Cluster-guided Imaging-based CFD Analysis of Airflow and Particle Deposition in Asthmatic Human Lungs

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Jiwoong Choi[1], Lawrence J. LeBlanc[1] , Sanghun Choi[2], Babak Haghighi[1], Eric A. Hoffman[1], Ching-Long Lin[1]

[1]The University of Iowa; [2]Kyungpook National University

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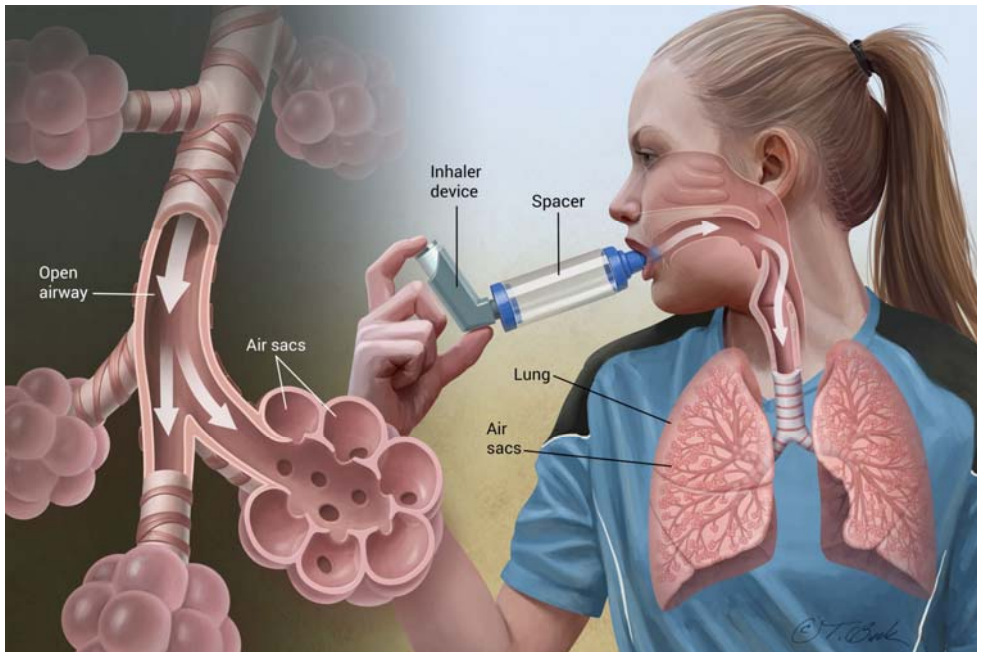
Disclosures: Eric A. Hoffman is a shareholder in VIDA diagnostics, a company that is commercializing lung image analysis software derived by the University of Iowa lung imaging group. He is also a member of the Siemens CT advisory board.

Particle inhalation in asthma

- Inhalation of medication (aerosolized bronchodilators and corticosteroids) is a major treatment for asthma,
- to relax airway smooth muscle and reduce airway wall inflammation, respectively.
- Current delivery methods are limited by low deposition in the peripheral lung regions,
- attributable to
  - lung structural variability,
  - aerosol size,
  - inspiration patterns, and
  - device misuse.

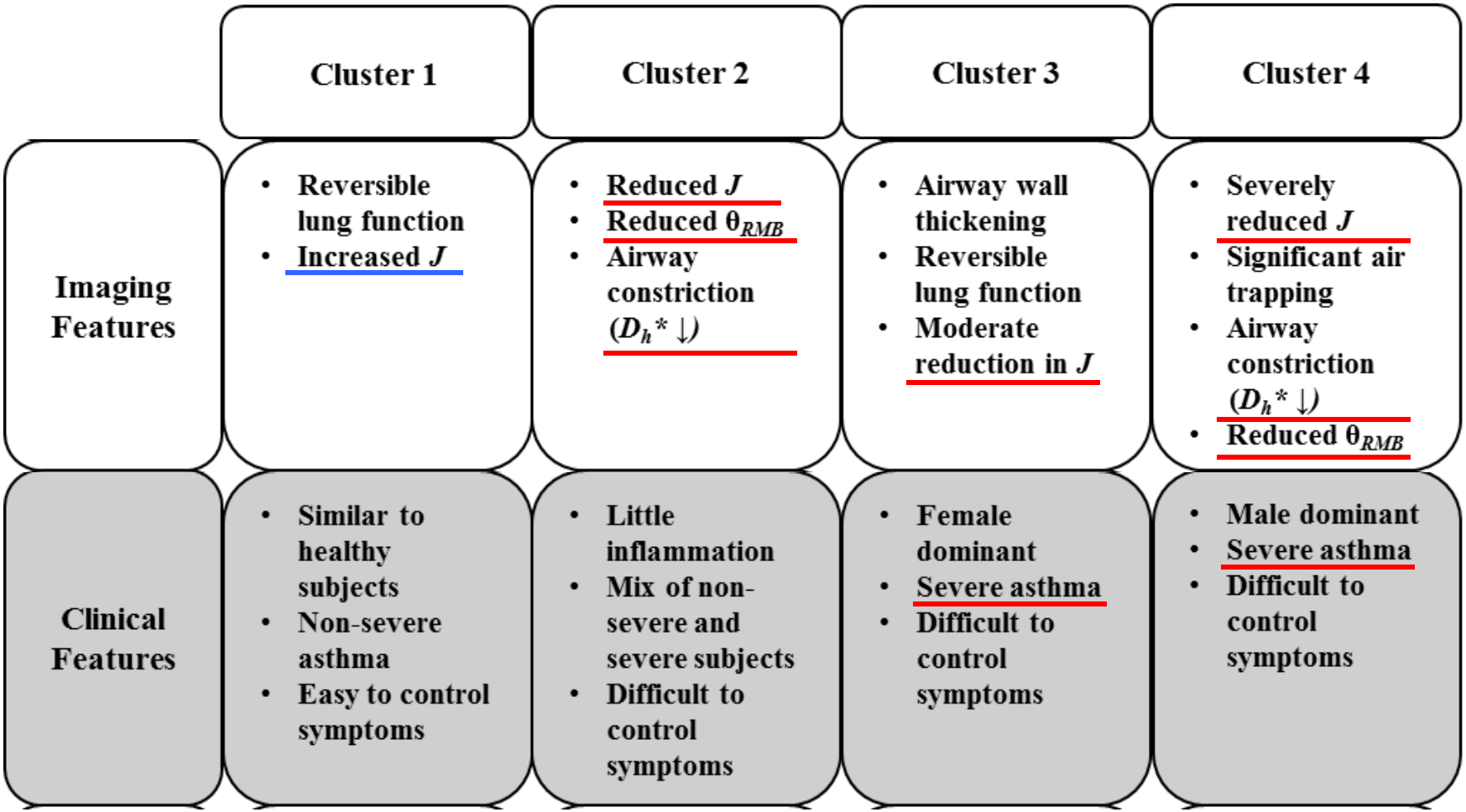


https://foundation.chestnet.org/patient-education-resources/asthma/

Objectives

- Goal: to assess inter-subject variability in delivery of orally inhaled drug products to small airways in asthmatic lungs.
- Aimed to address inter-subject variability via inter-cluster variability, based on distinctive structural and functional metrics for each cluster,
- utilizing CT-based CFD simulations of airflow and particle transport in human lung.

