NEUROSCIENCE

LECTURE 10: TECHNIQUES TO UNDERSTAND THE CHEMISTRY OF NERVOUS SYSTEM

TECHNIQUES TO UNDERSTAND THE CHEMISTRY OF NERVOUS SYSTEM:

Neuroimaging includes the use of various techniques to either directly or indirectly image the structure,function/pharmacology of the brain. It is a relatively new discipline within medicine and neuroscience/psychology.[1] Physicians who specialize in the performance and interpretation of neuroimaging in the clinical setting are neuroradiologists.

Overview

Neuroimaging falls into two broad categories:

- Structural imaging, which deals with the structure of the brain and the diagnosis of gross (large scale) intracranial disease (such as tumor), and injury, and
- functional imaging, which is used to diagnose metabolic diseases and lesions on a finer scale (such as Alzheimer's disease) and also for neurological and cognitive psychology research and building brain-computer interfaces.

Functional imaging enables, for example, the processing of information by centers in the brain to be visualized directly. Such processing causes the involved area of the brain to increase metabolism and "light up" on the scan. One of the more controversial uses of neuroimaging has been research into "Thought identification" or mind-reading.

History

In 1918 the American neurosurgeon Walter Dandy introduced the technique of ventriculography. X-ray images of the ventricular system within the brain were obtained by injection of filtered air directly into one or both lateral ventricles of the brain. Dandy also observed that air introduced into the subarachnoid space via lumbar spinal puncture could enter the cerebral ventricles and also demonstrate the cerebrospinal fluid compartments around the base of the brain and over its surface. This technique was called pneumoencephalography.

In 1927 Egas Moniz introduced cerebral angiography, whereby both normal and abnormal blood vessels in and around the brain could be visualized with great precision.

In the early 1970s, Allan McLeod Cormack and Godfrey Newbold Hounsfield introduced computerized axial tomography (CAT or CT scanning), and ever more detailed anatomic images of the brain became available for diagnostic and research purposes. Cormack and Hounsfield won the 1979 Nobel Prize for Physiology or Medicine for their work. Soon after the introduction of CAT in the early 1980s, the development of radioligands allowed single photon emission computed tomography (SPECT) and positron emission tomography (PET) of the brain.

More or less concurrently, magnetic resonance imaging (MRI or MR scanning) was developed by researchers including Peter Mansfield and Paul Lauterbur, who were awarded the Nobel Prize for Physiology or Medicine in 2003. In the early 1980s MRI was introduced clinically, and during the 1980s a veritable explosion of technical refinements and diagnostic MR applications took place. Scientists soon learned that the large blood flow changes measured by PET could also be imaged by the correct type of MRI. Functional magnetic resonance imaging (fMRI) was born, and since the 1990s, fMRI has come to dominate the brain mapping field due to its low invasiveness, lack of radiation exposure, and relatively wide availability. As noted above fMRI is also beginning to dominate the field of stroke treatment.

In early 2000s the field of neuroimaging reached the stage where limited practical applications of functional brain imaging have become feasible. The main application area is crude forms of brain-computer interface.

Brain imaging techniques

Computerized axial tomography:

Computed axial tomography (CAT), **computer-assisted tomography**, **computed tomography**, **CT**, or **body section roentgenography** is the process of using digital processing to generate a three-dimensional image of the internals of an object from a large series of two-dimensional X-ray images taken around a single axis of rotation. The word "*tomography*" is derived from the Greek *tomos* (slice) and *graphia* (describing).

Although most common in healthcare, CT is also used in other fields, e.g. nondestructive materials testing.

Instrumentation

The development of computed tomography (CT) in the early 1970s revolutionized medical radiology. For the first time, physicians were able to obtain high-quality tomographic (cross-sectional) images of internal structures of the body. Over the next 10 years, 18 manufacturers competed for the exploding world CT market. Technical sophistication increased dramatically, and even today, CT continues to mature, with new capabilities being researched and developed. Computed tomographic images are reconstructed from a large number of measurements of x-ray transmission through the patient (called projection data). The resulting images are tomographic "maps" of the x-ray linear attenuation coefficient. The mathematical methods used to reconstruct

