Magnetic Resonance Imaging: Window to a Watery World

Kavita Dorai

Mankind has continually striven to know more – about the environment, the earth, and the cosmos itself! Medicine and surgery turned our gaze inward, to the mysteries of the human body. Earlier on, the scalpel was the surgeon's sole tool to peep inside the patient. Later, when scientists began to understand the interaction of electromagnetic radiation with matter, techniques like X-ray computed tomography (CT scans), ultrasound, and positron emission tomography helped visualize the inside of the body. Magnetic resonance imaging (MRI) is the most sophisticated imaging method in use today. The technique uses a combination of radio waves and magnetic fields to reconstruct two- and three-dimensional images of soft tissue in the body.

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The physics behind MRI is the phenomenon called nuclear magnetic resonance (NMR). At the heart of all atoms and molecules are their nuclei – protons and neutrons, which have an intrinsic angular momentum called 'spin' In atoms with an even number of neutrons and protons, these spins pair off and cancel out and the nucleus has no overall spin. However, if the number of protons or neutrons is odd, the nucleus ends up with a net spin.

What happens when a tiny nuclear magnet like a hydrogen atom (which contains only one proton with a spin of 1/2) is placed in a magnetic field? Just like a compass needle aligns itself with the earth's magnetic field, the proton aligns itself either parallel or anti-parallel with the applied magnetic field. If a sample containing lots of protons is placed in a strong magnetic field, at thermal equilibrium there are more protons aligned parallel

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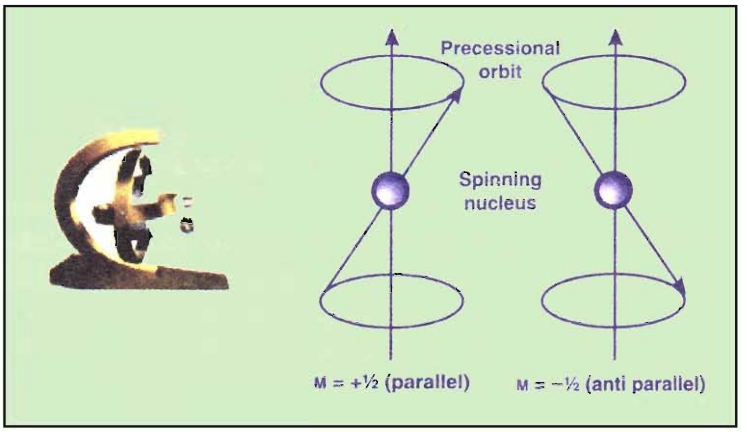

Figure 1. A gyroscope precessing in a gravitational field and a nuclear spin precessing in a magnetic field.

to the field (since the parallel alignment has lower energy than the anti-parallel), creating a net magnetization in the sample. Since protons also spin about their axes and have associated spin magnetic moments, in addition to aligning themselves with the magnetic field, they also 'precess' around the direction of the magnetic field. To picture this, recall what happens when a spinning top or gyroscope is placed in a gravitational field. It does not topple over, but instead performs a funny, wobbling movement (called 'precession') around the vertical axis. The torque produced by the gravitational field on its angular momentum makes the top's axis of rotation describe a cone around the axis of the field. In an exactly analogous way, the magnetic moment vector of a nucleus in a magnetic field precesses in a cone around the field, with a precession frequency $\omega = \gamma B_0$, where B_0 is the strength of the applied magnetic field. The quantity γ is called the gyromagnetic ratio (since it is a ratio of the gyroscopic precession rate to the magnetic field), and is a characteristic of the nucleus (see *Box* 1 for a more precise description of how nuclei behave in their quantum mechanical world). For hydrogen $\gamma = 42.57\text{MHz}T^{-1}$, so in a magnetic field of one Tesla (10,000 Gauss), protons precess at a rate of 42.57 million revolutions per second. This frequency is in the radiofrequency range of the spectrum of electromagnetic waves (the FM radio band is from 88 to 108 MHz).

Magnetic Resonance Imaging (MRI) is the most sophisticated imaging method in use today. The technique uses a combination of radio waves and magnetic fields to reconstruct the images of soft tissue in the body.

