ASSESSMENT OF REGIONAL LUNG DEPOSITION OF AEROSOL AERODONE IN IDIOPATHIC PULMONARY FIBROSIS PATIENTS USING FUNCTIONAL RESPIRATORY IMAGING

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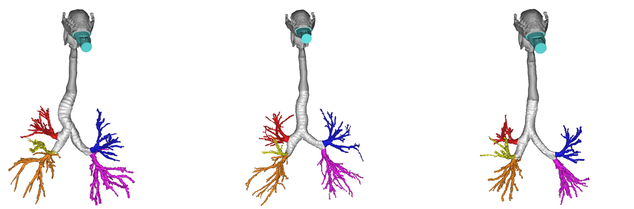
Objectives

Idiopathic pulmonary fibrosis (IPF) is a progressive and fatal disease characterized by an irreversible loss of lung function. Two oral drugs were recently approved for the treatment of IPF; Ofev® (nintedanib) and Esbriet® (pirfenidone). While each drug delivers significant, but limited slowing of IPF disease progression, side effects associated with their large oral dose challenge patient compliance, impede their combined use, and prevent dose escalation for additional efficacy. As an alternative approach, small inhaled doses are capable of delivering large local lung levels. Because inhaled doses are small, systemic exposure is minimized offering potential to reduce or eliminate oral-related side effects. With an improved safety and tolerability profile, the inhaled dose may be escalated for additional IPF efficacy.

In IPF, disease severity may reduce inhaled aerosol access to regions of desired deposition (distal and peripheral airways). In this study, Functional Respiratory Imaging (FRI) was used to measure aerosol pirfenidone (Aerodone™) lung deposition in patients of various IPF disease severity. (FRI has been validated in patients using SPECT CT[1] and gamma scintigraphy[2]). The impact of breathing pattern on deposition was also assessed.

Methods

Three-dimensional geometries of 3 IPF patients were selected according to disease severity; mild (FVC = 83% predicted), moderate (FVC = 60% predicted) and severe (FVC = 42% predicted).

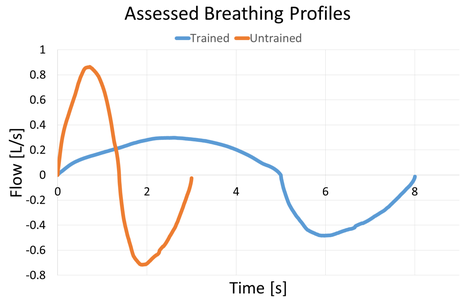


Male, 84 years
FVC = 83% predicted

Female, 75 years
FVC = 60% predicted

Female, 61 years
FVC = 42% predicted

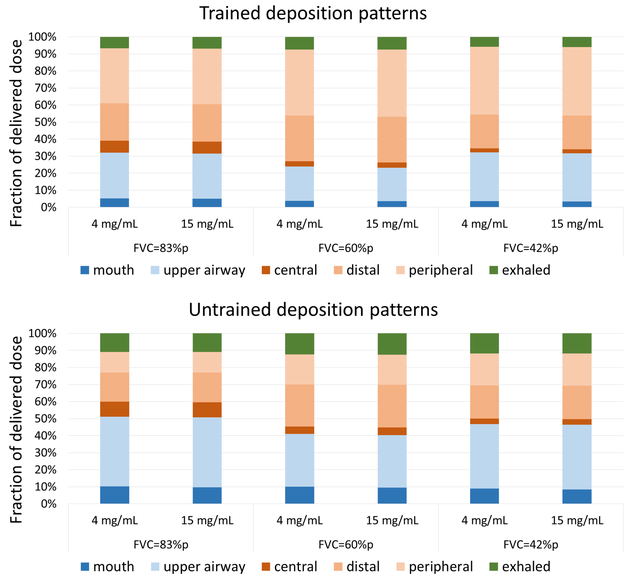
An average upper airway geometry was digitally coupled to each patient-specific intrathoracic region. Using FRI, the fraction of aerosol dose reaching different lung regions was assessed. Aerosols generated from two Aerodone formulations (4mg/mL and 15mg/mL) were studied. The volumetric mean diameter for each aerosol was 3.8μm and 3.7μm, respectively.



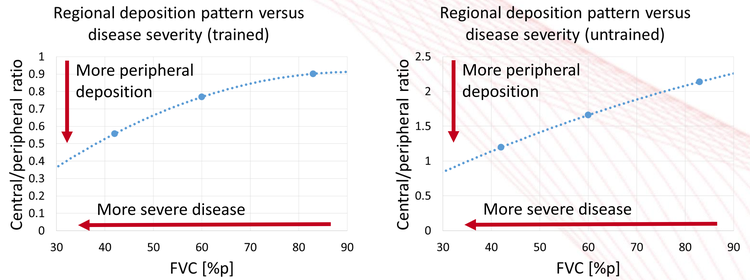
Two breathing patterns were simulated: a trained profile (Inhalation volume: 0.8L, Respiratory rate: 7.5bpm, Inspiration/Expiration ratio: 1.67) and an average untrained IPF profile (Inhalation volume: 0.8L, Respiratory rate: 20bpm, Inspiration/Expiration ratio: 0.85).

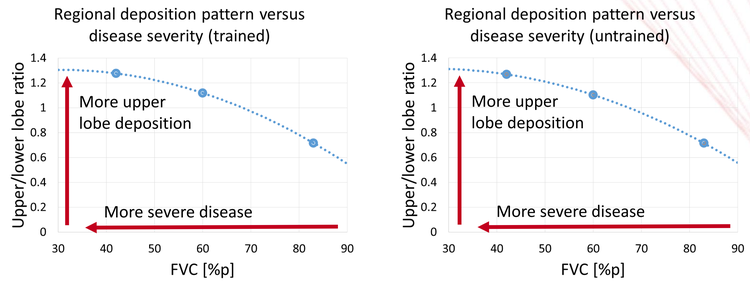
Results

Averaged together, the trained breathing profile resulted in high intrathoracic exposure (64.2%), and large distal (22.9%) and peripheral (37.1%) airway deposition. 6.8% of the trained dose was exhaled. Comparatively, the untrained IPF breathing profile resulted in efficient, albeit lower intrathoracic exposure (42.3%), similar distal (20.6%) and lower peripheral (16.2%) airway deposition. 11.7% of the trained dose was exhaled.



Total intrathoracic deposition was not influenced by disease severity. However, disease severity did correlate with increased upper lobe and peripheral airway deposition. No differences were observed between the two formulations.





Conclusions

Study results indicate that despite disease severity, inhaled Aerodone aerosol particles efficiently deposit in the distal and peripheral airways of the IPF lung. Results further suggest that training IPF patients to take long, slow breaths will improve total and peripheral aerosol deposition.

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References

[1] De Backer, JW, et al. Radiology 2010; 257:854-862

[2] Vinchurkar, S., et al. Inhal. Toxicol. 2012;24(2):81-8