71th APS DFD
Session L18: Biological fluid dynamics: Breathing

Assessment of Effects of Selective Airway Luminal Expansion on Inhaled Particle Deposition in Severe Asthmatic Human Lungs – A Numerical Study

November 19, 2018, 4:57-5:10pm
Room B305, Georgia World Congress Center, Atlanta, GA

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Acknowledgments

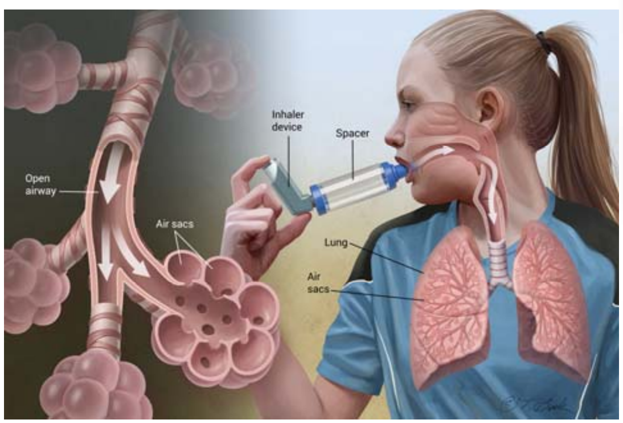
- FDA grant U01-FD005837; NIH grants U01-HL114494 and S10-RR022421.
- Views expressed in this work do not necessarily reflect the official policies of the Department of Health and Human Services and may not be quoted as being made on behalf of a reflecting the position of the US Food and Drug Administration; nor does any mention of trade names, commercial practices, or organization imply endorsement by the United States Government.
- We also thank the Extreme Science and Engineering Discovery Environment (XSEDE) (allocation MCA07S015) sponsored by the National Science Foundation for computational time and data storages at the Texas Advanced Computing Center (TACC) (Stampede2, Ranch) and the San Diego Supercomputer Center (SDSC) (Comet, Data Oasis).

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.
- A recent CT imaging-based cluster analysis (Choi S et al. 2017) classified asthma patients into 4 clusters.

	Imaging characteristics	Clinical characteristics
Cluster 1	• Normal airway structure • Increased lung deformation (Jacobian and ADI↑)	• Younger, early onset • Nonsevere asthma • Reversible lung function • Easy to control asthma symptoms
Cluster 2	• Airway luminal narrowing (D_h*↓) • No airway wall thickening (WT*) • Significant reduction of lung deformation (Jacobian and ADI↓)	• Nonsevere and severe asthma • Persistently altered lung function • Marginal to no inflammation • Difficult to control asthma symptoms
Cluster 3	• Airway wall thickening (WT*↑) • No airway luminal narrowing (D_h*) • Moderate reduction of lung deformation (Jacobian and ADI↓)	• Obese, female-dominant • Severe asthma • Reversible lung function • Blood lymphopenia • Difficult to control asthma symptoms
Cluster 4	• Airway luminal narrowing (D_h*↓) • Significant reduction of lung deformation (Jacobian and ADI↓) • Significant air-trapping (AirT%↑)	• Older, late onset, male-dominant • Severe asthma • Persistently altered lung function • Neutrophilic-dominant inflammation • Difficult to control asthma symptoms

