

## ABSTRACT

**RATIONALE:** The capability of predicting air flow and particle deposition with computation fluid dynamics (CFD) is desirable for understanding the structure and function relationship in the human lungs. In order to take into account the effects of physiologically consistent multiscale physics of the pulmonary air flow, we propose an integrative, image-based computational framework for subject-specific breathing lungs, and demonstrate the regional distribution of airflow properties in the entire conducting airway.

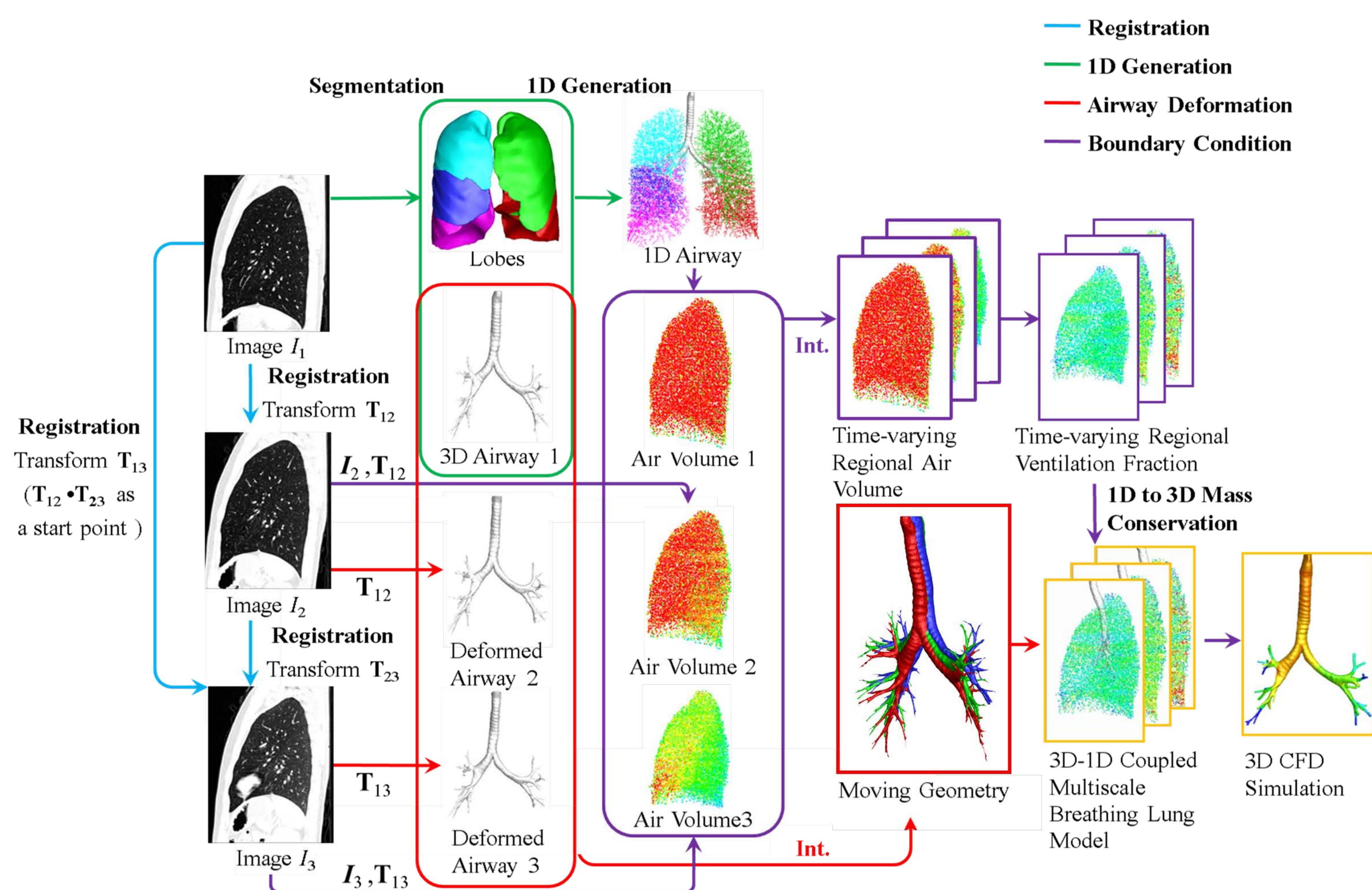
**METHODS:** The proposed three-dimensional (3D) and one-dimensional (1D) coupled framework, which spans from the mouth to the terminal bronchioles, is built to incorporate the desired level of geometric details. The image-derived deforming airway geometries and regional ventilation are acquired with a mass-preserving nonrigid image registration method to guide CFD simulation. An in-house parallel large-eddy simulation (LES) technique is adopted to capture turbulent-transitional-laminar flows in the central large airways (3D) and an energy-balance-based model is utilized to predict pressure drop in the peripheral small airways (1D), thus predicting ventilation and pressure in the entire conducting airways. Three volumetric multi-detector row computed tomography (MDCT) lung images of the same subject are used to derive non-linear time-varying deforming airway and regional ventilation. The CFD results in both normal and deep breathing conditions based on three images are compared against those of one or two images.

