^{129}Xe Apparent Diffusion Coefficient Anisotropy in Emphysema: Simulations using a 3-D Budded Cylinder Model

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INTRODUCTION

Recent developments in hyperpolarized noble gas Magnetic Resonance (MR) imaging have shown sensitivity to detecting emphysema *in vivo* [1]. Measuring apparent diffusion coefficients (ADCs) of hyperpolarized ^{3}He gas in the lungs can provide sub-voxel information on the disease severity [2]. Particularly, if measured at very short diffusion times, diffusion behaves anisotropically, thus ADCs can be modeled by two components [2]: (i) longitudinal component, D_L, the ADC along the airway and (ii) transverse component, D_T, the ADC transverse to the airway, towards the alveoli. ^{129}Xe may be better suited than ^{3}He for anisotropic diffusion studies because its smaller self-diffusion coefficient implies longer optimal diffusion times, which would be less strenuous on hardware. Furthermore, ^{129}Xe is more plentiful than ^{3}He and could provide a pathway to clinical applications in future.

The purpose of this study was to use a finite difference technique [3, 4] of solving the Bloch-Torrey equations for a 3-D budded cylinder model of the terminal airways (Fig. 1, introduced by Fichele *et al* [3]) to find the optimal ADC coefficient (D_L or D_T) and diffusion time to quantify emphysema using hyperpolarized ^{129}Xe MRI.

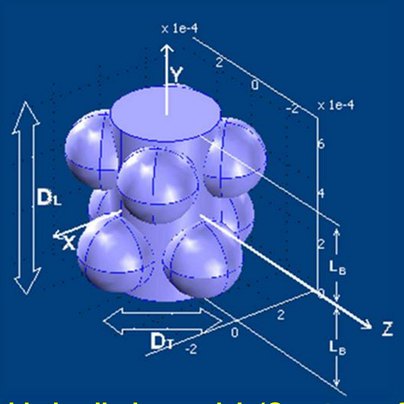

Figure 1. 3-D budded cylinder model. (Courtesy of X. Xu M.Sc. Thesis)

METHODS

A finite difference approach was used to numerically solve the Bloch-Torrey equations (1) in C.

$$\frac{dM(t)}{dt} = -i\gamma\left[\vec{G}(t)\cdot\vec{r}\right]M(t) + D\nabla^2 M(t) \quad (1)$$

Where *M* is the magnetization, γ is the gyromagnetic ratio of the nuclei, *G* is the magnetic gradient, *r* is the spatial position and *D* is the diffusion coefficient. The first term on the right side of (1) can be approximated by a Taylor expansion:

$$M(t+\Delta t,\vec{r}) = M(t,\vec{r})e^{-i\gamma[\vec{G}(t)\cdot\vec{r}]\Delta t} \quad (2)$$

The diffusion term of (1) can be solved by a stepwise spatial finite difference technique, shown in (3) for 3 dimensions.

$$\begin{aligned} M_{j,k,l}^{n+1} = M_{j,k,l}^{n} &+ D_{j-1,k,l}\frac{\Delta t}{\Delta x^2}\left(M_{j-1,k,l}^{n} - M_{j,k,l}^{n}\right) + D_{j+1,k,l}\frac{\Delta t}{\Delta x^2}\left(M_{j+1,k,l}^{n} - M_{j,k,l}^{n}\right) \\ &+ D_{j,k-1,l}\frac{\Delta t}{\Delta y^2}\left(M_{j,k-1,l}^{n} - M_{j,k,l}^{n}\right) + D_{j,k+1,l}\frac{\Delta t}{\Delta y^2}\left(M_{j,k+1,l}^{n} - M_{j,k,l}^{n}\right) \\ &+ D_{j,k,l-1}\frac{\Delta t}{\Delta z^2}\left(M_{j,k,l-1}^{n} - M_{j,k,l}^{n}\right) + D_{j,k,l+1}\frac{\Delta t}{\Delta z^2}\left(M_{j,k,l+1}^{n} - M_{j,k,l}^{n}\right) \end{aligned} \quad (3)$$

The integer indices i,j,k are for the spatial coordinates x,y,z respectively, and n is the integer indice for temporal steps.

A 23x40x23 matrix (x,y,z) was simulated using 42 µm *x* and *z* pixel size, and 16 µm *y* pixel size. Bipolar trapezoidal gradients were applied in 30 different orientations relative to the cylinder (0 to π rad) to simulate random orientation of airways in voxels [3].

Several assumptions were made for these simulations. (1) T_2* effects were ignored (2) Bulk flow of gas was not present (3) Magnetic field inhomogeneities (other than the applied gradients) were ignored (4) ^{129}Xe-tissue permeability was ignored (5) Prior to applying the bipolar gradients, the magnitude and phase of the transverse magnetization is homogeneous.

The xenon self-diffusion coefficient was set at 6.1 10^{-6} m^2/s. Diffusion times (Δ) ranged from 1 to 100 ms, and b-values ranged from 0.0011 to 7.32 s/cm^2. The boundary geometry is shown in Fig.1. The radius of the spheres (R_A) was set at 140 µm, distance between the two sets of spheres (L_B) was set at 160 µm and the distance from the center of the cylinder (R) was set at 210 µm. The radius of the cylinder R_D was varied depending on disease severity ("Healthy"=175 µm, "Mild"=245 µm,"Severe"=280 µm). The severity of the disease was interpreted as Fichelle did [4], with the $R_D/(R+R_A)$ ratio values. A phase wrapping boundary technique was used to simulate an infinite cylinder.

