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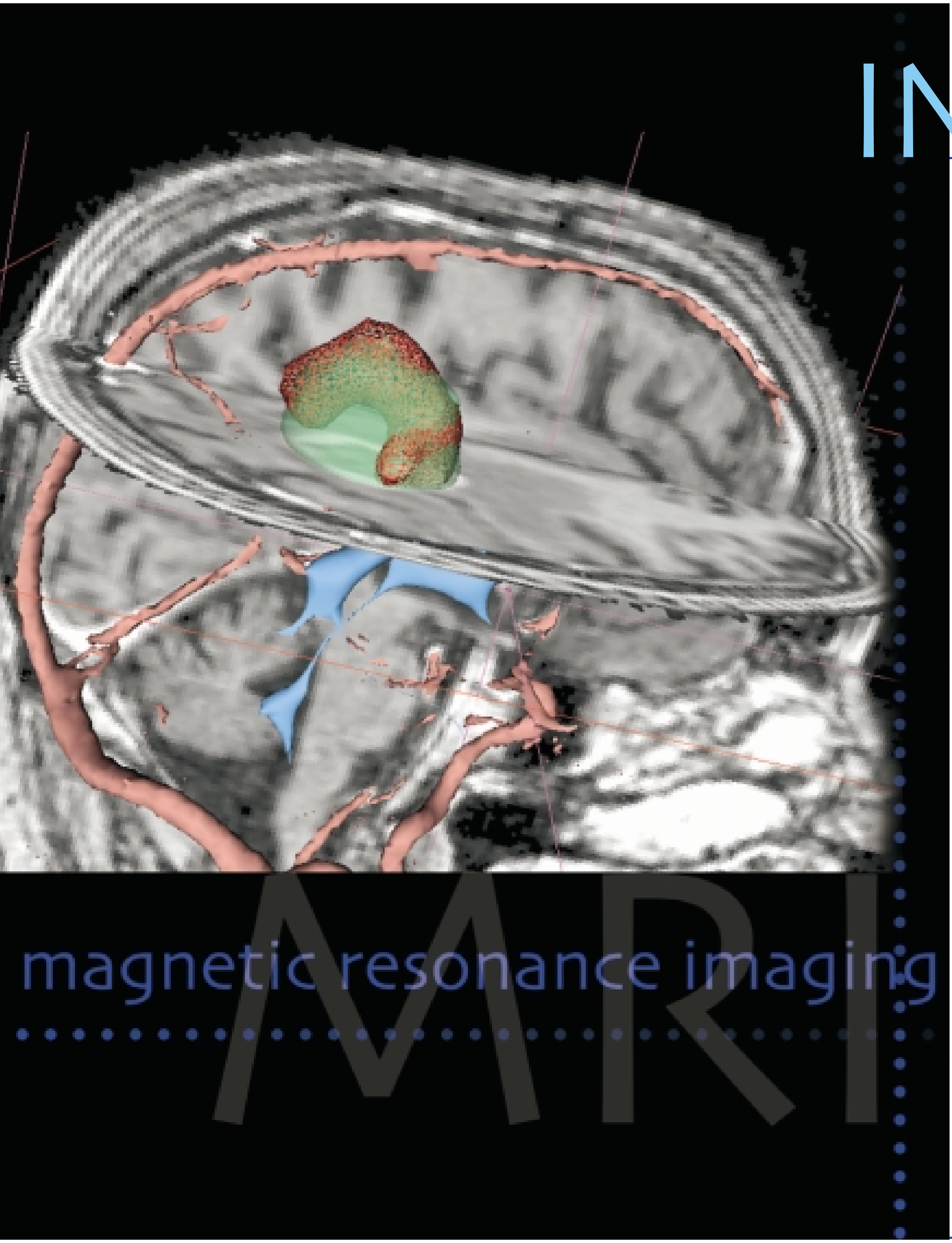

MRI

magnetic resonance imaging

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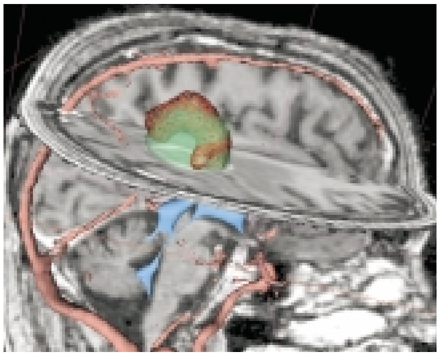

COVER IMAGE: An 3-D reconstructed MRI image of the human head highlighting the location of a brain tumor (green) and associated vasculature (red). The brain ventricles are highlighted in blue. The three-dimensional localization of the tumor is visualized in relation to sections of the brain in two different planes. This figure provided courtesy of Dr. Ferenc Jolesz, Brigham & Women's Hospital, MA.

