DEPOSITION OF PARTICLES IN THE UPPER RESPIRATORY TRACT

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Abstract

This study uses CFD simulations to examine the effect of using a 70/30 helium/oxygen (% vol) as the carrier gas for the delivery of inhaled medications to the lungs. The CFD mesh is a realistic computational mesh made from a cadaver throat (female, aged 84). Monosize droplets were used at four different sizes: 0.5µm, 2µm, 6µm, and 10µm. Flow conditions within the larynx and trachea affect the delivery of inhaled medications to the lungs. Deposition in these regions is considered undesirable and has been shown to be a particular problem for pediatric patients. This study further investigates the effects of carrier gas on particle deposition in the throat, using a CFD approach. The chosen inlet air velocity was based on an approximate adult breathing condition with a steady flow rate of 18 liters per minute.

Introduction

The advantage of pulmonary drug delivery through inhalation has recently led to the development of a series of new aerosol medications. For some medications this route is utilized because it offers topical treatment of specific lung conditions while limiting the whole-body effects. Modeling medical aerosol dynamics in the human throat may contribute to minimizing the amounts of medication deposited on the throat surfaces thus increasing the dose to the lungs. To accomplish this, a realistic throat model is necessary to accurately characterize the fluid mechanics and spray dynamics in this region. Numerical simulation utilizing a cadaver based throat mesh is performed in this study.

The deposition of aerosol medications in the throat has been demonstrated to be a particular problem for children, based on scintigraphy studies [4, 6, 11, 20]. Aerosol studies using in vitro models or casts of the mouth, throat and central airways have been performed [5, 14, 16, 17,18].

A few numerical studies have been performed by simplifying the larynx and trachea into a circular or elliptical pipe with a constriction. Martonen et al. (1993) conducted a 2-D larynx simulation with ventricular and glottal constrictions followed by a straight-tube tracheal section and a bifurcation [15]. This work is extended to three dimensions in Katz et al. [12, 13]. In their model, the ventricular and vocal fold constrictions were represented as ellipses. Stapleton et al. (2000) numerically studied aerosol deposition in the mouth and throat [19]. They chose to create an “average” geometrical model of the airways based on data from computed tomography (CT) scans, magnetic resonance imaging (MRI) scans, and direct observation of living subjects. By using this information, they constructed a model of the extra-thoracic airways using simple geometric shapes. For simplicity, the trachea was assumed to be a smooth circular tube and the cartilaginous rings were neglected. Gemci et al. numerically studied an inhalation flow containing a medicinal spray passing through a simple model of the larynx and trachea [7, 8]. In these studies, the constriction of the vocal folds within the larynx was represented by a semi-triangular shape based on an image from video bronchoscopy. Later, Gemci et al. (2001 and 2002) performed two more studies. The first, in Ref. [9], used the throat of a cadaver (female, aged 84) to create a computational mesh without the inclusion of a relative angle between the larynx and trachea. Afterwards, Gemci et al. (2002) used the same positive cast, including pharynx, larynx, and trachea, to create a computational mesh that included the proper relative angle between the larynx and trachea [10].

A technique currently used to increase lung deposition in pulmonary drug delivery is to use a 70/30 helium/oxygen (volume %) mixture of helium and oxygen, rather than normal breathing air. The density of helium is 0.1769 g/cm3, and the density of O2 is 1.4289 g/cm3, which makes the mass percentage of helium 22.42%, and the mass percentage of O_2 77.58%. The use of helium as a breathing gas has been shown to increase the amount of alveolar deposition of aerosol medication, possibly as a result of lower levels of deposition in the mouth and throat [3]. In Anderson’s study [3], ten subjects with asthma inhaled 3.6 micron particles labeled with radioactive Indium^{111} in air and in a helium-oxygen mixture (He-O2) at 0.5 and at 1.2 L/s. Lung retention was measured after zero and after 24 h, and the percentage 24-h retention (Ret24) was taken to represent the fraction deposited in the alveolar part of the lung. For both inhalation rates, Ret24 was significantly higher when particles were inhaled with He-O2 than with air. The increase in Ret24 seemed to be larger in

subjects with asthma than in healthy persons earlier studied. Ret24 was correlated with changes in both large and small airways, especially when the particles were inhaled with He-O2. Their data suggest that inhalation of drugs in He-O2 might be of therapeutic value when treating patients with severely obstructed airways.

