Diffusion Time: A Tuning Parameter for Lung Airspace Size Selection with Hyperpolarized 3He Gas Diffusivity Measurements?

D. D. Shanbhag[1], T. A. Altes[2], and J. Knight-Scott[3]

[1]Imaging Technologies, GE Global Research, Bangalore, Karnataka, India, [2]Department of Radiology, The Children's Hospital of Philadelphia, Philadelphia, PA, United States, [3]Department of Radiology, Children's HealthCare of Atlanta, Atlanta, GA, United States

Introduction and Theory

Hyperpolarized ^{3}He gas diffusion measurements in lungs present an opportunity to non-invasively probe the morphology of lung airspaces. A hyperpolarized ^{3}He q space spectroscopy technique has been utilized for detecting pathological changes of lung micro-structure in emphysema and shown to be sensitive to age related changes in lung microstructure [1]. Q-space describes NMR diffusion experiments in terms of reciprocal spatial vector q, which is defined as $(2\pi)^{-1}\,\gamma\delta G_d$ where γ is the gyromagnetic ratio of the observed nuclei, δ is gradient pulse duration and G_D is the gradient strength of bipolar gradient pulse. The q-space formalism provides a map of the distribution of the displacements of atoms within a geometrical structure in terms of displacement probability profile (DPP). The normalized signal from diffusion experiment is given by $E[q,\Delta] = \int DPP[R,\Delta]\exp[i2\pi q\cdot R]\,dR$. The signal attenuation due to diffusion in restricted environments is thus a function of two parameter domains: the effective observation time, Δ, and the gradient pulse area (provided by q), both of which are sensitive to the morphology of the porous structure [2]. An understanding of the variation of the q-space parameters in response to variations in different acquisition parameters might help in tuning the q-space sequence parameters for different restriction sizes. In present work, we have investigated the effects of variable diffusion times on diffusion measurements with *in vivo* lung ^{3}He gas diffusion data.

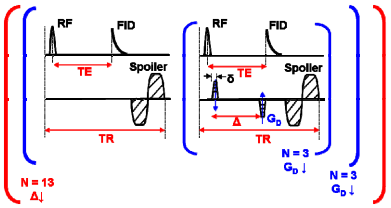

Figure 1. ^{3}He q-space DWS sequence. The colors indicate the parameters changing in the loop

Methods and Materials

Q-space Spectroscopy: ^{3}He diffusion-weighted spectroscopy (DWS) datasets were obtained from three healthy volunteers on a 1.5T Siemens Sonata MRI system using a ^{3}He flexible coil. To understand the effects of variable diffusion times, q-space spectroscopy data was collected for 13 different diffusion times Δ: 2.05 ms, 2.71 ms, 3.38ms, 4.04 ms, 4.7ms, 5.36, 6.02ms, 6.69 ms, 7.35 ms, 8.01 ms, 8.67 ms, 9.33 ms and 10 ms. For each value of Δ, 13 spectra were collected (9 diffusion weighted spectra and 4 non-diffusion weighted spectra) with q values varying from 2.008 mm^{-1} to 0 mm^{-1}. The q-space was traversed by fixing the value of δ at 1.63 ms and varying the diffusion sensitizing gradient amplitudes (along the A-P direction) from 38 mT to 0 mT. Since the q values were kept constant at each value of Δ, this resulted in the maximum b value being variable for different Δ. The maximum b value was thus highest (150 s/cm^2) for the longest Δ (10 ms) and lowest (35 s/cm^2) for the smallest Δ (2.05 ms). For each set of Δ, the TE/TR values changed accordingly, ranging from TE/TR =4.78/39.18 ms for Δ = 2.05 ms to 12.73/47.13 ms for Δ = 10 ms. Since the signal from ^{3}He gas decreases as acquisition progresses, measurements with higher Δ values were done first to maximize SNR. The entire dataset was collected within single breath hold of 7.5 s. **Data Analysis:** Data analysis has been described in detail in Ref [1] and a brief description is provided here. The signal intensities were calculated using the AMARES algorithm provided in jMRUI [v 2.0]. For each set of Δ, the diffusion weighted spectra were corrected for T_1 and flip angle related attenuation using the 4 q = 0 mm^{-1} (non-diffusion weighted) data points for that set. The zero-filled q-space curve was amplitude normalized and DPP obtained by Fourier transformation with respect to q. The DPP was fit to bi-Gaussian model: $DPP(x) = \sum_{n=1}^{m} Z_n e^{-0.5\left(\frac{x}{X_{rms,n}}\right)^2}$, $m = 2$ where, x is the displacement, Z_n is the zero-displacement probability (DPP(x=0)) and $X_{rms,n}$ is the rms displacement. Weighted average $X_{rms,WA}$ displacement was used as single metric for comparison $\left[X_{rms,WA} = \frac{(Z_1 X_{rms,1} + Z_2 X_{rms,2})}{(Z_1 + Z_2)}\right]$.