Magnetic Resonance Imaging:

From Atomic Physics to Visualization, Understanding and Treatment of Brain Disorders

She was watching TV when she was struck by a sudden, terrible headache, a fit of nausea, and powerful feelings of deja vu. Two days later, doctors at Boston's Brigham and Women's Hospital scanned this young college student's brain, using a technology called magnetic resonance imaging (MRI). The MRI revealed a tumor the size of a child's fist embedded in her temporal lobe that was beginning to cause seizures, and her eerie sense of deja vu was a sign of that. Left untreated, it likely would also have interfered with her speech and movement because circuitry controlling those functions is within the frontal lobe.

Before neurosurgeons began using MRI, standard procedures for treating such tumors were considered very risky for patients, and outcomes often proved as bad as the disease. Although slicing through brain tissue can kill neurons, which do not regenerate, redundancy in critical areas of this circuitry may spare speech if cutting is kept to a minimum. MRI now helps neurosurgeons meet a critical challenge, namely, doing the least possible damage during a vital procedure.

MRI does so by providing the clearest pictures of brain anatomy of any available imaging technology. By other means, the type of tumor growing within the young woman's temporal lobe is indistinguishable from healthy brain tissue. But MRI reveals such tumors with precision, and also shows blood vessels as well as other key landmarks within the brain, enabling neurosurgeons to navigate carefully through its delicate landscape. The surgeons, led by Dr. Peter Black, thus avoided inadvertent, potentially life-threatening damage as they cut through to the tumor and removed it.

Recent improvements in MRI provide additional means for neurosurgeons such as Dr. Black to avoid other potentially catastrophic mishaps. For instance, "functional" MRI enables them to picture critical centers of the brain as an individual responds to questions or other stimuli. Thus, when the young woman responded to a recited list of words such as "heat", "light", "fast", and "sky", her brain's language center "glowed" brightly in the functional MRI pictures, whereas her motor cortex was most active when she wiggled her fingers or toes. Those responses helped Dr. Ferenc Jolesz map those and other critical functions and advise Dr. Black on how not to damage the vital circuitry through which they act.

Meanwhile, the surgeons took advantage of yet another recent MRI wonder, a system developed jointly by researchers at Brigham and Women's Hospital and General Electric Medical Systems, called image-guided surgery. It permits them to work inside the magnetic coils of the MRI instrument, which furnishes updated 3-D images of a patient's brain every few minutes, and thus to track their progress in detail on a monitor that hangs above the surgical field (Fig.1). The successful surgery enabled the young woman to return to normal life where she ultimately resumed her class work, says Dr. Jolesz.

Figure 1. Using image-guided surgery, the surgeon is operating on the patient, who lies within the coils of the MRI. The screen, showing the patient's brain, is visible above the surgeon. This figure provided courtesy of Dr. Ferenc Jolesz, Brigham & Women's Hospital, MA.

MRI began to come into general use in the mid-1980s. But most of the tools Jolesz used to extract the temporal lobe tumor were unavailable before the mid-1990s. Until then, MRI had been very slow, like taking photographs in the days of the Civil War. A patient had to lie stock-still for 10–30 minutes for each picture. The slow image acquisition made it difficult to use MRI in much of the body, where the rhythms of life never cease. The beating of the heart, the pulsation of the lungs, and the peristalsis of the gastrointestinal tract inevitably blurred these slowly acquired images, making it impractical to use MRI throughout much of the body. But the MRI equivalent of shutter speed has risen exponentially, and image acquisition can take as little as one twentieth of a second.

The core of a magnetic resonance imaging machine is a magnet so powerful that it could drive a pen-sized piece of metal with the force of a bullet. Generally, it consists of a tubular structure large enough for the patient to lie inside while images are being made, although, specialized smaller magnets sometimes are used to image a patient's extremities, such as wrists, knees, or fingers. People approaching these powerful electromagnets must divest themselves of materials that are sensitive to magnets, such as any metal, and credit cards. Similarly, patients with metal plates, pacemakers, or other prostheses are not eligible for MRI tests. The electricity circulating in the coils of an MRI machine is roughly one-twelfth that produced by a typical commercial nuclear power plant.

One big advantage to MRI is that it is a non-invasive medical procedure. Nothing is inserted in a patient's body, no dyes are swallowed, and no contrast agents are injected, except under special circumstances. Moreover, patients are not exposed to ionizing radiation, as is the case with X-ray Computed Tomography (CT) imaging.