Imaging-based asthma cluster



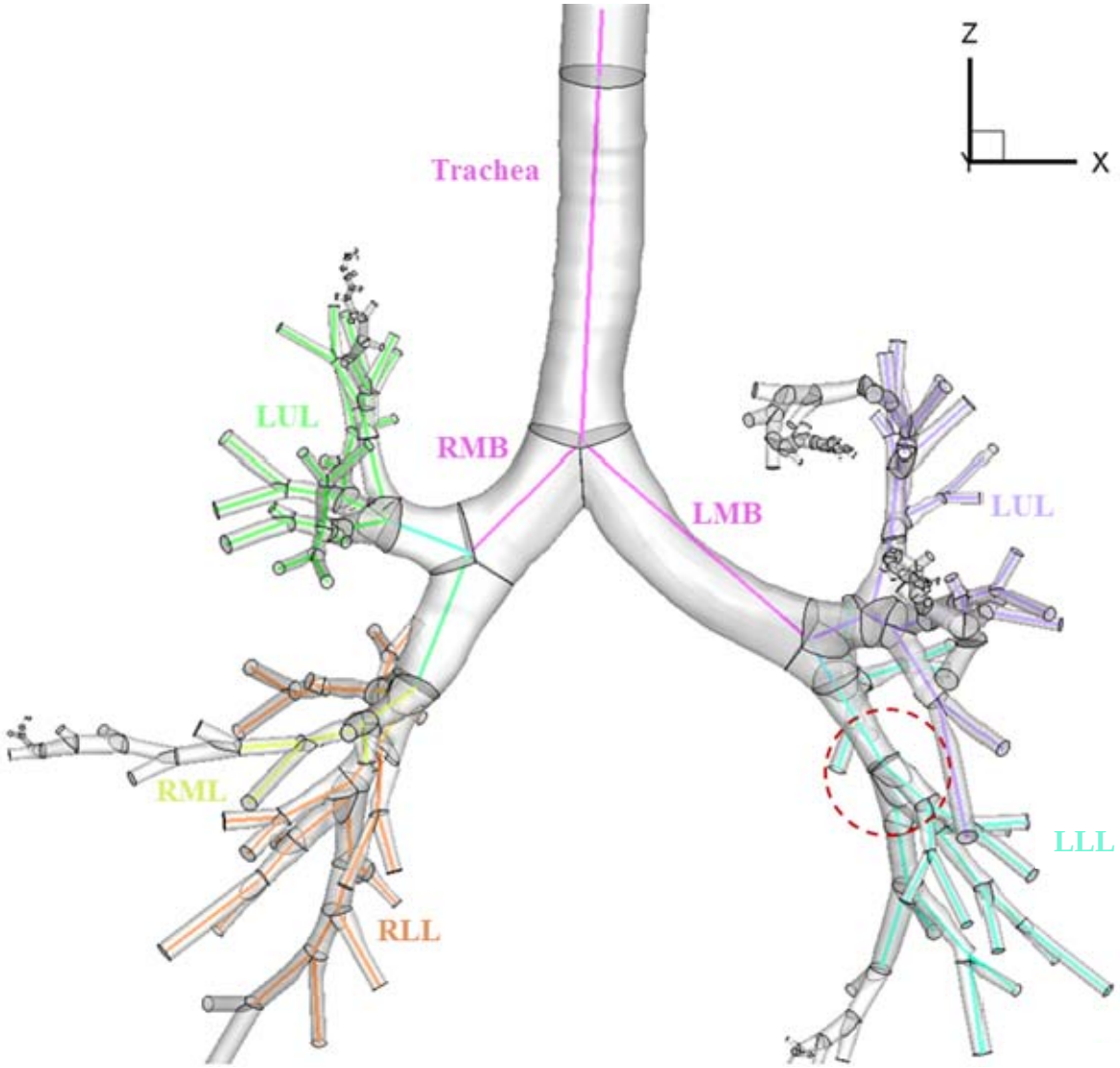
J, Local Jacobian determinant indicating local lung volume change.

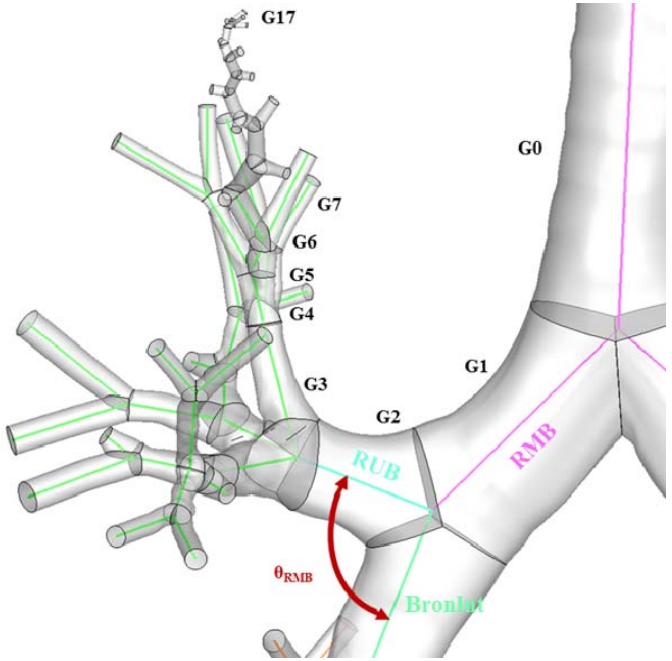
D_h^*, Hydraulic diameter of airway branch, normalized by healthy predicted diameter of the trachea

Choi et al. J Allergy Clin Immunol 2017;140(3):690-700.e8

Airway geometry and ROIs

CT-resolved large airways + 6 paths to terminal bronchioles





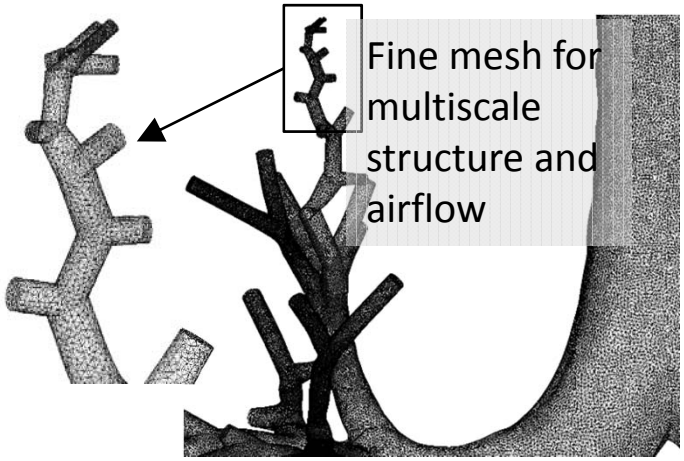
Structural alteration of interest

1. Airway narrowing (LLL)
2. Smaller branching angle (RMB)

Representative subject features

	HF	HM	C1	C2	C3	C4
Demography						
Gender	Female	Male	Female	Male	Female	Male
Age (yrs.)	29	28	20	52	49	51
Weight (kg.)	61.5	99.0	58.6	111.8	85.1	103.0
Asthma Severity	N/A	N/A	Non-severe	Non-severe	Severe	Severe
Features for Representative Subject Selection						
IC (Liters)	2.5 (2.2)	3.4 (3.1)	3.0 (3.2)	2.5 (1.8)	2.7 (2.0)	1.8 (2.1)
D_h^*(sLLL)	0.35 (0.34)	0.38 (0.33)	0.37 (0.34)	0.24 (0.27)	0.43 (0.34)	0.23 (0.28)
Structural Variables for Analysis						
D_h^*(sLLL)	0.35	0.38	0.37	0.24	0.43	0.23
D_h^*(sRUL)	0.34	0.37	0.35	0.24	0.39	0.20
ϑ_{RMB} (º)	90.0	90.0	94.8	74.8	91.3	67.9
Functional Variables for Analysis						
J	2.0 (2.0)	2.4 (2.1)	3.3 (2.5)	1.8 (1.7)	1.9 (1.9)	1.4 (1.5)
CFD Flow Inlet Conditions at Peak Inspiration (PI)						
Q_{PI} (L/min)	50.2	66.7	60.2	50.5	53.3	35.8
D_h^* (Trachea)	1.17	0.99	0.88	0.94	1.23	0.97
Re	4364	5364	6647	3905	3894	2742

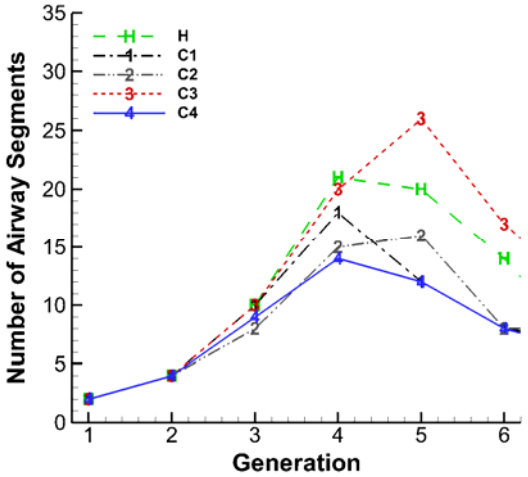
Subject specific multiscale CFD simulations

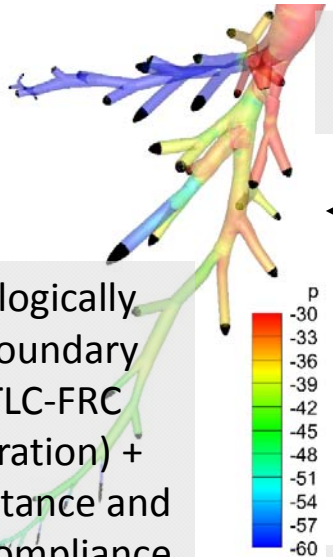


Fine mesh for multiscale structure and airflow

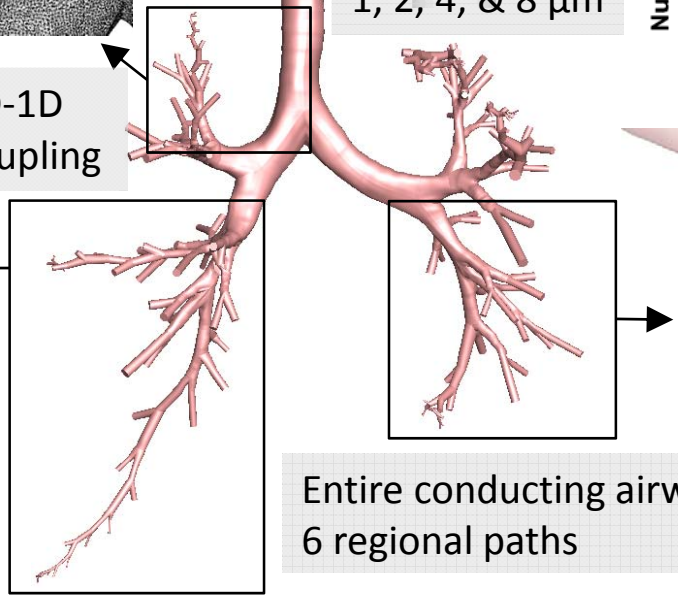
Slow and deep inhalation (CT-based inspiratory capacity)