Box 1. The Quantum Gyroscope

The nucleus is a quantum mechanical object and its spin angular momentum is quantized. It comes in chunks of $\hbar$ the Planck's constant, and only certain orientations of its magnetic moment with respect to the external magnetic field are allowed. A spin-1/2 can be pictured as being aligned parallel or anti-parallel with the applied magnetic field. It is not so easy to form vector pictures of a spin-1 particle or a spin-3/2 particle oriented in a magnetic field.

The energy of interaction for a magnetic moment in a magnetic field of strength B_0 is described by the Hamiltonian

$$H = -\mu.B_0. \qquad (a)$$

Since nuclear spin is quantized, only discrete energy states are allowed, given by

$$E_m = -\gamma\hbar B_0 m. \qquad (b)$$

For a proton (with spin quantum number $I = 1/2$), the energy eigenvalues are $E_{+1/2} = -\gamma\hbar B_0/2$ and $E_{-1/2} = +\gamma\hbar B_0/2$, with an energy difference of $\Delta E = \gamma\hbar B_0$.

Now let us apply a radiofrequency pulse, with an energy equal to the difference between the two energy levels, to a collection of these protons in a magnetic field. The spins flip between the two orientations absorbing/emitting photons. This emission/absorption of rf energy by the protons is what is detected as a *resonance*. The resonance matching condition is

$$\hbar\omega = \Delta E = \gamma\hbar B_0, \qquad (c)$$

where $\omega = \gamma B_0$ corresponds to the classical precession frequency.

If an rf pulse is now applied to the protons at the Larmor frequency, the protons are excited and 'flip' from the lower to the higher energy states. This is the phenomenon of *resonance*. Once the rf is switched off, the magnetization again precesses freely about the main magnetic field. According to Faraday's law of induction, this time dependent precession induces a current in an rf coil and which is detected as the NMR signal. This is how an NMR spectrometer 'sees' the protons (see *Box* 2 for a discussion on the major hardware components of a magnetic resonance imaging system).

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Living tissue consists of 60-80% water – truly a watery world! Nuclei of hydrogen atoms, i.e., protons (with spin of 1/2), are present in water and in lipids, and are the

Box 2. MRI Machines: Magnetic Personalities

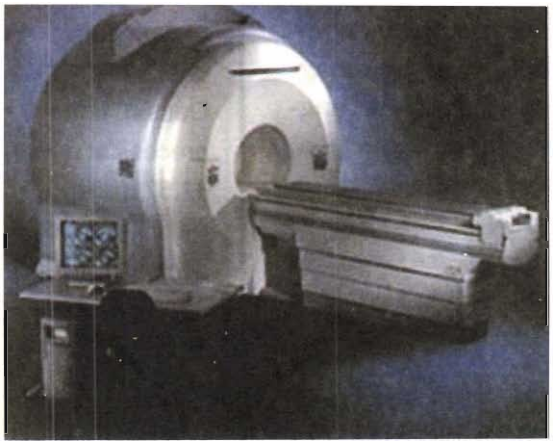
There are three different types of magnetic fields required for imaging: the main magnetic field, the gradient fields and the rf field for signal detection. The main MRI magnet is a forbidding looking object: typical magnets of today are superconducting, with field strengths of 0.5-2.0 T, a clear bore of 100 cm (through which the patient is inserted) and a mass of around 7000 kg. Superconductors are materials (certain alloys and metals) that exhibit no electrical resistance below a certain critical temperature in the range 10-20 K. The magnet is left running continuously, at a constant field and liquid helium temperatures.

Most MRI systems have gradient windings that produce three orthogonal field gradients. Essentially a gradient winding produces a quadrupole field. A gradient can be produced at any angle to the main field, as required when using projection reconstruction imaging methods. The function of the rf coil is to apply rf pulses to the patient and to receive the weak free induction signal emanating from the patient. The coils surround the patient and are tuned to the Larmor frequency. The magnetic energy stored in an MRI magnet is quite substantial.