**RESULTS:** The results show that the three-image-based breathing lung model yields physiologically consistent airway deformation and ventilation distributions. At peak inspiration during normal breathing, the 3D-1D coupled simulation yields an average pressure drop of 78 Pa (110 Pa) in the entire lung (in the lower lobes) from the mouthpiece to the terminal bronchioles. These values are within the typical range in normal breathing. And it agrees with known regional distribution of pressure drop in the lung. The detailed pressure distribution inside 3D airway is shown in Figure 8 in comparison with the one-volume-based case. The pressure drop is overall greater in the pathway of dorsal branches in Figure 8(a) due to the ventral-dorsal regional ventilation tendency. However, the one-volume-based model in Figure 8(b) under-predicts pressure drop and does not recover regional ventilation at the whole lung level. In addition, the two-volume-based model (results not shown), to some extent, can account for airway deformation and non-uniform regional ventilation, but not non-linear features of the lung.

**CONCLUSION:** The proposed multiscale breathing lung model from MDCT volumetric data sets acquired at different inflation levels, providing regional ventilation and airway deformation, predicts physiologically consistent air flow field in breathing lung. Three volumes allows dynamic behaviors of regional ventilation and non-linear motions of airway geometry.

## Flow chart: Multiple MDCT images to CFD

Mass-preserving nonrigid image registration (Yin et al., 2009, *Med Phys* 36(9):4213) derives airway and lobe geometry, regional ventilation map and deformation map, from multiple MDCT volume scans of lung. 1D airway tree generated by volume-filling (Tawhai et al., 2004, *J Appl Physiol* 97:2310) links CT-resolved airway to lung parenchyma where localized air volume changes are compared between global (total) lung volumes. Figure 1 shows the flow chart.

