# Regional Associations between CT Measures of Airway Structure and Hyperpolarized Helium-3 MRI Measures of Local Bronchodilator Response in Asthma

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## Introduction

- **Regional heterogeneity of ventilation** has been observed in asthma patients using hyperpolarized helium-3 gas (HP $^3$He) MRI and quantified using the segmental ventilation defect percent (SVDP). [1]

- **Changes in the size and number of ventilation defects** have been observed in response to inhaled bronchodilator:
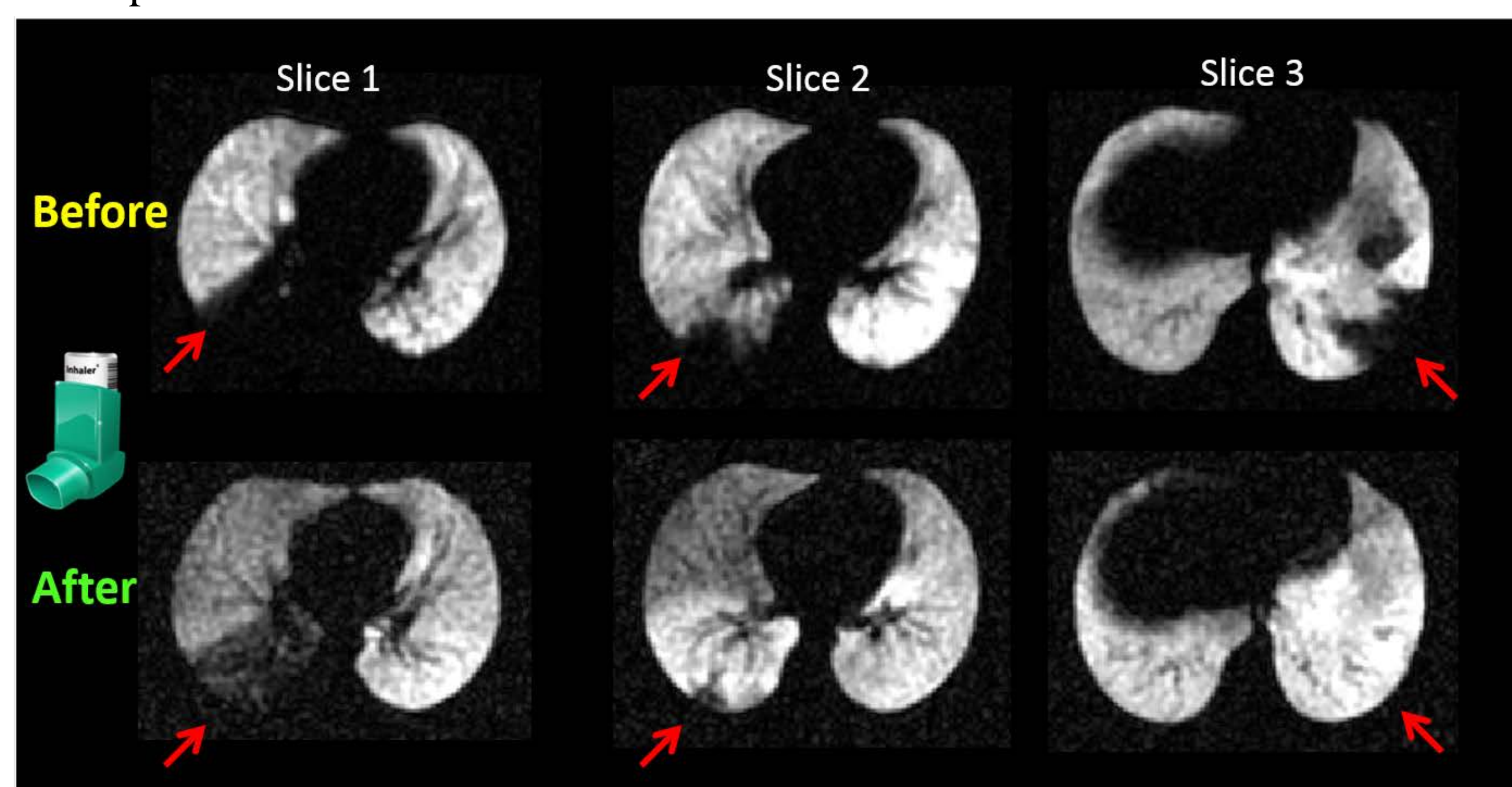


*Figure 1. Three axials slices from the same subject illustrate variable reversibility of ventilation defects following bronchodilator intervention.*

- Airway wall thickness in segmental feeding airway can be measured on CT using VIDA software (VIDA Diagnostics, Coralville IA)
- Measurements of airway wall thickness and wall area percentage using MDCT were found to be greater in subjects with severe asthma [2].
- Previous work has showed significant increase in wall thickness in airways leading to poorly ventilated regions [3].

