A Rapid Hyperpolarized ^{3}He Q-space Diffusion Spectroscopy Sequence for Sub-Second Breath Hold *in vivo*

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Introduction

Q-space describes 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 gyromagnetic ratio of the observed nuclei, δ is gradient pulse duration and G_D is the gradient strength of bipolar gradient pulse [1]. A q-space based hyperpolarized ^{3}He global spectroscopic technique has been utilized for detecting pathological changes of lung structure in emphysema and shown to be sensitive to age related changes in lung microstructure [2]. One of the primary motivations behind using the global diffusion weighted spectroscopy technique was to minimize the breathold times; especially attractive in pediatric patients and patients with severe lung disease. Examination of the q-space sequence reveals that most of the sequence duration is utilized for acquiring the FID and dense sampling at multiple q values. To minimize the total scan time of the sequence, we determined the minimum values for these parameters which yield acceptable errors by numerical simulations and verified these parameters *in vivo*.

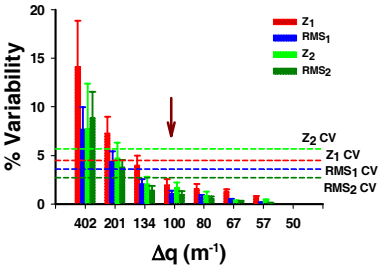

Figure 1. Plot of variability for the bi-Gaussian parameters as a function of Δq. The dashed lines indicate the mean CV_{intra} associated with different bi-Gaussian parameters while the arrow indicates the optimal sampling parameter (Δq = 100 m^{-1}).

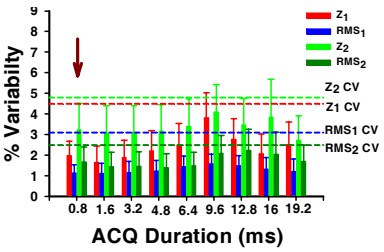

Figure 2. Variability plot for the bi-Gaussian parameters as a function of acquisition window duration. The arrow indicates the minimum acceptable acquisition duration (0.8 ms)

Methods and Material

Q-space Spectroscopy: All the studies were performed on a 1.5T whole body Siemens Sonata MRI scanner using a ^{3}He flexible chest coil. The 40 point q-space diffusion data (δ=1.63 ms, Δ=6.80 ms, q_{min} = 0 m^{-1}, q_{max} = 2008 m^{-1}, 10 kHz spectral width, 25.6 ms acquisition window, 256 complex points, ten additional interleaved q = 0 m^{-1} points for flip angle and T_1 related attenuation correction, ~2s total scan time) was acquired following inhalation of 40 mL of hyperpolarized ^{3}He with 950 mL of filler N_2 gas. As previously described, the data were processed and analyzed using a bi-Gaussian model [2]. **Repeatability Study:** 15 healthy adult volunteers underwent two q-space data acquisitions in the same breath hold and the intra-subject coefficient of variation ($\mathbf{CV_{intra}}$), as described in Ref. [3], was calculated for each of the four bi-Gaussian model parameters [2]. **Numerical Simulations**: Q-space data was acquired in 20 volunteers (14 healthy adult volunteers, 4 healthy children and 2 COPD patients). This data was used as input for the numerical simulations to assess the effects of varying the acquisition parameters. The number of q-space samples were varied, N = 5, 10, 15,…..40 points, corresponding to incremental q value (Δq) ranging from 402 m^{-1} to 57 m^{-1} respectively. The data for these incremental sampling rates were obtained by interpolating the 40 point q-space curve at the respective sampling points using the Piecewise Cubic Hermite Interpolating Polynomial (pchip) function provided in Matlab (Version 7.1). The ten interleaved q = 0 m^{-1} points, used to correct for flip angle and T_1 related attenuation, yield a decay parameter K_{10} [2]. By selecting the alternate q = 0 m^{-1} signals, the number of non-diffusion weighted acquisitions was reduced to 5, and the decay parameter K_5 was determined and compared to K_{10}. Next the minimum acquisition window duration was determined by truncating the 25.6 ms FIDs to 0.8 ms, 1.6 ms, 3.2 ms, 4.8 ms, 6.4 ms, 9.6 ms, 12.8 ms, 16 ms and 19.2 ms. The truncated FIDs from each volunteer were then phase corrected and signal intensities were obtained using the AMARES algorithm provided in jMRUI [v.2.1]. The data obtained at different incremental q-values and different acquisition window durations were analyzed using a bi-Gaussian model [2]. To determine the accuracy of the results with various parameters, the variation from the value obtained using the 40 point q-space curve was determined for each of the bi-Gaussian model parameters ($X_{rms,1}$, Z_1 , $X_{rms,2}$ and Z_2) as: $\text{var} = |\text{param} - \text{ref}|/0.5\times(\text{param} + \text{ref})$ [4]. A reduced parameter set was considered to have acceptable precision if the 95% confidence interval (CI) around the mean variability (var) of each of the bi-Gaussian parameters fell within the 95% CI of the intra-subject coefficient of variation [4]. The set of sequence parameters that achieved acceptable accuracy with the minimum acquisition time was determined. **Validation**: 8 healthy volunteers underwent in a single breath hold of ~3s two q-space acquisitions: the 40 point q-space acquisition described in "Q-space Spectroscopy" section and an acquisition with the optimized set of parameters. The resulting bi-Gaussian parameters were compared for accuracy.