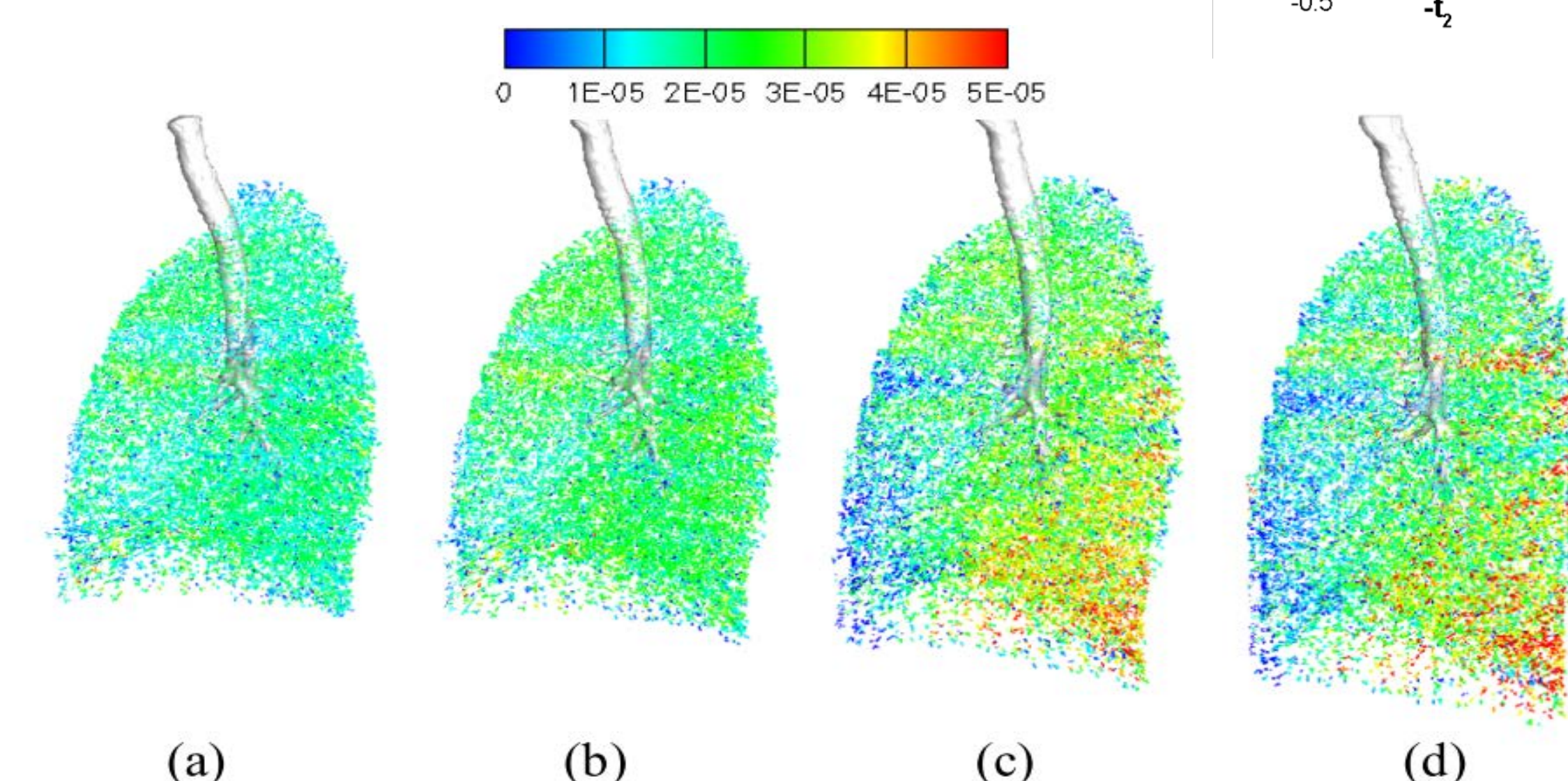


**Figure 1:** A flow chart of the entire process to develop the breathing lung model (Upper airway geometry and process are not shown).

