Diffusion MRI Based on SPatio-temporal ENcoding: Analytical Description and Validation

Eddy Solomon[1], Noam Shemesh[1], and Lucio Frydman[1]
[1]*Chemical Physics, Weizmann Institute of Science, Rehovot, Israel*

Introduction: Single-scan "ultrafast" MRI methods play an essential role in *in-vivo* diffusion studies. This reflects the need to overcome spontaneous subject motions inside the magnet, during an experiment that measures microscopic levels of water spontaneous displacement. As a single-shot scanning method that benefits from a number of advantages, including robustness vis-à-vis field inhomogeneities [1], ***SP***atio-temporal ***EN***coding (SPEN) could be a good candidate for diffusion-weighted imaging (DWI). Extracting self-diffusion coefficients (*D*) from these measurements, requires deriving expressions of b-values [2,3] for SPEN's particular progression of spatial and temporal encoding. Shrot and Frydman [4] have shown how the use of π/2 chirp or π adiabatic RF pulses in the presence of field gradients, can induce a molecular diffusion weighting on the spins for 2D MRS experiments. It follows from that study how a quantitative analysis of the internal random diffusion effects arising upon combining SPEN with PGSE can be carried out; the physics of that analysis are used in this study, to derive quantitative expressions on single-scan DW-SPEN MRI analyses of isotropic and anisotropic diffusion in model systems.

Theory: In SPEN, spins become subject to time and frequency (i.e., space) dependent manipulations, which make the influence of diffusion effects heterogeneous over the sample. Hence, the signal attenuation throughout the sample following a PGSE module will no longer in general be uniform. The overall local spatial variations of the spins required to derive this spatial attenuation, can be expressed (for a 1D case) in terms of the spatial derivatives $\partial\phi(t,z)/\partial z$ of the spins' dynamic evolution phases. Taking into account that these derivatives will in SPEN be a function of absolute position, we describe the attenuation factor as an extension of Karlicek and Lowe's [3] proposal:

$$A(t,z)=\exp\left[-D\gamma^2\int_0^t K^2_{local}(t',z)dt'\right]=\exp\left[-D\gamma^2\int_0^t\left(\frac{d\phi(t',z)}{dz}\right)^2 dt'\right] \quad (1)$$

which accounts for all gradients and all spatially-dependent RF manipulations. This expression can also be extended to 3D where one could draw the effective b-value acting in a SPEN diffusion MRI scan.

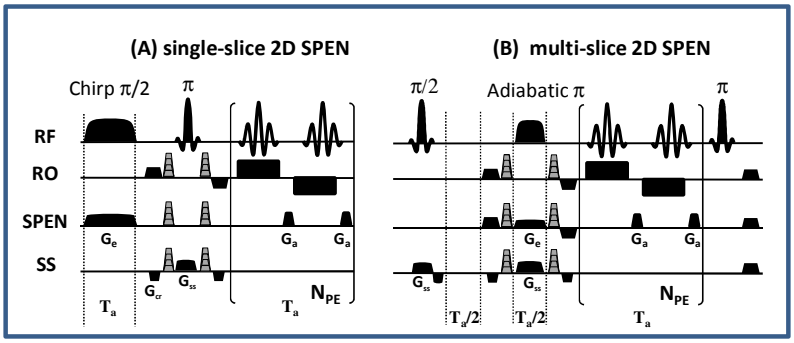

Fig. 1: Novel 2D SPEN of single-slice (A) and multi-slice (B) single-scan diffusion pulse sequences and timing definitions

Methods: Experiments were conducted to verify the theoretical treatment, using the two DW-SPEN 2D single-scan MRI sequences shown in Figure 1. A 7T (300/89) Varian VNMRS vertical-bore system using a single-coil probe with overall volume of 30×30×46 mm^3 was used. Analyzed samples: (a) $CuSO_4$-doped water sample scanned at ~20.5 ^{0}C with 30mm cubic FOV, resolution of 0.4×0.4×2 mm and 4 averages. (b) formalin-fixed swine spinal cord scanned with 20mm cubic FOVs, resolution of 0.28×0.28×1 mm and 20 averages. Diffusion parameters were δ=3ms, Δ=14ms and TR=5sec. The uncorrected b-values used in these experiments (dotted plots in Fig 2) were: 50 200 350 500 650 800 (s/mm^2), Stejskal-Tanner based:

$$b=\gamma^2G^2\delta^2\left(\Delta-\frac{\delta}{3}\right) \quad (2)$$

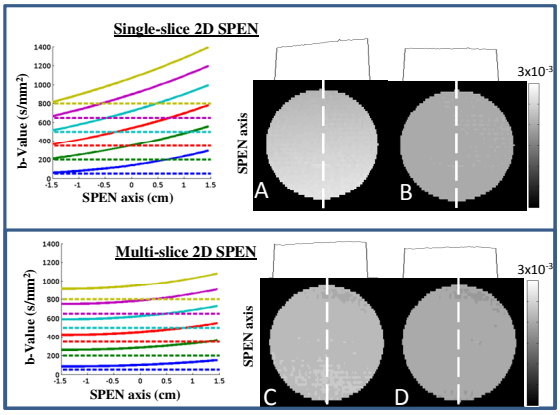

Fig. 2: single-slice 2D SPEN (top panel) and multi-slice 2D SPEN (lower panel) includes PGSE-derived *b*-values plots (dotted) and their ADC maps (A and C) and SPEN-derived corrected *b*-values plots (solid) and their ADC maps (B and D). The Cross-section lines shown on top of the ADC maps are along the SPEN axis diffusion measurement.

Results and Discussion: To validate experimentally our analytical calculations, Eq. (1) was used to derive the effective b-values for two novel DW single-scans 2D SPEN imaging schemes: the single-slice sequence in Fig. 1A, involving encoding by a chirp 90˚ excitation pulse and a slice-selective full refocusing, and the multi-slice sequence in Fig. 1B, involving encoding by a swept 180˚ adiabatic inversion. In both of these cases, bipolar diffusion gradients were placed symmetrically around a refocusing π pulse. The colored solid curves in Fig. 2, illustrate the curvature imparted by the SPEN process in these sequences on the PGSE-derived *b*-values (dashed lines). Unless properly accounted for, these extra weighting prevents accurate ADC mapping from SPEN experiments. Figure 2 further illustrates this with two diffusion experiments of a free water sample, where ADC maps were calculated before and after applying these corrections. The cross-section lines shown on top of Figs. 2A and 2C highlight the problem of ignoring these effects, as they show curved ADC values along the SPEN axis that are for this water sample are clearly artificial, and result from neglecting the additional SPEN-derived diffusion weighting as well as the cross-terms arising between the SPEN and the diffusion gradients. ADC maps obtained after employing the corrected-*b* formalism (Figs.2B and 2D) yield "flat" ADC profiles with no discrepancies *vs* the expected values. To further explore the usefulness of these SPEN-based diffusion schemes in biological tissues, SPEN DWI scans were collected on excised swine spinal cords. Fractional anisotropy (FA) maps were generated such that the orthogonal diffusion measurements where considered as λ_1, λ_2 and λ_3 respectively in the FA calculation. In the SPEN FA maps (Fig.3B-C), a clear contrast can be recognized between the white and the gray matter when compared to the EPI FA map (Fig. 3A). Two additional multi-slice 2D SPEN DWI variants were tested in this study (data not shown) showed similar diffusion results.

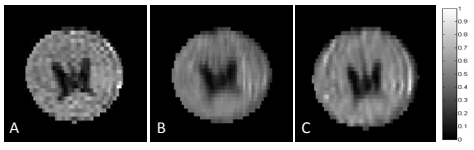

Fig. 3: FA maps of excised swine spinal-cord scanned with 2D EPI (A), single-slice 2D SPEN (B) and multi-slice 2D SPEN (C). FA scale is 0 for isotropic and 1 for fully anisotropic.

Conclusions: The analytical derivations calculated in this work present the formalism that is needed to accurately perform diffusion measurements using SPEN ultrafast MRI. This formalism extends Karlicek & Lowe's work by taking into account the spin interactions under the effect of adiabatic pulses, diffusion gradients and their cross-talk terms arising between them. The result is as a highly reliability ultrafast diffusion measurement MRI tool.

Acknowledgments: We are grateful to Dr. N. Ben-Eliezer, Ms. R. Schmidt and Dr. B. Baishya for insightful discussions. **Financial support:** ERC Advanced Grant #246754, a Helen Kimmel Award for Innovative Investigation, Kamin-Yeda Grant #711237 (Israel), DIP Grant #710907 (Germany).
References: [1] Ben-Eliezer, N., Shrot, Y., and Frydman, L., 2010, Magn Reson Imag, 28:77-86. [2] Mattiello, J., Basser, P. J., & Le Bihan, D., 1997. MRM,37:292-300. [3] Karlicek, R., & Lowe, I., 1980, J Magn Reso.,37:75–91. [4] Shrot, Y., & Frydman, L., 2008. J Chem Phys. 128: 164513.