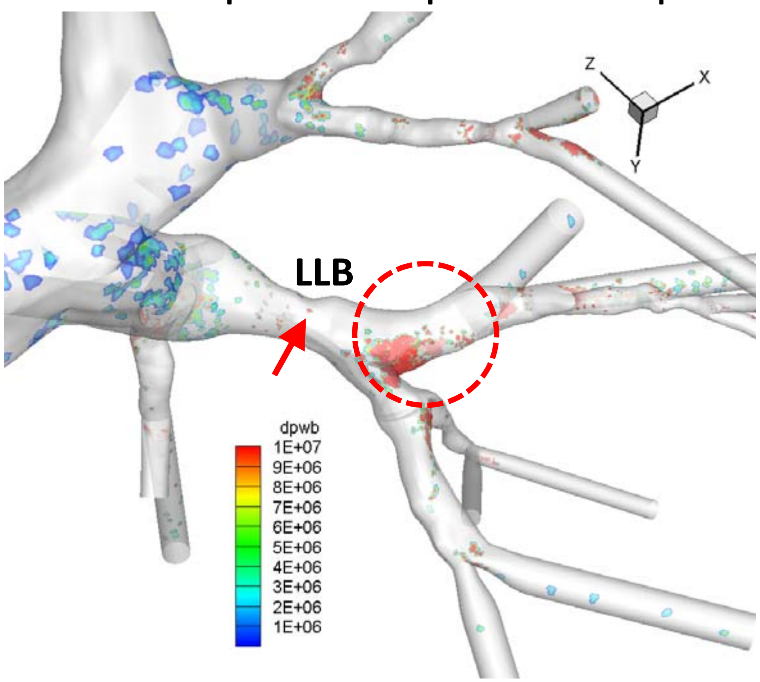


https://foundation.chestnet.org/patient-education-resources/asthma/

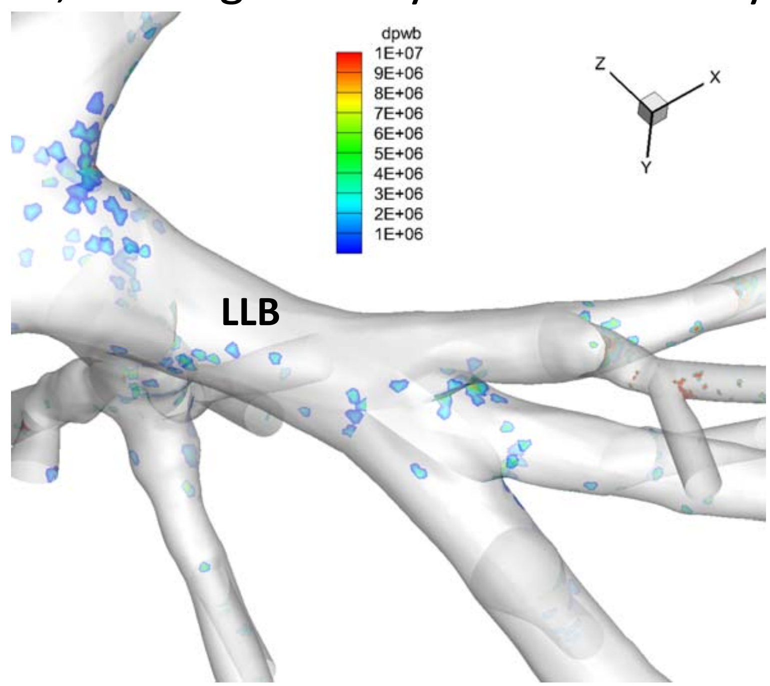
Choi S et al. 2017 J Allergy Clin Immunol 140(3):690-700

Particle inhalation in asthma

- Cluster-guided CFD analysis (Choi J et al. 2017 APS DFD) showed the proximal airway constriction of a severe asthmatic cluster (cluster 4) had increased proximal particle deposition, limiting delivery to small airways.



Cluster 4: D_h^* = 0.226



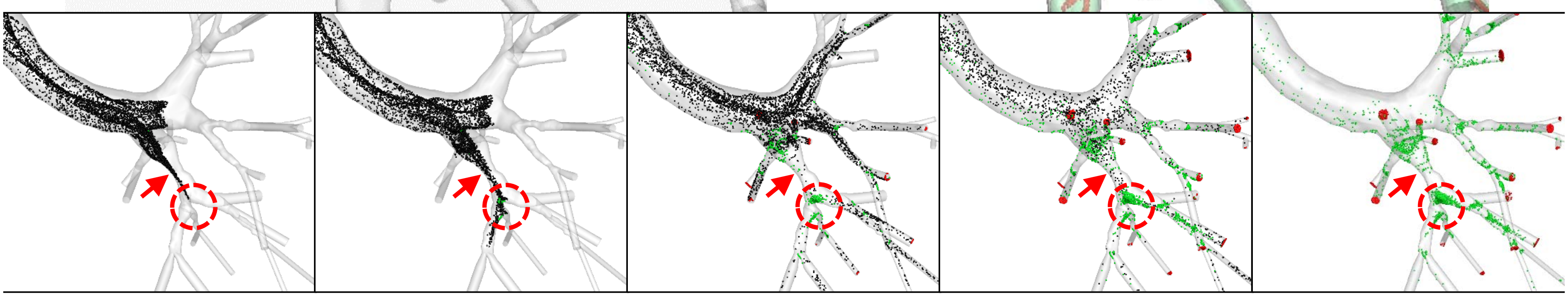
Healthy Male: D_h^* = 0.380

LLB: Left lower bronchus

D_h^*: Hydraulic diameter of airway lumen normalized by the predicted tracheal diameter.

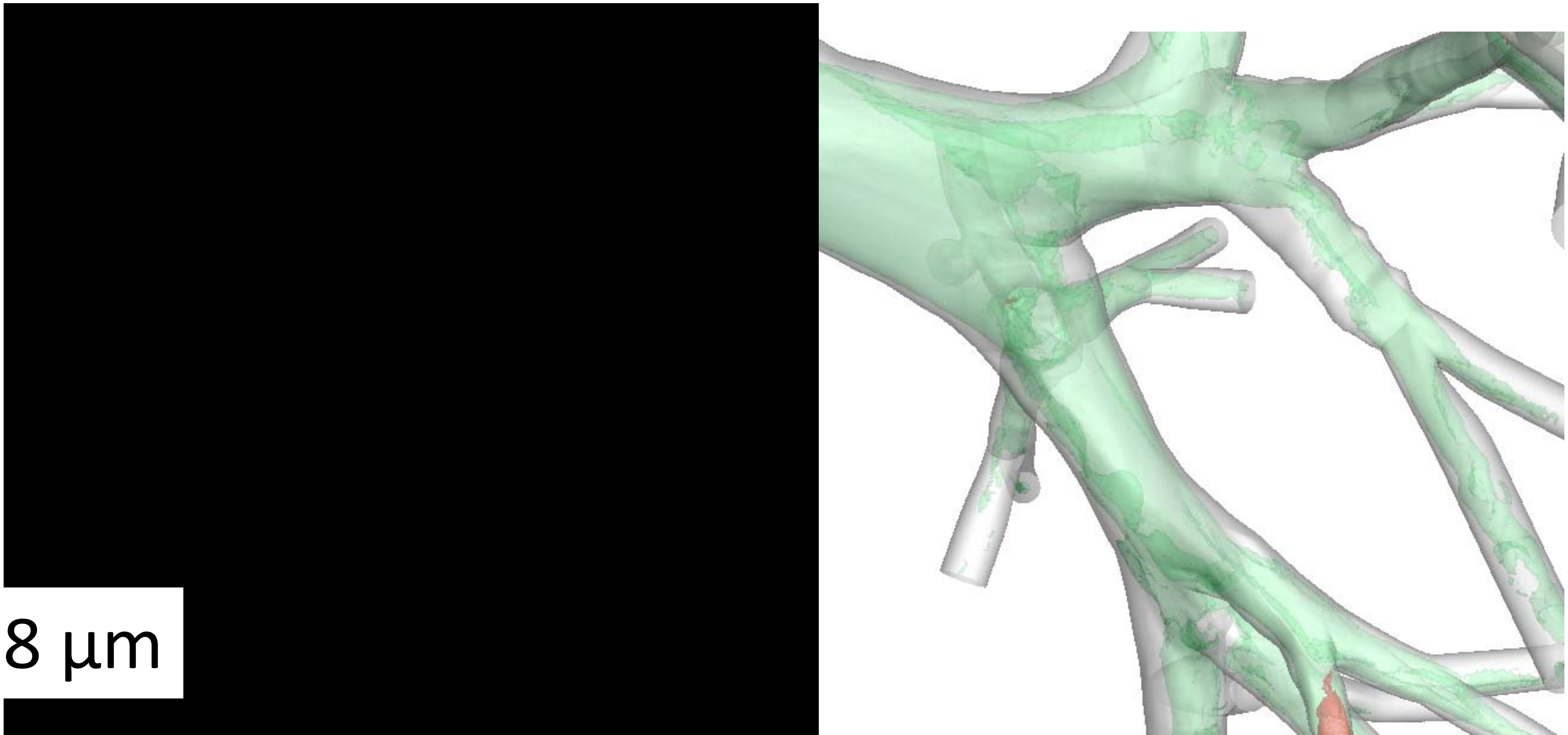
Airway constriction induces particle deposition hot spot