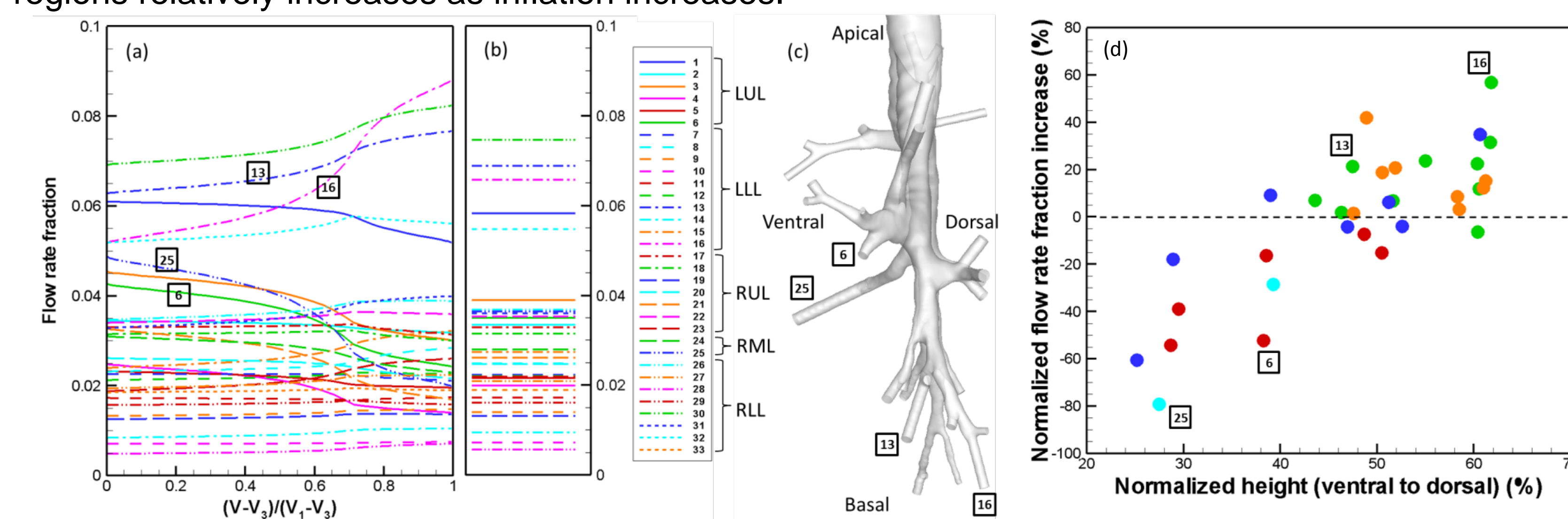
## Time-varying regional ventilation

Local properties such as air volume content at parenchymal units are determined as functions of the global lung volume by non-linear (linear) interpolation between registered image-derived data of three or more (two) volumes.

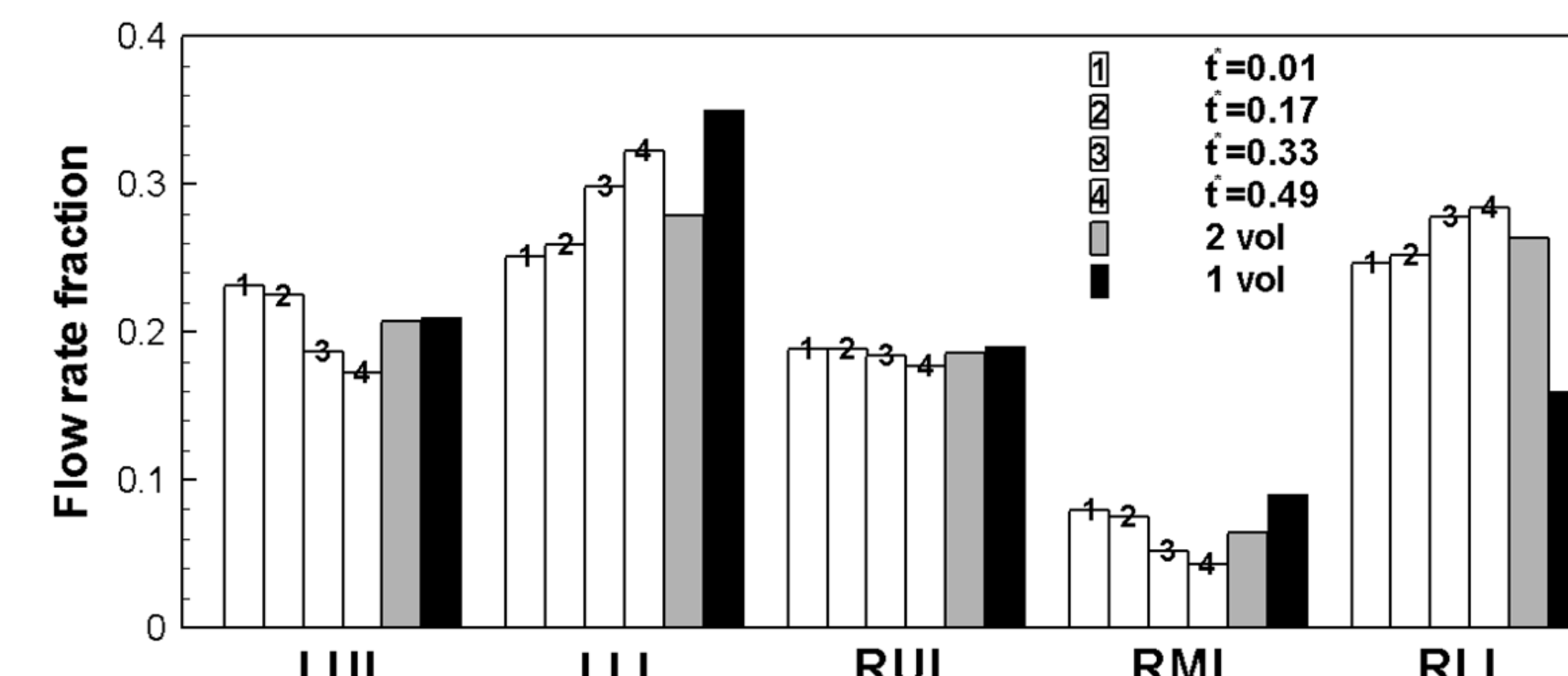
**Figure 2:** A schematic of the interpolation of time-varying local variable during a specific breathing cycle, with respect to global lung volume and reference time. Dashed (red) and dot-dashed (blue) lines represent two sections of respective interpolation curves based on three image data. Solid circles denote three image-derived data points.