To confirm this experimental observation, air vs. heliox delivery systems are compared using a CFD simulation. Gemci, et al. [10] demonstrated the effect of droplet size on deposition of medication in the throat via air delivery. In this paper, results for a similar study using a 70/30 heliox delivery system are presented.

Numerical Simulation

CFD simulations were performed by using KIVA-3V code [2]. KIVA-3V is a CFD program for the numerical simulation of transient, three-dimensional, chemically reactive fluid flows with sprays. Simulations are derived by solving the conservation equations of mass, momentum, and energy. The code is an extension of earlier KIVA codes for the complex mesh geometry of combustion chambers and valves in diesel engines. This code considers two-way coupling to account for the spray dynamics effects such as transport, coalescence, break-up, evaporation or condensation, deposition, and turbulent dispersion.

The complex turbulent air flows and high spray number densities in the throat affect the overall spray dynamics as they pass through the larynx constriction. The numerical simulation is performed with the standard k-ε turbulence model. The code solves the spray equation with the Stochastic Particle Technique and its complete description can be found in the KIVA-II code [1].

Typical human respiratory parameters and average droplet size distributions of medical nebulizers were then used to determine inlet and outlet boundary conditions for the numerical model. It was then run through the KIVA-3V code. The chosen inlet air velocity was based on an approximate adult breathing condition with a steady flow rate of 18 liters per second. This flow rate was divided into the inlet cross section area of the mesh and the simulation was started with an air inlet velocity value of 164 cm/sec. Four simulations were run using monosized droplet diameters 0.5 μm, 2.0 μm, 6.0 μm, and 10.0 μm. For all simulations, the coalescence, evaporation, and breakup sub-models were not activated in the spray calculations to focus only on the size effects of the droplets on throat deposition.

Mesh Generation

An RTV Silicone rubber cast of a human larynx from a cadaver was made. The human sample was suspended from a ring stand and positioned in approximately the anatomical position. A positive mold was then made using RTV Silicon rubber (GI-1110, Silicones Inc., High Point, NC). After the solidification, the tissue was removed, and the positive cast was used to produce a split mold of polyurethane (C-1506, Smooth-On Inc., Easton, PA). This mold was used to create a clean positive cast [5]. A reference axis in the model was established by inserting ink via a needle in a straight, vertical line into the throat when the throat was suspended in the anatomical position.

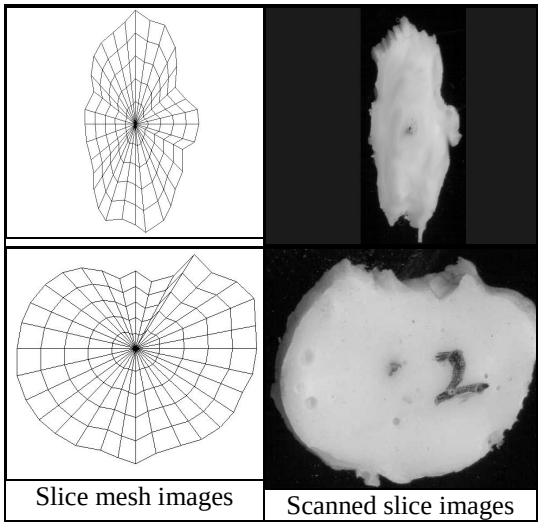

Figure 1: KIVA-3V mesh images from the constriction and bottom of trachea.

The cast was later cut into slices approximately 3mm thick, perpendicular to the reference axis. The true thickness of each slice was measured using dial calipers. Images of the slices were then digitized using a flatbed scanner (see right images in Figure 2). X-Y measurements about the outside of the slices, with reference to the axis, were made manually in Adobe Photoshop (Adobe Systems Inc., San Jose, CA) using the "Show

Coordinates" option, and recorded in a text file. A program was written to convert the coordinates in the text file into the proper block-structured mesh format required by KIVA-3V's meshing software (see left images in Figure 1).