The superconducting coil carries a typical current of 500 A and has a typical inductance of the order of 80 Henry. The magnetostatic energy E_M stored in an inductance L at a current i is given by

$$E_M = \frac{1}{2}Li^2 = 1 \times 10^7 J.$$

10 Mega Joules is the same amount of kinetic energy of a 100-ton engine moving at 14 m s^{-1}. If the superconducting magnet were to suddenly 'quench' (revert to becoming a normal conductor if the helium bath surrounding the coils suddenly evaporates), all this energy would be converted to heat. The remaining helium instantly vaporizes and blows out the top of the magnet in 30 sec, not a sight to be experienced at close quarters! However, such magnets are extremely stable and rarely quench.



A typical MRI scanner

objects that the MRI machine 'sees'. An MRI image is a map of the distribution of the water protons inside the body. MRI can quantify the amount of water in the tissue being imaged. It can also quantify the rate of flow and diffusion of water. By detecting the response of these tiny nuclear magnets (the water protons) to a colossal magnetic field, one can obtain amazing pictures of tissues, organs and even the human brain. Other nuclei like carbon, sodium and phosphorus also possess magnetic properties and in principle can be used for imaging. However, their gyromagnetic ratio and hence the magnetic resonance signal, is much less than that of hydrogen atoms. MRI of nuclei other than hydrogen is very difficult and is seldom attempted. We will now discover how to reconstruct an image of an object by probing its water density.

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Images from Inner Space

In a uniform magnetic field, all the water protons would resonate at the same precession frequency. The trick to obtaining an image of the protons is to differentiate them spatially. One way to do this is to make protons that are located in different regions in space resonate at slightly different frequencies. Since the gyromagnetic ratio of protons cannot be altered, this implies that the magnetic field should have different values at different points in space. In addition to the homogeneous field in the z direction, suppose a linear variation in the z direction is superimposed,

$$B_z = B_0 + zG_z, \tag{1}$$

where G_z is the field gradient. The term 'gradient' implies that the magnetic field is altered along a particular direction. The precession frequency of the proton is directly proportional to the applied field

$$\omega = \gamma B_z = \gamma B_0 + \gamma z G_z \tag{2}$$

The trick to obtaining an image of the protons is to differentiate them spatially. This is achieved in MRI, by applying linearly increasing magnetic field gradients.

A two-dimensional image is obtained in three steps. In the first step, called 'slice selection', spins in a slice are selectively excited. The next step is to distinguish the signal coming from different spatial locations within the slice. This is done by applying a gradient G_x (called the frequency encoding gradient).

and in this case is proportional to the proton's position on the z axis, as well as the strength of the applied gradient. Since G_z is a known gradient and ω can be measured, one can give the protons in a specific region, a unique address or a 'spatial label'.

A two-dimensional MR image is acquired in three steps. In the first step called 'slice selection', spins in the slice of interest are excited. This is achieved by applying the gradient G_z during an rf pulse of a specific frequency bandwidth. Instead of a single precession frequency, the NMR signal now contains a spread or bandwidth of frequencies, with the amplitude of each frequency component being proportional to the amount of those protons experiencing the corresponding field. Only nuclei in the plane with corresponding frequencies will be excited and a slice will be selected. No signals are excited or detected from areas outside the defined slice. The thickness of the excited slice Δz is related to the gradient amplitude G_z and the rf bandwidth Δf as

$$\Delta z = \Delta f / \gamma G_z. \tag{3}$$

A larger slice will be excited if Δf is increased to include more frequencies, or alternately if the strength of G_z is decreased. The location of the excited slice is varied by transmitting an rf pulse of a different central frequency. One has thus obtained a 1D projection of spin density. Of course, a 1D projection is hardly an image and something more creative will have to be done in order to get some real MRI pictures.

After the slice has been selected, the next step is to distinguish the signal coming from different spatial locations within this slice. This is done by applying a gradient G_x (called the frequency encoding gradient) in the x-direction during the time the signal is acquired. The acquired signal contains different amplitudes (due to varying water content) and different frequencies (due to the magnetic field gradients). A time-varying sig-

nal can be broken up into its various sinusoidal frequency components using a mathematical method called *Fourier transform*. In NMR, a Fourier transform of the time-varying rf signal gives us a spectrum of the different resonance frequencies of the nuclei in the sample. The MRI signal can be decomposed into its amplitude and frequency components using the Fourier transform. Since G_x is known, the frequency can be related to position and the MR image shows the spatial distribution of water.

