Mono- and Bi-exponential Behavior Coexist in ADC Maps of Subcutaneously Implanted Murine Renal Carcinoma

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Introduction

The calculation of apparent diffusion coefficients (ADCs) [1] often assumes a particular model of signal decay, usually either mono-exponential or bi-exponential, but not both. This abstract addresses whether or not both models are actually warranted. In addition, spatial localization of mono- versus bi-exponential behavior is investigated.

It has been observed that several tissue types exhibit two compartments, corresponding to the intra-cellular and extra-cellular spaces. Depending on the rate of exchange between the two compartments, signal decay with increasing gradient strength may exhibit either a mono-exponential or a bi-exponential rate [2,3]. In the case of a fast exchange, the decay is given by

$$S(b) = S_0 e^{-b(f_1 D_1 + f_2 D_2)}, \qquad (1)$$

where f_1, f_2 denote the fractional volumes of the two compartments (f_1=1-f_2), b is a function of the diffusion gradients, and D_1 and D_2 represent the respective diffusion coefficients. In the case of slow exchange, Eq. (1) becomes

$$S(b) = S_0 \left\{ f_1 e^{-bD_1} + f_2 e^{-bD_2} \right\}. \qquad (2)$$

From Eq. (1), it is clear that the behavior of fast exchange is mono-exponential, even though two compartments may exist. As a result only an average diffusion coefficient is calculated in this case. Since a number of different factors, such as transport resistances and different mobilities affect the rate of exchange between the two compartments [2], it is reasonable to expect that both behaviors may co-exist within the same tissue. We have investigated the diffusion behavior of water in murine renal carcinoma with mono- and bi-exponential decay models and found the existence of both in a regionally specific pattern.

Methods

Murine renal carcinoma, implanted subcutaneously in mice, was imaged at six weeks of growth. Diffusion weighted images (DWI) using the *z*-gradient as the diffusion gradient were acquired on a 400 MHz Omega imager (GE/Bruker). Imaging parameters were: TR=2s, TE=40ms, slice thickness = 1mm, and diffusion time =5ms. The image size was 256x128, with a FOV of 24mm. Eleven gradient steps (b = 0 to 4000 s/mm^2), were used.

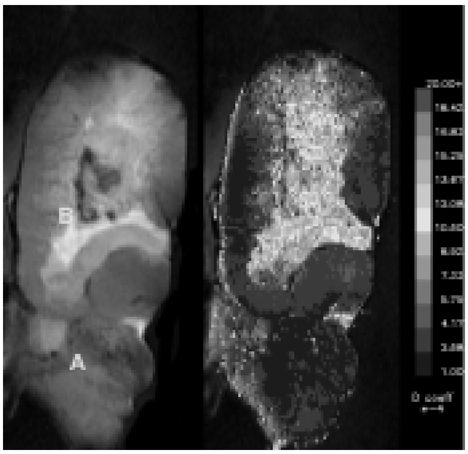

Figure 1. (L) Spin-echo image of a 1mm section of an implanted mouse tumor. (R) ADC map of the corresponding tumor slice (may be color-coded). For regions of bi-exponential decay, only the larger ADC was used.

Analysis

The datasets were analyzed using software developed in our lab and based on the Interactive Data Language (IDL) from Research Systems, Colorado. Each pixel in the tumor was fit to both Eqs. (1) and (2) using nonlinear least squares fitting based on a gradient descent algorithm. The correlation to the fit and its χ^2 values were computed for each model and for each pixel, and the model yielding the higher correlation and lower χ^2 value was kept. The analysis took approximately ten minutes.

Discussion

Both mono- and bi-exponential behavior of signal decay were seen in tumor tissue. This is in contrast to studies of normal human brain, where two compartments were found for all pixels in selected ROIs [4]. The ADC values observed in voxels with mono-exponential behavior ranged from 1e-4 to 5e-4 mm^2/s. In voxels with bi-exponential behavior, the larger ADC ranged from 5.6e-4 to 2e-3 mm^2/s, while the smaller ADC ranged from 1e-4 to 3e-4 mm^2/s. Figure 2 plots the logarithm of the intensity from points A and B of Fig. 1 versus the *b*-values to indicate the mono- and bi-exponential behavior, respectively. Note the exponential decay in Fig. 2 (R) compared to the straight line of Fig. 2 (L).

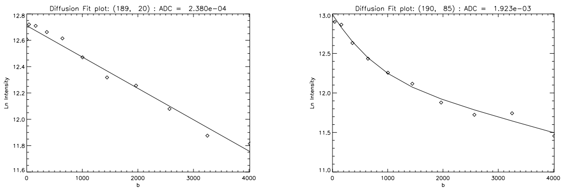

Figure 2. Semi-Log plot of (L) mono-exponential behavior, point A, (R) bi-exponential behavior, point B.

While it may seem reasonable to employ Eq. (2) for both mono- and bi-exponential models, in practice this is not as straightforward. Regression using Eq. (2) rarely yield f_2~0, even for mono-exponential signal decay. Also, D_2 or f_2 may often be negative for noisy data, if no constraints are used.

Spatially, bi-exponential behavior was observed near the center of the tumor, while mono-exponential behavior was seen in the outlying regions. The mono-exponential signal decay in the outlying areas indicated regions of fast exchange. The higher values of the ADCs, which occurred near the center of the tumor, indicated a higher amount of diffusivity. Higher ADCs were also observed in the center of implanted breast tumors in mice, and histology showed that these spatial locations were necrotic [5]. However, their b values ranged from 0 to 800 s/mm^2, so only the larger ADC could be observed. In our case, the higher *b*-values allowed us to observe the slower diffusion component, which resulted in a bi-exponential behavior.

Thus, we have shown that both models of signal decay co-exist. Furthermore, we have observed highly specific spatial distribution of the two different models. This may provide greater tumor characterization than using only the ADC values by themselves.

References

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