For medical purposes, the magnetic resonance imager usually is tuned to "see" hydrogen, which is the most abundant element within the body. The magnet first aligns hydrogen atoms that come within its field, and then a radio-frequency pulse is applied to jostle them momentarily. As they realign, special receivers pick up their signals and transmit that information into computers in which special programs convert those signals into vivid images. The various tissues and fluids are distinguishable from one-another largely because the concentration of hydrogen varies within different tissues and bodily fluids.

The images from MRI are cross sections of the brain or body, thin slices of tissue, like slices of bread from a loaf. Computer programs can be used to assemble these image slices into three-dimensional datasets. The computer power needed for this fast analysis, which was unavailable a few years ago, now fits on a desktop. Most of the time, however, doctors analyze those images slice by slice.

The non-invasive nature of MRI has opened new areas of research. Investigators learn much of what they know about human maladies

How MRI works

Medical imaging was far from the minds of Dr. Felix Bloch and Dr. Edward Purcell in 1946, when each independently discovered how to measure magnetic resonance, the breakthrough that led several decades later to MRI. Scientists already knew that the nucleus of an atom can absorb energy (i.e., resonate) from radio waves when placed in a magnetic field and that different atoms absorb different amounts of such energy. But until the two of them independently determined how to do so, no one could measure the phenomenon. For their analytic efforts, they shared the 1952 Nobel Prize in physics. "There was no idea that hidden inside this phenomenon was the possibility of making pictures," says Dr. Paul Lauterbur, a chemist at the University of Illinois, Champaign-Urbana, who has contributed significantly to this field of research.

Unfortunately for physicists, atoms usually are contained in molecules, which skew the signals and play havoc with the measurements that typically interest physicists. However, chemists seized upon the technique as a way of analyzing the structure of molecules, says Dr. Lauterbur. Nuclear magnetic resonance (NMR), as the technique was then called, by studying animal models. These may be animals that are bred to express particular genetic diseases like those in humans or animals in which specific diseases, such as cancer, HIV infection or other conditions are induced. Studies using MRI in these animal models may lead to similar applications in clinical investigations. For example, when the MRI technique called diffusion-weighted imaging was being developed for use in humans with strokes, researchers used the technique to perform imaging studies in animal models of stroke and then dissected the animals’ brains. The dissections showed the researchers how to interpret the diffusion-weighted images so that they would understand what they were seeing when they performed diffusion-weighted MRI in human stroke victims.

However, even without good animal models for many psychiatric maladies, including depression, dementia and schizophrenia, MRI provides a powerful means for visualizing how the brains of individuals with such disorders differ from those of others—without medical researchers resorting to surgery or other invasive procedures. For example, researchers from the Massachusetts General Hospital reported early in 2000, that certain regions of the brain are smaller than normal in individuals during the early stages of Alzheimer’s Disease. Indeed, these differences can be detected three years before other symptoms appear. Other researchers at Duke University are using magnetic resonance spectroscopy, which is closely related to MRI, to view direct brain responses to drugs among individuals being treated for this same disease. As with much of the basic and clinical research involving MRI, the National Institutes of Health (NIH) supports this work directly as well as through focused training and education programs.

Ever more powerful magnets and steady improvements in computers are raising the speed and increasing the precision of MRI imaging. Seven million MRI scans were performed on patients in 1998, up from virtually none before the mid-1980s. MRI is making brain surgery far more successful than it ever was, and once-impossible operations are now considered routine and can be finished faster with less harm to patients.

MRI arose following an obscure discovery in 1921 by physicists Otto Stern and Walther Gerlach, who found that magnetic fields can perturb the energy state of the nucleus within an atom. In 1946, physicists Felix Bloch and Edward Purcell figured out how to measure the energy required to drive those changes from one energy state to another.

“Through very esoteric research, with no apparent applications, physicists discovered the magnetic resonance phenomena, and chemists used it to learn about the structure and conformation of molecules,” says Representative Vern Ehlers from Michigan, who deals with science-related issues in Congress. “Doing similarly esoteric research on elementary particles, physicists developed very rapid computerized data gathering and analysis techniques. Combining these two,

can distinguish among different types of chemicals because the nuclei of each chemical element resonates to a particular frequency of radio wave and then emits signals at a characteristic frequency. Furthermore, and this is what bothered physicists, but pleased chemists, the electrons surrounding each nucleus slightly distort the resonant frequency. The technique soon proved powerful for determining structures of organic chemicals, the carbon-containing molecules found throughout living systems, as well as of many commercially useful chemicals, including drugs, plastics, and fibers. NMR is almost universally used in chemistry laboratories, and it is required for advanced chemical studies.

