Periciliary Liquid Depth Prediction in Multi-Scale CT based Dynamic Human Lung

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Rationale

- Periciliary liquid (PCL) is a critical component of the respiratory system for maintaining mucus clearance.
- Some *in vitro* studies have suggested that stress influences PCL volume regulation through stress mediated adenosine triphosphate (ATP) release, however whether this mechanism acts at the whole airway level is unclear.
- We have developed a CT image-based multiscale human lung model that integrates computational fluid dynamics (CFD) with a thermodynamics model and an airway epithelial cell model (Warren et al., 2010) to predict PCL depth distribution in a 3-D airway tree.

Methodology

1. Overview

- The CFD component solves 3D incompressible Navier-Stokes and transport equations for temperature and water vapor concentration by an in-house large-eddy simulation (LES) CFD code, providing airway wall shear stress and evaporation as inputs to the cell model.

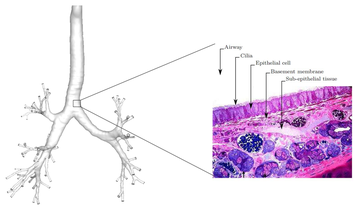

Fig. 1 The integration of CFD model with epithelial cell model

- The epithelial cell model implicitly solves a set of ODEs that describe four processes: shear stress induced ATP release and ATP metabolism, ATP binding to $P2Y_2$ receptor and activation of IP_3 production, IP_3 induced intracellular calcium release, and calcium mediated ion channel gating and osmotic driven fluid secretion, the last of which gives PCL depth.

2. Thermodynamic model

- Temperature and water vapor concentration transport equations are solved in the CT image-based human lung model:

$$c_p\rho\frac{\partial T}{\partial t}+c_p\rho u_i\frac{\partial T}{\partial x_i}=\frac{\partial}{\partial x_i}\left(k\frac{\partial T}{\partial x_i}\right);\quad \frac{\partial C}{\partial t}+u_i\frac{\partial C}{\partial x_i}=\frac{\partial}{\partial x_i}\left(D\frac{\partial C}{\partial x_i}\right)$$

- Conduction equation is solved through different tissue layers around the airway wall:

$$c_{pi}\rho_i\frac{\partial T_i}{\partial t}=k_i\left(\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial T_i}{\partial r}\right)\right),(i=1,2)$$

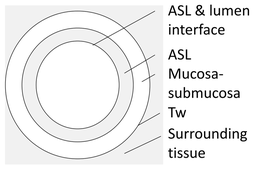

Fig.2 Different layers around the airway lumen

- Energy balance is imposed at the interface between ASL and lumen:

$$K_{asl}\left.\frac{\partial T}{\partial r}\right|_{R^+}=K_{air}\left.\frac{\partial T}{\partial r}\right|_{R^-}+D\Delta H\left.\frac{\partial C}{\partial r}\right|_{R^-}$$

- Evaporation is calculated by the gradient of water vapor concentration:

$$J_{evap}=\frac{1}{\rho_{water}}D\left.\frac{\partial C}{\partial r}\right|_{R^-}$$

3. Epithelial cell model

The epithelial cell model includes four separate models:

- ATP model
- Receptor model
- Intracellular calcium signaling model
- Fluid secretion model.

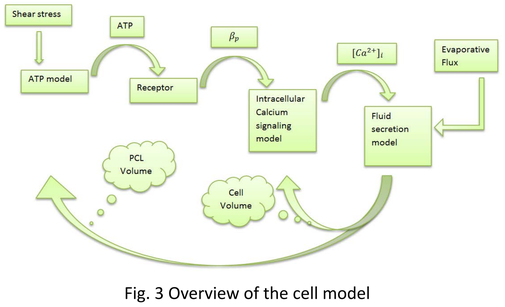

Fig. 3 Overview of the cell model

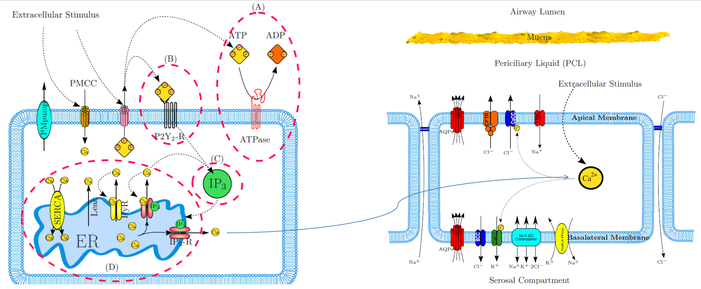

Fig. 4 Schematic of the cell model: (a) signaling pathways; (b) secretion (Warren 2010)

Fig. 4a shows the signaling pathway from ATP release to the intracellular calcium release. ATP binds with the G-Protein coupled receptor and triggers the inositol triphosphate (IP_3) Production, which opens the intracellular calcium channel and release calcium. Fig. 4b shows that after calcium is released, it opens the ion channels, which creates a osmolality gradient that drives the water flow across the membrane and changes the PCL depth.

