INFLUENCE OF GRADIENT DESIGN ON THE MEASUREMENT OF *S/V* USING DWI.

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Introduction

Cell density is an important marker of tumor agressivness than can be evaluated using diffusion weighted imaging. Unlike current apparent diffusion coefficient measurements, the surface to volume ratio (*S/V*) is directly linked to cell density. It can be determined by measuring the time dependent diffusion constant *D(t)*. The *D(t)* is time dependent since random walker "feel"restrictions as time evolves depending on the length scale of present microstructures. This connects *D(t)* to *S/V* under certain assumptions [2]. The determination of *S/V* rquires the measurement of *D(t)* in the short time limit when $D(0)t<<L^2$, where *L* is the typical length scale. It was proposed that this limit could be overcome by using a train of short alternating gradients [1]. The purpose of this work is to investigate if *S/V* can be determined using the oscilating gradients and to which extend the shape of the diffusion weighting gradients can be optimized to measure *S/V* using the *D(t)* approach in the limit $D(0)t<<L^2$ and for large *t*.

Theory

In the limit of $D(0)t<<L^2$, the time dependent diffusion constant is given by Eq.1 to 3, where *f(t)* is the normalized pulse profile (see [2] for details). By shaping the diffusion gradients, the two factors h_1 and h_2 can be modified. Here, h_1 is proportional to the b-value and corresponds to the double integral over the diffusion gradients [1], and h_2/h_1 determines the steepness of the square root term. Large h_1 values are favorable since this allows shorter echo times. Equ.1 is valid up to the second order of the expansion of $E\{\exp(i\phi)\}$ in the phase ϕ, where $E\{\}$ is the expectation value. Higher terms may be estimated by Eq. 4, which yields the condition $D(0)th_1<<L^2$. Here, this is automatically satisfied since h_1 is smaller than 1.

$$D(t) = D_0\left(1-\sqrt{D_0 t}\cdot(4/3/\sqrt{\pi})\cdot(h_2/h_1)\cdot(S/V)\right) \quad (1)$$

$$h_1 = \left\langle (t_2 - t_1)\right\rangle_2,\ h_2 = \left\langle (t_2 - t_1)^{3/2}\right\rangle_2 \quad (2)$$

$$\left\langle h(t_1,t_2)\right\rangle_2 = \int_0^1 dt_1 \int_{t_1}^1 dt_2\, f(t_1) f(t_2) h(t_1,t_2) \quad (3)$$

$$E\{\phi^{2n}/(2n)!\} \cong E\{\phi^2/2\}/n! \quad (4)$$

Methods

The values h_1 and h_2 were calculated numerically for 26 diffusion gradient shapes. Monte-Carlo simulations were performed for parallel slabs with a distance of 20 µm as in [3] with b = 100 s/mm², the signal was calculated for trains of alternating short gadients. Diffusion weighted images of two circular DTI fiber phantoms made of polyamide fibers (15 µm and 230 µm) with susceptibility adapted fluid [3] were measured (TR = 3 s, TE = 225 ms) using a 1.5 T scanner (Magnetom Avanto, Siemens Medical, Erlangen, Germany). with an echo planar imaging sequence. Diffusion weighting was achieved by a train of alternating gradients with gradient durations of Δ=5, 6, 7, 8, 10, 13, 16, 25 ms and a small b-value (b = 100 s/mm²), the gradient direction was perpendicular to the fibers.

Results

Fig. 1 shows h_2/h_1 versus h_1. In the limit $Dt<<L^2$, the optimal gradient shape is the classical Stejskal-Tanner scheme. It shows the largest h_1, which allows the smallest echo time. Moreover, its large value of h_1/h_2 stabilizes the determination of *S/V* (consider the limiting case of $h_1/h_2 \to 0$). In the MR measurements of the diffusion phantoms, $Dt<<L^2$ is violated (Fig. 2). Here, the measured diffusion of the two diffusion phantoms is independent of the gradient duration Δ within the gradient train. In the Monte-Carlo simulations, $Dt<<L^2$ is also violated and *D(t)* is dependent on the number of alternating gradient pairs (Fig. 3).These two findings clarify, that the alternating gradients can not overcome the limit $Dt<<L^2$ and that a train of short pulses is not equivalent to one single gradient pulse of the same length.

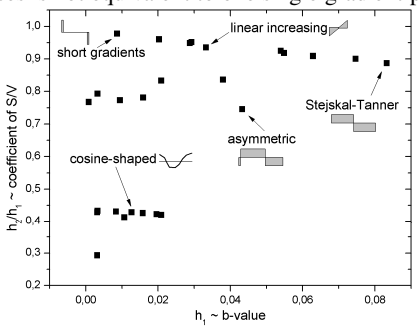

Fig.1: Numerical determined coefficient of *S/V* versus achievable b-value. Not all schemes are explicitly labelled due to limited space. In the limit $Dt<<L^2$, the Stejskal Tanner gradients are optimal since the achievable b-value is high and the coefficient of *S/V* in the *D(t)* curve (Eq. 1) is large enough to guarantee a stable measurement.

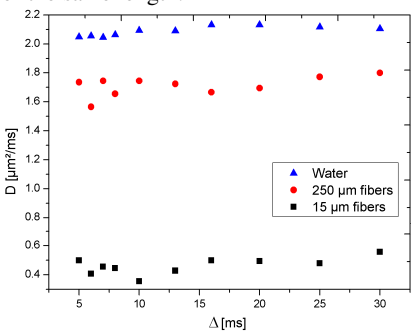

Fig.2: Measured diffusion constants of diffusion fibre phantoms and of water. A train of bipolar gradients was used for diffusion weighting. No dependence on the gradient length Δ is observable. Thus, a train of short pulses is not equivalent to one single gradient pulse of the same length.

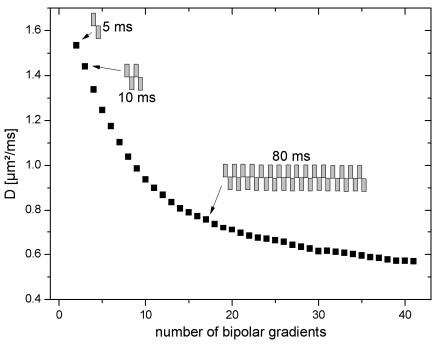

Fig.3: In Monte-Carlo simulations, the measured diffusion constant *D* shows a clear dependence on the number of bipolar gradients, contradicting the assumption that *S/V* can be easily measured in the regime $Dt>L^2$, otherwise, the curve had to be flat.

Discussion

We found no evidence that the condition $Dt<<L^2$ could be overcome by employing short alternating gradients as proposed in [1]. Although this regime is hardly accessible theoretically, our data supports the assumption that *S/V* can neither be determined properly for $Dt>L^2$ by shaping the gradients nor by using the *D(t)* approach. Thus, the Steskal-Tanner weighting should be used for the determination of *S/V* for $Dt<<L^2$. Assuming a typical cell size of 10 µm, D_0=2 µm²/ms and $2Dt$=0.1*L², a minimal diffusion time *t*=25 ms is required. For a b-value of 100 s/mm², this corresponds to a gradient amplitude G=27 mT/m, which can be achieved by clinical scanners and which will be evaluated in future works.

References

[1] Bihan, Raven Press 1995 [2] Grebenkov, Rev Mod Phys 2007 [3] Laun et al, Magn Reson Imaging 2008