MRI without the magnet

Daniel Raftery*
Department of Chemistry, Purdue University, West Lafayette, IN 47907

There is no doubt that magnetic resonance imaging (MRI) has had an enormous impact in science and medicine. Dating back to the initial "zeugmatography" work of Paul Lauterbur (1) and echo-planar imaging by Peter Mansfield (2) in the 1970s that resulted in their 2003 Nobel Prize, MRI has undergone dramatic progress over the ensuing years (3). For example, functional MRI is being widely used to diagnose disease and to probe some of the deep secrets in our brains in terms of how we respond to stimuli (4, 5). A number of technical enhancements, such as the use of multiple transmitter and receiver coils (6) or new pulse sequences, have improved sensitivity and selectivity significantly. However, one unfortunate requirement in MRI is the need to employ a large and expensive cryogenic high-field magnet, which is used both to polarize the sample and to help detect the image. Xu *et al.* (7) describe an innovative new approach in this issue of PNAS that eliminates these constraints. The work involves two advances, one previously reported in this journal (8), in which the signal of an MRI image is encoded in one region while the detection takes place in a separate region, and the second involving the use of a sensitive magnetometer in a unique way that performs detection. The basic idea of the experiment based on these two advances is depicted in the Fig. 1.

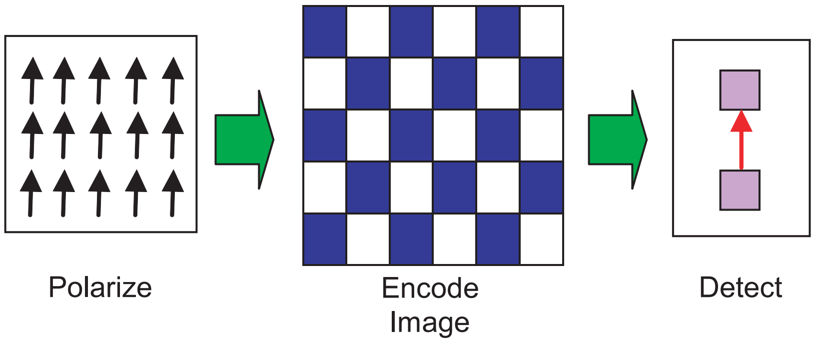

Fig. 1. Schematic diagram of the MRI experiment. MRI is normally performed by using a high magnetic field to create a large nuclear spin polarization, followed by a radio frequency pulse sequence and field gradients to encode the image spatially, and Faraday inductive detection. In the experiment described by Xu *et al.* (5), detection is carried out by using an atomic magnetometer, and only a small magnet is necessary to polarize the sample.

It is useful to put the work in context. Progress in imaging can be made on many fronts, including the three parts of the imaging experiment depicted in Fig. 1. The early work of Lauterbur and Mansfield involved the development of image encoding, and much innovative work in the form of new radio frequency pulse sequences is currently focused in this area. Enhanced images can also be made by creating a highly polarized sample because the signal-to-noise ratio (SNR) of the image is proportional to the initial nuclear polarization. In addition, because polarizations attainable in high magnetic fields are typically <100 ppm, there is plenty of room to make improvements. Beyond the use of larger (and more expensive) magnets, one approach that appears promising is the use of optical pumping (9) that creates an opportunity to improve the SNR of magnetic resonance dramatically (10). Currently, polarizations up to 70% have been reported under static and flowing conditions (11, 12). This approach was adapted quickly by the imaging community (13). Hyperpolarized gas imaging is attractive in that it can be used to image void spaces, including internal biological cavities (lungs, stomach, etc.) as well as being useful to carry polarization to other locations via the bloodstream (14). An alternative method for producing hyperpolarized tracer molecules is to use dynamic nuclear polarization (DNP), which also appears very promising (15). In this case, one can contemplate targeting proteins or tissues by using hyperpolarized ligands.

A third area of research involves advances in detection. Beyond the standard methods of inductive detection inside the MRI magnet, a number of approaches are being developed that may improve imaging systems. One approach involves the use of super conducting quantum interference devices (SQUIDs) (16), which dramatically improve the detection sensitivity at low frequencies. SQUIDs act as magnetometers in that they measure the size of the magnetic field or magnetization present, and they are exquisitely sensitive, with noise levels as low as 1 fT·Hz$^{0.5}$. However, they are somewhat finicky devices and are quite susceptible to stray magnetic fields. Their adoption by scientists in the magnetic resonance community has been slow, even though they have most notably been used for detecting and imaging brainwaves (magnetoencephalography) for some time (17). Wong-Foy *et al.* (18) previously showed how to combine the high polarization of optically pumped gases with remote SQUID detection to detect an image of the polarized gas at very low field. However, this approach has some drawbacks because of the difficulty of operating the SQUID detectors and their required cryogenic cooling.

Optical magnetometers also hold promise for improving the sensitivity of some NMR and MRI experiments. The use of optical magnetometers to detect the small, external magnetization of contained samples was reported almost 40 years ago (19). However, recent advances in optical magnetometry have prompted some new possibilities: The sensitivity has been improved to 0.5 fT·Hz$^{0.5}$ (20), and the magnetic resonance of hyperpolarized xenon and water has been reported using improved methods (21, 22). However, imaging has not been reported to date.

