Paul C. Lauterbur

Reflections on MRI

Magnetic resonance imaging (MRI) began as a problem that gave rise to an insight that was greeted with skepticism and outright disbelief by many colleagues, journal editors, patent experts, and scientists, and even by students doing the work. It was clear to me, however, that none of the doubters and disbelievers had thought deeply enough about the matter and were applying familiar, textbook reasoning about other physics to a new idea. The fact that the common lack of understanding could itself be easily understood and dismissed made persistence in these ideas easy and eliminated the doubts that often plague innovators and keep them awake at night.

The details are as follows: While observing some nuclear magnetic resonance (NMR) experiments on rat tissue specimens from newly sacrificed animals from the Johns Hopkins laboratory of Donald Hollis, I wondered whether this messy procedure, the most invasive imaginable, could be replaced by one that would identify the source of NMR signals in intact living animals (or humans). Although I had been using NMR to study molecules in homogeneous samples for many years and was familiar with the general theory, I knew of no way this could be done. Hours later, while relaxing with a friend over a restaurant dinner and explaining to him that it was not possible, I realized suddenly that in principle it was possible but in a way that was different from all other imaging methods. In a distorted magnetic field, each surface of constant field would give rise to a different NMR frequency. Each different shape or orientation of the field distortion would give rise to a different pattern, and the combination of a number of such patterns might make possible a solution to the problem, an image of the distribution of NMR signals within an object.

My first ideas about how that might be accomplished were unnecessarily complicated. But, I soon thought of an alternative, one that turned out to involve very similar mathematics to those, I later found out, used in CT scanning and in other fields as well, including radioastronomy and electron microscopy. Magnetic fields whose main component can be described, to a good approximation, as represented by a set of flat equidistant parallel planes over a limited region and range, can be generated at any orientation. More succinctly, these are described as having a linear magnetic field gradient in the direction normal to those planes. Reorientation of the gradient in another experiment gives a set of lines of constant field in two dimensions, and therefore of constant frequency for the NMR experiment. A third gradient allows each point to have a unique magnetic field in three dimensions. Simultaneous gradients sum like vectors, so that any desired gradient direction can be generated from three orthogonal components.

To generate an image from data obtained from NMR experiments in the presence of a set of successive gradients, I thought of an iterative method in which each of the integrated signals along a single line for each gradient orientation in a plane would be represented by a line crossing the image space. The sum of all those lines would be reprojected from the image space back to the normal of the initial gradient direction and compared to the measured value for that point. That total would then be adjusted, by an additive or multiplicative factor, to force agreement between the trial image and the measured data. The result would be an image independent of the electromagnetic wavelength ordinarily associated with that frequency. Most of the doubts initially expressed by many were based on the feeling that the results somehow violated the well-known Rayleigh resolution criterion, but the physics are completely different.

Although, for practical reasons, the first experimental realization of the principle was two dimensional, it differs from applications in three or more dimensions only in detail. But, to return for a moment to the two-dimensional example, I asked various colleagues in mathematics and computer science whether

In this issue we are honored to have Prof. Paul C. Lauterbur, Nobel laureate and co-inventor of magnetic resonance imaging (MRI), share his experience and thoughts with us. I am delighted that he has accepted my invitation to contribute this article, which contains a fascinating description of the breakthroughs in ideas, algorithms, and technologies that made the MRI possible.

An important point that Prof. Lauterbur makes is for the scientist (or engineer) to have the knowledge to be able to look beyond what the skeptics say is possible.

I invite you to read about the exciting development of the MRI and to join in thanking Prof. Lauterbur for helping make this life saving medical tool possible.

—Arye Nehorai
"Leadership Reflections" Editor

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such an “iterative back-projection” method was known (this was in 1971–1972, before CT scanning was widely known). All said it was not, some claiming that it was certain to work and others that it would never converge on a useful solution. As the “experts” disagreed, I just tried it myself, with four projections at 45° increments and a digital grid for the trial image. To my delight, these simple hand calculations converged very rapidly to a useful approximation of the synthetic test image. I later found that, if the iteration were continued through too many cycles, it diverged again; so, both groups of consultants were correct.