The final step in acquiring the 2D MR image is to encode the information of the second spatial dimension, i.e., the y coordinates of the protons. This is done by applying a second gradient G_y (called the phase encoding gradient) in the y direction. During the phase-encoding period, protons along the y direction experience different magnetic fields and acquire a phase angle. After the gradient is turned off, the protons revert to precessing at the frequency of the main magnetic field. However, they remember the previous event by retaining their y-coordinate dependent phase angles. The MR signal now contains both frequency and phase information and the protons are spatially labeled in both dimensions. However, one phase encode gradient of a particular strength enables us to acquire only a 1D image. To get a 2D image, the phase encode gradient has to be applied in increments of increasing strength. Each increment corresponds to a 1D profile across the sample being imaged in the second dimension. The MR signal can be thought of as being collected in spatial frequency space or the '*k-space*', because of the way the gradients are applied during the imaging sequence. Each point in *k-space* (usually plotted in two dimensions) represents the amount of a particular spatial frequency present in the imaged object. The final mathematical operation to be performed is the 2D Fourier transform. This then gives us the spatial map of the water protons in two dimensions in the

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object being imaged. The two frequency axes of the image correspond to the spatial axes x and y.

The frequency/phase encoding technique described above is just one way in which the MR image can be constructed and there have been many other methods since developed. One popular imaging technique based on 2D Fourier transforms emerged from the experiments of an Indian scientist Anil Kumar, while working in the group of Nobel laureate Richard Ernst, in Switzerland. The main idea is to scan *k-space* such that it provides sufficient information to construct the image after the Fourier transform. More rapid ways of scanning the k-space include spiral scanning, back projection and echo-planar imaging (EPI). The echo planar imaging method of Peter Mansfield is the fastest possible means of generating an MR image. The image is acquired using only a single Fourier transform for all points in the imaging plane. The gradient is reversed using a very fast switch, which generates multiple echoes in a single time dimension. The details of the EPI method are rather complex and a technical discussion is beyond the scope of this article.

The concept of a Fourier transform in two dimensions can be extended to three dimensions in order to construct three-dimensional MRI images. The amount of data to be collected and processed and the time to record the data are however prohibitively expensive in most of the cases. To give an idea of the time scales involved in obtaining images, a 2D MR image with a total of 128 pixels along each dimension has a total of $128^2 = 2^{14}$ pixels. The experiment requires 128 phase encode steps and the time taken to acquire the scan is 64 seconds (each phase encode step takes 0.5 seconds). The number of phase encode steps can be reduced to get a faster image, but the image resolution would get correspondingly reduced. 3D MR images use phase encoding in the third dimension as well. This means the time taken to

The echo-planar imaging method (EPI) of Peter Mansfield is the fastest possible means of generating an MR image.

acquire a 3D image with 128 pixels along each dimension is 128 times longer than the time taken for the 2D image!

Framing the Body: MRI as a Detective

Each pixel in the MR image corresponds to some voxel (volume element) in the subject being imaged. The composite signal is represented as pixel brightness. The brightness of the image is a direct measure of NMR signal intensity. How can one differentiate one region of the body from another in an informative way? The key to this question is *contrast*: using light/dark variation in pixel intensity to map different kinds of tissue. Even though proton concentration contributes to signal brightness, it varies only in a range of a few percent throughout most tissues so other parameters must be used for image contrast. Following excitation, all nuclei 'relax' to their equilibrium i.e return to their initial population distribution via a variety of relaxation processes. Spins relax in two different ways, categorized according to whether they exchange energy with their surroundings (spin-lattice relaxation, characterized by the time T_1) or with each other (spin-spin relaxation, characterized by the time T_2). The most common parameters used for tissue contrast in MRI are the two relaxation times T_1 and T_2. Protons in different tissues have different and very characteristic relaxation times and the brightness of pixels will then reflect these differences. For example, body fluids like the cerebrospinal fluid (CSF) and blood have T_1's of approximately 1 second, whereas water inside cells have T_1's which are an order of magnitude smaller. *Why* this is so is however a very complex question and the answer is not fully known as yet!