Results

1. Thermodynamic model

Conditions: Minute ventilation: 15L/min, inhale temperature 27 ^{0}C
absolute humidity 8.8 mg/L, relative humidity 34.7%

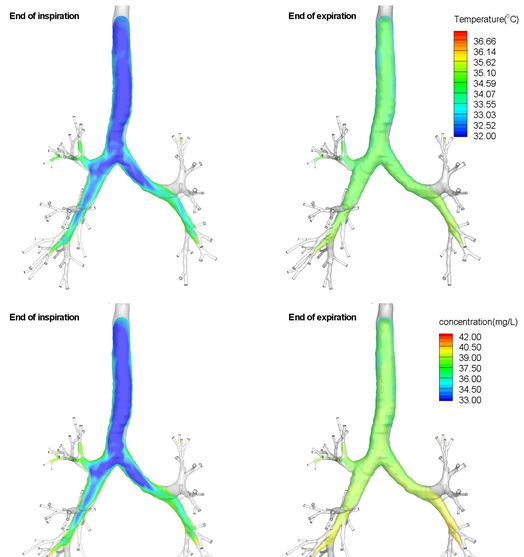

Fig. 5 The temperature (upper) and humidity (lower) distribution at the end of the inspiration (right) and end of the expiration (left)

- Both the temperature and humidity are lower during inspiration than those during expiration.
- During inspiration, the air is heated and water evaporates from the ASL.
- During expiration, the air is cooled down and water condensed on the ASL.

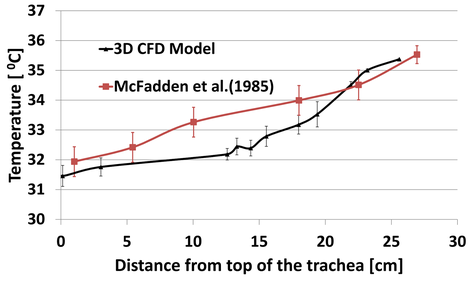

Fig. 6 The comparison between the 3-D model with the experiment at the end of the inspiration. Average value is calculated around the sample points in the center region of the airway, and standard deviation is provided.

2. Prediction of Periciliary Liquid Depth

Conditions: Minute ventilation: 15L/min, inhale temperature 27 ^{0}C
absolute humidity 8.8 mg/L, relative humidity 34.7%

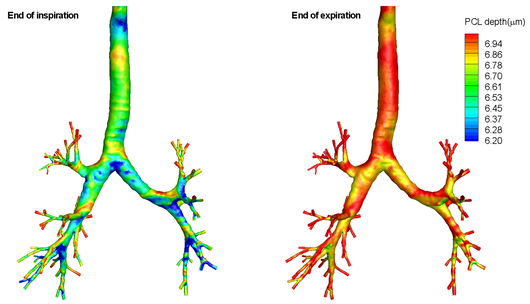

Fig. 7 The PCL depth distribution at the end of inspiration (right) and at the end of expiration(left)

- PCL depth is generally higher in the trachea than in the bronchi.
- PCL depth is lower at the bifurcation, which is correlated with local high evaporation rate and shear stress, perhaps due to local high air speed.

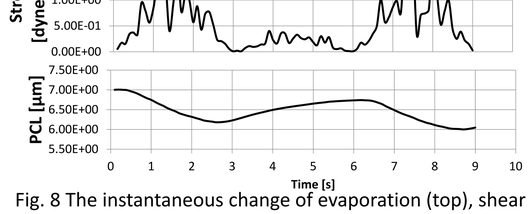

Fig. 8 The instantaneous change of evaporation (top), shear stress (middle) and the PCL depth (bottom) during 1.5 breathing cycles at the carina, starting from inspiration.

- PCL depth dehydrates during inspiration and recovers during expiration.
- Evaporation seems to be the major factor for the change of PCL depth.
- The shear stress is smaller during expiration, but its role in regulating the PCL depth is unclear.

Conclusion

- Evaporation seems to be the predominant factor of PCL dehydration, which is also the main cause of the lower PCL depth at the bifurcation.
- The effect of shear stress is very limited based on the current results. Although it shows the same trends with evaporation, whether it has the same or counter effect as the evaporation is unknown. However, theoretically the shear stress which increases the ATP level could be responsible for increasing the PCL depth. Thus, further study is required.

Future work:

- Cell culture experiment to study the relationship between extracellular ATP concentration and intracellular calcium release
- Coupled 3-D and 1-D thermodynamic model

Reference

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