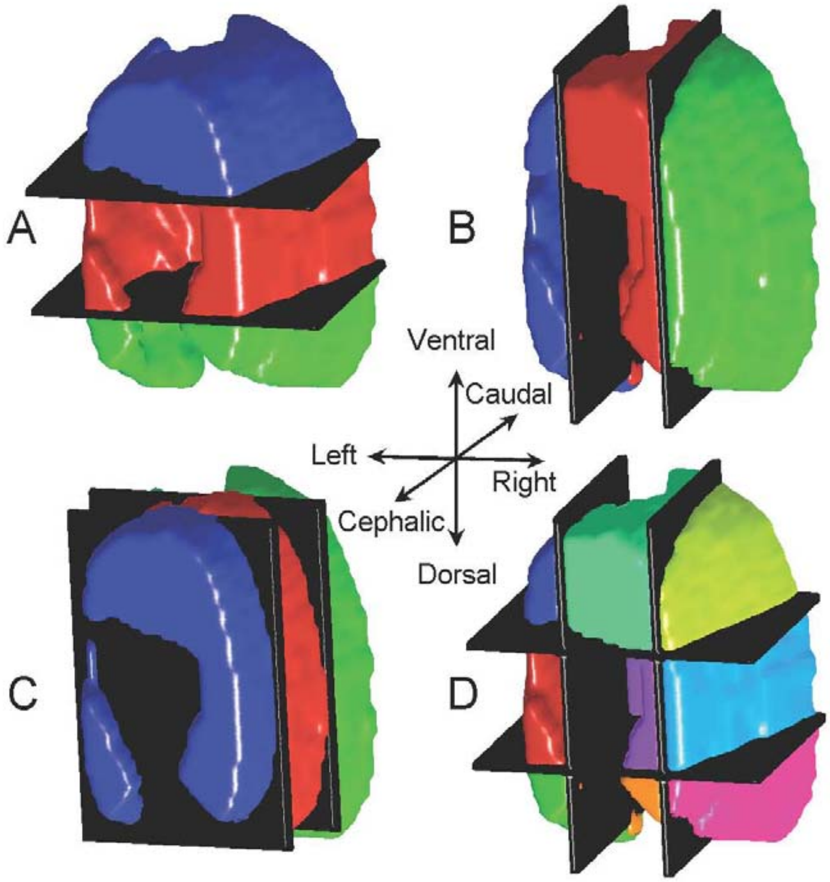
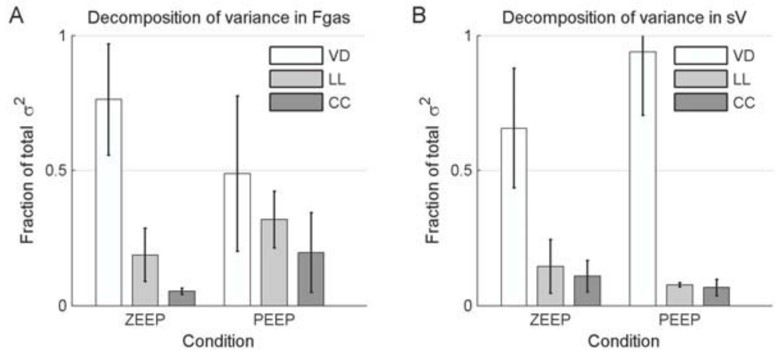
Supplemental Figure 1



SUPPLEMENTAL FIGURE 1. Examples of regions of interest (ROIs) used for analysis of per-breath specific ventilation ($s\dot{V}_B$) and specific lung volume change (sVol) shown at end-expiration. Colors are used to distinguish individual ROIs. Uni-dimensional division of the lung field results in either (A) ventral-dorsal ROIs separated by coronal planes; (B) latero-lateral ROIs separated by sagittal planes; or (C) cephalo-caudal ROIs separated by transverse planes. Multi-dimensional division creates a grid of ROIs, such as those divided simultaneously along the ventral-dorsal and latero-lateral axes (D). End-inspiratory lung fields were divided in the same manner.

Supplemental Figure 2



SUPPLEMENTAL FIGURE 2. Contributions of spatial position along the ventral-dorsal (VD), latero-lateral (LL), and cephalo-caudal (CC) axes to total variance (σ^2) in voxel estimates of (A) gas fraction (F_{gas}) and (B) specific ventilation ($s\dot{V}$). Experiments with zero end-expiratory pressure (ZEEP) and positive end-expiratory pressure (PEEP) are shown separately. Values are mean ± SD.

SUPPLEMENTAL APPENDIX

Model of Relationship Between Specific Volume Change and Specific Ventilation

We used a mathematical model of tracer dilution to examine the theoretical relationship between regional tidal expansion and ventilation (see Appendix in *(1)* for details). The model consists of two parallel compartments, each with an exclusive dead space, and accounts for the effects of tracer mixing in the common dead space as well as heterogeneity of regional air volume and ventilation.

