Experimental investigation of the limits of validity of the physical basis of a method for in vivo lung morphometry with ^{3}He diffusion MRI

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Introduction

An analytical model ("cylinder model") has been proposed [1] that attempts to estimate lung morphometry information from ^{3}He MR diffusion data. In this model, the non-monoexponential decay of the signal is attributed to originate from the superposition of the monoexponential signals of many individual non-connected cylinders. Inherent to this model is the assumption of Gaussian diffusion in each airway. The model has recently be extended with expressions obtained from Monte Carlo computer simulations [2] that attempt to account for non-Gaussian effects, but still relies on a fit of the cylinder model expressions to the signal decay. Despite the detailed theoretical treatments, experimental validation has only yet been done indirectly by comparison to computer simulations [3] or histological measurements [4]. In this work, the limits of validity of the basic underlying physical assumption of the cylinder model (i.e. Gaussian phase approximation) are investigated experimentally in simple geometric models. The accuracy of the relationship between ADC and airway radius for typical diffusion gradient timing parameters and strengths used in ^{3}He lung MR is also assessed in this work.

Methods

Experiments were performed on a 3T Philips system. Diffusion data was obtained from FID acquisition after bi-polar diffusion gradients with timing parameters as used in [1]. The gradient strength *G* was varied in 60 equal steps from -30 to 30 mT/m. Hyperpolarized helium of polarization ~25% was obtained using a Helispin polarizer (GE, USA). Polypropylene tubing of diameters 0.5, 0.76 and 1mm were used to build the phantoms (Fig. 1). Finite element computer simulations [3, 4] of the diffusion experiments in the same geometric models were implemented in Comsol Multiphysics and Matlab, and used compare to analytical theory and experimental data.

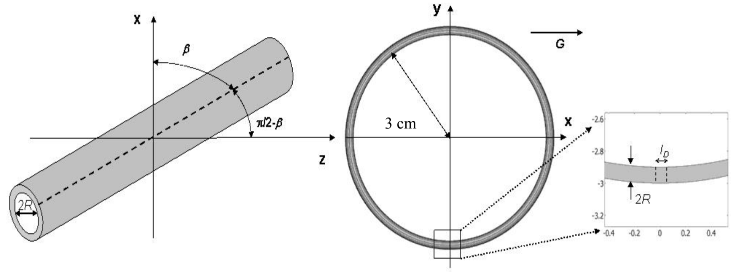

Figure 1. Diagrams of the phantoms consisting of parallel tubes (A), and circular turns (B). The curvature of the tubes in B is negligible over diffusion lengths l_D< 1mm.

Results and Discussion

Experiment 1: Experimental and simulation results (Fig.2) with phantom A and gradient perpendicular to phantom axis demonstrate that for gradient strengths (G >15 mT) typically found in lung ADC experiments, non-monoexponential signal decay can originate from a single cylinder and ADC is not independent of *G* as assumed by the cylinder model. The diameters calculated from the measured ADC are consistently larger than the known nominal diameters of the tubes, in agreement with previously published findings from simulations [3]. Our results identify the breakdown of the Gaussian approximation (in the onset of localized diffusion [6]) as a likely source of this over-estimation.

Diameter	D_T (cm^2/s)		
	β = 58°	β = 78°	Theory (independent of β)
0.51 mm	-0.151	0.042	0.029
0.76 mm	-0.108	0.136	0.113
1.02 mm	0.026	0.282	0.218

Table 1. Results of experiment 2 (D_0 = 0.88 cm^2/s).

Experiment 2: According to the cylinder model, for a cylinder forming an angle α with the diffusion gradient, $ADC(\alpha) = D_L cos^2\alpha + D_T sin^2\alpha$ (1) (1) where D_T and D_L are the transverse and longitudinal ADCs [1]. This equation can be tested by positioning phantom B parallel to the plane *xz* and forming an angle β with the *x* axis (Fig. 1A) and obtaining two ADC values D_X and D_Z from acquisitions with G in *x* and *z* directions respectively. From Eq.1 (assuming $D_L = D_0$), we obtain: $D_T = D_X + D_Z - D_0$ (2). If Eq.1 is valid, this estimate should be independent of β. Results (Table 1 and Fig. 3) show that D_T is not independent of β and in some cases even become negative for large G, which is physically impossible, indicating that Eq.1 becomes invalid as the localized diffusion regime (strong G) is approached.