To analyze a compound, researchers would place it in a tube, which then was put inside a magnet. The nuclei in the compound line up with the magnetic field in the same way that the needle of a compass points north in the earth’s magnetic field. Once in the magnet, the compound is zapped with a range of radio-frequency pulses, some of which cause the various nuclei in the chemical compound to resonate. The resonating nuclei then release energy, each at characteristic frequencies, which are displayed as peaks and valleys that vary with frequency. Chemists use such information to determine molecular structures.

MRI was developed, providing arguably the best medical diagnostic tool ever made, as well as an excellent biomedical research instrument. The point is simple but important: seemingly impractical research yields huge dividends and deserves substantial and stable funding." While applied research typically extends existing knowledge, basic research lays foundations from which truly novel technologies may arise.

Medical Applications

Multiple Sclerosis

MRI is providing scientists with a clear view of the circuitry of the brain, and it is showing them how the brain works, as well as how disease causes it to malfunction. For example, multiple sclerosis (MS) is a chronic, progressive disease that afflicts roughly a quarter-million Americans. Typical symptoms include loss of balance, paralysis, numbness, visual disturbances, incontinence, and even dementia. These symptoms, resulting when components of the immune system misguidedly attack specialized sheaths that insulate connections between nerve cells, vary greatly, making diagnosis difficult. But MRI can overcome such diagnostic uncertainties because it readily shows those damaged sheaths as small, whitish spots.

MRI also can help doctors determine whether or when a patient with early-stage MS needs treatment. Even when a patient appears clinically stable, the disease can be stealthily ravaging the brain, and such early-stage MS patients usually should be treated, whereas those whose MRIs show few active lesions may safely delay treatment.

Researchers are developing other, potentially more accurate ways to monitor MS with MRI. Dr. Richard Rudick and Dr. Elizabeth Fisher of the Cleveland Clinic Foundation use MRI to measure brain volumes with precision. Among healthy men and women 20-50 years old, 87 percent of the brain volume is tissue and the remaining 13 percent is water, with less than one percent variability. However, among individuals with MS, the tissue fraction declines by about 0.7 percent annually. Measuring these declining tissue volumes may enable physicians to determine how long individual patients have had MS and to more accurately predict the course of the disease. "It looks as if the atrophy severity and the change in atrophy score predict the patient's status 6-8 years down the line," says Dr. Rudick. This use of MRI also might help determine whether a patient's treatment is working, as well as the effectiveness of new drugs being tested in clinical trials.

Stroke

Another devastating brain disease, stroke, is the third leading cause of death in the U.S. About 550,000 strokes occur annually, killing roughly 100,000 people and leaving many others severely disabled. One such patient, a retired college professor who was writing a book when stricken, was left paralyzed and with so little short-term memory that she was usually unable to recall which close friend had visited her as recently as an hour earlier.

Although chemists quickly embraced this useful technology, applying it to medicine proved more challenging. For one thing, radio-frequency waves could not be captured on photographic film, or its equivalent. Thus, a quarter century passed before Dr. Lauterbur figured out how to apply this technology to imaging. In 1971, he saw some experiments which showed that different tissues, in this case, from a rat, produced different magnetic resonance signals. "People said, maybe we will be able to detect and diagnose cancer using biopsy specimens," says Lauterbur. At first, the method required removing tissue from the body, putting it into a tube like ordinary chemicals, and then placing the test tube within the magnet of then-available instruments. "I asked myself, is there any way one can tell where an NMR signal is coming from inside a complex object, for example, an animal?" he recalls. The answer was a resounding "Yes!"

MRI images used in medicine are based predominantly upon information from hydrogen nuclei, which are by far the most abundant element in the body, accounting for 63 percent of the atoms, including those in the water that bathes living tissue. Magnetic resonance is sensitive to signals that differ from one tissue to another as well as to relative concentrations of

Most strokes occur when a brain artery is blocked, either by a clot growing on the vessel wall, or, as in the case of this college professor, by one that the blood swept into the brain from elsewhere in the body. Less often, in about 20-25 percent of cases, a stroke may result from a ruptured blood vessel. In both cases, brain tissue that becomes deprived of oxygen quickly dies. However, knowing the cause of stroke is critical for determining how stroke patients are treated. Strokes caused by clots are treated with clot-busting thrombolytic drugs, provided the patient reaches the hospital within three to six hours of onset. However, if the stroke arises from a hemorrhage such drugs need to be resolutely avoided because they can make matters worse.