In KIVA's mesh generation code, K3PREP, the mesh design is based around a block structure. For this model, each slice was divided into 32 blocks in the azimuth direction. K3PREP designates left, right, front, derriere, bottom, and top faces to all blocks. For the blocks in this model, the left faces of all the blocks represented the central axis. The right faces represented the wall of the trachea. After the blocks were created, the fronts and derrieres were patched in the azimuth direction. Each block was then patched to the corresponding top and bottom blocks, and the appropriate inlet and outlet boundary conditions were applied. The top 7 slices of the throat were then tilted to the appropriate anatomical angle of 13 degrees, as observed on the cadaver model, using the NTILT function in K3PREP. The CFD mesh was created from 25 slices and last exit slice formed circularly. The total number of computational cells in the model was NX·NY·NZ=5x32x25=4000.

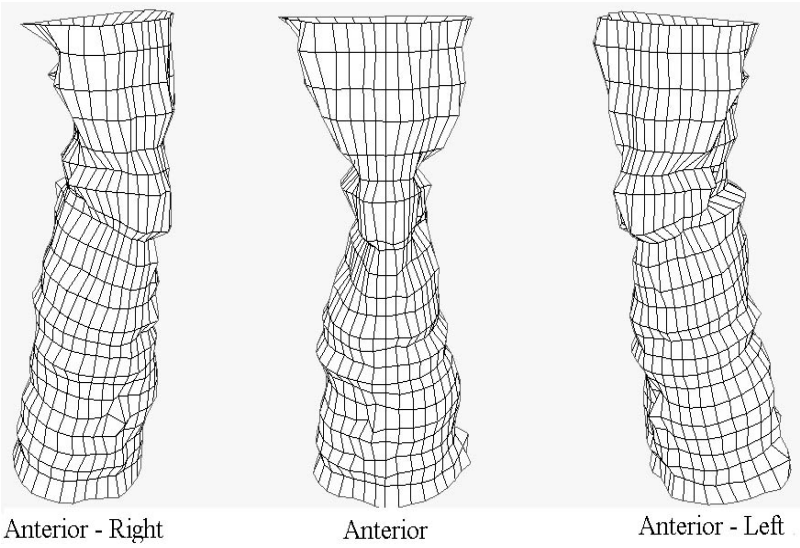

Figure 2: Three sample images of the entire tilted mesh of the larynx and trachea model in KIVA-3V.

Results

Figure 3 and Figure 4 compare the gas velocities when using heliox and air delivery systems in the anterior-right view and in selected cross-sections of the throat. The velocity field is dominated in each case by the laryngeal jet, where the maximum velocities in the flow can be found. The laryngeal jet is caused by the vocal fold constriction in the throat, as explored in Corcoran [5]. The laryngeal jet eventually ends near the bottom of the model, as seen in Gemci, et al [9]. Areas of higher and lower velocity occur in the same places in each simulation. However, for the heliox case, the maximum gas velocity is 15 cm/s (2.7%) higher than the maximum velocity for air.

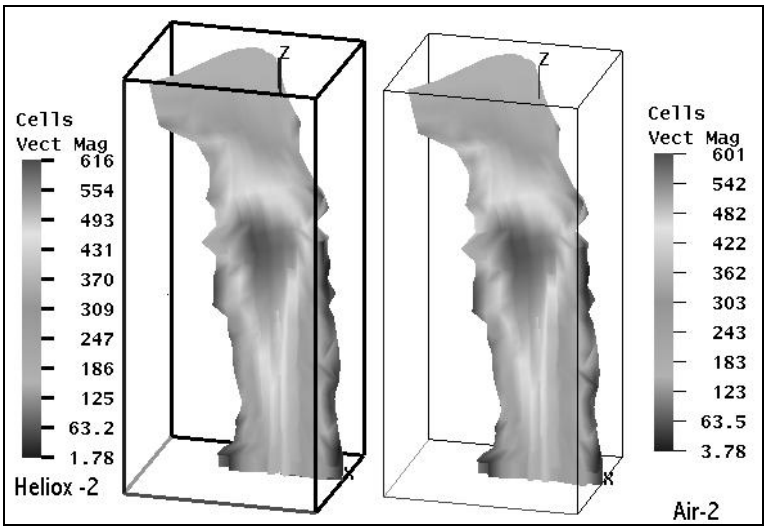

Figure 3: Right side view of gas velocities for heliox (left) and air (right) simulations