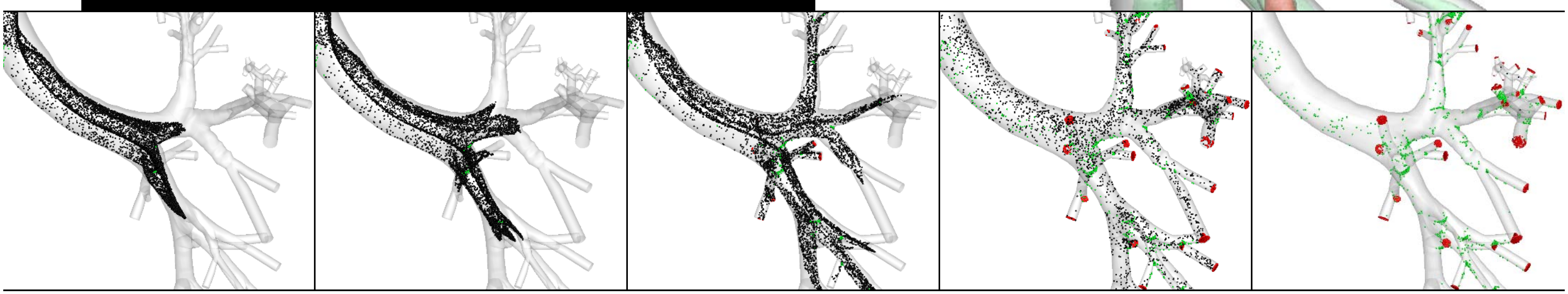
Cluster 4



Particle transport in a healthy human

Healthy



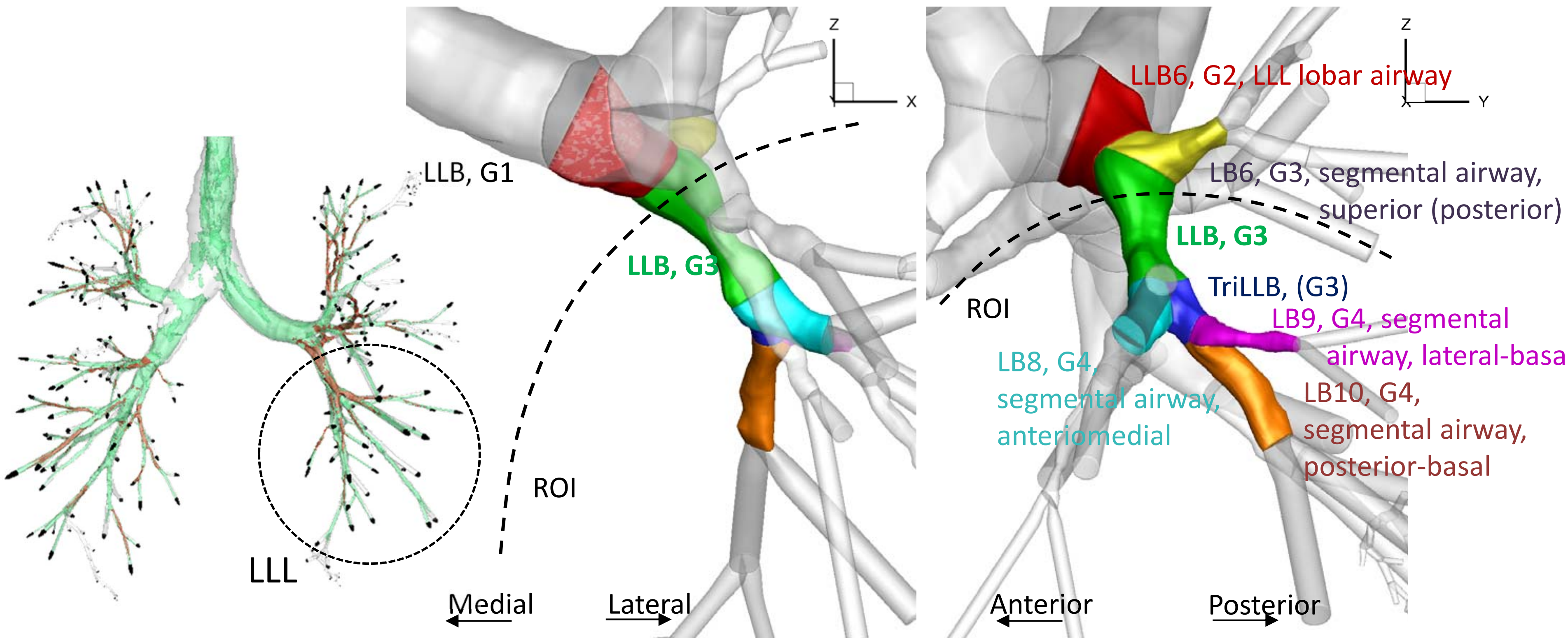


Objectives

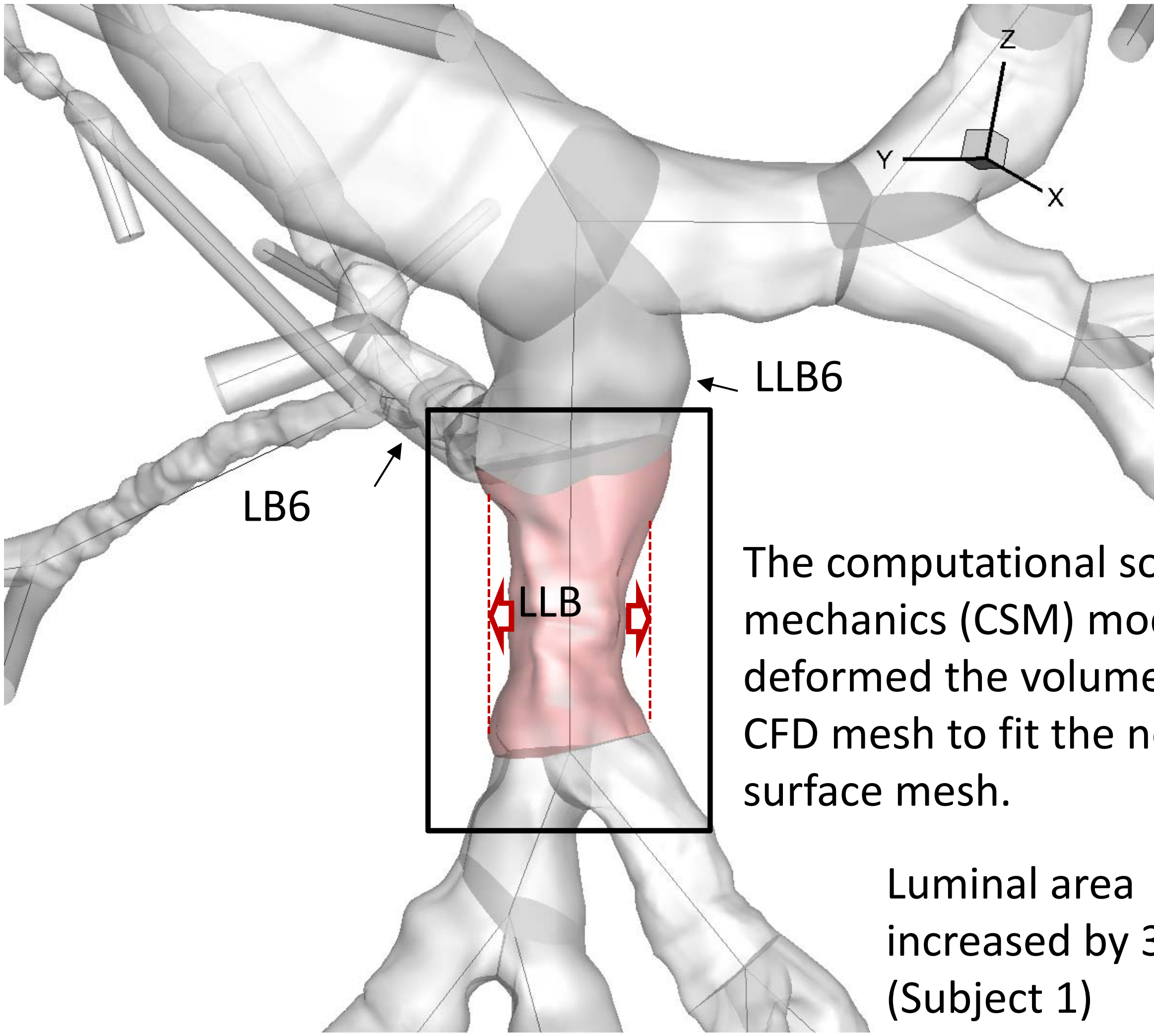
- The aim of the study is to assess the effects of luminal expansion of constricted proximal airways on inhaled particle deposition in severe asthmatic lungs,