The work by Xu *et al.* (7) combines some very promising features. By separating the image encoding and detection regions of their experiment, a larger region can be imaged without loss of sensitivity. Thus the imaged fluid, water, is transported from the two cylindrical tubes of 2.5-cm length to the magnetometer, which has a much smaller detection volume. In addition, the authors have worked out a very elegant method to improve the sensitivity of their magnetometer. The use of two oppositely oriented magnetometer detectors, arranged in an antiparallel configuration, makes the overall device sensitive to

Conflict of interest statement: No conflicts declared.

See companion article on page 12668.

*E-mail: raftery@purdue.edu.

differential signals. This approach allows a significant cancellation of background magnetic fluctuations because they tend to be relatively homogeneous in nature but varying in time. To detect the signal of interest, water, the fluid is transported to and from the detector in a U-shaped tube in such a way that one part of the magnetometer detects the ingoing magnetic flux (i.e., the south pole) of the incoming fluid, whereas the other half of the magnetometer detects the emanating flux (the north pole) of the outgoing fluid's magnetization. This arrangement gives rise to the desired differential signal, which improves the SNR dramatically over background noise signals. The authors can thus detect the magnetization from 10 μl of water in 0.1 sec without the presence of a large magnetic field. Improvements to the experiment should provide significant enhancements beyond these initial results, according to the authors.

One constraint that still remains is that the sample must be transported into the magnetometer. This constraint may limit the new approach to flow imaging or at least make many types of human imaging challenging because of the difficulty of accessing fluids (such as in brain imaging). However, with further development, a number of possible applications come to mind. It should be possible, for example, to make certain types of MRI portable, because the large magnetic field and cryogenic cooling are no longer required. In addition, because the magnetometer detector is relatively inexpensive and compact, it may be miniaturized and multiplexed. Further development of magnetometer-based imaging may make the expensive parts of MRI optional and lead to a wealth of opportunities.

1. Lauterbur, P. C. (1973) *Nature* **242,** 190–191.
2. Mansfield, P. (1977) *J. Phys. C: Solid State Phys.* **10,** L55–L58.
3. Callaghan, P. T. (1991) *Principles of Nuclear Magnetic Resonance Microscopy* (Oxford Univ. Press, New York).
4. Weiller, C., May, A., Sach, M., Buhmann, C. & Rijntjes, M. (2006) *J. Magn. Reson. Imaging* **23,** 840–850.
5. Peper, M. (2006) *J. Physiol. (Paris)* **99,** 293–307.
6. Sodickson, D. K., Hardy, C. J., Zhu, Y. D., Giaquinto, R. O., Gross, P., Kenwood, G., Niendorf, T., Lejay, H., McKenzie, C. A., Ohliger, M. A., *et al.* (2005) *Acad. Radiol.* **12,** 626–635.
7. Xu, S., Yashchuk, V. V., Donaldson, M. H., Rochester, S. M., Budker, D. & Pines, A. (2006) *Proc. Natl. Acad. Sci. USA* **103,** 12668–12671.
8. Moule, A. J., Spence, M. M., Han, S. I., Seeley, J. A., Pierce, K. L., Saxena, S. & Pines, A. (2003) *Proc. Natl. Acad. Sci. USA* **100,** 9122–9127.
9. Walker, T. G. & Happer, W. (1997) *Rev. Mod. Phys.* **69,** 629–642.
10. Raftery, D., Long, H., Meersmann, T., Grandinetti, P. J., Reven, L. & Pines, A. (1991) *Phys. Rev. Lett.* **66,** 584–587.
11. Ruth, U., Hof, T., Schmidt, J., Fick, D. & Jänsch, H. J. (1999) *Appl. Phys. B* **68,** 93–97.
12. Knagge, K., Prange, J. & Raftery, D. (2004) *Chem. Phys. Lett.* **397,** 11–16.
13. Albert, M. S., Cates, G. D., Driehuys, B., Happer, W., Saam, B., Springer, C. S. & Wishnia, A. (1994) *Nature* **370,** 199–201.
14. Kilian, W., Seifert, F. & Rinneberg, H. (2004) *Magn. Reson. Med.* **51,** 843–847.
15. Golman, K., Ardenkjær-Larsen, J. H., Petersson, J. S., Månsson, S. & Leunbach, I. (2003) *Proc. Natl. Acad. Sci. USA* **100,** 10435–10439.
16. Clarke, J. (1997) *Curr. Opin. Solid State Mater. Sci.* **2,** 3–10.
17. Hämäläinen, M., Hari, R., Ilmoniemi, R. J., Knuutila, J. & Lounasmaa, O. V. (1993) *Rev. Mod. Phys.* **65,** 413–497.
18. Wong-Foy, A., Saxena, S., Moule, A. J., Bitter, H. M., Seeley, J. A., McDermott, R., Clarke, J. & Pines, A. (2002) *J. Magn. Reson.* **157,** 235–241.
19. Cohen-Tannoudji, C., DuPont-Roc, J., Haroche, S. & Laloë, F (1969) *Phys. Rev. Lett.* **22,** 758–760.
20. Kominis, I. K., Kornack, T. W., Allred, J. C. & Romalis, M. V. (2003) *Nature* **422,** 596–599.
21. Yashchuk, V. V., Granwehr, J., Kimball, D. F., Rochester, S. M., Trabesinger, A. H., Urban, J. T., Budker, D. & Pines, A. (2004) *Phys. Rev. Lett.* **93,** art no. 160801.
22. Savukov, I. M. & Romalis, M. V. (2005) *Phys. Rev. Lett.* **94,** art no. 123001.