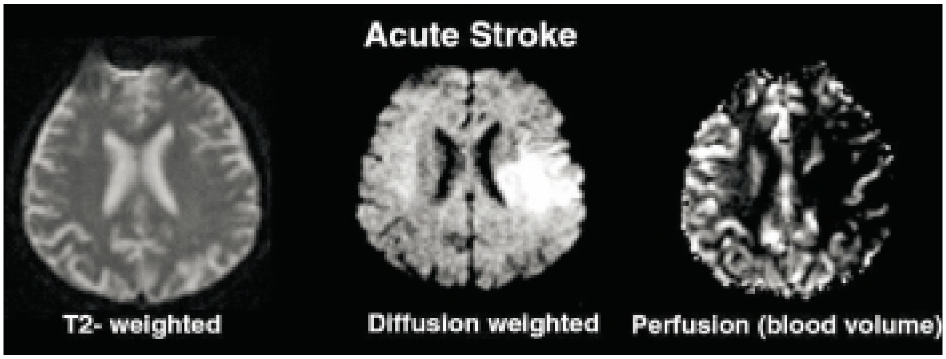

Figure 2. Three different MRI imaging protocols of a patient 20 min after a stroke event. The T2 weighted image in the first panel shows some structural information about the patient's brain but no evidence of the site of the stroke. The diffusion weighted image, which monitors the random movement of water, shows a distinct lesion on the right side of the patient (right side of middle panel). This is representative of decreased water diffusion in the area of the stroke, where there are dead neurons. The third panel shows a perfusion image, which demonstrates regions of the brain where there is reduced blood flow. The region of reduced blood flow in this patient (dark areas) is identifiable by the lower contrast and structural detail. This is larger than the area highlighted in the diffusion-weighted image, which may indicate that there may be additional neuronal cell loss. Courtesy of Drs. Steven Warach and Lawrence Lautor, National Institutes of Neurological Disorders and Stroke, National Institutes of Health, MD.

Most patients with an acute stroke receive a CT scan before MRI, because CT is particularly sensitive to bleeding in the brain and also because such instruments are cheaper and thus more widely available than MRI. While CT shows bleeding, MRI can reveal the size and location of the stroke far more accurately and precisely than CT. This more detailed information can be vital when making treatment decisions.

A recently developed MRI technique, called diffusion imaging (Fig.2), can diagnose strokes within minutes, revealing the location and size of damage. Diffusion imaging highlights the random movement, or diffusion, of water, which decreases when a stroke kills nerve cells. Thus, where neurons are dying, there is a net flow of water from the extracellular spaces into the cells. Since water diffuses relatively freely outside cells, while its movement is constrained inside cells by all the cellular machinery, there is less than ordinary diffusion in the vicinity of the stroke, and this difference shows up clearly on diffusion MRI. That movement of water from the extracellular spaces into the dying

hydrogen in tissues and fluids. As with conventional NMR, tissues are placed within a magnetic field, and then subjected to a radio-frequency pulse. That momentary pulse quickly aligns the hydrogen nuclei within it, but then they realign more slowly with the constant magnetic field within the magnetic resonance device. This realignment, or relaxation, takes several hundred milliseconds to a few seconds, depending on the environment surrounding the hydrogen atoms. For instance, hydrogen nuclei in water have a long relaxation time, as they do in blood and in cerebrospinal fluid. In tissues, their relaxation time is much shorter, and it is shortest in fat — around 300 milliseconds. These differences in relaxation times appear as degrees of brightness within the MRI image. In scientific shorthand, relaxation time is called T_1.

Yet another phenomenon, called T_2, makes MRI still more versatile when it comes to distinguishing one tissue from another. To understand T_2, imagine nuclei behaving like tops, says Dr. David Fisher of the University of Washington. Tops spin around their axes, but as they spin, they also lean. That leaning constantly shifts direction, from north to west to south to east and north again, tracing circles. Nuclei have a property, called spin, which resembles this directional leaning of tops. Now imagine many tops all leaning in the same direction, all shifting direction together. This neurons takes place because normal, healthy cells, including neurons have a lower concentration of salt than the surrounding extracellular fluids. Therefore salt leaks into the neurons, like water seeping into a boat through tiny holes in the gunwales, and so the neurons have to bail it. They have special pumps just for this task. But as a clot chokes off the blood, the bailing pumps lose their energy supply and stop working, and the cell dies. Salt flows inward and water follows.

One challenge in treating strokes is that most victims do not reach the hospital quickly enough to be candidates for thrombolytic drugs, which ordinarily are effective only when used within about three hours of onset. But Dr. Chelsea S. Kidwell of the University of California, Los Angeles and her colleagues are developing a means for using MRI imaging information to predict whether particular patients might benefit from such thrombolytic treatments at times following that usual three-hour window. “We believe that the information we are obtaining from the MRI will indicate if there is still salvageable tissue beyond these absolute time windows, and that this information could then be used to make treatment decisions,” says Dr. Kidwell.