CT images from projection data are discussed in the next section. In this section, the hardware and instrumentation in a modern scanner are described. The first practical CT instrument was developed in 1971 by DR. G. N. Hounsfield in England and was used to image the brain [Hounsfield, 1980]. The projection data were acquired in approximately 5 minutes, and the tomographic image was reconstructed in approximately 20 minutes. Since then, CT technology has developed dramatically, and CT has become a standard imaging procedure for virtually all parts of the body in thousands of facilities throughout the world. Projection data are typically acquired in approximately 1 second, and the image is reconstructed in 3 to 5 seconds. One special-purpose scanner described below acquires the projection data for one tomographic image in 50 ms. A typical modern CT scanner is shown in Fig. 5, and typical CT images are shown in Fig. 6. The fundamental task of CT systems is to make an extremely large number (approximately 500,000) of highly accurate measurements of x-ray transmission through the patient in a precisely controlled geometry. A basic system generally consists of a gantry, a patient table, a control console, and a computer. The gantry contains the x-ray source, x-ray detectors, and the data-acquisition system (DAS).

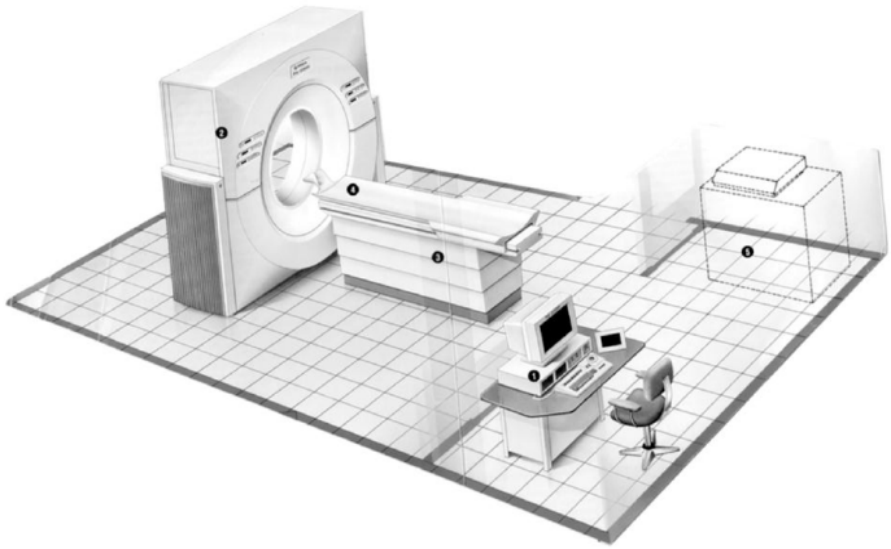

Figure 5 Schematic drawing of a typical CT scanner installation, consisting of (1) control console, (2) gantry stand, (3) patient table, (4) head holder, and (5) laser imager. (Courtesy of Picker International, Inc.)

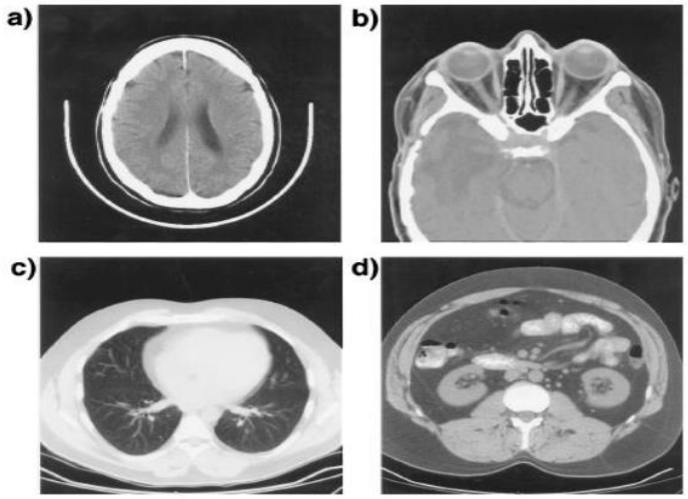

Figure 6 Typical CT images of (a) brain, (b) head showing orbits, (c) chest showing lungs, and (d) abdomen.

Data-Acquisition Geometries Projection data may be acquired in one of several possible geometries described below, based on the scanning configuration, scanning motions, and detector arrangement. The evolution of these geometries is descried in terms of "generations," as illustrated in Fig. 7, and reflects the historical development [Newton and Potts, 1981; Seeram, 1994]. Current CT scanners use either third-, fourth-, or fifthgeneration geometries, each having their own pros and cons.