- utilizing CT-based CFD simulations of airflow and particle transport in two representative cluster 4 patients.

Region of interest (ROI) in the left lower lobe (LLL)

Airway constriction in LLL is a key structural characteristic of asthma cluster 4.



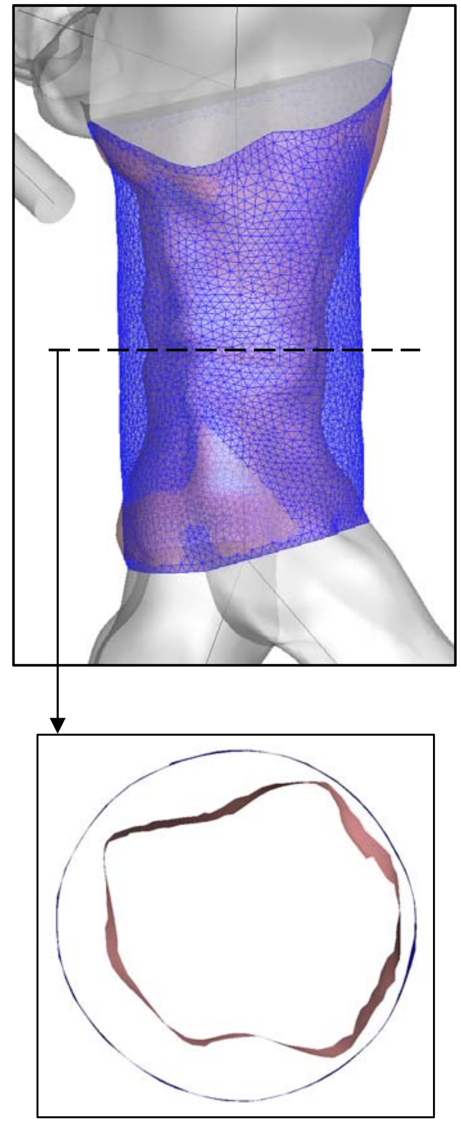
Luminal expansion



The computational solid mechanics (CSM) model deformed the volumetric CFD mesh to fit the new surface mesh.