Purpose: To establish **regional associations between defect reversibility** in response to bronchodilator treatment **and deviation from predicted airway wall thickness** as a means to explore fixed vs. reversible ventilation defects.

## Materials and Methods

### Study Population Demographics

|  | CT | CT + MRI Subset |
|---|---|---|
| Total N | 65 | 21 |
| Gender | 23 M 42F | 7M 14F |
| Age | 45.0 ± 14.9 years | 47.3 ± 16.6 years |
| Asthma Severity | 13 mild (20%) | 4 mild (19.0%) |
|  | 12 moderate (18.5%) | 3 moderate (14.3%) |
|  | 40 severe (61.5%) | 14 severe (66.7%) |

CT performed post-bronchodilator (BD) in all subjects. MRI performed both pre- and post-BD in the CT+MRI subpopulation.

All imaging performed under **stable conditions** (subjects excluded if within 6 weeks of asthma exacerbation or respiratory complications).

**We created two statistical models:**

(1) Predicted Wall Thickness. *All subjects.*

(2) Predicted Wall Thickness vs. Reversibility. *CT + MRI subgroup.*

## Materials and Methods (cont.)

### Segmental Ventilation Defect Percent (SVDP)

$$SVDP = \frac{\text{Segmental Ventilation Defect Volume (HP 3He MRI)}}{\text{Segment Volume}} \cdot 100\%$$
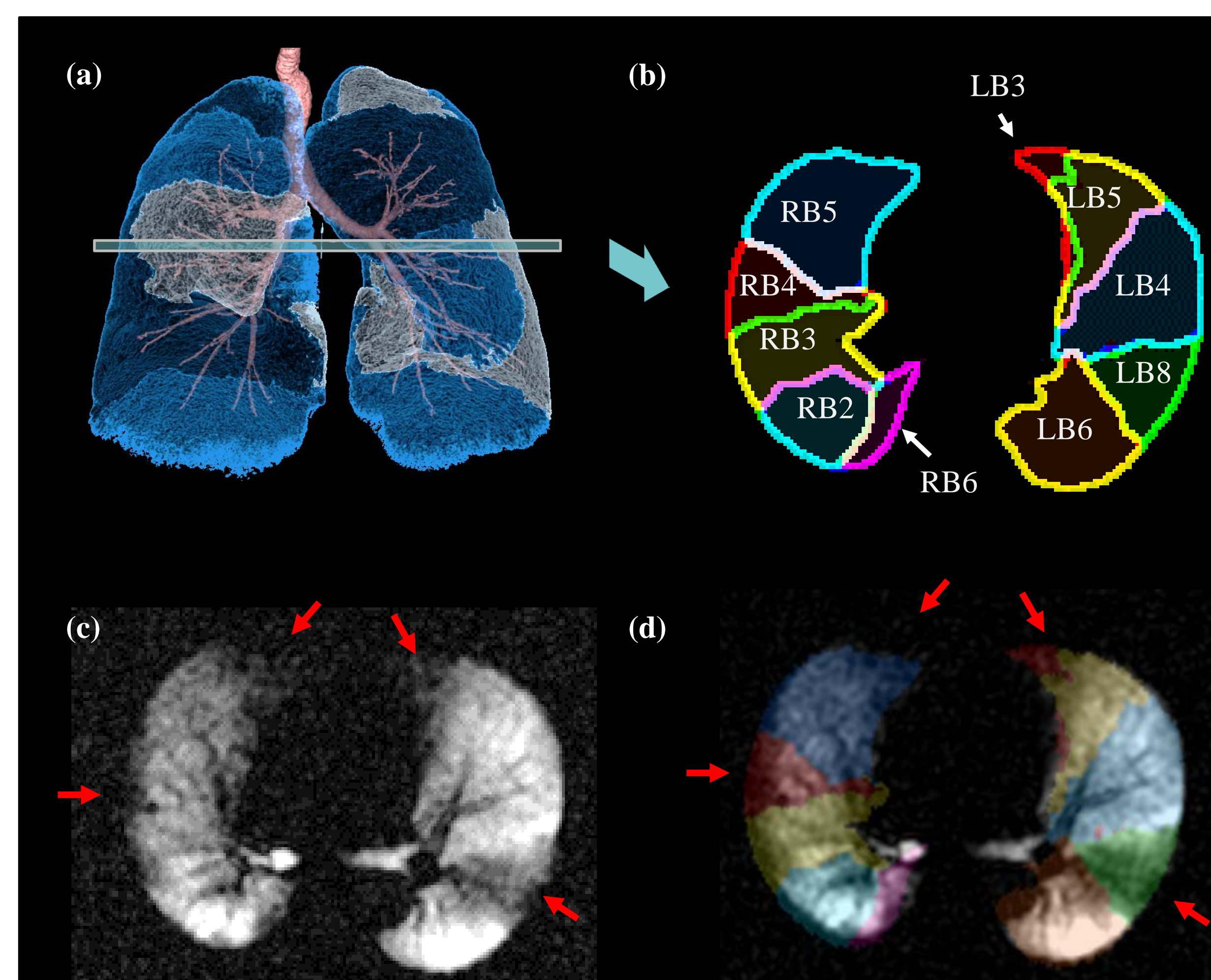