By 3D-1D coupling and mass conservation, the flow rate distribution at the distal ends of 3D airway model is determined from regional ventilation map at terminal bronchioles as a function of the global lung volume. Both in parenchymal level and in large airways, ventilation in the dorsal and basal regions relatively increases as inflation increases.



**Figure 4:** Time varying ventilation at distal ends of 3D model. (a) The time-varying flow rate fractions with respect to the global lung volume and (b) the two-image-based constant flow rate fractions at distal ends of 3D airway model illustrated in (c). (c) A side (left) view of 3D airway model. The upper airway is not shown. Boxed numbers denote the indices of four selected boundaries. (d) The ventral-to-dorsal dependency of the flow rate fraction increases at normalized by the average values between  $V_1$  and  $V_3$ .

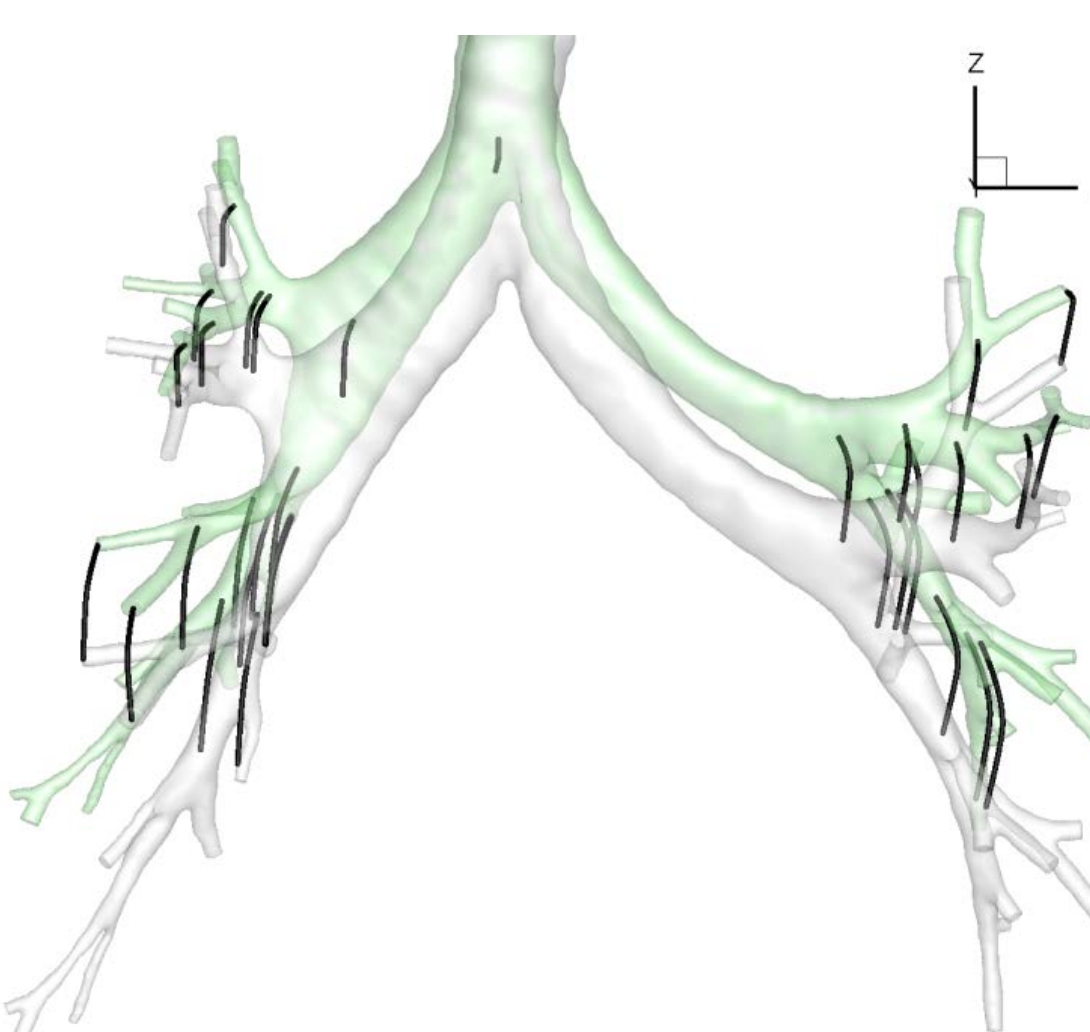


