Inhaling Hyperpolarized Noble Gas Helps Magnetic Resonance Imaging of Lungs

Since the late 1970s, Princeton physicist William Happer had been investigating spin-exchange optical pumping as a means of polarizing nuclei. Along the way, he had given thought to practical things one might do with large collections of nuclei thus polarized, among them the enhancement of fusion in tokamaks, the creation of new kinds of polarized targets for high-energy physics and the improvement of clinical magnetic resonance imaging. "But I was always too busy to think seriously about imaging," Happer told us. "Then, when I came to Washington in 1991 [to become, for a time, director of energy research at DOE] I ruptured a disk and they did an mri scan of my spine. I was in great pain, and that concentrates the mind wonderfully."

Thus began the effort by Happer, Gordon Cates and collaborators to do clinical magnetic resonance imaging with noble gases whose nuclei have been polarized by laser optical pumping. And now we have the first results: In a recent issue of *Magnetic Resonance in Medicine*,[1] a collaboration led by Happer and Allan Johnson of the Duke University Medical Center presented a sequence of mri images of guinea pig lungs filled with polarized helium-3. Last fall Happer's Princeton group, working with biophysical chemist Arnold Wishnia and colleagues at the State University of New York, Stony Brook, published mri images[2] of the excised heart and lungs of a mouse, made with nuclear-polarized xenon-129.

All this comes almost precisely half a century after the first observation of nuclear magnetic resonance, the physical phenomenon underlying mri. (See the letter by Edward Apgar in last month's PHYSICS TODAY, page 88.)

Lungs are very hard to image. Magnetic resonance imaging of inhaled noble gases optically pumped to high levels of nuclear polarization may offer the solution clinicians are looking for.

Lungs are a challenge

Imaging lungs has always presented a particular challenge for clinicians and biologists. X-ray pictures of the lungs can show fluid accumulation, neoplasms and calcified scars; but short exposures hardly show the very porous lung tissue, let alone inhaled gas. Lung function is sometimes imaged by having patients inhale radioactive xenon-133, a gamma emitter. But that diagnostic procedure exposes the patient to radiation doses one would rather avoid.

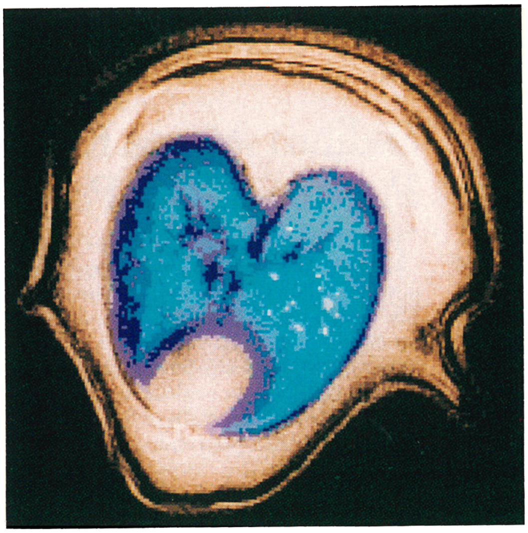
Conventional mri looks only at free protons, that is to say, ^{1}H nuclei. Because there's so much hydrogen (most of it in water) in the human body, the very small "thermal" polarization of proton spins in the 15-kilogauss magnetostatic field of a typical mri scanner is sufficient for most clinical imaging. At body temperature the tiny energy difference between the up and down nuclear spin states in such an external field yields a net polarization of only a few protons in 10^6. But that's adequate for imaging ^{1}H, with its high concentration in the body and, incidentally, the highest magnetic moment of any spin-½ nuclear species.

High-resolution magnetic resonance imaging with any other spin-½ nucleus, resident or inhaled, in the human body would require much higher polarization levels. An inhaled gas would have to be "hyperpolarized" to levels on the order of 10%. The mri signal, which comes from the precession of nuclear spins tipped by an rf pulse, is proportional to the concentration of the nuclear species times its polarization.

Optical pumping

That's where the Princeton group's long history of optical-pumping experiments comes in. Suppose you shine circularly polarized laser light on a vapor of alkali atoms at the wavelength that's just right for exciting the lone valence electron from its S-wave ground state to the first excited P-wave state. Conservation of the polarized photon's angular momentum imposes the selection rule $\Delta m = 1$ on this excitation, where m is the magnetic quantum number. But the subsequent relaxation back down to the S-wave ground state is subject to no such restriction. The net result, therefore, is that the incident circularly polarized light steadily pumps ground-state valence electrons from the $m = -½$ orientation to $m = +½$. This pumping process is admirably efficient. Promoting one alkali atom to the desired m substate costs, on average, only two laser photons.

But so far we've only discussed the polarization of atomic *electrons*. What the Princeton group was ultimately interested in, and what's needed for mri, is polarized *nuclei*. In 1960, Thomas Carver and coworkers at Princeton demonstrated that optically pumped rubidium vapor in an atmosphere of ^{3}He can



MAGNETIC RESONANCE IMAGE of a live guinea pig in thoracic cross section. The lungs (shown in blue) were imaged with inhaled ^{3}He with a nuclear polarization of 20%. The surrounding anatomy was imaged by conventional hydrogen mri. The animal's back is at the top. Taken recently at Duke University, this is the first mri image of living lungs ever made with hyperpolarized gas.

transfer its electron polarization to the helium nuclei by hyperfine interaction in collisions.