200,000 particles 1, 2, 4, & 8 µm

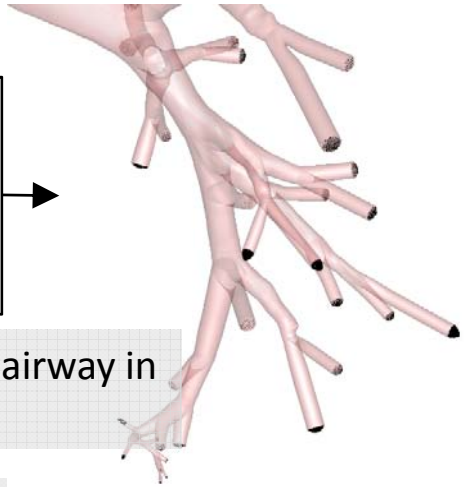




3D-1D coupling



Pathophysiologically consistent boundary condition. (TLC-FRC image registration) + (airway resistance and peripheral compliance model)

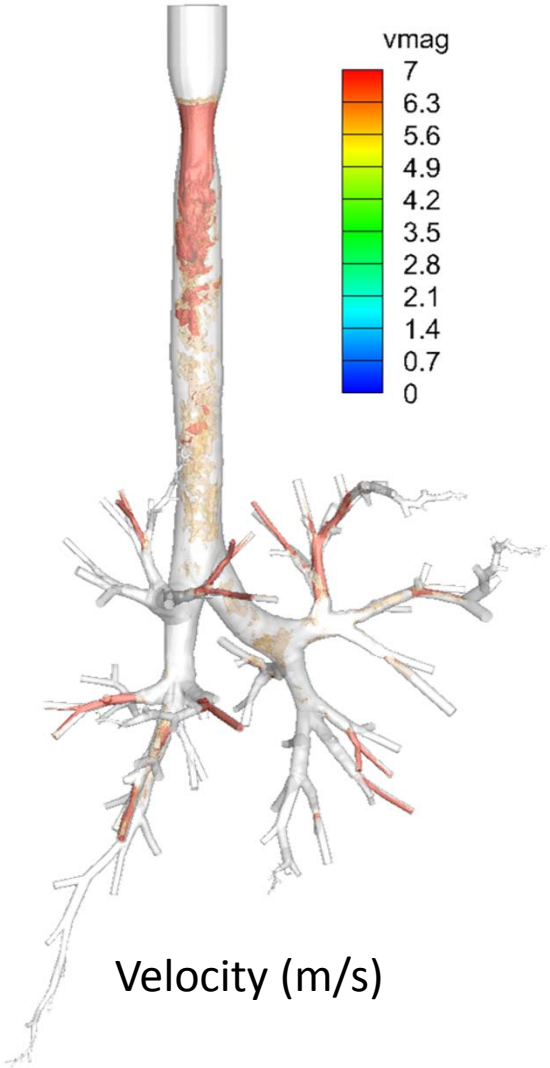


Entire conducting airway in 6 regional paths

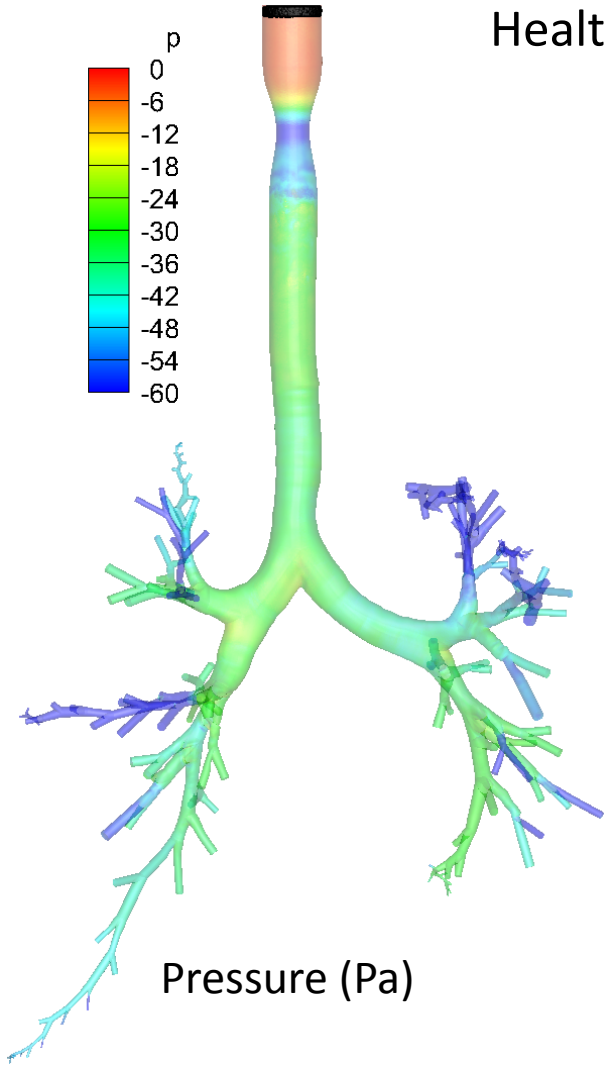
Large eddy simulations on a MPI-based finite element framework (160-320 CPU cores)

Choi et al. 2009 PoF 21 (10), 101901; Yin et al. 2010 J Biomech 43 (11), 2159-2163; Lin et al. 2013 WIREs Syst Biol Med 5:643–655

Airflow and particle transport

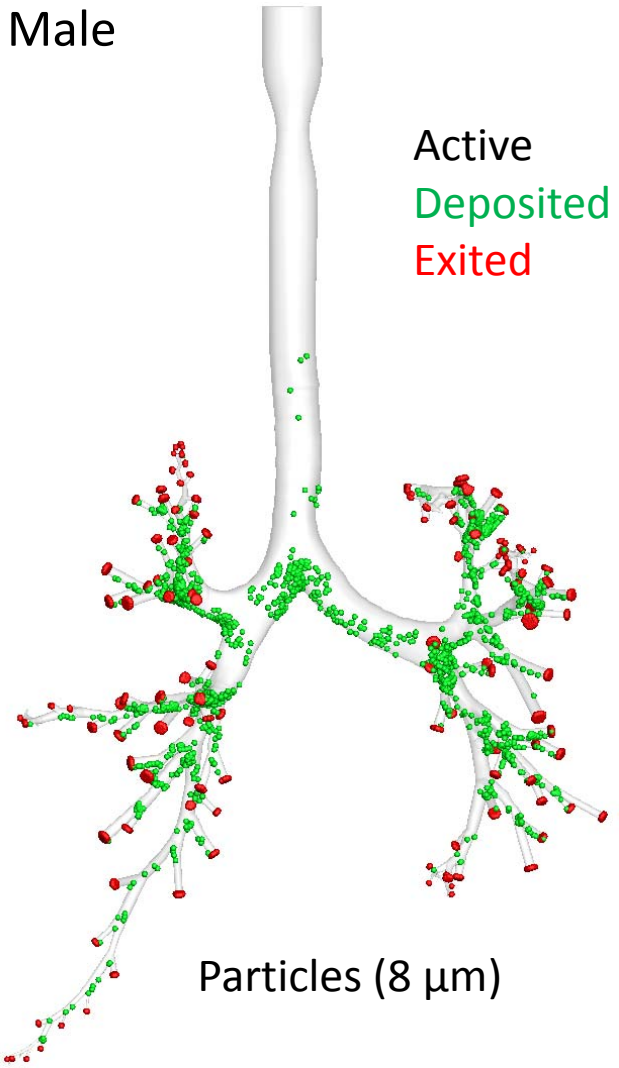


Velocity (m/s)