The most common parameters used for tissue contrast in MRI are the two relaxation times T_1 (the spin-lattice relaxation time) and T_2 (the spin-spin relaxation time).

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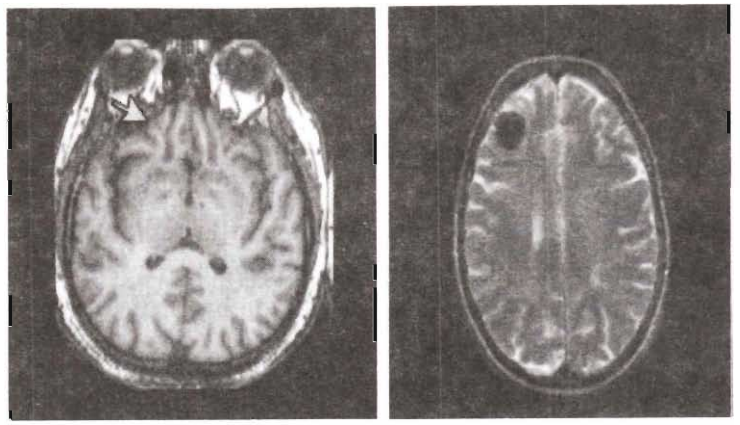

An MR view of a healthy brain.

MR image of a brain with a tumor (a metastatic adenocarcinoma).

Figure 2. MR images of the brain showing tissue contrast and relaxation-weighted differences.

Pictures courtesy the whole brain atlas of the Harvard medical school. http://www.med.harvard.edu/AANLIB/home.html

clear images of organs located within dense bone structures that tend to block X-ray penetration. It is an important tool in angiography for studying heart function and blood flow. MRI is also the best technique for detecting brain damage in multiple sclerosis, for detecting brain tumors, and for characterizing spinal cord injuries. MR images of a healthy brain and a brain with a tumor are shown in *Figure* 2.

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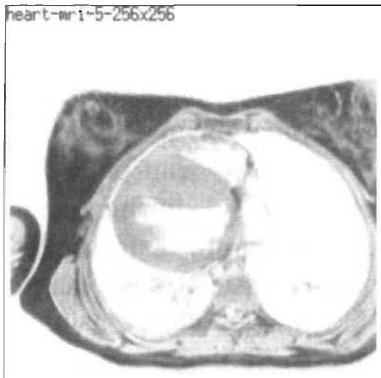
While most soft tissues can be nicely imaged, the heart poses a unique problem. A single heart beat cycle occurs in only a fraction of a second which causes severe motional artifacts in the MR image. The 'shutterspeed' of the MRI camera is not fast enough to freeze the motion and obtain a clear image of the heart. *Cardiac gating* is the technique used to acquire MR images stroboscopically in synchrony with the heart beat. An electrocardiograph monitors electrical activity by detecting small voltages in electrodes attached to the chest. This electrical signal is used to pace the data acquisition and adjust the timing of the RF pulses. The image is then obtained in 128 or 256 heartbeats. Using cardiac gating one can also obtain magnetic resonance *angiograms* which are pictures of moving blood in the vascular system. Two images are subtracted – one obtained during



An MR image of a beating human heart.

An angiogram of a kidney.

Figure 3. MR image of the heart in a patient with hypertrophic cardiomyopathy (i.e a very thick heart muscle), and an angiogram of a kidney after a catheter has been placed in the renal artery. The images were obtained using cardiac gating.

Pictures courtesy the NCI-Frederick Institute. http://www.lecb.ncifcrf.gov/flicker/heartMrIFlkPair.html and the National Institutes of Health http://dir.nhlbi.nih.gov/lrp/labs/cardiology/renalmra.htm respectively.

the *systole* where the left ventricle of the heart is contracted and experiences a surge of blood and the other during the *diastole* when the ventricle is relaxed and the flow rate is lower. An angiogram and an MR image of a beating heart are shown in *Figure* 3.

