**Validation of computational models of aerosol transport in the human lung: what type of experimental data do we need?**

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In recent years, there has been a substantial development of sophisticated subject-specific computational models of aerosol transport and deposition in human lungs. However, experimental validation of predictions from these new models is sparse. The aim of this study was to conduct aerosol deposition studies in subjects that also completed CT scans from which 3D/CFD models of aerosol transport are being developed with the ultimate goal of evaluating model performance.

We collected aerosol retention and exhalation profiles in six healthy volunteers (FEV1 > 80%pred) and four mild to moderate COPD patients (FEV1 = 56-69 %pred) in the supine posture. Total deposition was measured during continuous breathing of 1 and 3 µm-diameter particles at a tidal volume of 1L and a flow rate of either 0.3L/s or 0.75L/s. Bolus inhalations of 1 µm particles were also performed to penetration volumes of 200, 500 and 800 ml at a flow rate of 0.5L/s. Aerosol bolus dispersion, deposition, and mode shift were calculated from these data.

There was no significant difference in total deposition between COPD and healthy subjects. Total deposition increased with increasing particle size and decreased with increasing flow rate. Similarly, there was no significant difference in aerosol bolus deposition between subject groups. Yet, the rate of increase in dispersion with increasing penetration volume was higher in COPD patients than in healthy volunteers (0.53 ± 0.12 ml/ml vs. 0.75 ± 0.24 ml/ml, p=0.031) indicating larger ventilation inhomogeneities in the COPD than in the healthy group. There was also a significant effect of disease (p=0.034) on mode shift. Mode shift was larger in COPD patients than in healthy volunteers, suggesting increased flow sequencing in the COPD group.

In conclusion, in the supine posture, deposition appears to lack sensitivity for assessing the effect of lung morphometry and/or ventilation distribution alteration induced by mild to moderate lung disease on the fate of inhaled aerosols. Our data suggest however that other parameters such as aerosol bolus dispersion and mode shift may be more sensitive parameters for evaluating lung models with moderate disease.

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