The central area of the stroke,

Functional MRI

Functional MRI (fMRI) enables researchers and physicians to visualize parts of the brain that are active during specific tasks. This technique highlights fast-moving blood, and blood moves fastest in those parts of the brain that are working hardest. Active regions glow more brightly than inactive regions in functional magnetic resonance images.

Functional MRI aids neurosurgeons so that they can avoid damaging critical areas of the brain when performing delicate brain surgery. It highlights regions of brain activity upon performance of some task, sensory or motor. A cutaway of a three-dimensional reconstructed image of a human head shows the location of an identified tumor (green) in relation to brain regions of auditory (red), visual (blue) and motor (yellow) activities as identified using functional MRI. This figure provided courtesy of Dave Gering, Artificial Intelligence Laboratory, MIT. © Dave Gering

fMRI is fomenting a revolution of sorts within the neurosciences. Throughout science and medicine, researchers typically address large and complex questions by first breaking them into smaller, more manageable components. Among neuroscientists, for instance, one particularly important but also highly complex question, how does communication change between specific nerve cells when an individual learns a new skill and its memory becomes encoded, could not be addressed because they lacked the tools needed to get at its inherent complexity. “While reductionism [the strategy of asking small, manageable questions] has done wonderful things for science, you need to put the pieces together and see how the whole thing works,” says Dr. Just. “In neuroscience, fMRI has been one of the first tools to let you see how the parts work together.”

fMRI also is revolutionizing brain surgery, helping surgeons to avoid damaging areas of the brain that are critical to speech, movement, and other necessary functions. Someday such information may enable researchers to develop better teaching methods and to redesign work environments for those performing complex jobs, such as air traffic controllers. Perhaps a new field of brain ergonomics[1] will emerge.

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[1] Ergonomics is an applied science concerned with designing and arranging things people use so that they can be used efficiently and safely.

coordinated leaning is roughly what happens when whole bunches of nuclei are “in phase”. When a radio-frequency pulse is applied during MRI, the nuclei align and the spins come into phase. When the pulse ceases, the spins of the nuclei gradually “dephase”, and the signal weakens. The further out of alignment they fall, the weaker the signal becomes. When the spins are entirely random, the signal disappears. The time required for the spins to fall completely dephase is T_2.

Like relaxation, the rate of dephasing depends on characteristics of the tissue being imaged, but those characteristics where the blood supply is choked off, may be surrounded by an area where the blood flow is merely restricted, stressing the still-undamaged nerve cells. A recently developed technique called perfusion-weighted MRI can measure this blood flow (Fig. 2). Combined with diffusion-weighted images, it can provide valuable information about how the stroke may progress. If an area of low blood flow surrounds the central area of the stroke, the stroke is likely to spread, unless normal blood flow is quickly restored. But if not, doctors can be pretty sure that the stroke has run its course and that further treatment with thrombolytic drugs offers no benefit.

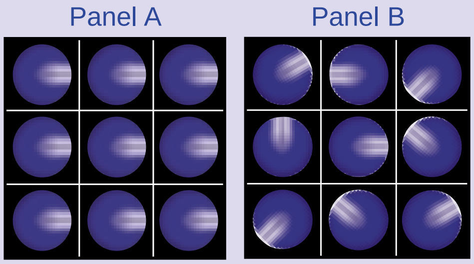
Within hours following a stroke, the brain begins adapting to its new limitations, marshalling regions that normally have nothing to do with the tasks that the damaged region had been performing. Sometimes, however, the damage overwhelms this limited ability of other brain segments to adapt to performing new activities. Using functional MRI (see box previous page), Dr. Marcel Just of Carnegie Mellon University is developing therapies that aim at improving the damaged brain's capacity to deal with its changed circumstances. For instance, patients whose language networks are damaged by stroke often can no longer understand complex sentences. Based on functional MRI studies, Dr. Just learned that the undamaged brain sometimes enlists the prefrontal cortex to reason through unfamiliar tasks. To engage the prefrontal cortex to help language-impaired stroke patients overcome some of their speech-associated difficulties, Dr. Just has presented them with sentences, asking them to find the verb, and to explain the action. He finds that, over a month, some patients improve so much that they could again analyze complex sentences as quickly as subjects with normal brains. Functional MRI studies indicate that the patients' prefrontal cortices again are active when the patients converse.

