INTRODUCTION: The dead space volume in measurements of lung ventilation using gaseous contrast agents (e.g. hyperpolarized 3He) can be a substantial source of error if their magnitude is not carefully incorporated in the gas distribution model. The dead space in lung ventilation can be divided into two main components (Figure 1.a): (1) Dynamic Dead Volume, \( V_D \); contains the major conductive airways and the portion of the ventilator after the respiratory valve, including endotracheal tube which experiences a bi-directional flow during respiration; (2) Static Dead Volume, \( V_S \): contains part of the ventilator system that only uni-directionally carries the source contrast gas towards the respiratory valve’s inlet, primarily containing the transmission line between the \(^3\)He chamber and the respiratory valve. The primary distinction between \( V_S \) and \( V_D \) is that the portion of the respiratory gas residing in \( V_S \) from the previous breath is re-inhaled with each new breath; known as rebreathing.

METHODS: THEORY: A lumped three-compartment model is proposed as illustrated in Figure 1.b to model the system dead volumes. The rightmost compartment comprises the acinar airways and contains the magnetization \( M_C \); the middle compartment comprises the combination of major conductive airways and the respiratory valve, and contains the magnetization \( M_R \); and the leftmost compartment includes the transmission line (with magnetization \( M_T \)) that carries the \(^3\)He from the source \((M_S)\). For the serial ventilation sequence [1], the magnetization build-up can be expressed as:

\[
M_S(t) = M_0 \exp \left( -\frac{t}{\tau_1} \right) + \left( 1 - \exp \left( -\frac{t}{\tau_2} \right) \right) \exp \left( \frac{t}{\tau_3} \right)
\]

where \( r = r_A', r_S'(1-r_S') \) is the apparent fractional ventilation, including the rebreathing effect of conductive airways, and \( r_S'/V_S \). The RF and oxygen decay mechanisms are governed by \( D_{O2} = N_{O2} + \ln(\cos\alpha) \) and \( D_{O2} = r/F_{O2} \), with \( F_{O2} = \frac{\gamma}{PO_2} \). It is implied that the arriving magnetization from the conductive airways, \( M_R \), at each breath is a combination of the arriving HP \(^3\)He from the transmission line and the exhaled gas from the previous breath. Since the gas in the transportation line travels only in one direction towards the respiratory valve, it is assumed that the entrance of HP \(^3\)He gas from the source pushes the same amount of gas \((V_T)\) out of the static dead volume (Figure 1.c). For a relatively small \( V_S \) compared to \( V_T \) \((r_S' = V_S'/V_T < 1, \text{ e.g. in rodents})\), the concentration of the gas delivered from the transmission line \( M_T \) increments increases with each breath. However for large tidal volumes \((r_S' > 1, \text{ e.g. in humans})\), the entire contents of the static dead space is purged with the first breath.

SIMULATION: The magnetization and signal build-up history in acinar airways were simulated using: \( M_S = 1 \times [a_1, a_2, \ldots, a_5, \ldots, a_n] \), \( N_S = 30 \), \( \tau_1 = 1 \) s, \( N_{O2} = 64 \), \( P_S = 140 \) mbar, \( V_T = 2 \) ml, and \( V_S = 6 \) ml. All initial magnetizations are zero. Introduction of the two types of dead space affects the magnetization and signal build-up in very different ways (not shown). Adding \( V_D \) to a no-dead-space system \((r_D = 0 \text{ and } r_S = 0)\) is reflected as a lower steady state magnetization, \( M_S \), and a lower apparent fractional ventilation. Introduction of \( V_S \) to a no-dead-space system, on the other hand, increases the rise time of magnetization build-up curve. This curve however eventually reaches the same \( M_S \) as that of the no-dead-space system. PHANTOM: An artificial lung phantom was constructed with a 10-ml glass syringe (ID=1.46cm), loaded with a nonmagnetic beryllium-copper compression spring \( (3.248 \text{ free length } @ 0.145 \text{ lbf/cm}) \). A residual volume of \( V_T = 4 \) ml was enforced. The syringe-spring assembly was ventilated with three different tidal volumes \( V_T = 1.1, 2.5 \) and \( 4.5 \) (equivalent to \( r_A = V_T/(V_T+V_S) = 0.22, 0.38 \) and 0.53). Dead spaces were directly measured as \( V_S = 0.5 \) ml and \( V_D = 3.2 \) ml. Imaging was performed using a GEMS pulse sequence on a 50-cm 4.7-T MRI scanner equipped with 12-cm 25 G/cm gradients and a quadrature 8-leg birdcage body coil \((152.95 \text{ MHz}, \text{ID}=7\text{cm})\), with: projections at \( \text{FOV}=6 \times 6\text{cm}^2\), \( \alpha = 4-5^\circ\), \( \text{MS}=64 \times 64 \) pixels, \( T_A=6.6 \) ms and \( T_E=3.3 \) ms.

RESULTS: Fractional ventilation was measured in the spring-syringe setup with each measurement repeated three times. The experimental results \((0.22, 0.37 \) and \(0.52)\) were in good agreement with \( a \text{ priori} r_A \) values. The fractional ventilation \( r_A \) and dynamic dead space ratio \( r_D \) are related through\( r = r_D' (1 - r_D') \). Therefore the relative error in \( r_A \) as a function of uncertainty in \( r_D \) is governed by \( \Delta r_A = \Delta r_D / r_D \). The constructed model with a nominal \( r_A = 0.3 \) and above parameters, were solved numerically for the unknown \( r_A \) and \( r_D \in [0.0, 0.9] \) and the relative error \( \Delta r_A \) was calculated (Figure 2.a) showing a monotonic dependence of \( \Delta r_A \) on \( r_A \) variation. The relative error is larger for smaller \( r_A \) values. For instance, an error of \( +0.05 \% \) in \( r_A \) results in \( 80\% \) overestimation of \( r_A \) as \( 0.15 \), whereas it only affects \( r_A \) as \( 0.45 \) by \( 45\% \). The sensitivity of the model was also assessed to entirely ignoring static dead space using \( r_D \in [0.1, 0.9] \) and solving for \( r_D \) by setting \( r_S \rightarrow \infty \). The net result of ignoring \( V_S \) is underestimation of \( r_A \) value, again with a larger relative error for smaller \( r_A \) values. The model however quickly becomes less sensitive as the actual \( r_A \) value grows beyond \( 0.6 \) (Figure 2.b).

DISCUSSION: Simulation and experimental results both indicate that inclusion of dead space volume in the ventilation model allows for a better fit to the data by providing additional degrees of freedom to the signal build-up model. As shown in simulation, as well as the syringe phantom experiment, in presence of a static dead volume, the signal build-up curve starts resembling an S-shaped curve. In the absence of the static dead space model the signal build-up is mathematically incapable of exhibiting such a behavior and therefore adversely affects the estimation of \( r_A \) value. This model has a greater significance in small animals and rodents where the tidal volume is of the same order of magnitude as dynamic and static dead space volumes. On the other hand it, is important to note that inaccurate estimation of system dead volumes can lead to error in \( r_A \) calculation as well, and therefore it is necessary to balance the tradeoff between the two factors through direct and accurate measurement of system dead spaces and estimating the volume of major conductive airways in the imaged subject.