Nominal diameter	D_T (theory) (cm^2/s)	D_T (cm^2/s)	D_L (cm^2/s)	Estimated diameter
0.760 mm	0.106	0.116	0.969	0.785 mm
1.020 mm	0.226	0.276	0.956	1.125 mm

Table 2. Results of experiment 3 (D_0 = 1.01 cm^2/s).

Experiment 3: Diffusion signals were acquired from phantom B with G parallel to the plane of the circular turns (Fig. 1B). This way, a full loop can be considered equivalent to a collection of elemental long cylinders uniformly distributed with orientations in all possible (2D) angular directions. For this model, the signal dependence upon b-value can be calculated to be: $S(b) = S_0 \exp\left[-\frac{b\{D_T+D_L\}}{2}\right] I_0(b\{D_T - D_L\}/2)$ (3), where I_0 is the modified Bessel function. Eq.3 is the equivalent in 2D of the cylinder model. Fig. 4 shows that the signal from these experiments follows the non-monoexponential behaviour typical of lung diffusion experiments. The estimated D_T values (Table 2) are always larger than theoretical values, while D_L is smaller than D_0. The diameter of the tubes calculated from the estimated D_T is always over-estimated, which again agrees with previously published numerical simulations [3]. The deviation of the signal decay from a monoexponential (Fig. 4), though significant, is less than theoretically predicted by the cylinder model, which may be due to superposition of competing effects of non-Gaussian signal behaviour in different parts of the phantom which experience different intermediate diffusion regimes as they approach localized diffusion.

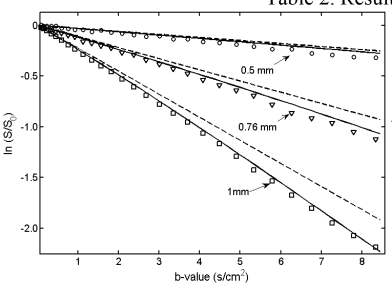

Fig. 2. Comparison of experimental signal decays (phantom A) to theory (Eq.8 in [1], dashed lines) and simulations (solid lines).

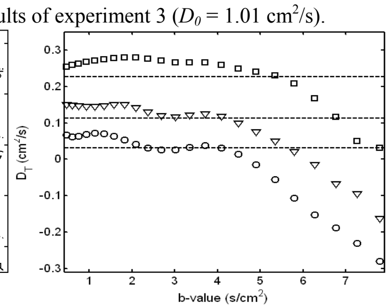

Fig. 3. Experimental D_T values for β = 78° become negative for large *b*. Dashed lines: theory (Eq. 8 in [1]).

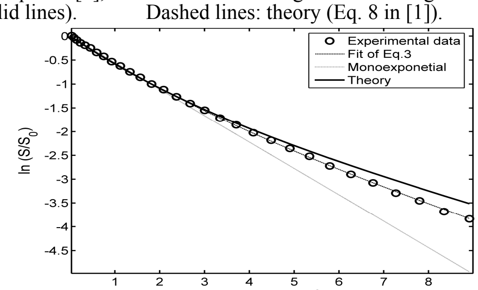

Fig. 4. Comparison of experiments (phantom B) and the cylinder model (Eq.3), assuming $D_L = D_0$ and D_T as calculated using Eq.8 in [1].

Conclusions

Simple experimental tests have highlighted limitations of the cylinder model. Breakdown of the Gaussian phase approximation was experimentally demonstrated for gradient strengths commonly used in lung ADC experiments. The physical assumptions of the cylinder model are only valid if the localized diffusion regime and its neighboring intermediate regimes are avoided. The phantoms and experimental procedures shown here may provide a framework to validate future models.

References
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