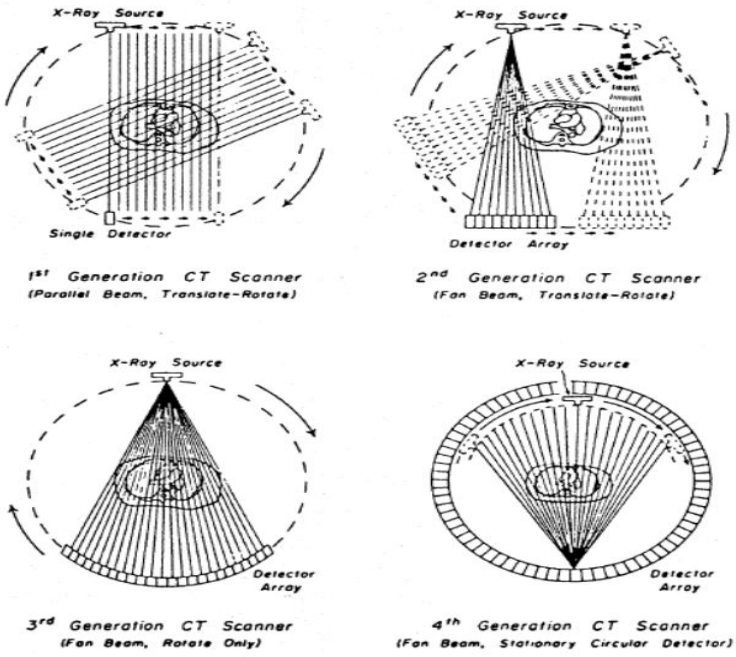

Figure 7 Four generations of CT scan

First Generation: Parallel-Beam Geometry Parallel-beam geometry is the simplest technically and the easiest with which to understand the important CT principles. Multiple measurements of x-ray transmission are obtained using a single highly collimated x-ray pencil beam and detector. The beam is translated in a linear motion across the patient to obtain a projection profile. The source and detector are then rotated about the patient isocenter by approximately 1 degree, and another projection profile is obtained. This translate-rotate scanning motion is repeated until the source and detector have been rotated by 180 degrees. The highly collimated beam provides excellent rejection of radiation scattered in the patient; however, the complex scanning motion results in long (approximately 5-minute) scan times. This geometry was used by Hounsfield in his original experiments [Hounsfield, 1980] but is not used in modern scanners.

Second Generation: Fan Beam, Multiple Detectors Scan times were reduced to approximately 30 s with the use of a fan beam of x-rays and a linear detector array. A translate-rotate scanning motion was still employed; however, a larger rotate increment could be used, which resulted in shorter scan times. The reconstruction algorithms are slightly more complicated than those for first-generation algorithms because they must handle fan-beam projection data.

Third Generation: Fan Beam, Rotating Detectors Third-generation scanners were introduced in 1976. A fan beam of x-rays is rotated 360 degrees around the isocenter. No translation motion is used; however, the fan beam must be wide enough to completely contain the patient. A curved detector array consisting of several hundred independent detectors is mechanically coupled to the x-ray source, and both rotate together. As a result, these rotate-only motions acquire projection data for a single image in as little as 1 s. Third-generation designs have the advantage that thin tungsten septa can be placed between each detector in the array and focused on the x-ray source to reject scattered radiation.

Fourth Generation: Fan Beam, Fixed Detectors In a fourth-generation scanner, the x-ray source and fan beam rotate about the isocenter, while the detector array remains stationary. The detector array consists of 600 to 4800 (depending on the manufacturer) independent detectors in a circle that completely surrounds the patient. Scan times are similar to those of third-generation scanners. The detectors are no longer coupled to the x-ray source and hence cannot make use of focused septa to reject scattered radiation. However, detectors are calibrated twice during each

rotation of the x-ray source, providing a self-calibrating system. Third-generation systems are calibrated only once every few hours. Two detector geometries are currently used for fourth-generation systems: (1) a rotating x-ray source inside a fixed detector array and (2) a rotating x-ray source outside a nutating detector array. Figure 8 shows the major components in the gantry of a typical fourth-generation system using a fixed-detector array. Both third- and fourth-generation systems are commercially available, and both have been highly successful clinically. Neither can be considered an overall superior design.