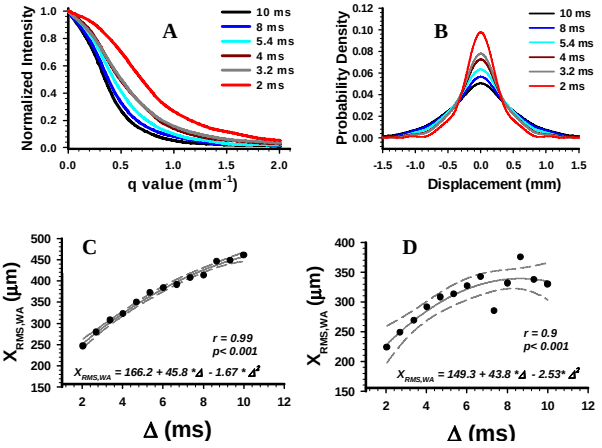

Figure 2. Effect of Δ on the DPP obtained *in vivo*. **A**. Q-space curves. **B**. DPP broadens and lowers with increasing Δ. **C** The $X_{rms,WA}$ curve was found to be quadratic, function of Δ. **D** Similar effect in other adult volunteer

Results and Discussion

As seen from figure 2, the primary effect of increasing the diffusion time (Δ) is to broaden and lower the DPPs. Overall, in all three volunteers, the weighted average rms displacement ($X_{rms,WA}$) increased in quadratic manner with increasing diffusion time Δ (Figure 2C and 2D). Table 1 shows the variation of the individual parameters in the bi-Gaussian model with increasing Δ. When the individual components of DPP were examined, it was observed that variation in $X_{rms,1}$ was smaller compared to the larger $X_{rms,2}$. Moreover, the zero-displacement probability associated with the narrower component (Z_1) was found to have maximum change and decreased in an inverse polynomial function ($Z_1 = a0 + a1 * \Delta^{-1}$) in all the three volunteers (Figure 3). Since Z_1 is associated with restrictiveness of the acinus, the results suggest that increasing diffusion time results in gas atoms exploring more of the acinar structure [1]. However, for none of the bi-Gaussian parameters, was an asymptotic value reached. This suggests that the diffusion motion in lungs is hindered rather than strictly restricted. The variation of rms displacements with diffusion times suggests that *Δ might be used a "tuning" parameter to make the diffusion measurements in the lungs more sensitive to a particular geometrical length scale for different lung disease cases.* Since the rms displacements and ADC values are coupled by the root-mean-square relationship, the results here have implications for ^{3}HE ADC imaging as well. The result indicates that strong caution should be exercised when comparing q-space parameters/ADC values obtained from different experiments (different δ, Δ and G_d) as the restricted diffusion coefficients are a highly sensitive to these experimental parameters. ***This also hints that a set of standard diffusion gradient waveform parameters should be adopted so that results of ^{3}He lung diffusion measurements from different groups can be easily compared.***

Volunteer	(Minimum, Maximum, %Coefficient of Variation)			
	$Z_1\downarrow$	$X_{rms,1}$ (μm) $\uparrow$	$Z_2\downarrow$	$X_{rms,2}$ (μm) $\uparrow$
#1	0.017, 0.060, 40%	172, 262, 13%	0.029, 0.044, 13%	364, 605, 16%
#2	0.027, 0.114, 48%	171, 242, 10%	0.013, 0.054, 36%	337, 532, 17%
#3	0.015, 0.08, 45%	155, 220,7%	0.027, 0.045, 12%	329, 497, 12%

Table 1. Bi-Gaussian model parameters in three volunteers. Arrows indicate the general trends in each parameter as ***Δ increases.***

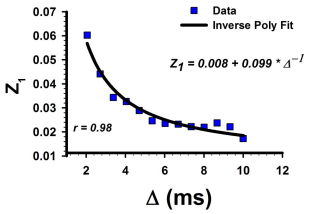

Figure 3. Zero displacement probability Z_1 shows an inverse polynomial relation with increasing Δ and contributes to maximum change seen in $X_{rms,WA}$ **for all three volunteers**.

References [1]. Shanbhag DD, et. al. *J Magn Reson Imaging.* 2006; 24: 84-94. [2]. Callaghan PT, AE et.al. *J Magn Reson* 1995; 113: 53. [3]. Assaf Y, Basser PJ. Neuroimage 2005;27(1):48-58.