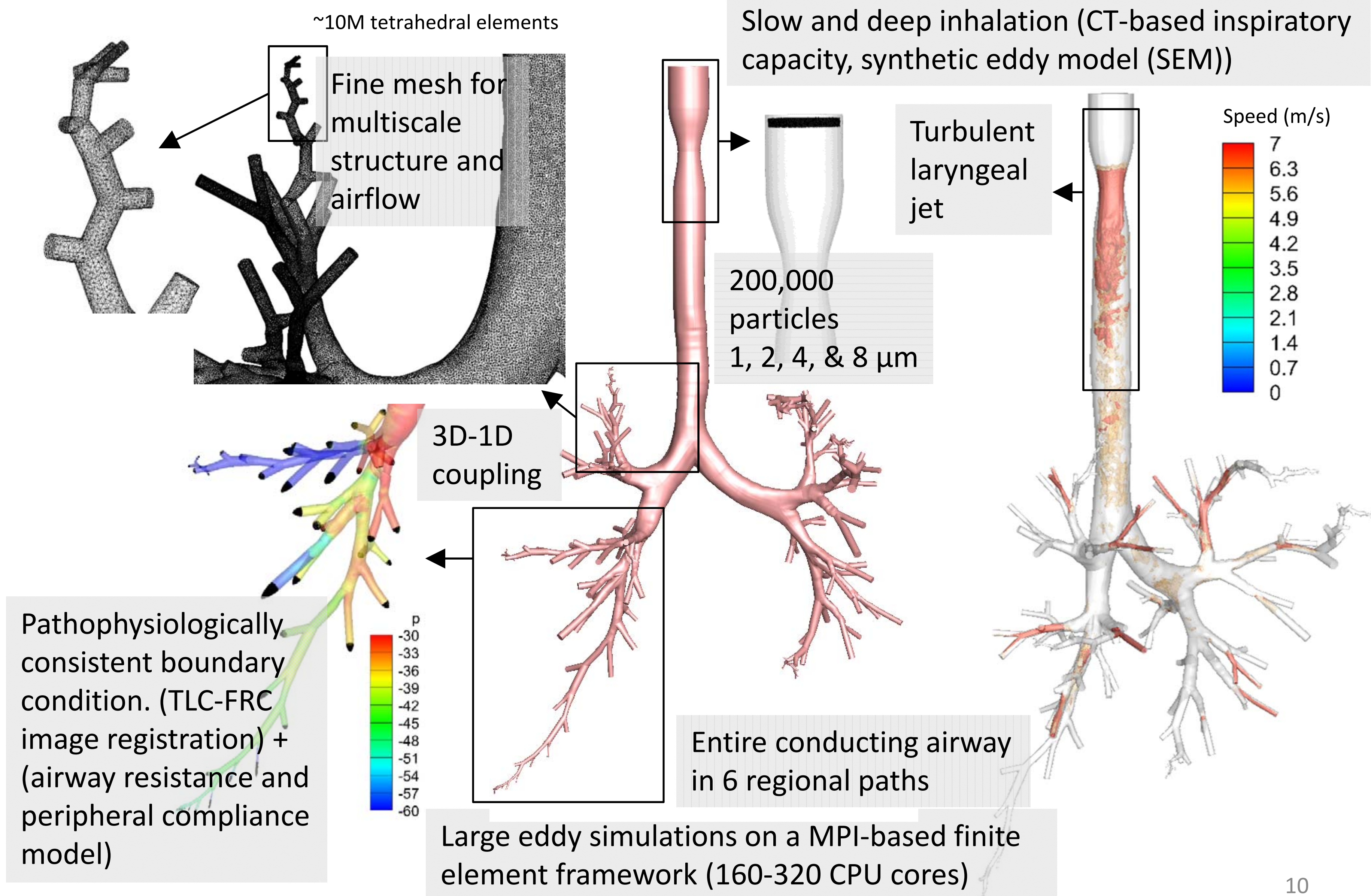
Luminal area increased by 33% (Subject 1)

New surface mesh



Flow boundary conditions remained unchanged for comparison.