**Figure 5:** Comparison of lobar ventilation (flow rate fractions) of three-volume-based regional ventilation model at 4 reference times of deep breathing with the two-volume-based constant regional ventilation model and the one-volume-based model with uniform velocity.

## Non-linear deformation

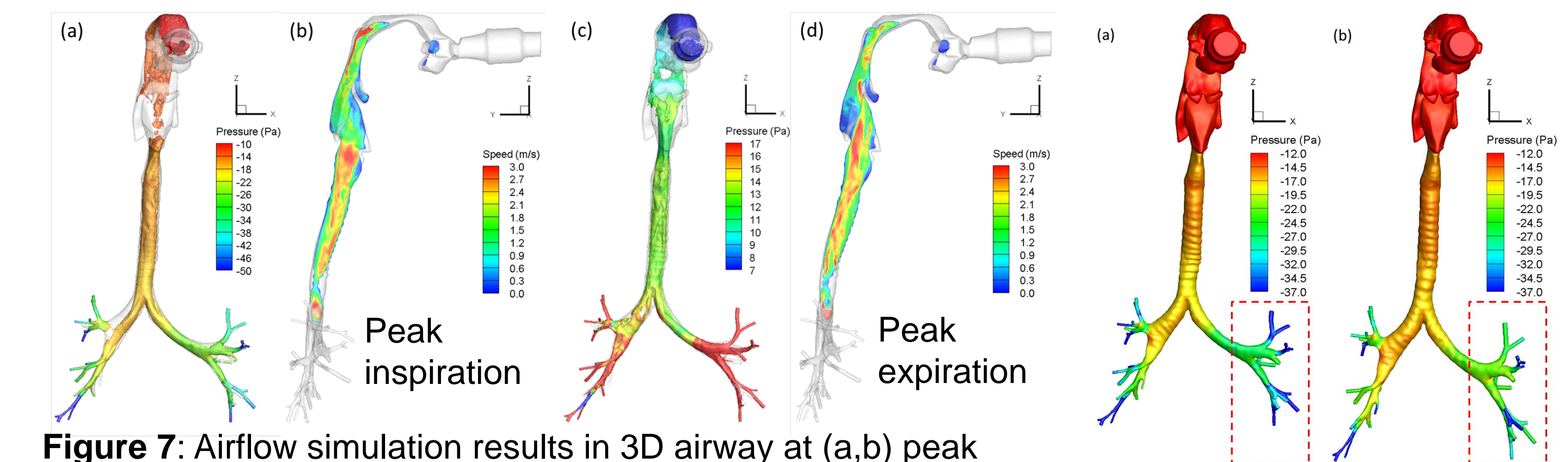
Local coordinates of airway and lobe surfaces are obtained as C1-continuous functions of the global lung volume, as described in Figure 2.

**Figure 6:** Connected lines of black symbols show trajectories of selected local points in the airway during non-linear deformation. The airway surfaces of  $I_1$  and  $I_3$  are denoted by the light gray and the light green, respectively.