For the simulations to converge, the spatial steps size (Δx, Δy and Δz) needs to satisfy the Nyquist criteria. We required greater than 1% accuracy, thus the following condition was always satisfied.

$$\Delta x \leq \frac{\pi}{10G\gamma\Delta} \quad (4)$$

Similarly, the temporal step size (Δt) satisfied the following condition:

$$D\frac{\Delta t}{\max(\Delta x,\Delta y,\Delta z)^2} \leq 0.27 \quad (5)$$

RESULTS

D_L and D_T were extracted from the data by fitting the data to the Yablonskiy anisotropic diffusion model [2]:

$$S = S_0 exp(-bD_T)\left[\frac{\pi}{4b(D_L - D_T)}\right]^{1/2}\Phi\left\{[b(D_L - D_T)]^{1/2}\right\} \quad (6)$$

where b is the b-value of the bipolar trapezoidal gradient sequence[2], S_0 is the signal for b = 0 s/cm^2, and Φ is the error function. This model was fitted to the data using a nonlinear least squared Matlab algorithm (lsqcurvefit.m, The Mathworks, Natick MA). Results are shown in Table 1 and Figs. 2

Time (ms)	ΔD_L – Severe (cm^2/s)	ΔD_L – Mild (cm^2/s)	ΔD_T – Severe (cm^2/s)	ΔD_T – Mild (cm^2/s)
1	0.0003	0.0002	0.0154	0.0110
2	0.0004	0.0003	0.0188	0.0132
5	0.0175	0.0183	0.0118	0.0052
10	0.0263	0.0192	0.0050	0.0026
20	0.0272	0.0196	0.0019	0.0007
50	0.0281	0.0194	0.0000	0.0000
100	0.0279	0.0196	-0.0002	-1.00E-04

Table 1. Change in longitudinal (ΔD_L) and transverse (ΔD_T) diffusion coefficients between healthy airways and severely/mildly diseased airways. Highlighted cells show the greatest change in D_L and D_T.

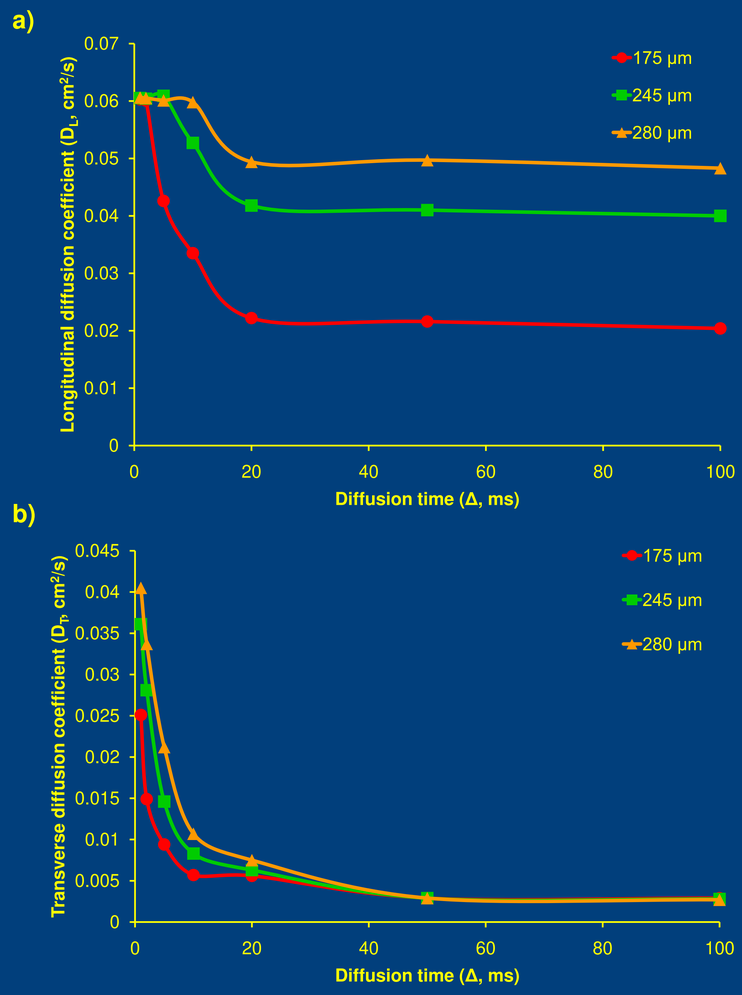

Figure 2. Simulated anisotropic ADCs as a function of diffusion time for healthy (R_D = 175 µm), mild (R_D = 245 µm) and severe (R_D = 280 µm).

DISCUSSION AND CONCLUSIONS

In Fig 2(a), D_L plateaued for diffusion times greater than 20 ms (122% increase for severe emphysema compared to healthy tissue). In Fig. 2(b), D_T had optimal change for a 2 ms diffusion time (126% increase for severe emphysema compared to healthy tissue). These results will aid choosing the best diffusion times to detect emphysema *in vivo* using ^{129}Xe MRI. For these long diffusion times, a low field system may be ideal for *in vivo* investigations as T_2* is longer due to reduced air-tissue susceptibility differences, though diffusion times up to 20 ms may be possible at 3.0 T.

Smaller spatial step sizes in future simulations would allow larger b-values to be simulated, as these are limited by the Nyquist criterion [3,4]. It's important to note that behavior at long diffusion times will alter from our simulations due to the branched structure present *in vivo*, thus investigating other models may be useful in determining optimal diffusion times for ADC measurements.

ACKNOWLEDGEMENTS AND REFERENCES

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