The brain is the most important organ of the human body and the least understood. The cerebellum is involved in the regulation of movement and is also involved when a new skill has been learned. For example, when learning to play the violin, at first the cerebral cortex controls the fingers, but upon learning, the cerebellum takes over. The thalamus acts as an intermediary in transferring information to the cerebral hemispheres. The hippocampus plays a role in long term memory storage while the hypothalamus mediates emotions and controls hormonal release. The reticular formation, medulla and pons regulate alertness, blood pressure and respiratory mechanisms. What we know about the brain is extremely sketchy, but new models are being evolved every day, and MRI is contributing to our understanding in a major way.

Functional MRI (fMRI) can identify parts of the brain involved in processing sensory data (like perceiving flashing lights) or involved in motor tasks (like clenching the

Functional MRI (fMRI) can identify parts of the brain involved in various activities. Activation results in increased blood flow to that part of the brain.

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fist or flexing the fingers). Activation of the part of the brain engaged in this particular activity results in increased blood flow to that part. The magnetic properties of blood depend on the amount of oxygen it carries and can then be used by NMR to identify that part. By subtracting T_2-weighted images obtained during a rest period and while the brain is performing a particular task, only those areas that experience neuronal activation can be highlighted in the MR image. *Figure* 4 shows the results of an fMRI study where different parts of the brain are activated when human subjects were asked to use Spanish and English words to name the same object. The study shows that the brains of bilingual subjects show more activity in diverse areas of the brain as compared to those who are proficient only in a single language. The fMRI technique is helping us understand the basic functioning of the brain, and can be used to study how the brain functions in psychiatric disorders.

Concluding Remarks

MRI has become the most popular medical diagnostics tool in use today. The major advantage of MRI is its non-invasive character. Unlike X-ray or CT scans, it has no radiation risks, and hence does not destroy or damage tissues. To honor this important breakthrough, the Nobel Prize in medicine was awarded on October 6th 2003 jointly to a chemist and a physicist for their contributions to MRI. Paul C Lauterbur, a professor at the University of Illinois (USA), first demonstrated that two-dimensional images could be obtained by applying field gradients to the main magnetic field. Sir Peter Mansfield, emeritus professor at Nottingham University (UK), mathematically analyzed the MRI signal, and also developed methods to obtain very fast images (the echo planar imaging technique briefly mentioned earlier).

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The future of MRI is promising: already cognitive psychologists and neurobiologists have begun to use fMRI

