APPLICATION BRIEF

Targeted Delivery of Antiviral Therapeutics via Atomized Aerosol Inhalation

Coronavirus disease 2019 (COVID-19) is most dangerous for people with underlying conditions such as COPD. COVID-19 can cause severe and life-threatening pneumonia and acute respiratory distress syndrome (ARDS), with accumulated mucus blocking the airways. There is no specific treatment recommended for COVID-19, and no vaccine is currently available. One possible future method of treatment is to deliver an atomized mixture of therapeutic aerosols to the lungs through the mouth. However, delivering aerosols to small airways is difficult since it is known that a large amount of medication will deposit in the mouth-throat region. Only a small fraction of the medication reaches the designated lung sites, i.e., the small airways of which the diameter is less than 2 mm and usually encompass generation 8 (G8) to alveoli, leading to unexpected side effects and ineffective therapeutic outcomes.

Products Used:

Ansys Fluent
Ansys Mechanical

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Research Objective

Our research objective is to use our unique CFD model to demonstrate pulmonary targeted drug deliveries to treat viruses effectively, in a short timescale, by enhancing the therapeutic aerosol delivery to small airways, or even a specific lobe/region of the lung, to be more precise.

Findings

By modulating (1) the size distributions of the atomized therapeutic aerosols, (2) the patient inhalation flow rate and (3) the drug release position at the mouth front, targeted delivery to a specific region of the lung — the lesion sites — can be achieved. Simulation results indicate that this targeted delivery method can deliver more than 90% of the drugs to a single lobe compared with only around 25% using conventional inhalation therapy. This should be also achievable when targeting a certain generation of the lung. We hope the research will be able to advance fundamental understanding and provide a positive impact to clinical practices.

Some Specs of the Simulation

1. Pulmonary therapeutic aerosol droplets/particles ranging from nanometers to tens of microns in diameter. The condensation/evaporation-induced droplet/particle size changes in the humid airways are also modeled.

2. The average inhalation flow rate of the patients ranges from 15 L/min to 90 L/min, depending on the medical device they will use. The inhalation boundary condition is transient waveforms.

3. Subject-specific human respiratory system geometries usually are reconstructed from CT/MRI scanned data. The airway geometry contains mouth/nose to generation 6 (G6), and sometimes can be up to generation 9 (G9) if the CT/MRI images are high-resolution.

4. Disease-specific airway deformation can be integrated using either a dynamic mesh method or fluid–structure interaction (FSI) to accurately describe the disease's influence on the inhalation of the therapeutic aerosols.

Outputs

The outputs we used to disseminate the powerful CFD results are:

1. Therapeutic release map at the mouth front. The drug particles/droplets released at the mouth front are colored by their destinations in the lung (Figure 1).

2. Pulmonary airflow field, including air velocity, pressure, turbulence characteristics, etc. (Figure 2b).

3. Localized therapeutic particle deposition in lung airways (Fig. 2c).

4. After-deposition dynamics, such as the pharmacokinetics and immune system responses. Pharmacokinetics data include the concentration of the therapeutic ingredient in different organs and the blood as a function of time (Fig. 3).

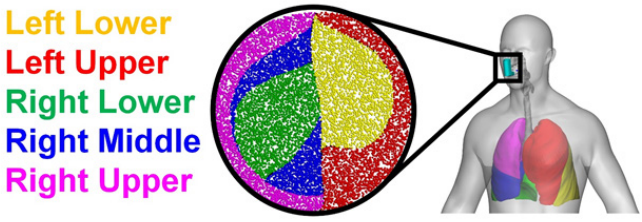

Figure 1. Example of release map of the therapeutics colored by its deposition sites

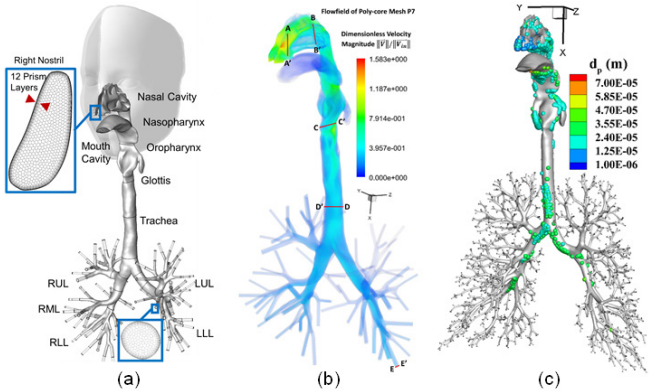

Figure 2. Examples of numerical setup and outputs: (a) subject-specific airway and CFD mesh, (b) airflow field visualization; and (c) droplet deposition with diameter changes

Long-term Goals

Our long-term goal is to build the full 3D physiologically realistic and patient-specific elastic whole-lung modeling system to noninvasively evaluate the therapeutic efficacy of medical interventions via pulmonary aerosol drug delivery with the next-generation virtual human lung model.

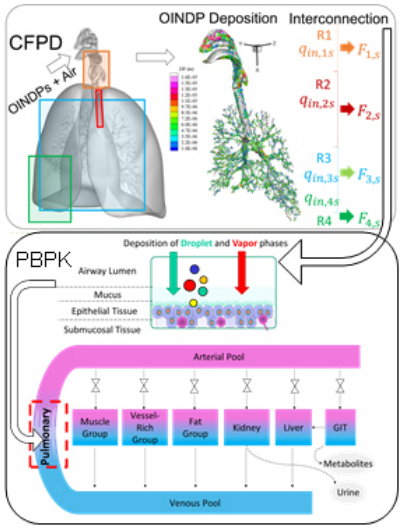

Figure 3. Example of pharmacokinetics modeling

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Disclaimers
These simulations were designed to replicate physical behaviors under specific circumstances. They should not be considered medical guidance and do not account for environmental variants, such as wind or humidity.