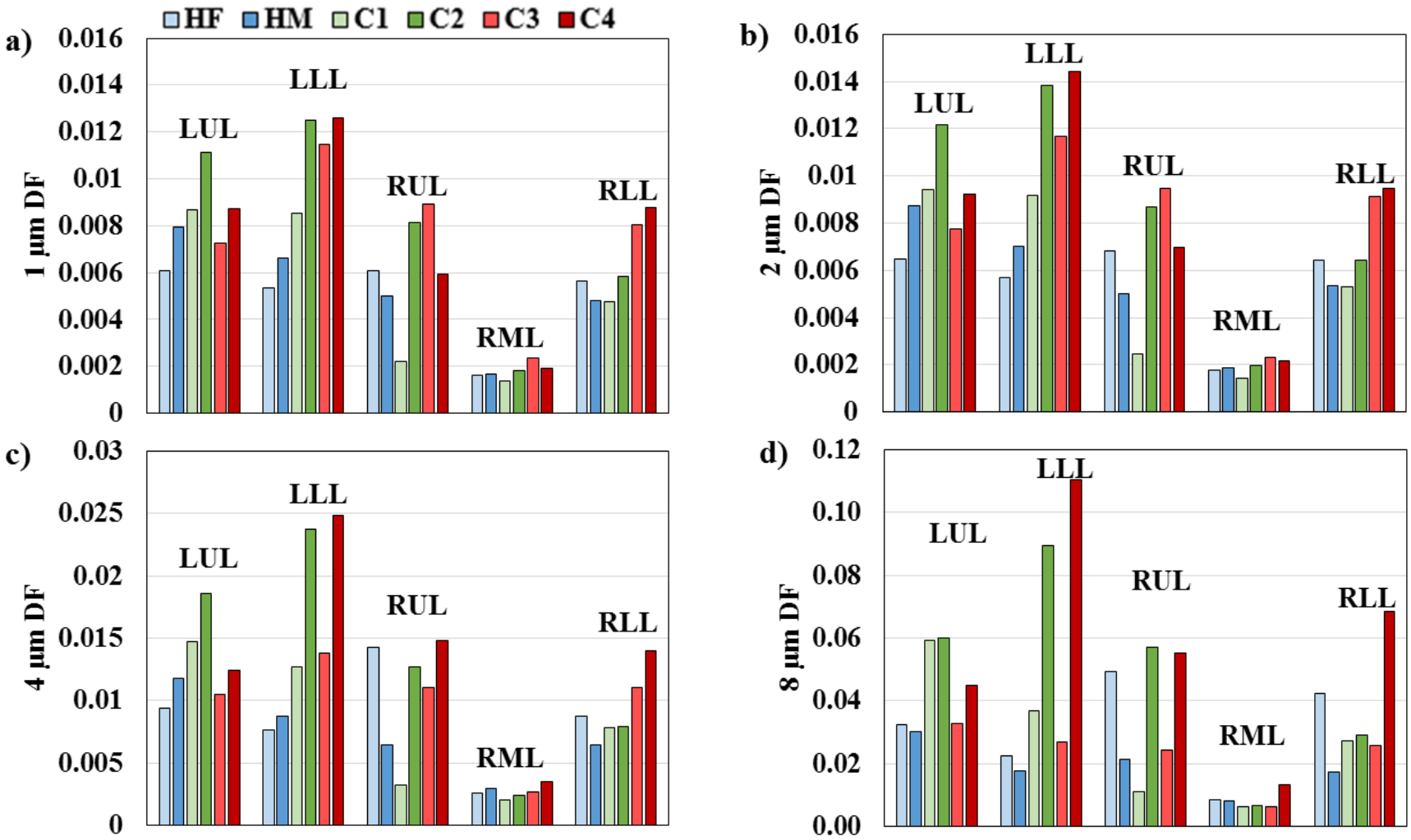
Pressure (Pa)

Healthy Male

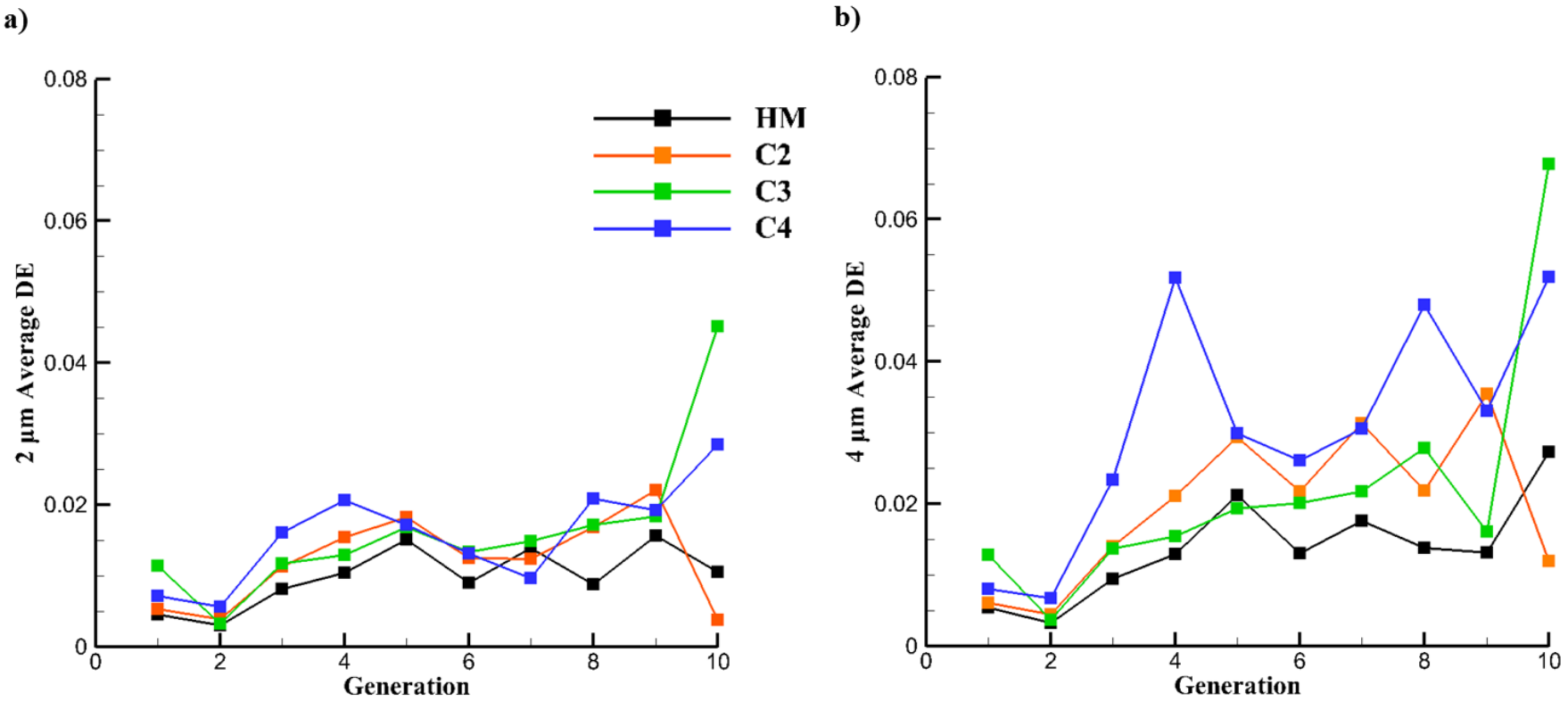


Particles (8 µm)