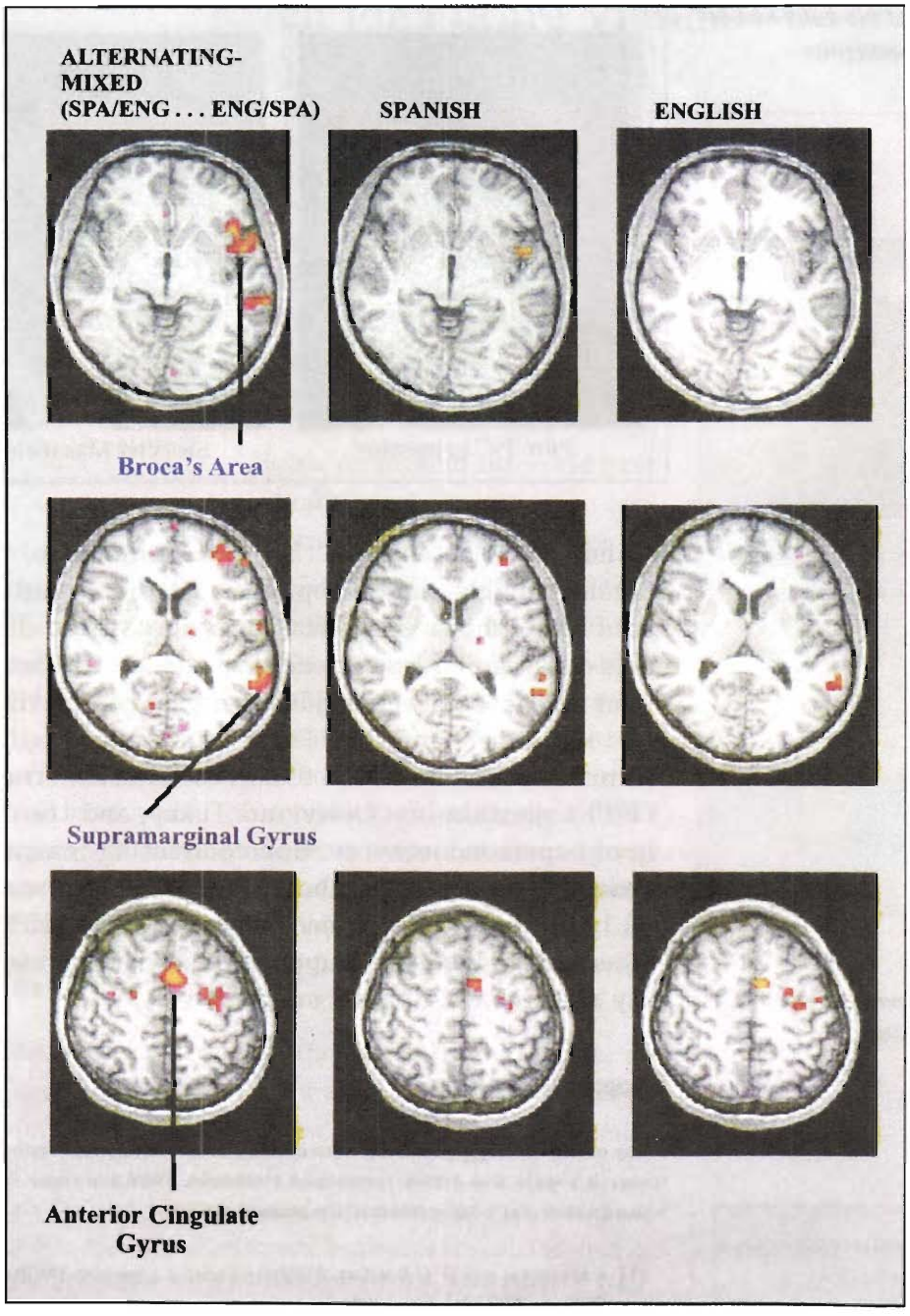
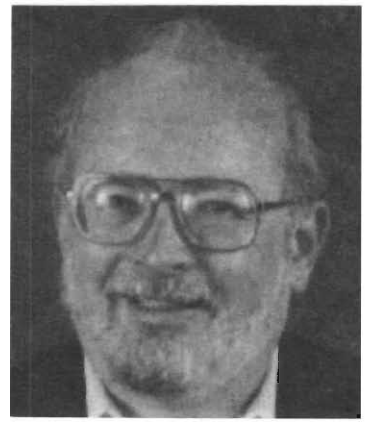


Figure 4. fMRI images of the brain during a language study involving performance between single-language and dual-language picture naming in a group of three Spanish-English bilingual subjects.
Picture courtesy researchers at the University of California, San Diego http://crl.ucsd.edu/bilingual/fMRI3.html.

Winners of the 2003 Nobel prize in medicine.



Prof. P C Lauterbur

Sir Peter Mansfield

to find out what parts of the brain respond to various human thoughts and perceptions. MRI is a good example of how the cross-fertilization of ideas from different fields of research leads to exciting science. In fact, MRI might not have developed into a viable medical diagnostics tool, had it not been for the advent of high speed computers, the invention of the Fast Fourier Transform (FFT) algorithm by Cooley and Tukey, and the discovery of superconductivity. Superconducting magnets are crucial components of the hardware of MRI scanners, and by a happy coincidence, this year's Nobel Prize in Physics was awarded to superconductivity and superfluidity research. But that's another story!*

* See *Resonance*, Vol.9, No.2, pp.50-63, 2004.

Suggested Reading

Many of the developments referred to in this article are as yet described only in research papers and highly specialized textbooks. Here are some books and websites that may be of interest to the general reader.

[1] **R Hashemi and W G Bradley, *MRI:the basics*, Lippincott Williams and Wilkins, Philadelphia, 1997.**

[2] **M A Brown and R C Semelka, *MRI: Basic principles and applications*, Wiley-Liss, New York, 1995.**

[3] **J P Hornack, *The basics of MRI*, http://www.cis.rit.edu/htbooks/mri/**

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