Subject specific multiscale CFD simulations

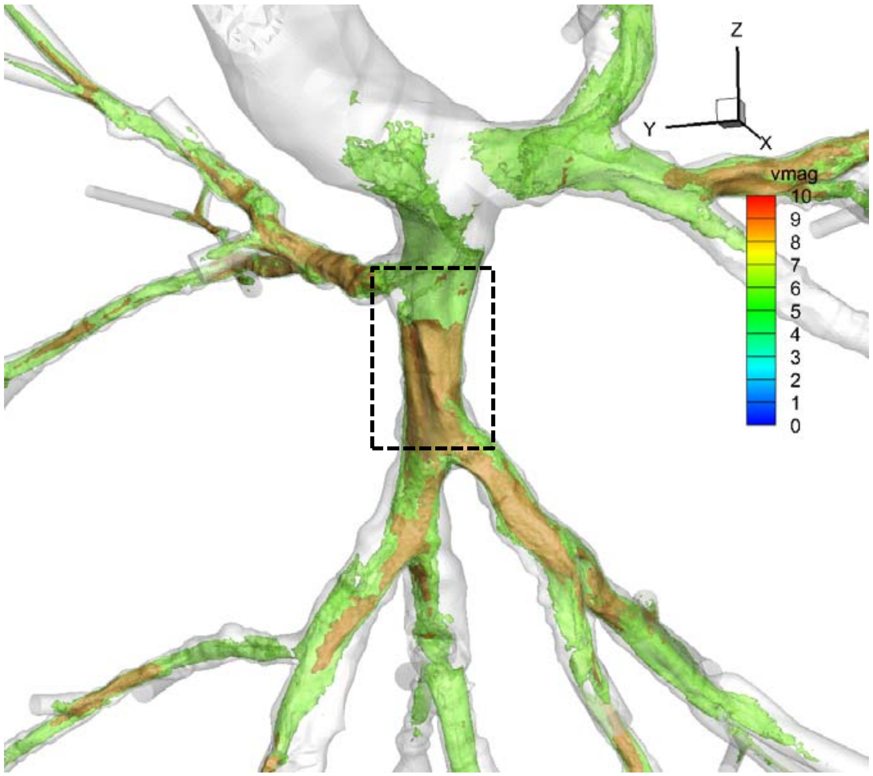


Choi et al. 2009 PoF 21 (10), 101901; Yin et al. 2010 J Biomech 43 (11), 2159-2163; Lin et al. 2013 WIREs Syst Biol Med 5:643–655

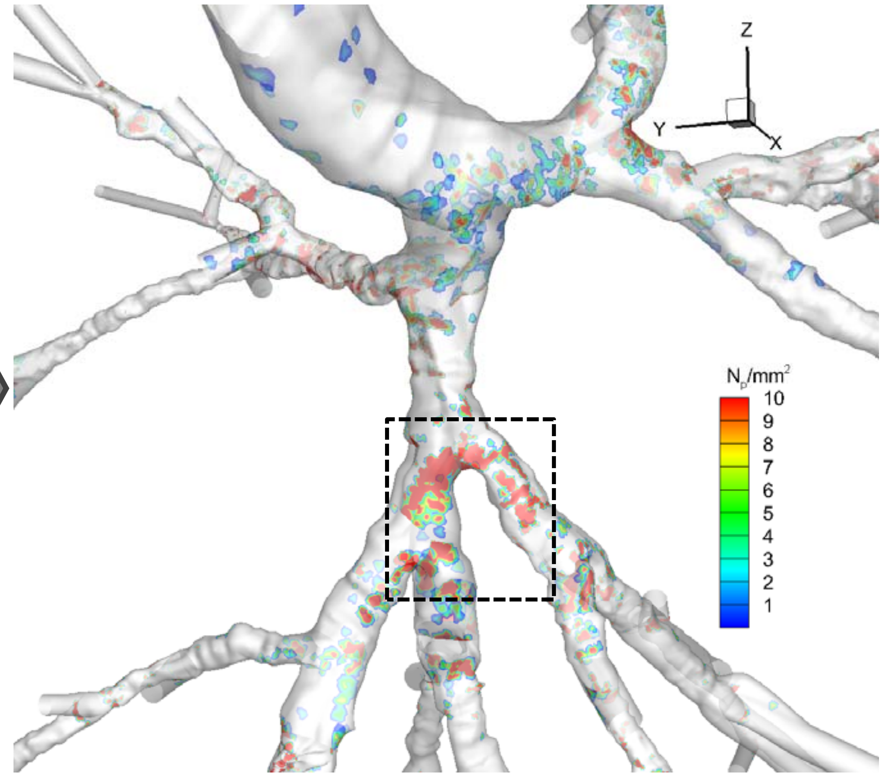
Before luminal expansion (Subject 1)