Lobar particle deposition fractions

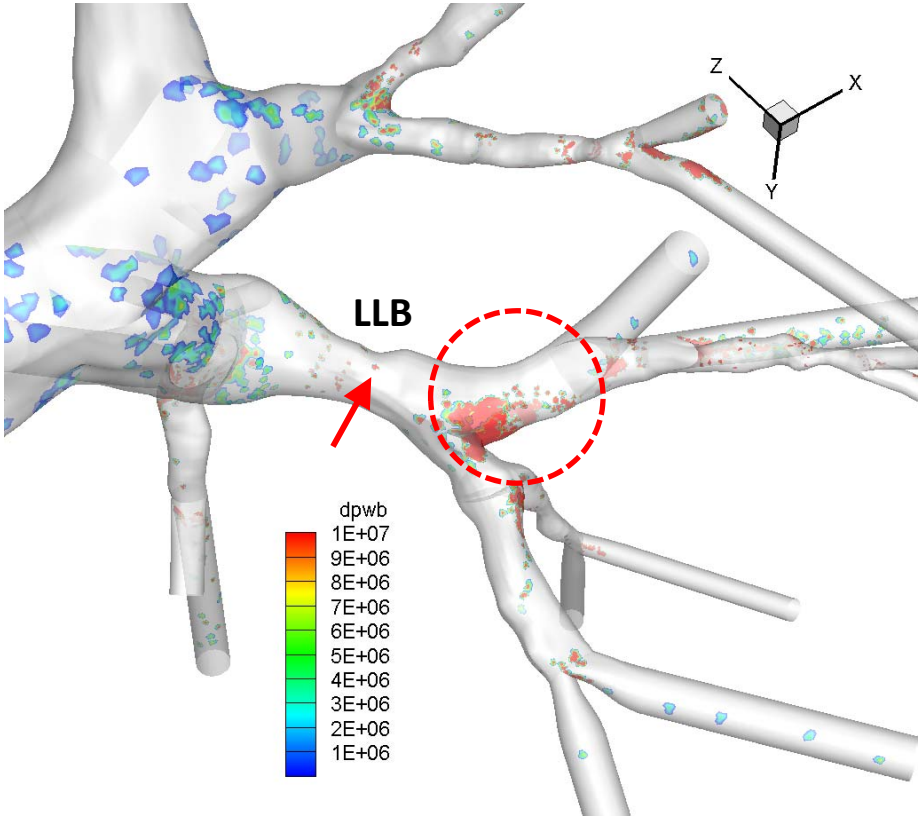


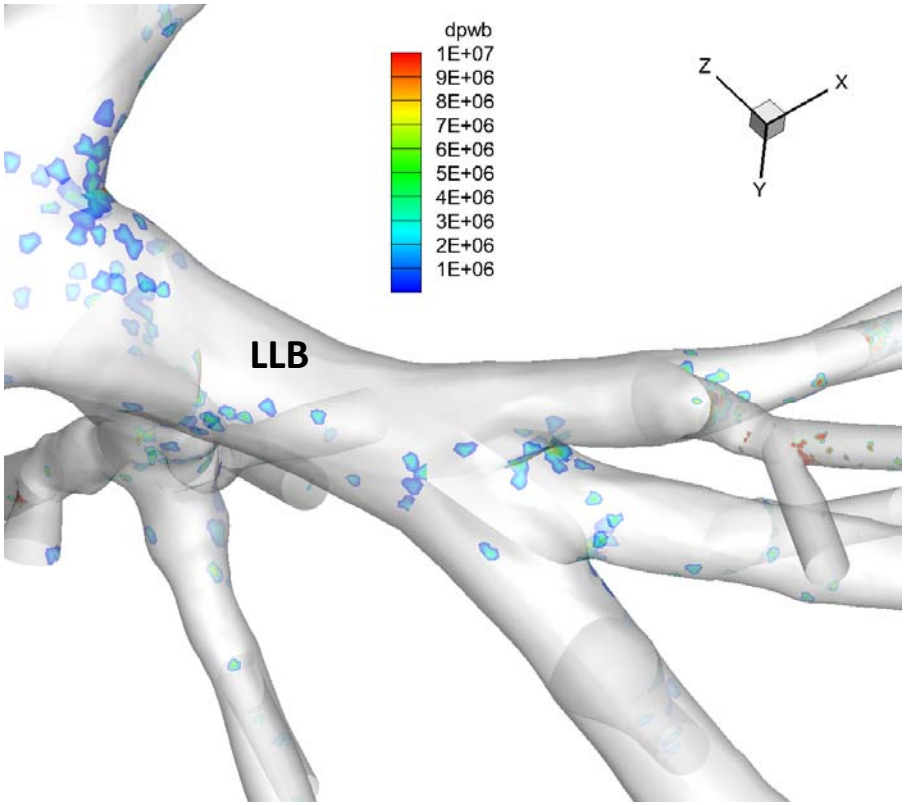
Generational particle deposition efficiency



Particle deposition fraction and efficiency both increased in one severe (C4) and one non-severe (C2) asthmatic cluster subjects characterized by segmental airway constriction, as compared with the other two cluster subjects (one non-severe and one severe asthmatics) without airway constriction.