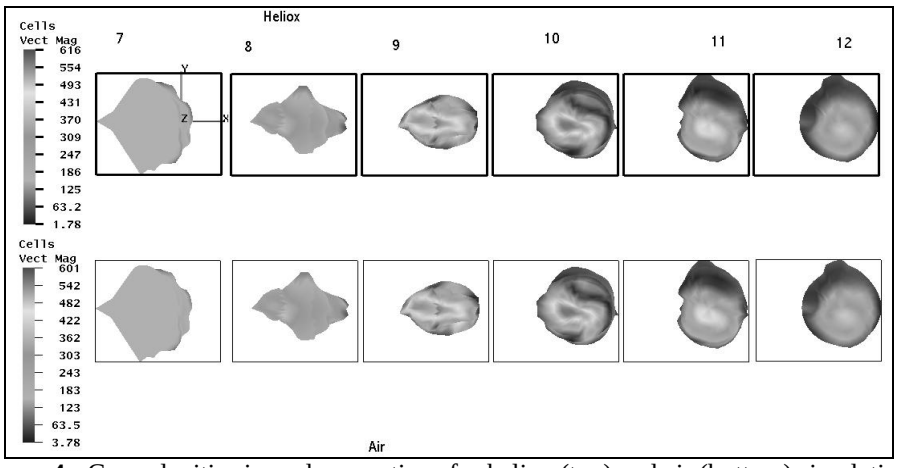

Figure 4: Gas velocities in z-plane sections for heliox (top) and air (bottom) simulations. The image's right side is anterior for all sections.

Figure 5 shows the turbulent kinetic energy in the heliox and air simulations. The maximum turbulent kinetic energy of the air is 4.2% higher than the maximum turbulent kinetic energy in the heliox case. There is also a slightly more pronounced difference between the turbulent kinetic energy distributions. In the heliox simulation, the high turbulence areas tend to be spread out over a slightly larger area than in the case of air. An area of high turbulence to the right of the main laryngeal jet is more prominent in the heliox case than the air case.

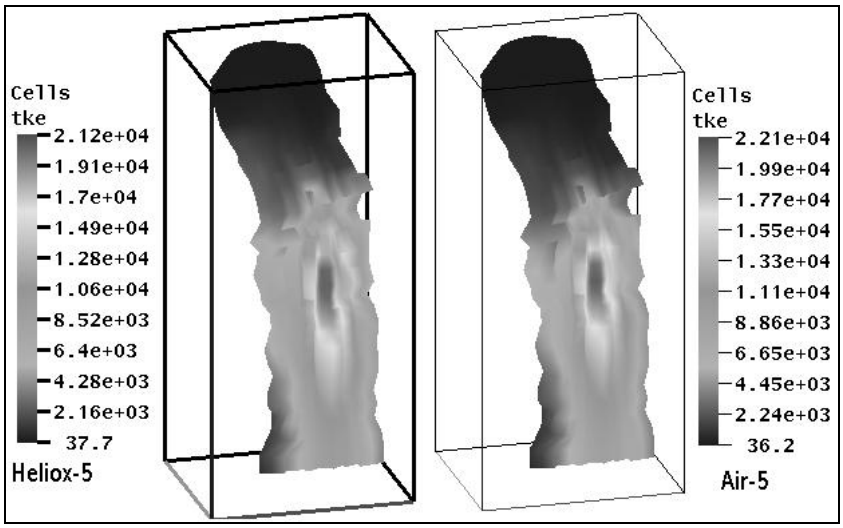

Figure 5: Turbulent kinetic energy for heliox (left) and air (right) simulations

Figure 6 compares the individual droplet velocities when using air (left) and heliox (right) as the carrier gas. The droplet velocity fields show marked differences here, with a pronounced effect on the width of the fields. Droplets in heliox follow a narrower path through the laryngeal jet and at a lower velocity magnitude (maximum 623 cm/s) then droplets in a comparable air carrier field (maximum 652 cm/s). Effectively this decreases particle dispersion away from the laryngeal jet leading to fewer errant particles as the droplets pass through the larynx and thus reducing deposition.

