Abstract #02192 ISMRM ABSTRACT

[USGOV] Low-field, high-gradient diffusion NMR on in vivo mouse brain

Primary: Physics & Engineering - Low-Field MRI) **Secondary:** Diffusion - Microstructure) **Presentation:** Oral, PowerPitch Oral, Digital Poster) **Keywords:** PRECLINICAL GRADIENTS NEW DEVICES RESTRICTED DIFFUSION SINGLE-SIDE MRI

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Impact

We demonstrate the use of a portable low-field, single-sided magnet with a strong static gradient to measure spin echo signals at unprecedented diffusion weightings in the in vivo rodent brain. Attenuation curves show evidence of motional averaging or localization.

Synopsis

Motivation: There is a need for portable, low-field MR devices for measuring water diffusion and probing brain tissue microstructure in vivo.
Goals: Preclinical low-field high-gradient diffusion method development.
Approach: A chamber and RF coil are developed for *in vivo* mouse measurements. Static gradient spin echo-based diffusion measurements using a single-sided permanent magnet with a 15.3 T/m static gradient are performed on anesthetized mice.
Results: Signal is measured out to $b = 4000\ \mathrm{ms}/\mu\mathrm{m}^2$. Attenuation at high b values is well-fit by a model for motional averaging, estimating an apparent cell radius of of 1.2 $\mu\mathrm{m}$, and providing signatures of restricted water diffusion.

Introduction

Stejskal and Tanner's 1965 works showed the benefits of pulsed gradients (PG), enabling the subsequent development of diffusion MRI [1]. Despite their universal use in dMRI, constraints on the maximum PG strength and slew rate limit the diffusive length and timescales one can probe, and hardware advances are increasingly costly and less portable[2]. Ideally, we desire a high gradient system on a low-field portable low-cost scanner to address these limitations.

Hahn's first spin-echo diffusion measurements in 1950, in which a static gradient (SG) was modulated using rapidly switching RF pulses[3], offers a strategy to overcome these limitations. Various schemes exist to incorporate SGs in the main magnetic field even in low-field MRI[4,5]. Gradients stronger than 10 T/m can be achieved by single-sided permanent magnets[6], posing challenges for conventional MRI, but benefits for high temporal and spatial resolution diffusion measurements, albeit only in one direction[7]. Here, hard RF pulses are used to modulate a $g = 15.3$ T/m gradient produced by an NMR-MOUSE system to measure diffusion in the *in vivo* mouse brain. Signals show restricted diffusion scaling (motional averaging or localization)[8–10], clarifying the patterns which begin to emerge at lower b-values accessible with PGs[11,12].

Methods

NMR measurements were performed at 13.79 MHz using a Kea2 console and PM-10 NMR-MOUSE (Magritek). An isoflurane chamber was built in-house and passed WAG leak testing. Vitals (respiration rate, SpO_2, heart rate) were monitored with pressure, IR, and ECG sensors (SAI). Heated water circulated through the aluminum base of the chamber to control temperature. The animal's oral temperature was measured continuously with a fiber optic probe (Opsens), and was maintained at 36 °C. The recessed base minimized magnet distance and held a multi-turn transmit and receive coil built with copper wire and a capacitive tuning and matching network. The coil was oriented horizontal to the magnet's surface, creating a B_1 orthogonal to B_0 (Fig. 1).

Under an approved IRB protocol, Swiss Webster mice (P6–P10; Taconic) were induced with 3% isoflurane at 300 ml/min (electronic vaporizer, Kent Scientific) within the chamber, positioned supine with the back of the head recessed in the RF coil, then maintained at 0.5–1.5% at 150 ml/min, adjusted according to continuous vital monitoring. The magnet was positioned to maximize signal, which was found between 2.7 and 4.0 mm deep into the head.