8 µm

Airflow speed



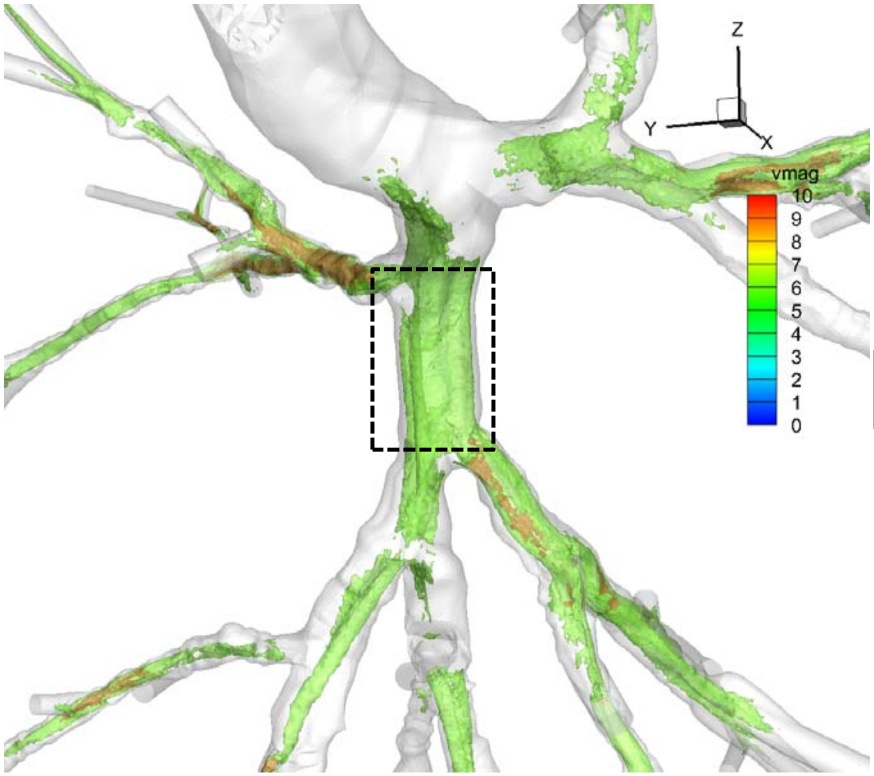
Particle deposition density



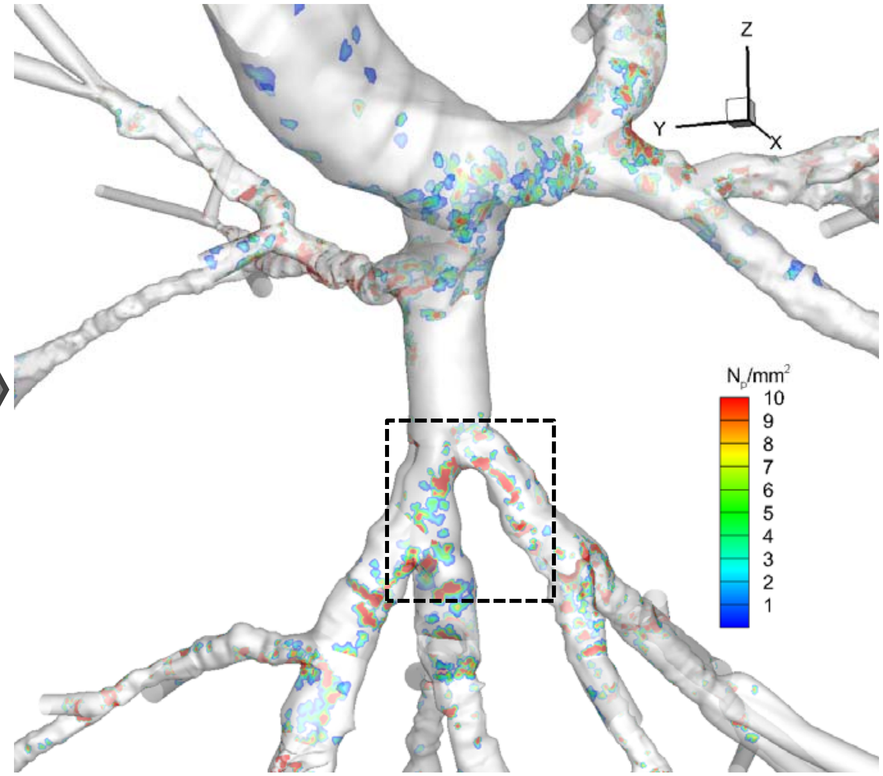
- Local airway constriction induces high speed jet-like flow (brown in the left side figure),
- which impinges on the downstream wall,
- forming particle deposition hot spot (red in the right side figure) and
- limiting particle delivery to the distal small airways (primary target sites of asthma).

After luminal expansion (Subject 1)

Airflow speed



Particle deposition density

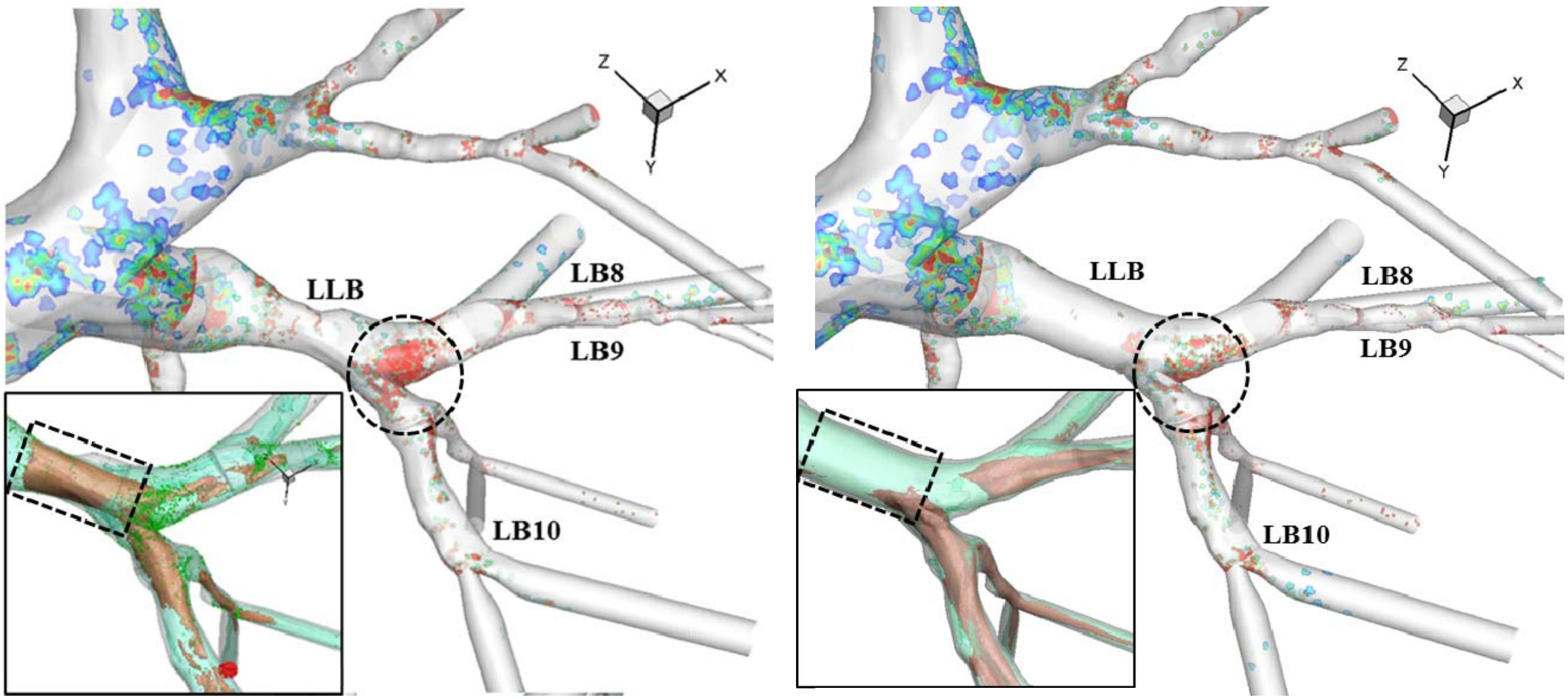


DF (4µm)	Pre	Post
LUL	0.0431	0.0427
LLL	0.0534	0.0427
RUL	0.0190	0.0191
RML	0.0125	0.0124
RLL	0.0409	0.0409

- Constriction-induced high speed jet disappeared.
- Hot spot has been markedly reduced. Proximal deposition decreased by 16-38%.