Figure 7 compares the velocity profiles of different sized droplets in heliox. As the sizes of the droplets increase, the droplets become less evenly distributed throughout the flow. They tend to shift more toward the anterior side of the throat as size increases. The maximum velocity of the droplets tends to decrease as the size increases. For the 0.5µm droplets, the maximum velocity is 696 cm/s, but for the 10µm droplets, the maximum velocity is 624 cm/s. Figure 8 shows the mass percentage of spray deposited in the trachea vs. the size of the droplets in the spray. There are four simulations shown for heliox, which are compared against results done by Gemci, et al (2002) [10]. All droplets are monosized for each case, and the inlet velocities are the same. For the heliox simulations, the amount of deposition in the throat increases as the droplet size increases. This trend matches well with trends found in real breathing condition experimental data provided by Heyder et al. (1986) in Figure 9 [11]. At the smallest droplet size of 0.5 µm, 31.8% of the injected spray mass was deposited on the walls of the throat. This is a 17% improvement over the 38.7% of total injected mass that was deposited when

an air delivery was used for the same inlet conditions and droplet diameter. The difference between the heliox and air simulations grows smaller as the drop size increases, but for the four drop sizes studied, there was an average improvement of 7.1% in eliminating deposition.

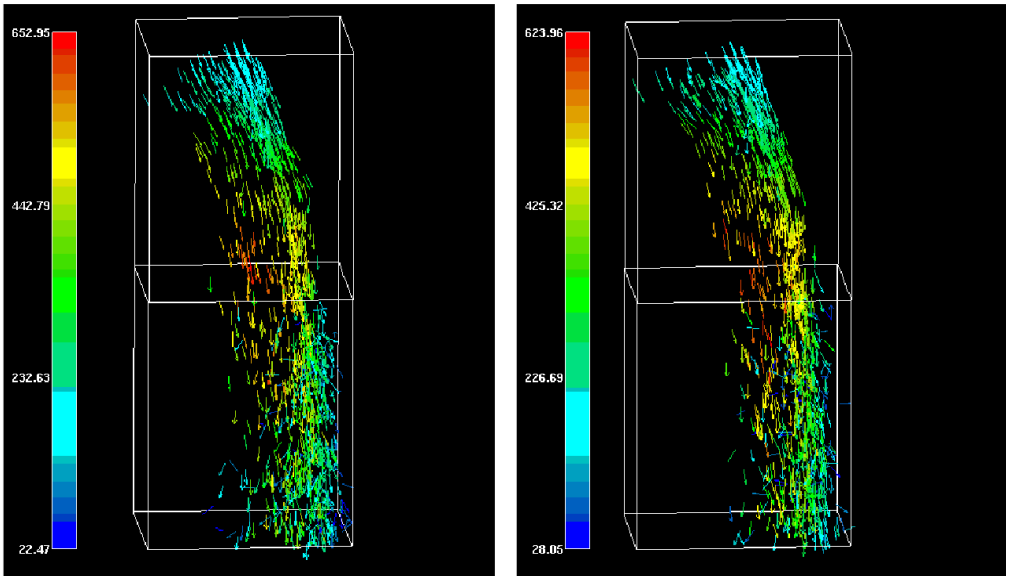

Figure 6. Droplet velocity profile for 0.5 µm monosized droplets in Air (left) and Helium (right)