LLB constriction

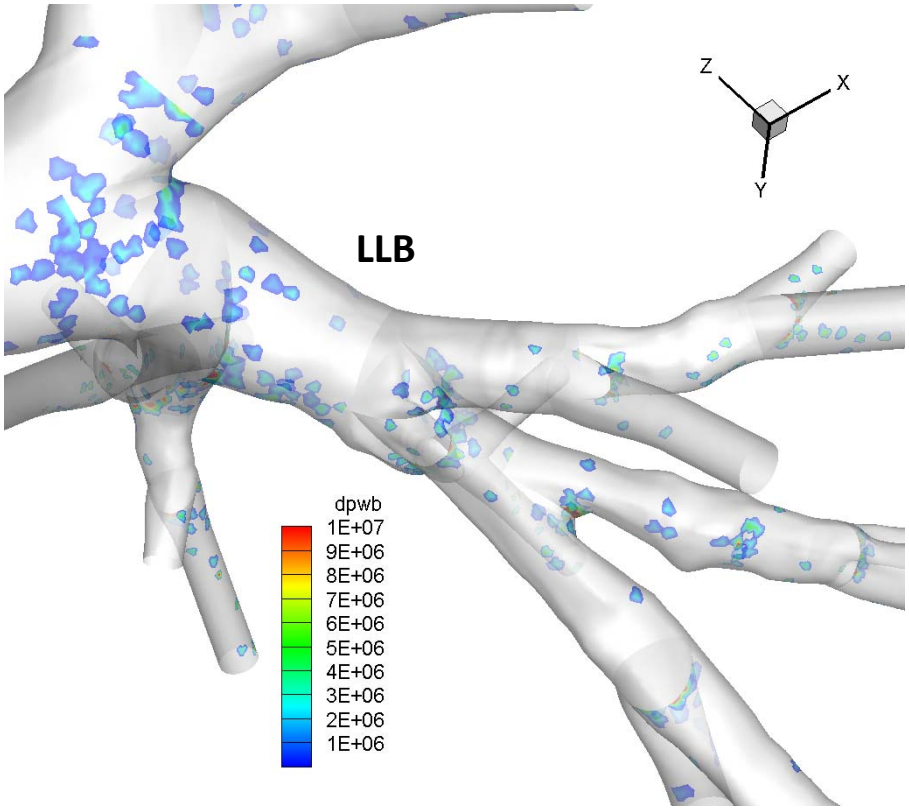


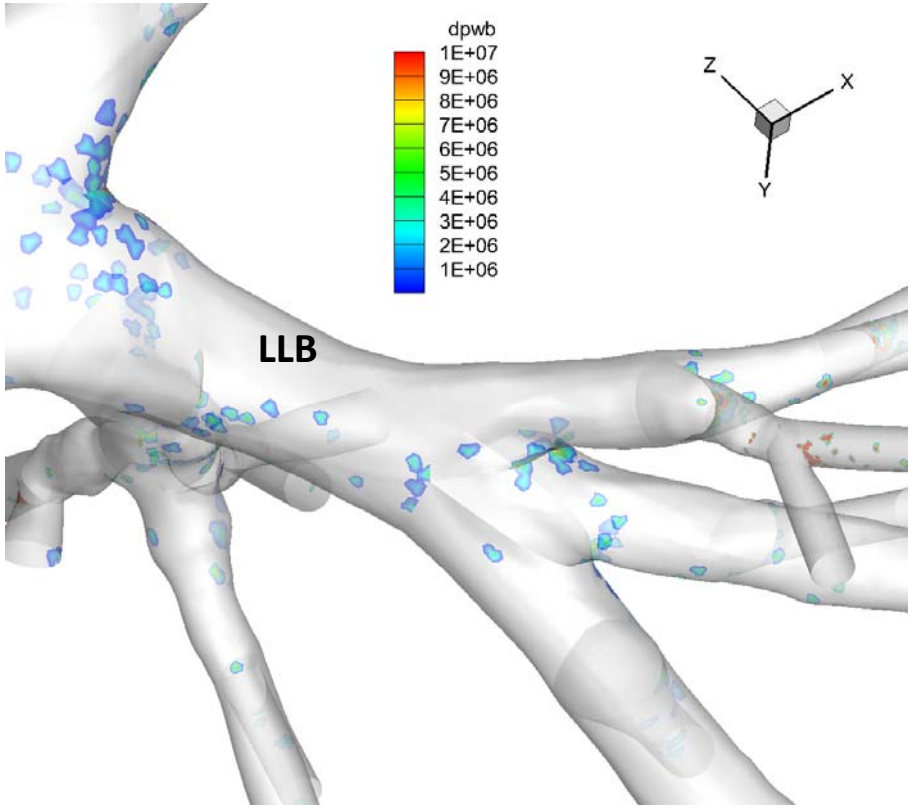


Cluster 4: D_h* = 0.226

Healthy Male: D_h* = 0.380

LLB constriction



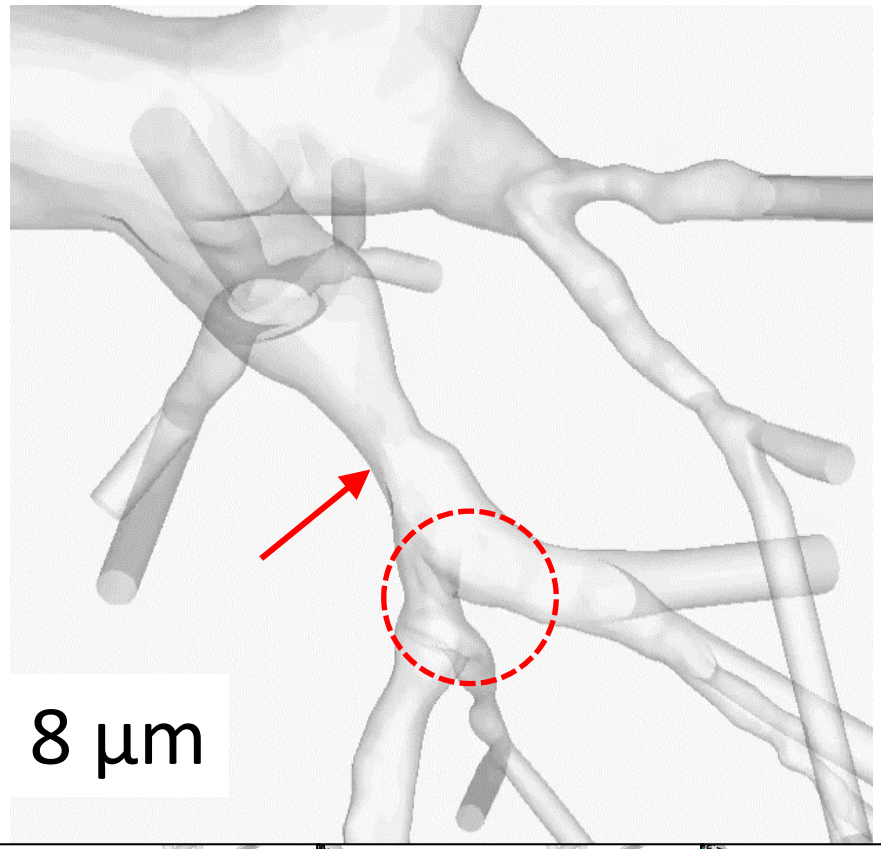


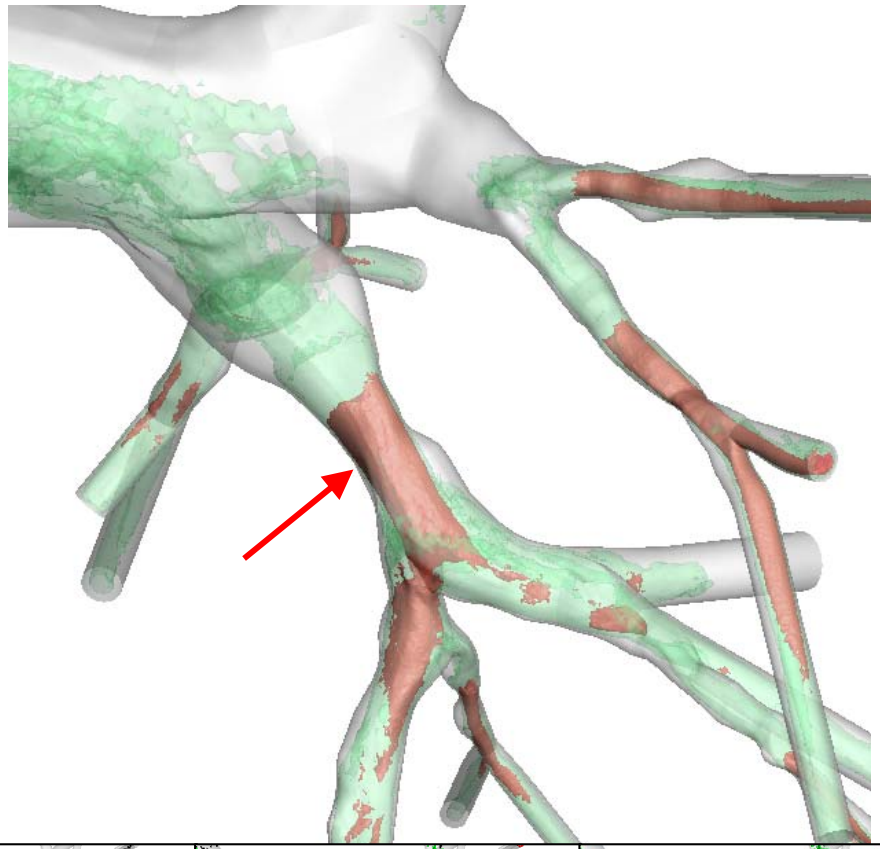
Cluster 3: D_h* = 0.428

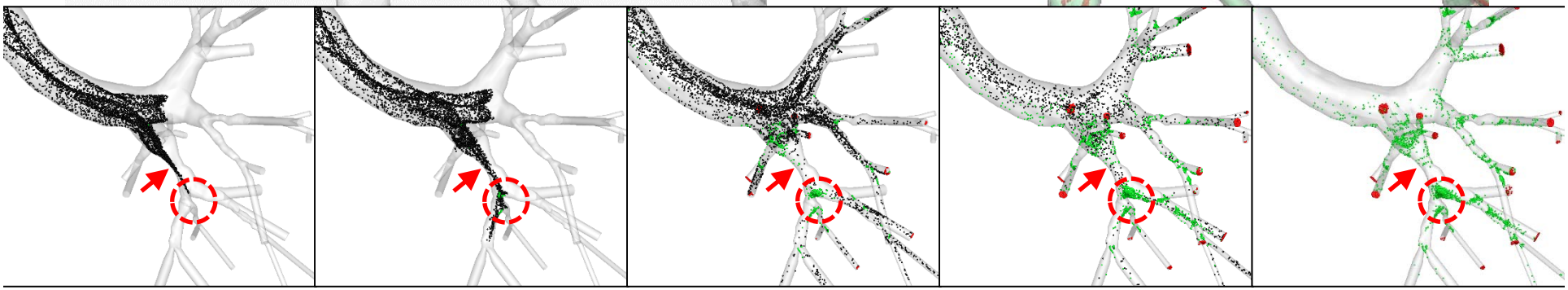
Healthy Male: D_h* = 0.380

LLB constriction

Cluster 4

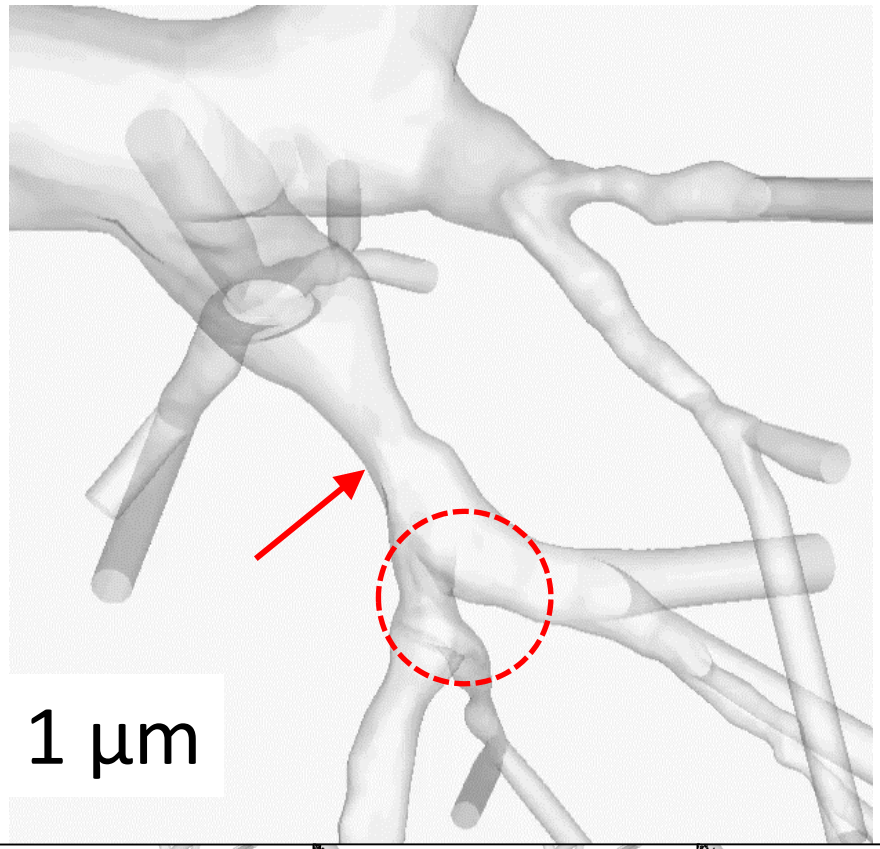


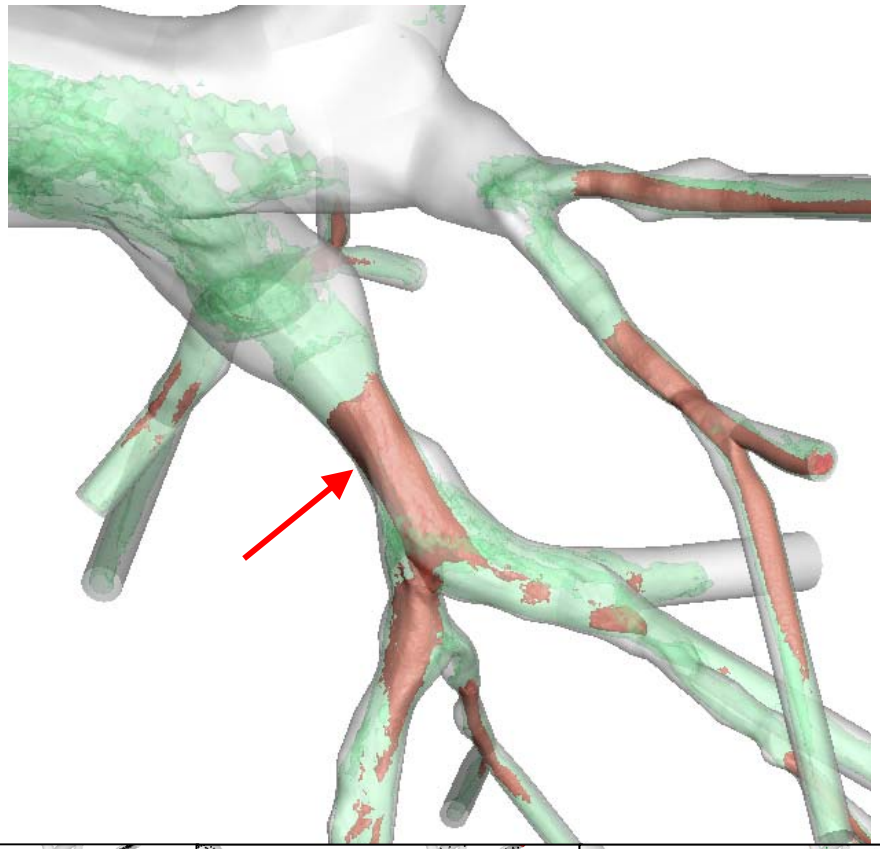


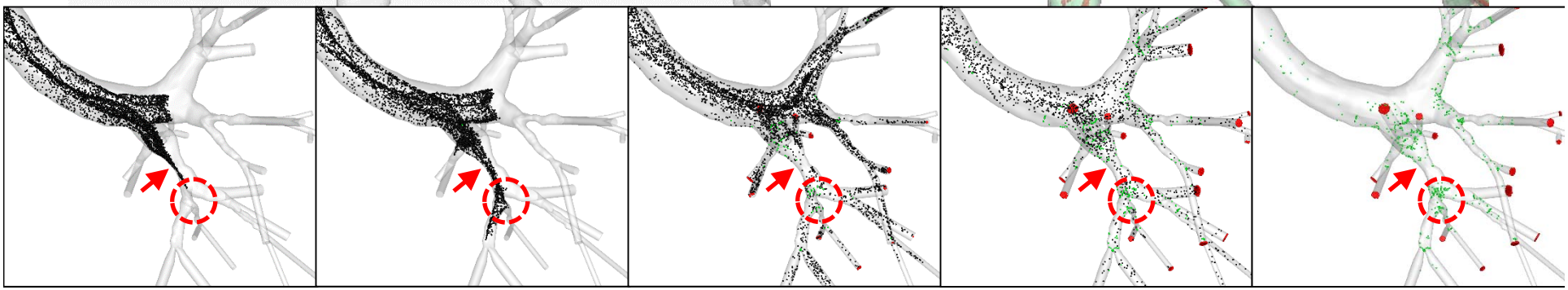


LLB constriction

Cluster 4

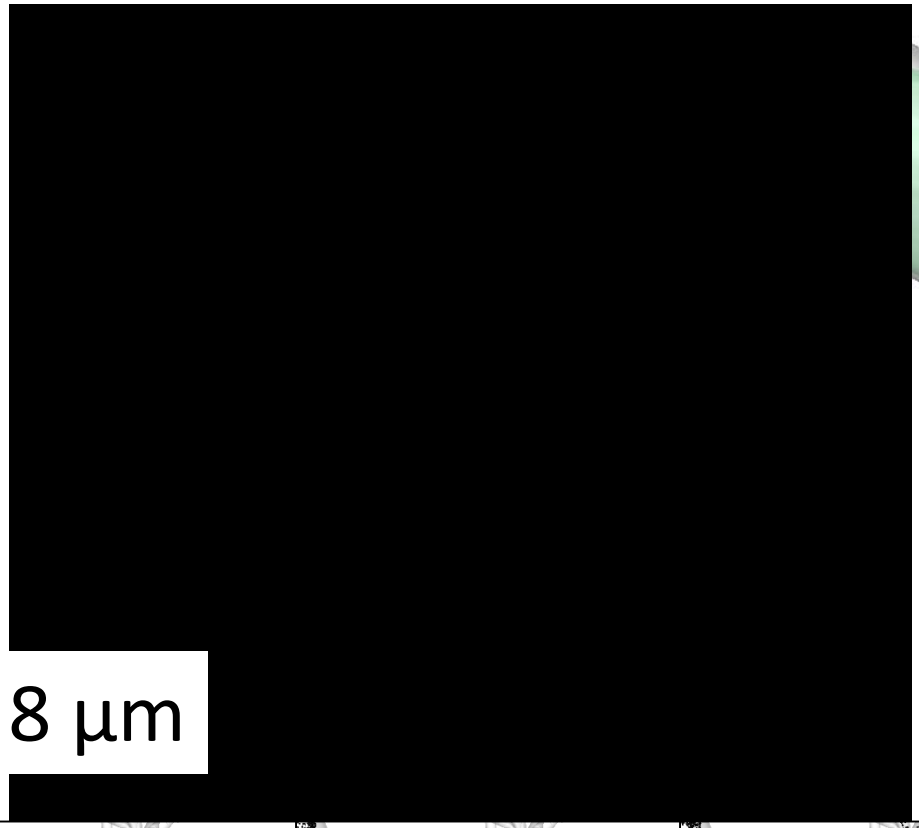


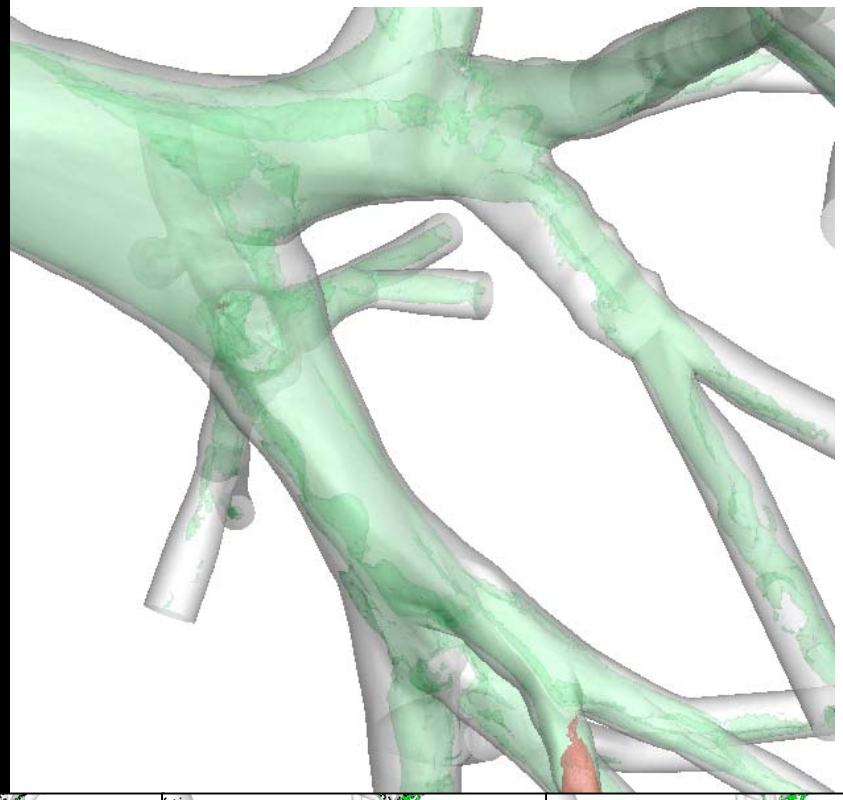


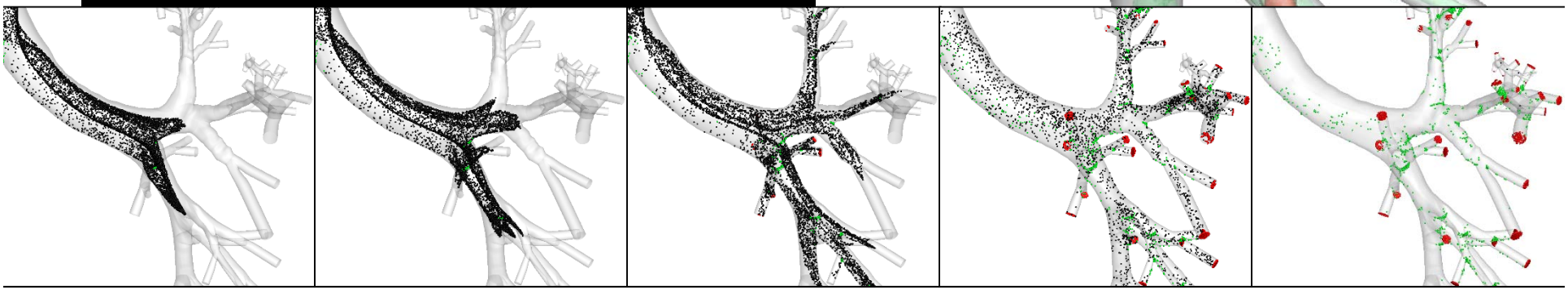


LLB constriction

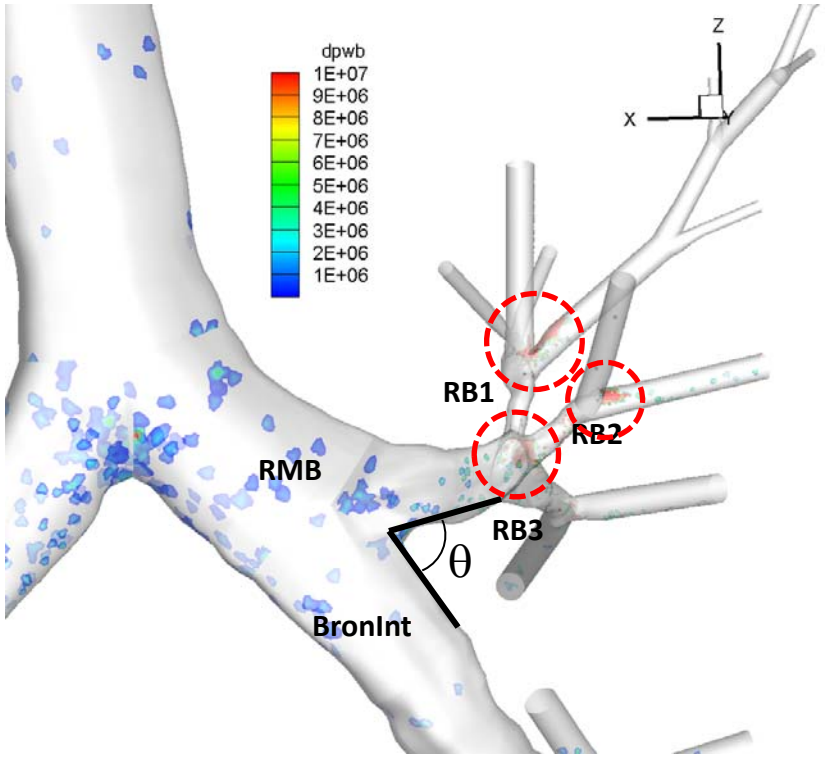
Healthy



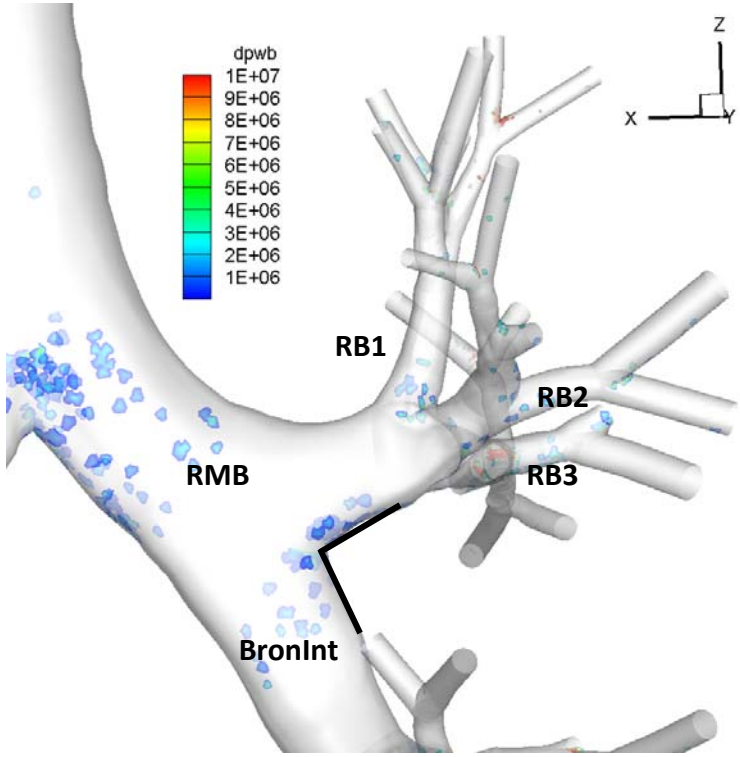




RMB branching angel, θ



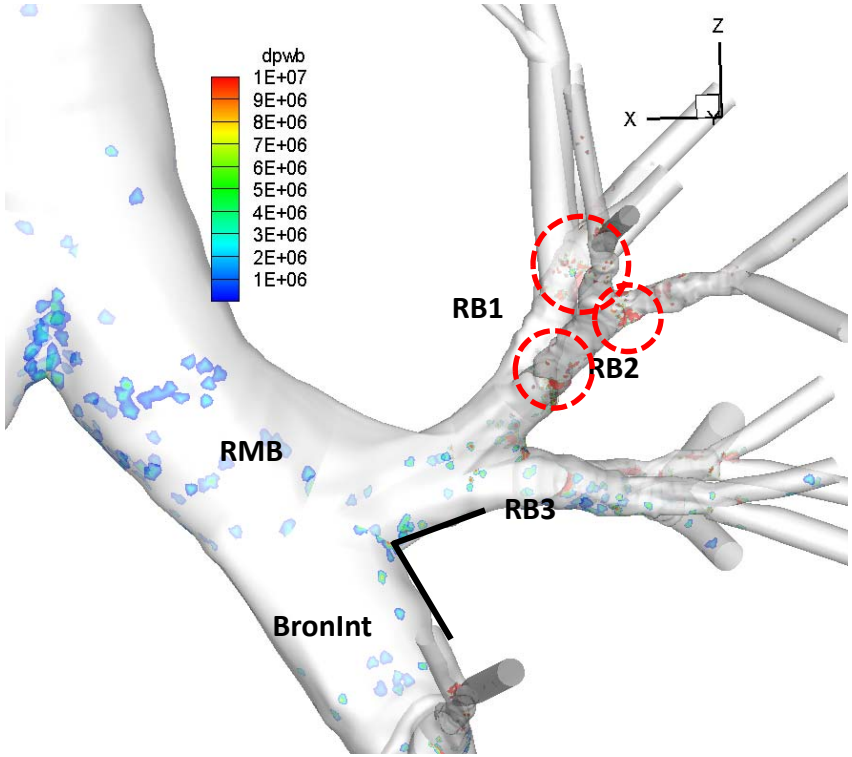
Cluster 4: θ = 68 °



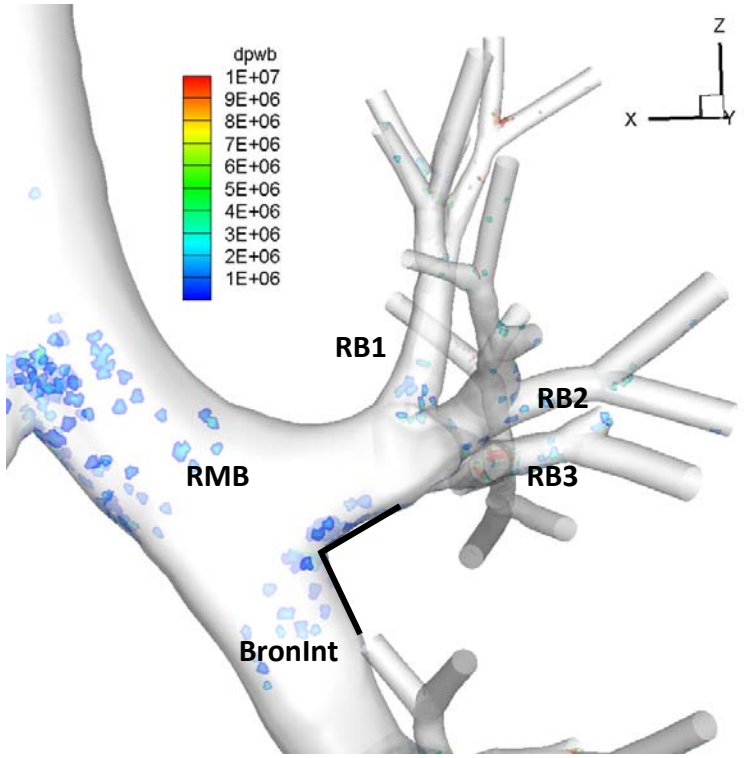
Healthy Male: θ = 90 °

*View of RMB is from behind.

RMB branching angel, θ



