Q-space Analysis of Lung Morphometry in vivo with Hyperpolarized ^{3}He spectroscopy

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Introduction:

For diffusion in heterogeneous systems, q-space based diffusion analysis is a powerful tool because it yields information that is directly related to the structure without resorting to complex models. Q-space measurements provide a profile of the root mean square (RMS) displacements that occur during a given observation time. Since it is the translational diffusive displacement that is actually detected in the PFG experiment, q-space provides unequivocal information about the processes responsible for the diffusion weighted contrast in different pathologies. The purpose of this study was to develop a ^{3}He global spectroscopic q-space technique for examining lung morphometry *in vivo*. Here we report on preliminary studies comparing the spectroscopic q-space method to ^{3}He diffusion weighted imaging (DWI) We demonstrate that a global spectroscopic q-space approach provides equivalent about lung microstructure as DWI but using a very low dose of inhaled HHe gas and short breathold times.

Theory :

Q-space describes NMR diffusion experiments in terms of displacement probabilities, using the reciprocal spatial vector q, which is defined as $(2\pi)^{-1}\,\gamma\delta G_D$ m^{-1} where γ is the gyrometric ratio of observed nuclei, δ is gradient pulse duration and G_D is the gradient strength of bipolar gradient pulse. The normalized signal from diffusion experiment is given by $E[q,\Delta] = \int \overline{P}[R,\Delta]\exp[i\,2\pi\, q\cdot R]\,dR$ [1] where $\overline{P}[R,\Delta]$ is the displacement probability profile(DPP) DPP is not a map of the underlying geometrical structure, but describes the distribution of the displacements of atoms within the geometrical structure being probed. The flexibility of q-space approach lies in the simple Fourier relationship between the measured NMR signal and the displacement probability profile.

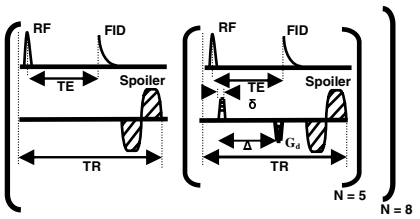

Figure 1. Sequence diagram for q-space spectroscopy in human lungs.

Methods and Materials:

^{3}He DWS data was collected from eleven healthy adult (HY), five healthy children (PED) and two COPD volunteers. All the experiments were performed on a 1.5T whole body Siemens Sonata MRI system using a ^{3}He flexible chest coil. For each subject, 48 global lung spectra were collected during a 2 s breathold using a non-selective 6°, 400μs gaussian RF pulse by inhaling 40 cc of HHe diluted with ~1L of filler N_2 gas. Bipolar trapezoidal gradients (δ=1.63 ms, Δ=6.80 ms) were used for diffusion sensitization along the *anterior-posterior* (**A-P**) anatomical direction. 40 q-values were uniformly sampled by varying G_D from 38 mT/m to 0 mT/m. The maximal q value for the experiment was 2008 m^{-1} while the maximal b value was 100 s/cm^2. The displacement resolution was limited to 0.5mm which was improved to 125 μm by zero-filling the q-space curve to 160 points. The data were corrected for flip angle dependent attenuation and T_1 relaxation using the method described in Knight-Scott et.al. [2]. The zero-filled q-space curve was amplitude normalized and DPP obtained by Fourier transformation with respect to q. The DPP was fitted to a bi-gaussian model $P = \sum_{n=1}^{m} Z_n e^{-0.5\left(x/RMS_n\right)^2}$, $m = 2$. For all but one volunteer, standard HHe diffusion weighted images were collected (b: 0 and 1.6 s/cm^2)

Results and Discussion:

The DPP obtained *in vivo* appears to have two distinct length scales: a narrower one which has a mean RMS value of 189 um in HY volunteers, and morphmetrically equivalent to diameter of alveolar sacs and Broader component which has dimensions of 488 um, the dimension of the respiratory bronchioles [3]. In case of COPD patients examined, the DPP is extremely broad indicating highly free diffusion environment for HHe; concordant with the pathological condition of emphysema: destruction of alveolar walls and airspaces. Excellent correlation was obtained with mean value of the histogram obtained from diffusion weighted imaging performed on same volunteers : ADC vs RMS_1 (r = 0.87), ADC vs RMS_2 (r = 0.92).The q-space data shows broadening and lowering of DPP with age (figure 2). Good correlation was obtained for age related changes in lung structure (age vs RMS_1: r =0.78 , age vs RMS_2:r =0.9). Table 1 summarizes the results for three different volunteer groups.

Table 1

Volunteer Groups	DWI $\overline{ADC}$ (cm^2/s)	$\overline{Z_1}$	$\overline{R.M.S._1}$ (μm)	$\overline{Z_2}$	$\overline{R.M.S._2}$ (μm)
Peds (N=5)	0.149±0.01	0.058±0.013	167±4	0.038±0.002	382± 22
HY (N=11)	0.232±0.04	0.036±0.005	188±10	0.037± 0.004	474±44
COPD (N=2)	0.383±0.09	0.018±0.006	265±71	0.029±0.006	699±125

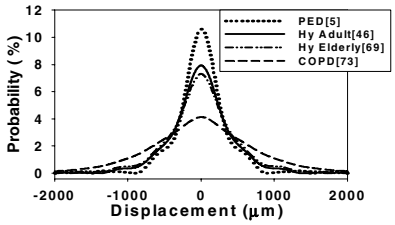

Figure 2. Representative DPPs obtained from volunteers of different age. Numbers in brackets indicate the age of respective volunteers.

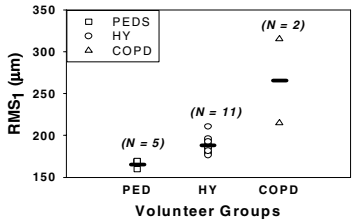

Figure 3. Scatter plot for the RMS_1 volunteer groups. The (-) on the scatter plot of each volunteer group indicates the mean RMS.

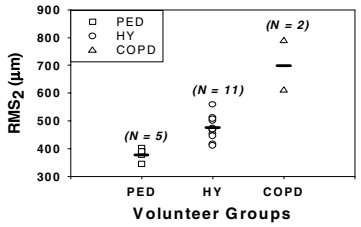

Figure 4. Scatter plot for the RMS_2 volunteer groups. The (-) on the scatter plot of each volunteer group indicates the mean RMS.

Conclusion:

The parameters obtained from q-space analysis correlate well with the current morphometry data available *in vitro*. The technique is well suited for longitudinal studies to understand impact of age, environmental exposures such as smoke and pollutants as well as pharmaco-therapy on lung microstructure. The technique holds promise of translation as a clinical tool due to the low volume of HHe gas required compared to DWI.

References:

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