

Diffusion MRI: Past, Present, and Future

Peter J. Basser, Ph.D.

Section on Tissue Biophysics and Biomimetics, NICHD, National Institutes of Health, Bethesda, MD, USA

The measurement of the translational diffusion of water in tissue via MRI provides unique biological and clinical information about its microstructure, and architectural organization non-invasively and without exogenous contrast agents.

Erwin Hahn first described the effect of molecular diffusion on the NMR signal (1). Carr and Purcell then (2) employed Hahn's NMR spin echo (1) in the presence of a static magnetic field gradient (2) to make the first NMR measurements of the self-diffusivity of water protons. Their work also established the non-perturbing and highly accurate NMR measurement of the self-diffusion coefficient of water and other solvents as a "gold standard". Torrey later incorporated diffusion of spins explicitly into the Bloch equations (3) as another NMR relaxation mechanism (4). Analytical solutions followed for freely diffusing species during a spin echo experiment (5) and later, for restricted geometries (e.g., see (6-8)).

Stejskal and Tanner's pulsed-field gradient NMR (9) method then allowed the diffusion time and the lengthscale probed to be varied independently (7). Their proposed Fourier relationship between the NMR signal attenuation and the conditional displacement distribution became the basis of q-space NMR (10,11). Tanner's definition of the "apparent diffusion coefficient" (ADC) (12) was useful to describe diffusion in complex media, like tissue.

Following a decade of NMR measurements of diffusion properties in muscle and nerve tissue, MRI was invented by Lauterbur in 1973 (13). Although he suggested it, diffusion MRI was not realized until 1984 by Wesbey, Moseley and Ehman (14,15), whose ADC maps were shown to be useful in following a stroke in progress (16). Diffusion MRI, however, failed to describe anisotropic diffusion in brain white matter. Diffusion Tensor MRI (DTI) was invented in the early '90s, providing a more comprehensive and accurate description of diffusion in such heterogeneous, anisotropic tissue (17).

In the past decade, several non-parametric displacement MRI methods have been proposed to characterize features of restricted diffusion observed in nerve axons or anomalous diffusion observed in complex, hierarchically organized tissues. The future appears bright to continue developing displacement MRI methods to measure key microstructural and architectural features of living tissues.

1. Hahn EL. Spin-echoes. *Phys Rev* 1950;80(4):580-594.
2. Carr HY, Purcell EM. Effects of diffusion on free precession in nuclear magnetic resonance experiments. *Phys Rev* 1954;94(3):630-638.
3. Bloch F. Nuclear induction. *Physical Review* 1946;70(7 and 8):460-474.
4. Torrey HC. Bloch equations with diffusion terms. *Physical Review* 1956;104(3):563-565.
5. Douglass DC, McCall DW. Diffusion in paraffin hydrocarbons. *J Phys Chem* 1958;62:1102.
6. Neuman CH. Spin echo of spins diffusing in a bounded medium. *J Chem Phys* 1974;60(11):4508-4511.
7. Stejskal EO. Use of spin echoes in a pulsed magnetic-field gradient to study restricted diffusion and flow. *Journal of Chemical Physics* 1965;43(10):3597-3603.
8. Wayne RC, Cotts RM. Nuclear-Magnetic-Resonance study of self-diffusion in a bounded medium. *Phys Rev* 1966;151(1):264-272.
9. Stejskal EO, Tanner JE. Spin diffusion measurements: spin echoes in the presence of time-dependent field gradient. *Journal of Chemical Physics* 1965;42(1):288-292.
10. Callaghan PT. *Principles of nuclear magnetic resonance microscopy*. Oxford: Oxford University Press; 1991.
11. Cory DG, Garroway AN. Measurement of translational displacement probabilities by NMR: an indicator of compartmentation. *Magn Reson Med* 1990;14(3):435-444.
12. Tanner JE. Transient diffusion in system partitioned by permeable barriers. Application to NMR measurements with a pulsed field gradient. *Journal of Chemical Physics* 1978;69(4):1748-1754.
13. Lauterbur PC. Image formation by induced local interactions: examples employing nuclear magnetic resonance. *Nature* 1973;242:190-191.
14. Wesbey GE, Moseley ME, Ehman RL. Translational molecular self-diffusion in magnetic resonance imaging. II. Measurement of the self-diffusion coefficient. *Invest Radiol* 1984;19(6):491-498.
15. Wesbey GE, Moseley ME, Ehman RL. Translational molecular self-diffusion in magnetic resonance imaging. I. Effects on observed spin-spin relaxation. *Invest Radiol* 1984;19(6):484-490.
16. Moseley ME, Mintorovitch J, Cohen Y, et al. Early detection of ischemic injury: comparison of spectroscopy, diffusion-, T2-, and magnetic susceptibility-weighted MRI in cats. *Acta Neurochir Suppl (Wien)* 1990;51:207-209.
17. Basser PJ, Mattiello J, Le Bihan D. MR diffusion tensor spectroscopy and imaging. *Biophys J* 1994;66(1):259-267.