \), \( P \sim P_c \), where \( P_c \) is an arbitrary pressure scale. The Navier–Stokes equation can then be written in nondimensional terms as

\[
\frac{\rho D^2}{\mu} \frac{\partial u^*}{\partial t^*} + \frac{\rho DU}{\mu} \left[ u^* \nabla u^* \right] = - \frac{PD}{D\mu} \nabla P^* + \nabla^2 u^* \tag{A3}
\]

where the * denotes the nondimensional variables. Three dimensionless parameters are found in the nondimensional equation. The first parameter, Reynolds number, defined by \( Re = \rho DU / \mu \) determines the role of the steady inertia forces relative to viscous forces. The second parameter, \( B = \rho D^2 / \mu \), determines the role of the nonsteady inertia forces, The Womersley number [32] is defined as \( Wo = (D/2) \sqrt{2 \pi f / \nu} \), which is related to the nondimensional parameter \( B, B = 4 \rho / Wo \). The third nondimensional parameter is \( C = P/\rho D / \mu U \), which defines the resulting scale of \( P_c \).

The Reynolds and Womersley numbers for in vivo alveolar sacs are much less than unity, therefore, the left-hand side of the Navier–Stokes equation is small compared with the viscous terms. Since pressure is required to interact with dominant flow terms, the pressure gradient term balances the viscous term and the parameter \( C \) is chosen to be 1, which sets the pressure scale as \( P_c = \mu U / D \). In the limit of small \( Wo \) and \( Re \), then, the Navier–Stokes equation thus reduces to

\[
- \nabla^2 P^* + \nabla^2 u^* = 0 \tag{A4}
\]

which when coupled with the continuity equation yields Stokes' description for steady flow.

Appendix B

The Lagrangian pathline calculation and error analysis was performed. The position \( x \) at any numerical step \( k \) was calculated by numerical integration in time according to

\[
x_k = x_0 + \sum_{i=1}^{k_{\text{max}}} u_i \Delta t_{\text{int}} \tag{B1}
\]

where \( x_0 \) was the initial position, \( \Delta t_{\text{int}} \) was the integration time, the summation term is the total distance traveled and \( \Delta t \) may be related to real time \( t \) by \( t = k \Delta t_{\text{int}} \). Several integration steps occur for each measurement file and each measurement file is only used when \( t \) corresponds to the time of that particular measurement. For example, if the time separating the data files was 0.1 s and the \( \Delta t \) was 0.01 s there would be \( m = 10 \) integration steps for each vector field. The velocity for each velocity vector solution file was defined as

\[
u_{i} = \frac{d_{j} + \varepsilon}{\Delta t_{j}} \tag{B2}
\]

where \( d_{j} \) was the interpolated displacement for the velocity vector solution time, \( \varepsilon \) was the assumed constant RMS 0.1 pixel PIV error [27] and \( \Delta t \) was the time separating the frames used for the cross correlation, which ranged between 0.02 s and 0.2 s. The \( d \) and \( \Delta t \) varied for each velocity vector solution file; the \( \Delta t \) was chosen such that \( \varepsilon \) would be much smaller than \( d \) but small enough so that the PIV particles did not travel outside of the interrogation region. The integration error was minimized by decreasing the \( \Delta t \) until convergence was met in the pathline distance calculation. The pathline calculation error, independent of integration error, was given by

\[
E_{(k,j)} = \frac{1}{k} \sum_{j=1}^{m} \frac{\varepsilon}{\Delta t_{j}} \tag{B3}
\]

Equation (B3) was utilized to access the error in pathline calculations. The average \( d \) was about 2.38 pixels, the average \( \Delta t \) was 0.13 s, the \( \Delta t_{\text{int}} \) was 0.2 s, the \( \vareference


