# Long-Range Diffusion of $^3$He in Lungs: Evidence for Collateral Ventilation Pathways from Comparison of Computer Simulations and Measurements

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## INTRODUCTION

Using hyperpolarized $^3$He and magnetization tagging techniques, the rate at which gas diffuses across long distances (1-3 cm) within human and canine lungs has been determined by us and others in both healthy and emphysematous lungs [1-3]. In this study a regular symmetric dichotomous branching model of human lungs [4,5] has been implemented in computer simulations of diffusion that allow the long-range diffusivity to be determined. In the simulations, diffusion was allowed through the branching airways but not through collateral ventilation pathways. *In vivo* measurements have shown that resistance through collateral pathways decreases with increasing lung volume [6]. As a preliminary investigation into the effect of increased collateral ventilation, the long-range diffusion was measured in a healthy 24 year old volunteer at two disparate lung volumes.

## MATERIALS AND METHODS

A computer routine for solving differential equations from arbitrary initial conditions with a time-step of 25 ms was used to monitor the diffusion of gas in simulated lungs. This routine was tested thoroughly, including using it to solve the diffusion equation in a smooth tube of specified length, for which the results agreed with the known analytical solution. An algorithm was used to generate the Cartesian coordinates of dichotomously branching stochastic trees terminated at the acinar level. The lengths and diameters of the airways came from accepted morphometric measurements [4, 5]. To produce the initial conditions of simulated magnetization tagging experiments, a sinusoidally varying magnetization was applied to gas within the lungs. The time decay behavior of the striped pattern was quantified by tracking the value of the relevant spatial Fourier coefficient as a function of time within the simulation.

For imaging in a healthy volunteer, $^3$He was polarized to ~40% using SEOP. The subject inhaled to (1) approximate functional residual capacity (FRC) and (2) total lung capacity (TLC); decay at TLC is shown in Figure 1. Magnetization tagging of $^3$He used two 45° pulses separated by a gradient pulse. The decay of the resulting sinusoidal modulation was followed over 10 seconds by subsequent FLASH imaging.

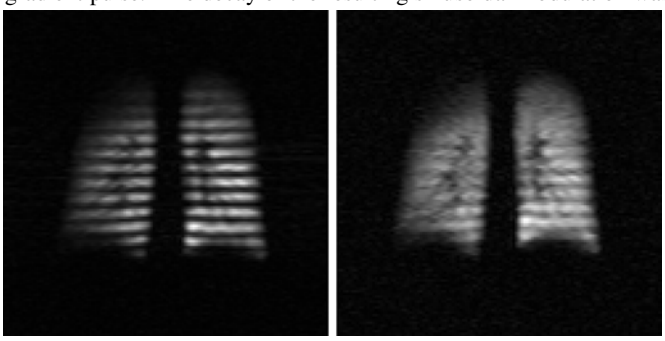

**Figure 1 - Initial magnetization tagging stripes at TLC have substantially decayed 4 seconds later in this healthy volunteer.**

## RESULTS

For a tagging wavelength of 2 cm in 32 simulated lungs, approximately exponential decay of the modulated magnetization was observed with an average time constant $\tau$of 115 s, corresponding to a long-range effective diffusivity $D_e$ of 0.00088 cm$^2$/s (using $1/\tau = 4\pi^2 D_e/\lambda^2$ from the diffusion equation). By comparison, the reported diffusivity in healthy humans [1], dogs [2] and explanted normal human donor lungs [3] is around 0.02 cm$^2$/s—20 times larger than the simulation results. Varying the details of the simulated lung structure, such as varying the branching half-angle from 35° to 45°, produced only minor changes in the simulated $D_e$. The more rapid experimental decay suggests that additional pathways for gas diffusion are at work. In the healthy volunteer, $D_e$ was found to be 0.027 cm$^2$/s at FRC (consistent with previously reported results) and 0.068 cm$^2$/s at TLC.

## CONCLUSIONS

Experimentally measured long-range diffusion is much faster than simulated diffusion through the airways proper, indicating the presence of an additional mechanism that transports gas over distances of several centimeters. In living humans, bulk mixing of gas via cardiogenic pumping may explain these results in part, but similar results from motionless explanted donor lungs show that it cannot be the full explanation. Microscopic or macroscopic collateral ventilation pathways may significantly promote the diffusion of gas throughout the lung parenchyma over distances of centimeters, even under static conditions. The significantly higher diffusivity seen in the healthy volunteer at TLC compared to FRC is preliminary evidence that collateral pathways, whose resistance to flow is known to drop at higher lung volumes, may play an important role in long-range diffusion in healthy lungs.

## REFERENCES

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