Particle deposition density on C4 subject (Subject 1)

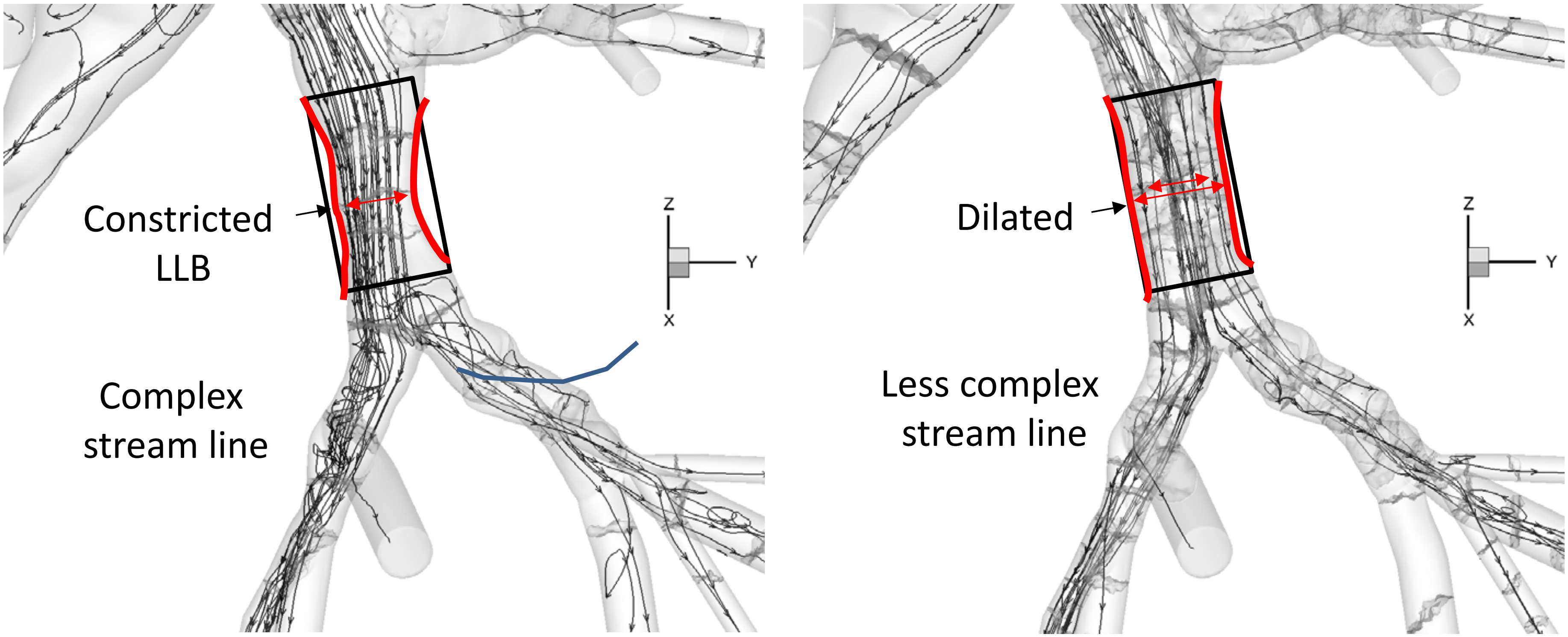
Before After



- 50% luminal area expansion
- Constriction-induced high speed jet disappeared.
- 22-35% proximal deposition decrease for 1-8 μm particles

Flow structure

Original | After virtual BT



- High speed core flows with surrounding complexity (fluctuation) propagate into the child branches.
- After luminal expansion, fluctuation in LLB and the child branches is reduced.

Change in lobar particle deposition fraction (DF) and advection fraction (AF) in LLL

	Subject 1				Subject 2			
Size	DF (pre)	ΔDF* (%)	AF (pre)	ΔAF* (%)	DF (pre)	ΔDF* (%)	AF (pre)	ΔAF* (%)
1μm	0.0096	-38	0.0044	13	0.0126	-22	0.2717	1
2μm	0.0205	-16	0.0434	-6	0.0144	-27	0.2694	1
4μm	0.0534	-20	0.1029	5	0.0249	-25	0.2573	3
8μm	0.1923	-17	0.0903	46	0.1102	-35	0.1656	23

- After luminal expansion of LLB, lobar deposition fraction in LLL decreased by 16-38% for 1-8 μm particles.
- 8 μm particle advection into small airways was increased by 46% and 23% for subjects 1 and 2, respectively.

ΔDF* (%) and ΔAF* (%) are percent change in DF and AF w.r.t the original cases.

Summary

- CT image-based CFD simulations of slow and deep inhalation of air and aerosol particles showed that luminal expansion of local constriction of a proximal airway branch eliminated formation of the particle deposition hot spot.
- The results imply that the use of imaging-based clustering and enlargement of constricted proximal airway may help improve delivery of orally inhaled drug aerosols to small airways specifically for large particles in severe asthmatic lungs.
- The analysis can be useful for the investigating the effect of bronchial thermoplasty treatment in severe asthma patients.