Results and Discussion

Repeatability Study: The mean intra subject variation, CV_{intra}, and the 95% CI for the four bi-Gaussian model parameters were: Z_1 = 4.58 %, 3.04% to 5.71%, $X_{rms,1}$ = 3.16%, 1.97% to 4.01%, , Z_2 = 4.81%, 2.69% to 6.25%, $X_{rms,2}$ = 2.51%, 1. 1% to 3.39%. **Numerical Simulations:** For Δq of 100 m^{-1} (N = 20), the variability for each of the four parameters is within the 95% CI for the CV_{intra} associated with that parameter (Figure 1). The percent difference between K_5 and K_{10} was less than 0.03%, indicating that interleaving the sequence with five q = 0 mm^{-1} points is sufficient for correction of T_1 and flip angle related effects. For the four bi-Gaussian parameters, the 95% CI for the variability for different acquisition window durations is within the 95% CI limit imposed by the intra–subject CV_{intra} (Figure 2). The plot indicates that a sampling window of 0.8ms, 1.6ms and 3.2 ms predict similar variability (~2.7% for Z_1 and ~1.8% for Z_2, ~1.2% for $X_{rms,1}$ and $X_{rms,2}$) for the different bi-Gaussian parameters. While according to our selection criteria, 0.8 ms window would thus be optimal, the current spectroscopy programming environment (VA 25B) on 1.5T Siemens Sonata systems allows a minimum acquisition window of only 3.2 ms. Hence, we used this acquisition window in the reduced scan time sequence. **Validation:** For the reduced scan time q-space sequence, the parameters were as follows: TE: 9.38ms, TR = 19.5 ms, vector points = 64 points, spectral BW = 20 kHz, $N_{q\text{-}values}$ = 24 (19 non-zero-q points and 5 q = 0 mm^{-1} points for T1 and flip angle attenuation correction) ranging from 2 mm^{-1} to 0 mm^{-1}.The total scan time for this sequence was ~ 0.5 s. The mean variation for each of the bi-Gaussian parameters obtained from reduced scan time sequence were as follows: Z_1 = 3.93%, $X_{rms,1}$ = 1.8%, Z_2 = 2.4%, $X_{rms,2}$ = 1.65% (Figure 3). While these variations are higher than those predicted using simulations, the variability is less than the measured intra subject variation, CV_{intra}, for each of these parameters.

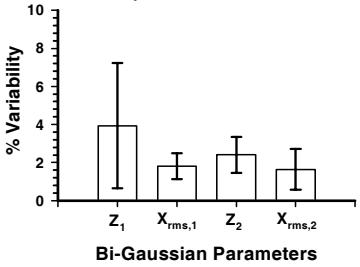

Figure 3. The variability of bi- Gaussian parameters obtained from the optimal sequence compared to those obtained from Q-ref sequence. Except for Z_1, the mean variability is less than 3% for other

Conclusions

We have determined a set of parameters for the q-space sequence which allows the diffusion data to be collected in-vivo with a 0.5 s scan time and which yields results similar to the long scan time (~2 s) q-space sequence. Thus, the reduced scan time sequence can be used interchangeably with the previously described sequence, with applications such as: increased utility in subjects who have a limited breath holding ability, dynamic assessment of lung structure during respiration and multi-direction diffusion tensor spectroscopy.

References:

1. Callaghan, P. T.; Coy, A.; MacGowan, D.; Packer, K. J.; Zelaya, F. O. *Nature* **1991**, 467-469.
2. Shanbhag DD, Altes TA, Mata JF, Miller GW, Knight-Scott J. *J Magn Reson Imaging.* 2006; **24**: 84-94
3. Bland JM, Altman DG. (1996). *BMJ*, Vol. 313**, 7049:** 106. 4. Bland JM, Altman DG. (1986). *Lancet*, **i**, 307-310.