With the knowledge that a mathematical imaging algorithm was possible, I calculated (using equations from a standard reference) possible signal-to-noise ratios for the NMR signals from an object in a large, fairly low-field magnet. I found that they could be adequate, despite some doubts from experienced workers in the field. I also found in the literature, designs for large, practical resistive magnets with rather uniform fields, so that there seemed to be no obvious major impediments to working toward a human imaging capability.

To evaluate the potential usefulness of such a procedure, I began to read the medical literature, including atlases of cross-sectional anatomy. I decided that a good medical imaging technique would also pass the “so, what?” test. Therefore, I gradually phased out my other research projects and concentrated on imaging, writing papers and giving lectures on the subject.

At the same time, patent issues naturally arose. A friend who was a patent attorney started to prepare an application but then dropped it for personal reasons. An invention disclosure to the State University of New York resulted in its agent for such matters deciding that it did not make economic sense to apply for a patent, so I decided to promote the imaging idea vigorously and hope that others would take up the challenge. One of these early talks, at the meeting of the International Society of Magnetic Resonance (ISMAR) in Bombay (now Mumbai) in 1974, was to have important consequences. In the audience were two physicists working in Nottingham, England, a faculty member named Bill Moore and an American postdoctoral fellow named Waldo Hinshaw. As they chatted about the meeting on the flight back to London, they concluded that there must be a better way of making NMR images than I had described. Upon their return to Nottingham, they developed the “sensitive point method,” using alternating gradient polarities with the “steady-state free precession” NMR technique, producing scanned, exquisitely detailed slice images without any need for a computer or mathematical algorithms. Its drawbacks were slow scanning speed, poor contrast, and sensitivity to motion (so much so that one radiologist described it as a “great technique for noninvasive autopsy”). A postdoctoral fellow and I were working on a similar method, but he saw Hinshaw’s paper first and put a copy on my desk with a single comment “Grrr!!!”

At the same time, we stumbled into another lively controversy about “selective irradiation,” intended also to yield single slice images. We were developing it not only for ordinary anatomical imaging, but also for so-called “chemical shift imaging” in which each point would be associated with a chemical composition, as revealed by its NMR spectrum. This was achieved by producing an impulse signal limited to a single plane and subjecting it to a Fourier transform to generate the spectrum then back-projecting each spectral intensity separately to give the desired image. Peter Mansfield was also pursuing selective excitation slice selection imaging at this time, but David Hoult insisted to both of us that it was physically impossible. It took a while, but eventually we realized that we were all, in a sense, correct. In the linear limit, the signal response would overlap the excitation; but with large enough NMR flip angles, a response would persist until it could be observed, as a student in my lab, David Kramer, found by explicit simulation. This was perhaps the last of the fundamental controversies over MRI physics.

The practical aspects of the technique, however, were completely changed by an unexpected development. Everyone in the field had initially used resistive magnets and relatively low magnetic fields, but it was found by magnet manufacturers that whole-body size superconducting magnets were practical, if expensive. The increase in imaging speed and clarity at higher fields and the magnet stability catalyzed medical and industrial acceptance. My group continued to work in the field for many years, but the contributions of others steadily increased, so that our efforts, although often novel and scientifically interesting, decreased in relative clinical importance.

Applications continued to grow, however, becoming important enough to the practice of medicine to attract the attention of the Swedish Academy, who honored all those who made the development possible with the award of a Nobel Prize in 2003.

Of course, none of these things would have happened as they did if my education had not prepared me to see the possibilities and relationships and to build on that base the necessary ideas to carry the project along though a wide variety of interdisciplinary stages. Those required enough knowledge of physics, chemistry, engineering, mathematics, biology, and medicine to recognize the nature of the problems and decipher where the solutions might be sought. That knowledge also supported the informed optimism that is often required when things go wrong, as they so easily can in an innovative project, and could have in this one.

AUTHOR

Paul C. Lauterbur was born in Sidney, Ohio, grew up in that small town and on a nearby farm, obtained a B.S. in chemistry at Case Institute of Technology in 1951, and then went to work at the Mellon Institute. While there, he did graduate work part time at the University of Pittsburgh, both interrupted by military service, and moved to the State University of New York at Stony Brook after he received a Ph.D. in chemistry in 1962. In 1985, he moved to the University of Illinois at Urbana-Champaign. SP