Washout of tracer gas from each compartment was described by the following difference equations for end-expiratory concentrations:

$$F_A[i] = \frac{F_A[i-1]\cdot(V_A+V_{DA}) + F_D[i-1]\cdot V_D\cdot f_{VA}}{V_A+f_{VA}\cdot V_T} \qquad \text{Eq. A1}$$

$$F_B[i] = \frac{F_B[i-1]\cdot(V_B+V_{DB}) + F_D[i-1]\cdot V_D\cdot(1-f_{VA})}{V_B+(1-f_{VA})\cdot V_T} \qquad \text{Eq. A2}$$

$$F_D[i] = f_{VA}\cdot F_A[i] + (1-f_{VA})\cdot F_B[i] \qquad \text{Eq. A3}$$

where F_X[i] is the tracer concentration in compartment x (A, B, or common dead space D) at the end of breath i, V_X is the end-expiratory volume of compartment x, V_{DX} is the dead space unique to compartment x, V_D is the common dead space volume, and f_{VA} is the fraction of tidal volume (V_T) assigned to compartment A.

For washout simulations, the initial concentration in all compartments was set to 1.0, and respiratory rate (RR) was set at 20 breaths per minute (bpm). Model input parameters were taken either directly from experimental data or derived from them (Table A1). Conditions of zero and high positive end-expiratory pressure (ZEEP and PEEP, respectively) were differentiated by the end-expiratory lung volume, with the ZEEP simulation having a smaller and more heterogeneously distributed volume. All other parameters were equivalent for both conditions. Ventilation heterogeneity was simulated by varying the fraction of tidal volume to compartment A from 0.2 to 0.6 in steps of 0.2.

To compute per-breath specific ventilation ($s\dot{V}_B$) for each compartment, the end-expiratory concentrations were plotted on a logarithmic axis during washout, and the slope of the line of best-fit to the first three washout points (m_{wo}) was used in Equation A4.

$$sV_B = -\frac{m_{wo}}{RR} \qquad \text{Eq. A4}$$

Specific volume change (sVol) of each compartment was computed from the tidal volume and compartment volume according to Equation A5.

$$sVol = \frac{f_{V_x} \cdot V_T}{V_x} \qquad \text{Eq. A5}$$

Figure A1 depicts the relationships between $s\dot{V}_B$ and sVol for the simulated parameters. The ranges of points for both simulations, as well as the slopes and y-intercepts of the regression lines, are consistent with the experimental data (see Fig. 2 of main text). The larger y-intercept for the ZEEP condition is also consistent with the data, and results from a higher dead space to total lung volume ratio. Interestingly, the R^2 values are both less than 1. This effect is caused by tracer mixing in common dead space and heterogeneity of regional volume and ventilation, which are both present in real experimental conditions.

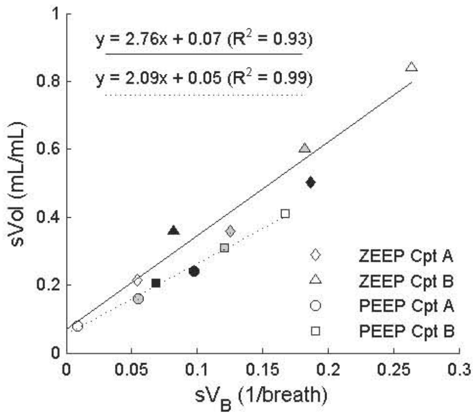


FIGURE A1. Relationships between $s\dot{V}_B$ and sVol for washout simulations. For each simulation (ZEEP and PEEP), the fraction of ventilation to Compartment A was increased from 0.3 to 0.6 in steps of 0.1 (white → black symbols). The points were well described by a linear fit (ZEEP, solid line; PEEP, dotted line). Note the larger slope and y-intercept for the ZEEP simulation.

TABLE A1

Simulation Input Parameters

V_T (mL)	180
V_D (mL)	60
V_{DA}, V_{DB} (mL)	20
V_A (mL)	250 (ZEEP), 450 (PEEP)
V_B (mL)	150 (ZEEP), 350 (PEEP)
f_{VA}	0.2, 0.4, 0.6

V_T, tidal volume; V_D, common dead space volume; V_{DA}, V_{DB} compartmental dead space volumes; V_A, V_B, compartment volumes; f_{VA} fraction of ventilation to compartment A

SUPPLEMENTAL REFERENCES

1. Vidal Melo MF, Harris RS, Layfield D, Musch G, Venegas JG. Changes in regional ventilation after autologous blood clot pulmonary embolism. *Anesthesiology*. 2002;97:671-681.