Noble gases

What's so special about ^{3}He and ^{129}Xe? They turn out to be the only noble gas isotopes with spin-½ nuclei. One could polarize the nuclei of the hydrogen isotopes and other gases by this kind of optical pumping and collisional spin exchange. But only in the noble gases, with their perfectly symmetrical, closed electron shells, does the nuclear polarization last for hours and even days. In ordinary reactive atoms, molecular configurations formed in collisions couple to the nuclear spins and promptly depolarize them. Furthermore, the chemical inertness of the noble gases makes them harmless inhalants (except for radioisotopes like ^{133}Xe) for clinical applications. The spin-½ nuclei are essential for mri. Spinless nuclei like ^{4}He obviously don't experience magnetic resonance, and spins higher than ½ involve electric quadrupole moments that promote depolarization.

The subject lay largely dormant until 1978, when Bruce Grover at Litton Industries, trying to devise a nuclear-magnetic-resonance gyroscope, succeeded in polarizing ^{129}Xe and krypton-83 nuclei with optically pumped rubidium. "Grover's work rekindled my interest in this field," Happer told us. Undertaking a systematic study of the spin-exchange mechanisms from alkali vapors to noble gas nuclei, Happer and colleagues Nat Bhaskar and Thomas McClelland were able to achieve 5% nuclear polarization of ^{129}Xe with a tunable laser in 1982. In all the earlier work, the optical pumping had been done with lamps.

Before turning its attention to mri applications, the Princeton group in 1988 began to work on creating polarized ^{3}He targets for nuclear and particle physics. That work, led by Cates, culminated a few years later in the building of a foot-long, 9-atmosphere ^{3}He target with a nuclear polarization of about 35% at the business end of the two-mile-long Stanford linear accelerator. High-energy experiments carried out with this target have contributed crucial information about the role of quarks in the spin structure of the neutron.[3]

"Achieving that level of polarization required, at the time, an expensive, powerful laser system that our little atomic physics group could never have afforded," recalls Happer. "The relatively generous funding for high-energy physics came to the rescue." But in just the last year or two the availability of small, efficient diode-laser arrays has made it possible to do optical pumping for mri at modest expense.

A breathing guinea pig

The thoracic cross section of a guinea pig shown on page 17 is, Johnson told us, the first hyperpolarized magnetic resonance image ever made with a living, breathing animal. (The guinea pig imaged several months earlier for reference 1 had just been "euthanized.") It was made at Duke, by Robert Black, Hunter Middleton and coworkers, with inhaled ^{3}He polarized to about 20%. The picture is actually a composite of the ^{3}He lung scan (shown in shades of blue) and a conventional ^{1}H mri scan of the rest of the body. The ^{3}He scan took less than 20 seconds. (The scans are synchronized with the animal's breathing.) Obtaining comparable signal-to-noise for lung tissue with conventional mri takes much longer, and then one still doesn't see the inhaled gas. "This is the only lung-imaging technique I know of," says Johnson, "that promises both high resolution *and* capability for functional studies."

The 20% ^{3}He nuclear polarization was obtained by several hours of optical pumping with circularly polarized laser light tuned to 795 nm, the appropriate excitation wavelength for rubidium, the alkali vapor mixed in with the helium at about a part per million. The nuclear polarization thus achieved lasts for several hours. Collisions with the wall of the containing vessel contribute significantly to depolarization. "Much of our effort has gone into learning how to make the walls benign," Happer told us. "With carefully prepared walls we can get relaxation times of days, which lets us pump the helium beyond 50% nuclear polarization."

In ^{129}Xe, the noble gas used in last year's mri experiments at Stony Brook, one can maintain the nuclear polarization for days without having to worry about collisions, simply by freezing the gas. Xenon has the potentially attractive property of lipophilia: Unlike helium or water, it is readily absorbed by fatty tissue. The hydrophobia of lipids presents imaging problems for conventional mri. Another promising attribute of ^{129}Xe for mri is its very large "chemical shifts." In the magnetostatic field of an mri scanner, the resonant precession frequency of a hydrogen nucleus has a very slight dependence on its immediate molecular environment. Such chemical shifts can be exploited to identify biochemical details in magnetic resonance imaging. The chemical shifts of the ^{129}Xe nucleus turn out to be orders of magnitude higher than those of hydrogen.

No listing of the virtues of xenon for mri would be complete without mentioning that inhaling xenon, which has well-known anesthetic properties, produces a subjectively pleasant effect. "There's been no shortage of volunteers for the human trials planned for Duke," Happer told us. "We're still quite far from knowing whether any of this will prove to be clinically useful," he notes. "But in the current political climate it's important to point out that it all began as curiosity-driven physics research. If we had set out simply to find a better way to image lungs, we wouldn't have gotten this far."

Bertram Schwarzschild

References

1. H. Middleton, R. Black, B. Saam, G. Cates, G. Cofer, R. Guenther, W. Happer, L. Hedlund, G. A. Johnson, K. Juvan, J. Swartz, Magn. Reson. Med. **33**, 271 (1995).
2. M. Albert, G. Cates, B. Driehuys, W. Happer, B. Saam, C. Springer, A. Wishnia, Nature **370**, 199 (1994).
3. P. Anthony *et al.*, Phys. Rev. Lett. **71**, 959 (1993).

Sodium Atoms Kicked by Standing Waves Provide a New Probe of Quantum Chaos

Several features of quantum chaos have been demonstrated in a system of sodium atoms interacting with a modulated standing wave of light. The system can be tuned continuously from a regime that can be described classically to one where a quantum description is necessary.

The question of how to quantize a system whose classical dynamics is chaotic has long been a puzzle. The hallmark of classical chaos is sensitive dependence on initial conditions: A small perturbation of the system changes its evolution in a way that grows exponentially with time. But in quantum mechanics a small perturbation of the initial state will in general be mapped into a small perturbation of the final state. In re-