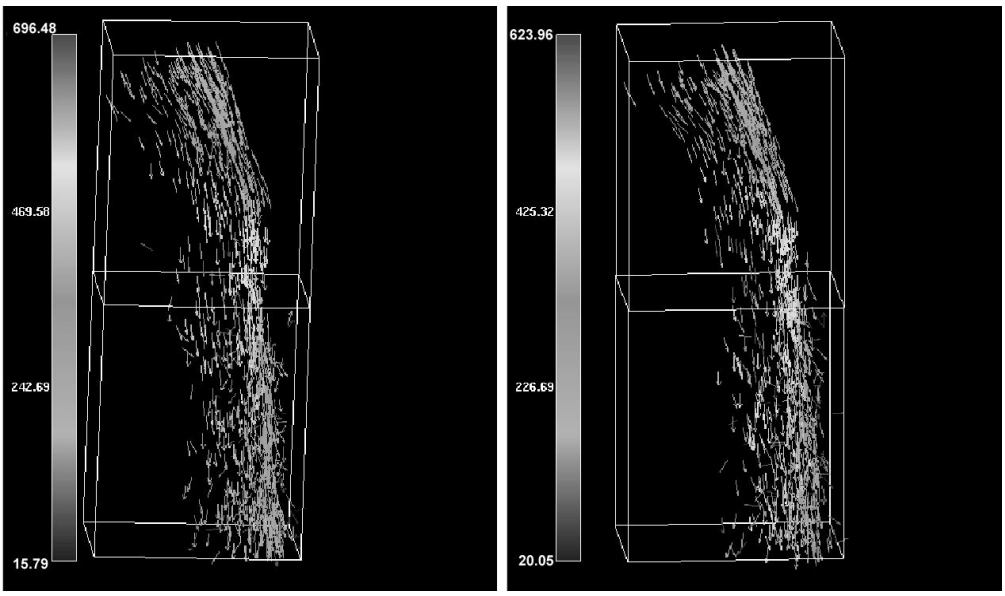

Figure 7. Helium Droplet Velocity field for monosized droplets of 0.5 µm (left) and 10 µm (right).

Conclusions

This preliminary data supports the hypothesis that using heliox as a breathing gas may lower the level of aerosol medicine deposition in the throat, allowing an increase in lung deposition. The data shows an average decrease of 7% in throat deposition when using a 70/30 helium/oxygen (vol. %) mixture. This decrease in throat deposition means that more droplets will get through the throat and down to the lungs, where most inhalation therapy drugs are required.

The effects of the heliox mixture at other droplet sizes must be examined in order to ensure that the trend is constant. Also, the effects of a polydispersed spray must be examined, since this is what will be realistically produced by medical nebulizers. Furthermore, it would be useful to examine a dynamic breath in order to see what the effects of heliox are when gas velocities are changing with time, as in a normal breath.

Acknowledgments

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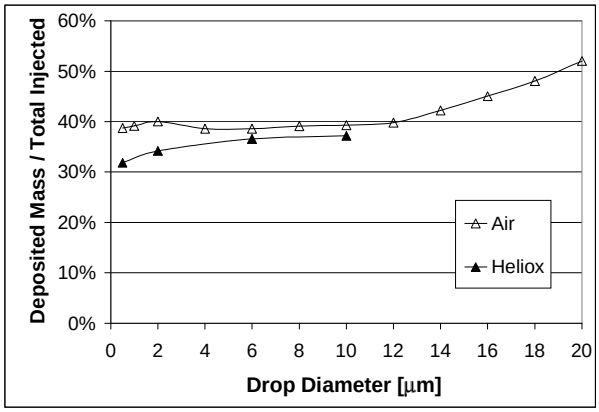

Figure 8: Deposition vs. size for air and heliox.

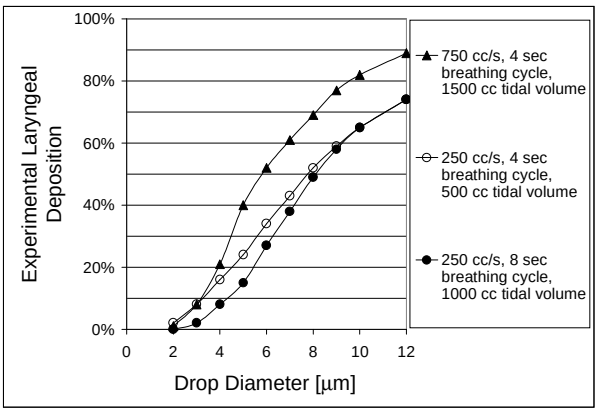

Figure 9: Experimental deposition study in [11]

References

[1] Amsden, A.A., O'Rourke, P.J. and Butler, T.D., "KIVA-II: A computer program for chemically reactive flows with sprays," *Los Alamos National Laboratory report* LA-11560-MS (1989).

[2] Amsden, A.A., "KIVA-3V: A block-structured KIVA program for engines with vertical or canted valves," *Los Alamos National Laboratory report* LA-13313-MS (1997).