Brain Surgery

It is no accident that brain surgeons use many, if not all, the MRI tools that are available. Operating on the brain is delicate and complex for many reasons. The skull is difficult to penetrate, nerve cells are easily damaged and slow or impossible to repair, and anatomic landmarks are difficult to discern. Even with MRI to help in visualizing the functional anatomy of the brain, brain surgeons are afforded a view that is more like that from a tiny porthole rather than a picture window.

Thus, despite their value, conventional MRI maps of the brain have shortcomings. When tumors or otherwise diseased tissues are extracted, the brain undergoes seismic-like shifts, rendering the original map inaccurate. "When the tumor comes out, it leaves this hole," says Dr. Jolesz of Brigham and Women's Hospital. "The remaining cortex is falling in, and so there are deformations.

differ slightly from those that affect T_1 relaxation times. In effect, tinkering with these two signal sources provides a way of sharpening MRI images, much like adjusting contrast in a black-and-white TV picture. Moreover, certain agents, notably gadolinium, can be injected into a patient to increase contrast by reducing T_1 values.


Panel A

Panel B

The alignment of water nuclei are demonstrated for in phase (panel A) and out of phase (panel B). The nuclei are "in phase" following a radio-frequency pulse, while they are "out of phase" or dephased in their natural relaxed state.

Dr. Lauterbur also figured out how to translate magnetic resonance signals into a two- and then a fully three-dimensional grid, no small feat. Spin rate rises with the strength of a magnetic field. When a tissue slice is subjected to two magnetic fields, parallel to the plane of the slice, but perpendicular to each other, the spin will vary from lowest at one corner of the slice to highest at the opposite corner. Those differences enable the magnetic resonance equipment to determine where in the slice each signal, whether T_1 or T_2, is coming from. To produce a three-dimensional image, a series of consecutive two-dimensional slices is compiled one on top of the other, and a computer assembles all these two-dimensional images into a three-dimensional image. Beyond this basic MRI technology, improvements have involved ever more sophisticated developments in mathematics, engineering, and software.

You can't use the original image to guide the surgery." Edema, or swelling that occurs during surgery may also shift the terrain. At Brigham and Women's, however, recent improvements being made to conventional MRI mapping procedures are changing all that.

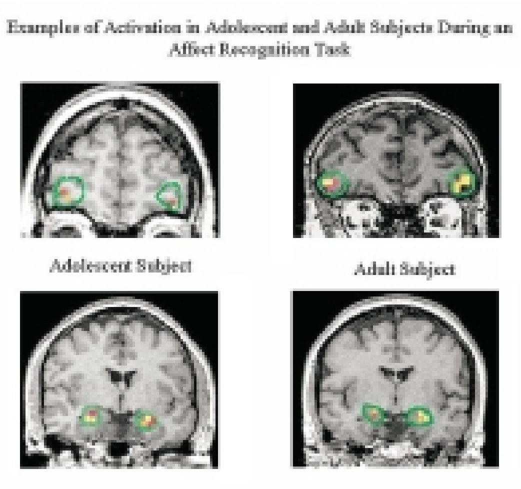
Before surgeons ever scrub for surgery, they review three-dimensional composites of various MRI images of their patients' respective brains to plan the best path to a particular damaged area and to avoid causing incidental damage, such as "big bleeds." First, conventional MRI provides a structural map, pinpointing the tumor and major arteries in its vicinity. Additionally, functional MRI maps help to locate centers of speech, movement, and other critical functions.

Typically during MRI-guided brain surgery, a patient lies upon a platform that spans two magnets shaped like huge tires that are spaced far enough apart for members of the surgical team to stand between them. Initially, a monitor above the surgical field displays the same image that the surgeon studied, but aligned precisely with the patient's brain, providing the surgeon with the virtual equivalent of X-ray vision. Throughout the operation, the MRI system provides a series of fresh images, each new one overlaying its predecessor on the screen, thereby updating any shifts within the anatomic terrain. Moreover, a special probe enables the surgeon to monitor specific sites along the incision within the brain, providing fresh images that appear immediately upon the screen above.

The Change in Brain During Adolescence is Plain

Some researchers, including Dr. Deborah Yurgelun-Todd of McLean Hospital in Belmont, Massachusetts, are investigating how the brain changes during adolescence and into adulthood. Different centers of the brain, each with distinctive roles, sometimes are at odds with one another. For instance, the thumb-sized piece of brain tissue called the amygdala, is a seat of emotion and impulse, whereas the frontal cortex is a center for executive functions such as planning, understanding the consequences of behaviors, and regulating emotions. Should one drive after drinking a six-pack of beer? Engage in sex with an unknown partner? Embark on an expedition to the South Pole? Start a new company? While the amygdala may be urging action, the frontal cortex is thinking through what the repercussions of that action might be.