Diffusion measurements were performed with TR=2s and PL=3-6 $\mu\mathrm{s}$ using the static gradient spin echo (SGSE) sequence (Fig 2). τ was varied linearly over 22 points between 0.05 and 3.3 ms. The initial attenuation from points $2-4$ ($b = 0.01 - 1.5\ \mathrm{ms}/\mu\mathrm{m}^2$) and final attenuation from points $7-22$ ($b = 10.4 - 400\ \mathrm{ms}/\mu\mathrm{m}^2$) were fit with a free diffusion model $I(b) = I_0 \exp(-bD)$ where $b = 2/3\gamma^2 g^2 \tau^3$ used to estimate D. The final attenuation was also fit with a motional averaging model $I(\tau) = I_0 \exp(-\tau M)$ to estimate an effective radius R from $M = 16/175 R^4 \gamma^2 g^2 / D_0$ of an (assumed) spherical restriction[8].

Results and discussion

On a scale of b, a sample containing pure artificial cerebrospinal fluid (aCSF) at 35°C shows monoexponential signal attenuation with a free diffusion model fit yielding $D_0 = 2.74\ \mathrm{ms}/\mu\mathrm{m}^2$ (Fig. 3a). Differences between in vivo mouse samples are apparent in the larger standard deviation of the attenuation. Within a representative sample, a free diffusion fit of the initial attenuation yields an apparent diffusion coefficient $0.62 \pm 0.07\ \mu\mathrm{m}^2/\mathrm{ms}$. A fit of the final attenuation yields $0.0095 \pm 0.0002\ \mu\mathrm{m}^2/\mathrm{ms}$, but is not valid in the presence of restriction and does not fit the data well. These fits

appear as straight lines in Fig. 3a, whereas the data is clearly multiexponential at all b. Alternatively, the motional averaging model decays exponentially with $(b \times D_0)^{1/3}$ or τ at $b \times D_0 \gg 1$, giving it the appearance of a multiexponential decay in Fig. 3a, though it is from water within a single sized compartment, and a single exponential decay in Fig. 3b. The fit yielded an effective $R = 1.161 \pm 0.004\ \mu\text{m}$, which is similar to the length scales of neural cells in the brain[13]. Adjusting for the full model form [8], the motionally-averaged signal fraction accounts for 30% of the total. This model clearly fits the final attenuation better than the free diffusion model. It should be noted that localization and exchange also cause decay which is exponential with $(b \times D_0)^{1/3}$ or τ at $b \times D_0 \gg 1$.

Conclusion

Low-field, high-gradient NMR is sensitive to localization or motional averaging of water near surfaces in the in vivo rodent brain. This presents new opportunities for low-field hardware design, diffusion encoding, and tissue microstructure contrast.

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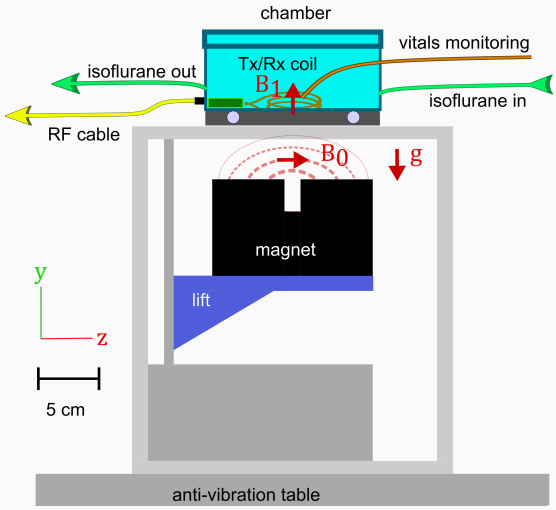

Figure 1: *In vivo low-field, high-gradient NMR setup, showing the isoflurane chamber and the NMR MOUSE magnet. The chamber shows wiring and connections for vitals, RF, and isoflurane, and the RF coil with the direction of B_1. The magnet (drawn in the "service" position) projects a B_0field bending between the poles, with the active region roughly 10 mm above its surface, and a gradient which decays away strongly with distance from the surface. The motorized lift moves the magnet into position.*