*Figure 2. Identification of segmental volumes on CT in (a) allows for axial segment mask shown in (b) [3]. This mask can be overlaid on HP $^3$He MRI image (c) to identify spatial distribution of ventilation defects and calculate segmental VDP (SVDP). RB2-3 are segments of RUL, RB4-5 of RML, and RB6 of RLL; LB3-5 are segments of LUL, LB6 and LB8 of LLL. Note spatial overlap of prominent ventilation defect (red arrows) with segment LB8.*

SVDP was measured both pre- and post-BD in the MRI + CT population [1, 4].

### Airway Wall Thickness on CT

**Segmental feeding airway wall thickness measured on CT population using VIDA software (VIDA Diagnostics, Coralville IA).**

### Predictive Model of Segmental Airway Wall Thickness

- Linear mixed effects model based on CT population
- **Predicted Wall Thickness WT** is outcome. (Subject is random effect).

WT_pred ~ age + sex + BMI + severity + segment + subject

Thus wall thickness percent predicted (WTPP) is $\frac{\text{WT Observed}}{\text{WT Predicted}} * 100$

### Bronchodilator Response vs. WTPP

- Generalized additive mixed effect model based on CT + MRI population
- **Outcome is SVDP post-BD**
- Input parameters SVDP pre-BD, segment, WT PP, and subject (random effect).

SVDP_post ~ SVDP_pre + segment + WT PP + subject

## Results



Airway Wall Thickness (mm)