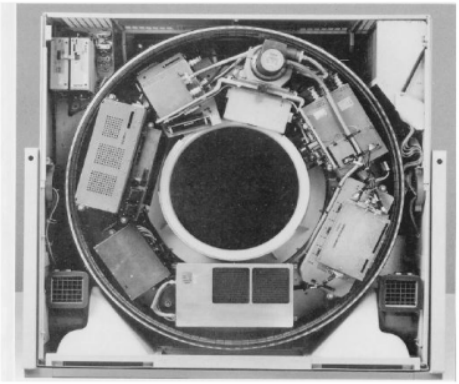

Figure 8

Fifth Generation: Scanning Electron Beam Fifth-generation scanners are unique in that the x-ray source becomes an integral part of the system design. The detector array remains stationary, while a high-energy electron beams is electronically swept along a semicircular tungsten strip anode, as illustrated in Fig. 9.

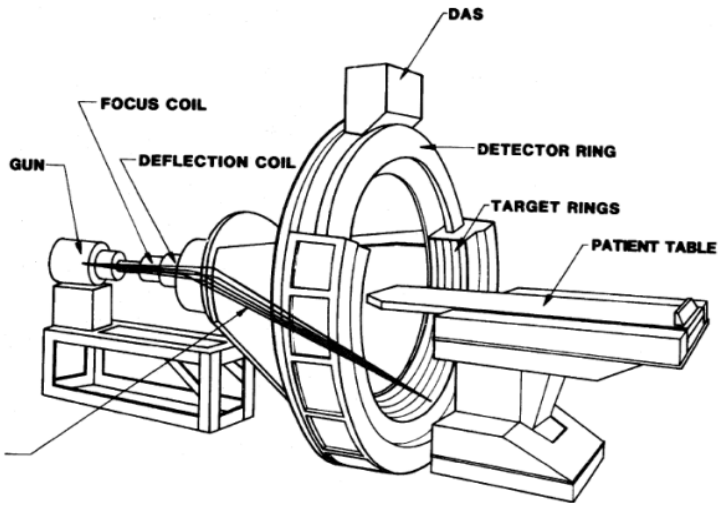

Figure. 9

X-rays are produced at the point where the electron beam hits the anode, resulting in a source of x-rays that rotates about the patient with no moving parts [Boyd et al., 1979]. Projection data can be acquired in approximately 50 ms, which is fast enough to image the beating heart without significant motion artifacts [Boyd and Lipton, 1983]. An alternative fifth-generation design, called the dynamic spatial reconstructor (DSR) scanner, is in use at the Mayo Clinic [Ritman, 1980, 1990]. This machine is a research prototype and is not available commercially. It consists

of 14 x-ray tubes, scintillation screens, and video cameras. Volume CT images can be produced in as little as 10 ms. Spiral/Helical Scanning The requirement for faster scan times, and in particular for fast multiple scans for three-dimensional imaging, has resulted in the development of spiral (helical) scanning systems [Kalendar et al., 1990]. Both third- and fourth-generation systems achieve this using self-lubricating slip-ring technology (figure 10) to make the electrical connections with rotating components.

Figure 10

This removes the need for power and signal cables which would otherwise have to be rewound between scans and allows for a continuous rotating motion of the x-ray fan beam. Multiple images are acquired while the patient is translated through the gantry in a smooth continuous motion rather than stopping for each image. Projection data for multiple images covering a volume of the patient can be acquired in a single breath hold at rates of approximately one slice per second. The reconstruction algorithms are more sophisticated because they must accommodate the spiral or helical path traced by the x-ray source around the patient, as illustrated in Fig. 11.

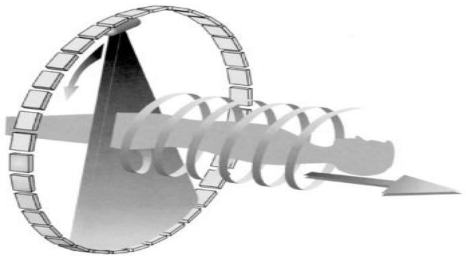

Figure 11

X-Ray System

The x-ray system consists of the x-ray source, detectors, and a data-acquisition system.

X-Ray Source

With the exception of one fifth-generation system described above, all CT scanners use bremsstrahlung x-ray tubes as the source of radiation. These tubes are typical of those used in diagnostic imaging and produce x-rays by accelerating a beam of electrons onto a target anode. The anode area from which x-rays are emitted, projected along the direction of the beam, is called the focal spot. Most systems have two possible focal spot sizes, approximately 0.5 × 1.5 mm and 1.0 × 2.5 mm. A collimator assembly is used to control the width of the fan beam between 1.0 and 10 mm, which in turn controls the width of the imaged slice.