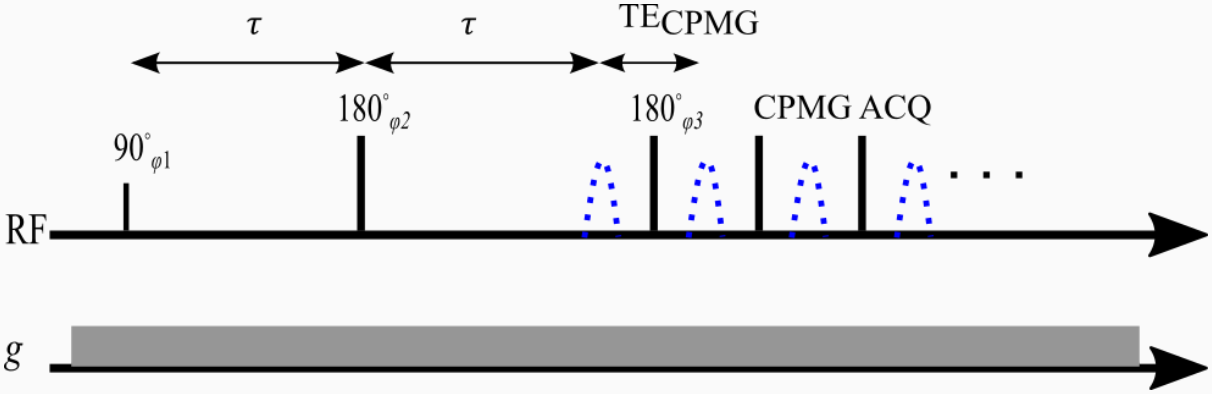

Figure 2: *Static gradient spin echo (SGSE) pulse sequence. Signal was acquired in a CMPG train with 700 or 2000 echoes and 70 $\mathrm{\mu s}$ TE. The real component was summed for a data point.*

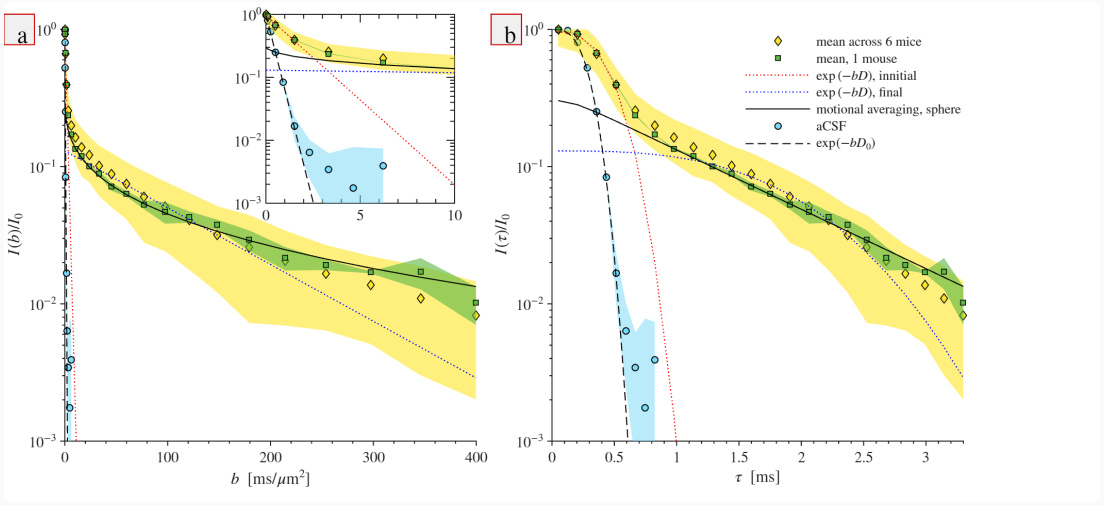

Figure 3: *SGSE diffusion signal attenuation curves showing the mean (symbol) and standard deviation (shaded band) from measurements on mice and pure artificial cerebrospinal fluid at 35°C , and fits (see legend), plotted on scales of$b$ where free diffusion appears linear (a), and $\tau$where restricted diffusion (localization or motional averaging) appears linear at $b\times D_0 \gg 1$(b). In (a), a zoomed-in regions shows b-values typically accessed with PGs.*