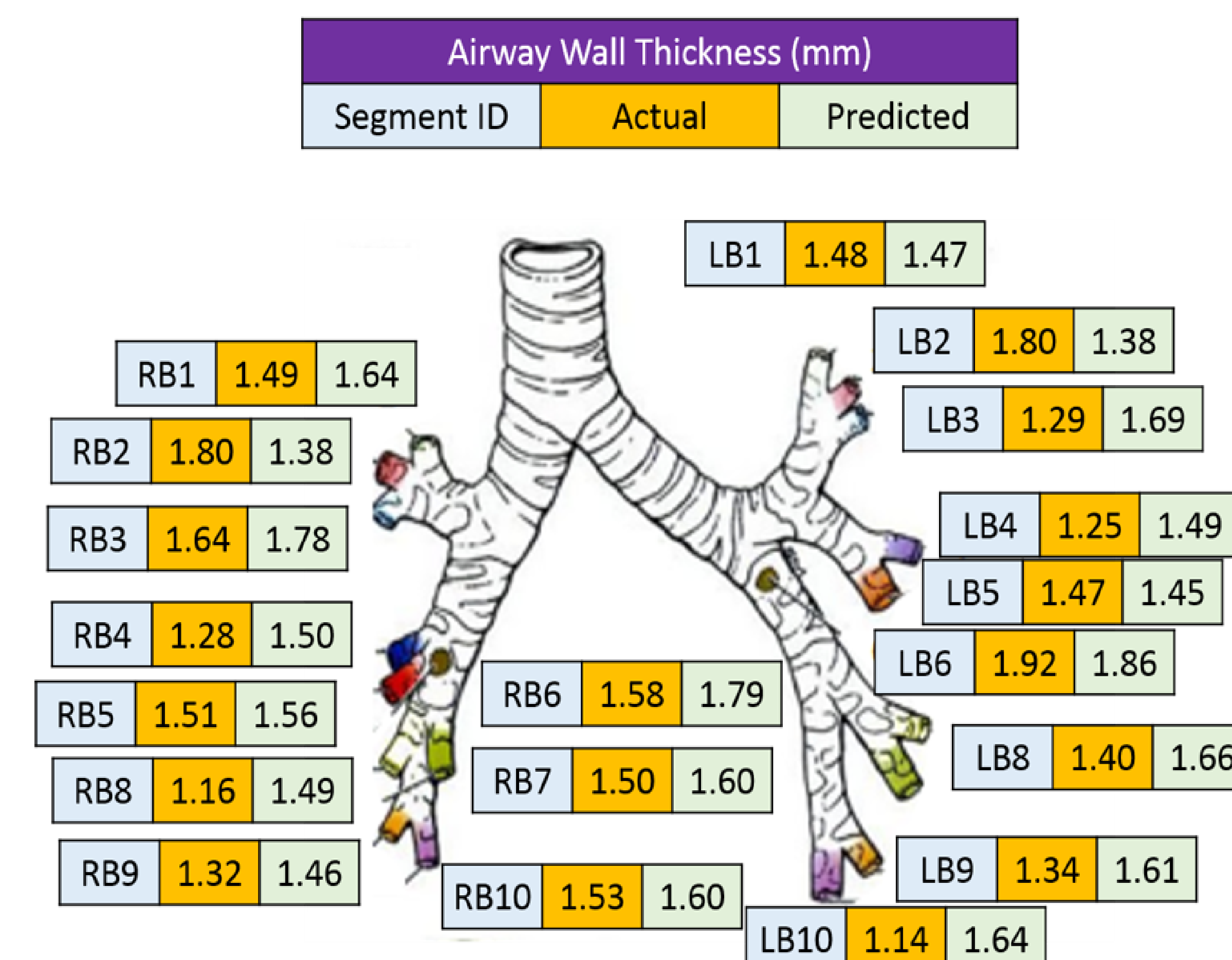| Segment ID | Actual | Predicted |
|---|---|---|
| LB1 | 1.48 | 1.47 |
| RB1 | 1.49 | 1.64 |
| LB2 | 1.80 | 1.38 |
| RB2 | 1.80 | 1.38 |
| LB3 | 1.29 | 1.69 |
| RB3 | 1.64 | 1.78 |
| LB4 | 1.25 | 1.49 |
| RB4 | 1.28 | 1.50 |
| LB5 | 1.47 | 1.45 |
| RB5 | 1.51 | 1.56 |
| LB6 | 1.92 | 1.86 |
| RB6 | 1.58 | 1.79 |
| RB8 | 1.16 | 1.49 |
| RB7 | 1.50 | 1.60 |
| LB8 | 1.40 | 1.66 |
| RB9 | 1.32 | 1.46 |
| LB9 | 1.34 | 1.61 |
| RB10 | 1.53 | 1.60 |
| LB10 | 1.14 | 1.64 |

*Figure 3. Illustration of predicted vs. actual wall thickness by segmental feeding airway in a single subject from the study population.*

- **In the WT prediction model,** segment and sex were significant factors.

**In the model of wall thickness percent predicted (WTPP) vs bronchodilator response, greater segmental WTPP was associated with reduced segmental defect reversibility (p=0.04).**

- **Whole lung VDP** across the population was (median [1st quartile, 3rd quartile]) 7.37 [2.43, 9.73] pre-BD and 5.35 [0.62, 7.76] post-BD (p < 0.05).

## Discussion and Conclusion

- Hyperpolarized gas MRI enables functional imaging before and after intervention with no exposure to ionizing radiation.

This work suggests that **a significant fraction of segments refractory to bronchodilator intervention** also exhibit **airway remodeling.**

- Smooth muscle relaxant effects of bronchodilator may have reduced efficacy in the presence of thicker airway wall .

- Further analysis in this area may improve understanding of regional mechanisms of airway obstruction and their relationship with disease progression, severity, and response to targeted therapies.

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## References

[1] Thomen et al. *Radiology* 2014.
[2] Aysola et al. *Chest* 2008.
[3] Mummy et al. *ATS International Coneferece* 2016
[4] Zha et al., *Acad. Radiology* 2016

## Acknowledgements