[3] Anderson M, Svartengren M, Bylin G, Philipson K, Camner P. , "Deposition in asthmatics of particles inhaled in air or in helium-oxygen." Am Rev Respir Dis 1993 Mar;147(3):524-8

[4] Chua, H.L., Collis, G.G., Newbury, A.M., Chan, K., Bower, G.D., Sly, P.D., Le Souef, P.N., "The Influence of Age On Aerosol Deposition in Children with Cystic Fibrosis," *Eur Respir J*, 7:2185-2191 (1994).

[5] Corcoran, T.E. and Chigier, N., "Characterization of the Laryngeal Jet Using Phase Doppler Interferometry," *J of Aerosol Medicine*, 13(2):125-137 (2000).

[6] Diot, P., Palmer, L.B., Smaldone, A., DeCelie-Germana, J., Grimson, R., Smaldone, G.C., "Rhdnase I Aerosol Deposition and Related Factors in Cystic Fibrosis," *Am J Respir Crit Care Med*, 156:1662-1668 (1997).

[7] Gemci, T., Corcoran, T.E., and Chigier, N., "Dispersion and deposition of inhalation therapy sprays in the larynx and trachea using experimental and numerical methods," *ICLASS-2000*, July 16-20, Pasadena, CA.

[8] Gemci, T., Corcoran, T.E. and Chigier, N., "A Numerical and Experimental Study of Spray Dynamics In A Simple Throat-Model," *Aerosol Science and Technology*, 36:18-38 (2002).

[9] Gemci, T., Corcoran, T.E., Yakut, K., Shortall, B. and Chigier, N., "Numerical Simulation of Particle and Air Velocity Fields in A Model of A Cadaver Throat," *ILASS-AMERICAS-2001*, pp. 131-136, Dearborn, MI.

[10] Gemci, T., Shortall, B., Corcoran, T.E., and Chigier, N., "Deposition Study of an Inhalation Therapy Spray in a Cadaver Throat," *ILASS Americas, 2002*, pp. 297-303, Madison, WI, May 14-17, 2002.

[11] Heyder, J., Gebhart, J., Rudolf, G., Schiller, C.F., Stahlhofen, W., "Deposition of Particles in the Human Respiratory Tract in the Size Range 0.005-15 μm Range," *J Aerosol Science*, 17:2185-2191 (1986).

[12] Katz, I.M. and Martonen, T.B., "Flow patterns in the three-dimensional laryngeal models," *J of Aerosol Medicine*, 9(2):501-511 (1996).

[13] Katz, I.M., Davis, B.M. and Martonen, T.B., "A numerical study of particle motion within the human larynx and trachea," *J Aerosol Science*, 30(2):173-183 (1999).

[14] Martonen, T.B., "Measurement of Particle Dose Dsitribution in a Model of a Human Larynx and Tracheobronchial Airways," *J Aerosol Science*, 14:11-22 (1983).

[15] Martonen, T.B., Zhang, Z., and Lessmann, R.C., "Fluid Dynamics of the Human Larynx and Upper Tracheobronchial Airways," *Aerosol Science and Technology*, 19:133-156 (1993).

[16] Schlesinger, R.B. and Lippmann, M., "Particle Deposition in Casts of the Human Upper Tracheobronchial Tree," *Am. Industrial Hygene Assoc. Journal*, 237-251 (1972).

[17] Schlesinger, R.B. and Lippmann, M., "Particle Deposition in the Trachea: In Vivo and in Hollow Casts," *Thorax*, 31:678-684 (1976).

[18] Schlesinger, R.B., Bohning, D.E., Chan, T.L., and Lippmann, M., "Particle Deposition in a Hollow Cast of the Human Tracheobronchial Tree," *J Aerosol Science*, 8:429-445 (1977).

[19] Stapleton, K.W., Guentsch, E., Hoskinson, M.K., and Finlay, W.H., "On the Suitability of k-ε Turbulence Modeling for Aerosol Deposition In the Mouth and Throat: A Comparison with Experiment," *J Aerosol Science*, 31(6):739-749 (2000).

[20] Svartengren, K., Lindestad, P-A., Svartengren, M., Philipson, K., Bylin, G., Camner, P., "Deposition of Inhaled Particles in the Mouth and Throat of Asthmatic Subjects," *Eur Respir J*, 7:1467-1473 (1994).