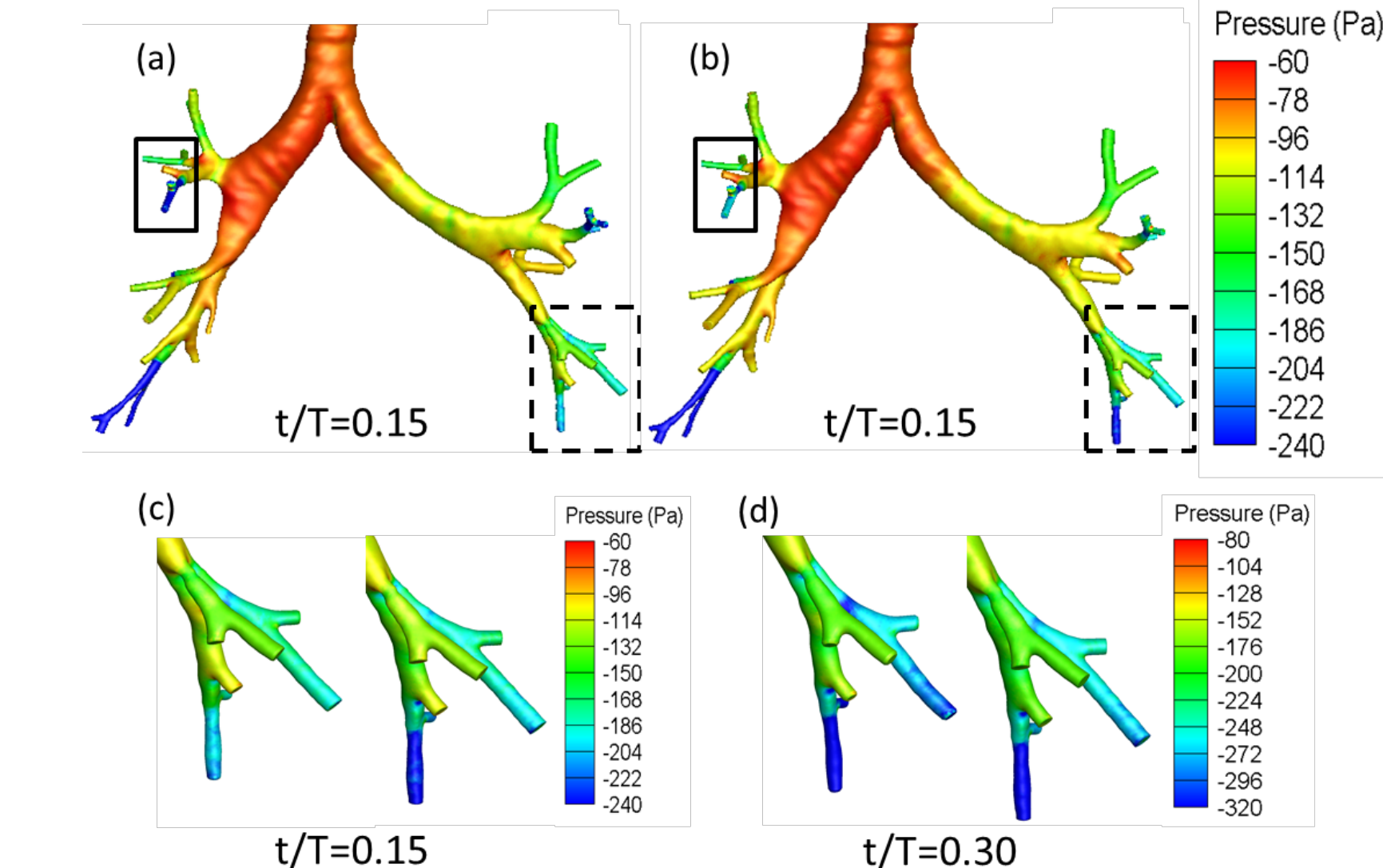


## Airflow simulation: normal and deep breathing

In-house parallel finite element LES code (Lin et al., 2007, *Resp Physiol Neurobiol* 157:295; Choi et al., 2009, *Phys Fluids* 21:101901) provides physically accurate predictions of multiscale airflow physics according to the physiologically consistent breathing conditions such as normal breathing with end expiratory volume at FRC and tidal volume of 500 ml and deep breathing. Three-volume-data model predicts reasonable regional distributions of ventilation and pressure at a given time, while single-volume-data leads to relatively lower and randomly distributed pressures at distal airways without modeling deformation. Geometry and pressure distributions from two-volume-data model deviate from three-volume-data results.