Dr. Yurgelun-Todd conducted functional MRI studies on adolescents ages 11-18 and on adults performing tasks mediated by the frontal cortex. Those studies indicate that the frontal cortex is least active in the youngest adolescents, but that this activity rises steadily with age until it reaches adult levels. Moreover, the amygdala appears more active in teenagers than in adults. "That, in particular, made us think that the likelihood for impulsive behavior might be greater in adolescents than in adults," says Dr. Yurgelun-Todd. Lower activity in the frontal cortex of youths is consistent with their frequently impulsive behavior, but MRI analysis by itself cannot prove this explanation, she points out.



These images show the difference in brain activity between healthy adolescents and adults who were presented with pictures of faces displaying different emotions, and asked to name the emotion being displayed on each face. The top two figures show the lateral prefrontal cortex, which is involved in planning, regulating emotions, and understanding the consequences of behavior, and the bottom two figures show the amygdala, a seat of emotion and impulse. The adult prefontal cortex shows higher activity as represented by the yellow color and larger colored area. (The brighter, more yellow colors indicate areas of high activity, while red indicates areas of lower activity.) This figure provided by Deborah Yurgelun-Todd, McLean Hospital, Belmont, MA.

Not only does this MRI-based technology reduce the danger of damaging the brain, it also enables surgeons to remove more of each tumor that they encounter. Before this image-guided surgery became available, up to 80 percent of operations ultimately failed because they left bits of low-grade tumor behind.

Anticipated Applications in Medical Practice

MRI-guided imagery soon may help surgeons to substitute focused beams of ultrasound or lasers for conventional scalpels as a way of removing brain tumors, essentially cooking them to death. Ultrasound beams already can be aimed and synchronized electronically, guided by MRI. Laser light can also be used to kill certain tumors, but applications are still limited. Yet another recently developed variety of magnetic resonance, which is heat sensitive, makes it possible to monitor the temperature of a tumor and its surroundings, to insure that tumor, not healthy tissue, is being destroyed during such procedures (Fig. 3).

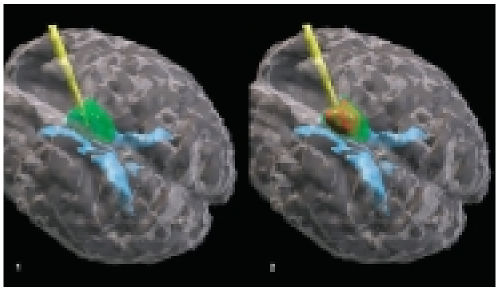


Figure 3. Using a computer-assisted MRI three-dimensional reconstruction of a patient's brain, a tumor (green) has been identified which can then be characterized by taking a biopsy (first panel). This same approach can be utilized to kill the tumor with heat by using a laser fiber (second panel). This innovative MRI-assisted technique illuminates heated tissue (in red), guiding the surgeons so that they can avoid killing normal tissue. The blue regions are the ventricles of the brain. This figure provided courtesy of Dr. Ferenc Jolesz, Brigham & Women's Hospital, MA.

Other MRI techniques are opening new windows into the brain. One approach involves using MRI to detect changes in nuclei of elements other than the usual hydrogen. For example, MRI can be used to detect changes in sodium ions, which move in and out of nerve cells when they transmit signals throughout the brain. This MRI-based approach thus might provide new insights about changes to the brain following a stroke or other diseases. It also might help in pinpointing brain areas involved in epilepsy that sometimes need to be removed in cases that cannot be controlled by drugs. MRI analysis of nuclei other than hydrogen or sodium, within experimental or established psychiatric drugs may provide insights about how such drugs are working and where they interact with the brain.

"Unlike other imaging modalities, which essentially have one tool, MRI is a big toolbox," says Dr. Cecil Charles, head of radiology at Duke University. Choosing what kind of MRI to use may depend on whether a specific disease involves changes in blood flow, metabolism, structural anomalies, or particular interactions with therapeutic drugs. "The only difficulty with MRI is deciding which tool to use," he says.

Biographies

David Holzman writes about science, medicine, and automobiles from Lexington, Massachusetts. He has written for Smithsonian, The Atlantic Monthly, the Journal of the National Cancer Institute, The Washington Post, the Boston Globe, Science, and numerous other publications. He is a contributing editor to Physician's Weekly and a medical correspondent for WebMD.

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References

Information on NIH research activities on magnetic resonance technologies can be found at the National Center for Research Resources web page at http://www.ncrr.nih.gov/ncrrprog/btdir/bt-c.htm.

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