Cluster 2: θ = 75 °



Healthy Male: θ = 90 °

*View of RMB is from behind.

Discussion

	Cluster 1	Cluster 2	Cluster 3	Cluster 4
Clinical Features	• Similar to healthy subjects • Non-severe asthma • Easy to control symptoms	• Little inflammation • Mix of non-severe and severe subjects • Difficult to control symptoms	• Female dominant • Severe asthma • Difficult to control symptoms	• Male dominant • Severe asthma • Difficult to control symptoms
Imaging Features	• Reversible lung function • Increased J	• Reduced J • Reduced θ_{RMB} • Airway constriction ($D_h^* \downarrow$)	• Airway wall thickening • Reversible lung function • Moderate reduction in J	• Severely reduced J • Significant air trapping • Airway constriction ($D_h^* \downarrow$) • Reduced θ_{RMB}
CFD Features	• Reduced Re • Increased Stk • Similar to healthy subjects	• Reduced Re • Increased Stk • LLL DF ↑ • DE ↑ in segmental and sub-segmental airways • DE ↑ distal to θ_{RMB}	• Reduced Re • Increased Stk • Generational DE similar to healthy subjects • Particle FF ↑ in RUL	• Reduced Re • Increased Stk • LLL DF ↑ • DE ↑ in segmental and sub-segmental airways • DE ↑ distal to θ_{RMB}

Summary

- The aim of this study was to utilize imaging-based cluster membership in conjunction with lung CFD to assess the effects of cluster-specific, imaging-based variables on air flow, particle transport, and deposition.
- Structural metrics such as airway narrowing in C2 and C4 clusters contributed to higher deposition in lobar, segmental, and selective sub-segmental airways.
- Characterization of inter-cluster variability with respect to particle transport could potentially help improve inhalation drug delivery in asthma sub-populations.
- Results demonstrate the power of understanding MICA features, and using them as a means of exploring the asthma drug treatment implications of structural and functional differences within an asthmatic population, and assessing the efficacy of orally-inhaled drugs.

Thank You