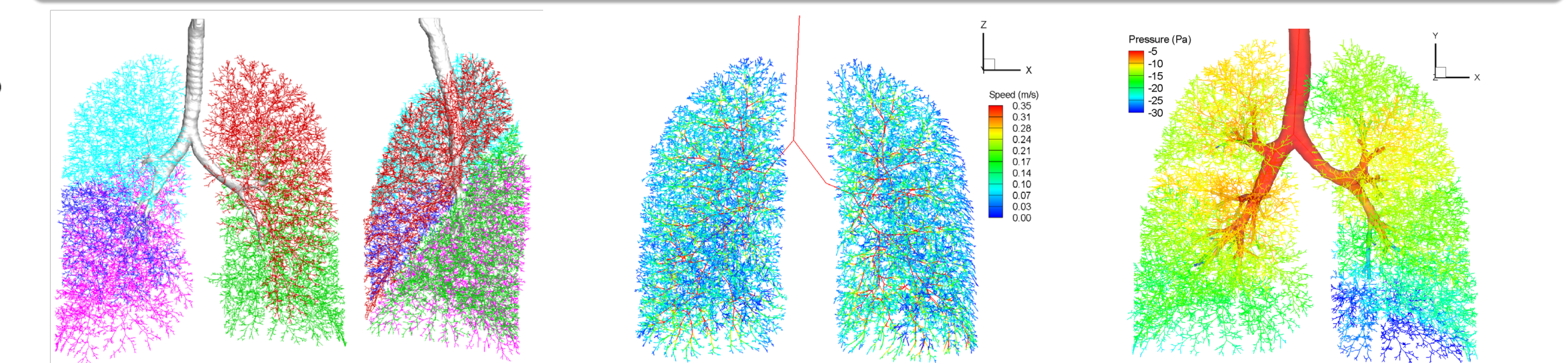
**Figure 7:** Airflow simulation results in 3D airway at (a,b) peak inspiration and (c,d) peak expiration of normal breathing. (a,c) show the isosurface at air speed of 5 m/s color-coded by pressure contours. (b,d) show the instantaneous air speed contours in a vertical plane through the trachea.



**Figure 8:** Comparison of pressure at the peak inspiratory flow between (a) the three-image-based realistic normal breathing case and (b) the single-image based case near 78%VC with traditional boundary condition (uniform flow).

**Figure 9:** Comparison of pressure drop at an inspiratory phase of  $t/T = 0.15$  of deep breathing, using the approaches based on (a) three images and (b) two images. (c) Enlarged views of LLL (dashed box) from (a) (left) and (b) (right). (d) The same views at later time  $t/T = 0.30$ .

## Multiscale features in entire conducting airway



**Figure 10:** 3D-1D coupled entire conducting airway model. Each color denotes each of five lobes.

**Figure 11:** Distribution of average air speed in individual airway segments at peak inspiration of normal breathing.

**Figure 12:** Demonstration of pressure distribution in the entire conducting airway at inspiration.

## SUMMARY

We proposed a technique to build a multiscale breathing lung model from MDCT volumetric data sets acquired at different inflation levels. Three-(two-) volume-data model allows predicting subject-specific time-varying (time-constant) regional flow rate fractions and non-linear (straight-trajectory) motions of airway deformation, thus providing physiologically consistent regional ventilation and deformation in addition to physically accurate predictions of airflow field in the entire conducting airway according to global lung volume change of breathing cycles. In contrast, physiologically consistent deformation and regional distributions of ventilation and pressure are not available with single volume data. Parts of this work has been submitted for publication and is under review.

## ACKNOWLEDGMENTS

This work was supported in part by Roche Pharmaceuticals PostDoc Fellowship Program, NIH Grants R01-HL-094315, R01-HL-064368, R01-EB-005823, and S10-RR-022421. The computer time was supported by the Texas Advanced Computing Center and San Diego Supercomputer Center which are parts of NSF-supported TeraGrid/XSEDE.

**Disclosure:** Eric A. Hoffman is a share holder in VIDA diagnostics which is commercializing lung image analysis software derived by the University of Iowa of Iowa lung imaging group.