The power requirements of these tubes are typically 120 kV at 200 to 500 mA, producing x-rays with an energy spectrum ranging between approximately 30 and 120 keV. All modern systems use highfrequency generators, typically operating between 5 and 50 kHz [Brunnett et al., 1990]. Some spiral systems use a stationary generator in the gantry, requiring high-voltage (120-kV) slip rings, while others use a rotating generator with lower-voltage (480-V) slip rings. Production of x-rays in bremsstrahlung tubes is an inefficient process, and hence most of the power delivered to the tubes results in heating of the anode. A heat exchanger on the rotating gantry is used to cool the tube. Spiral scanning, in particular, places heavy demands on the heat-storage capacity and cooling rate of the x-ray tube.

The intensity of the x-ray beam is attenuated by absorption and scattering processes as it passes through the patient. The degree of attenuation depends on the energy spectrum of the x-rays as well as on the average atomic number and mass density of the patient tissues. The transmitted intensity is given by

$$I_t = I_o e^{-\int_0^L \mu(x)dx}$$

where Io and II are the incident and transmitted beam intensities, respectively; L is the length of the x-ray path; and μ(x) is the x-ray linear attenuation coefficient, which varies with tissue type

and hence is a function of the distance x through the patient. The integral of the attenuation coefficient is therefore given by

$$\int_0^L \mu(x)\,dx = -\frac{1}{L}\ln\left(I_t / I_o\right)$$

X-Ray Detectors

X-ray detectors used in CT systems must (a) have a high overall efficiency to minimize the patient radiation dose, have a large dynamic range, (b) be very stable with time, and (c) be insensitive to temperature variations within the gantry. Three important factors contributing to the detector efficiency are geometric efficiency, quantum (also called capture) efficiency, and conversion efficiency [Villafanaet et al., 1987]. Geometric efficiency refers to the area of the detectors sensitive to radiation as a fraction of the total exposed area. Thin septa between detector elements to remove scattered radiation, or other insensitive regions, will degrade this value. Quantum efficiency refers to the fraction of incident x-rays on the detector that are absorbed and contribute to the measured signal. Conversion efficiency refers to the ability to accurately convert the absorbed x-ray signal into an electrical signal (but is not the same as the energy conversion efficiency).

Overall efficiency is the product of the three, and it generally lies between 0.45 and 0.85. A value of less than 1 indicates a nonideal detector system and results in a required increase in patient radiation dose if image quality is to be maintained. The term dose efficiency sometimes has been used to indicate overall efficiency.

Modern commercial systems use one of two detector types: solid-state or gas ionization detectors.

Solid-State Detectors.

Solid-state detectors consist of an array of scintillating crystals and photodiodes, as illustrated in Fig. 12. The scintillators generally are either cadmium tungstate (CdWO4) or a ceramic material made of rare earth oxides, although previous scanners have used bismuth germanate crystals with photomultiplier tubes. Solid-state detectors generally have very high quantum and conversion efficiencies and a large dynamic range.

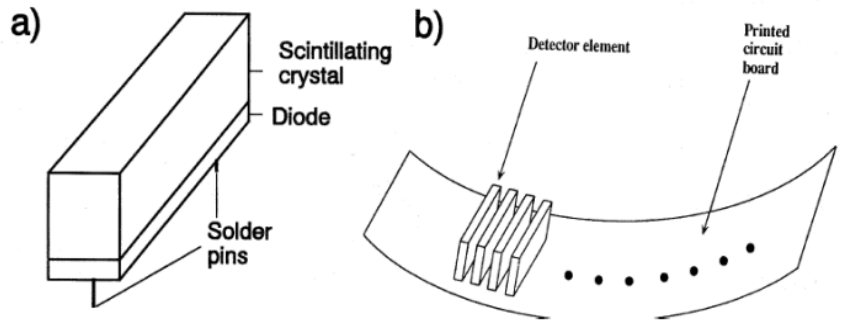

Figure 12. (a) A solid-state detector consists of a scintillating crystal and photodiode combination. (b) Many such detectors are placed side by side to form a detector array that may contain up to 4800 detectors.

Gas Ionization Detectors. Gas ionization detectors, as illustrated in Fig. 13, consist of an array of chambers containing compressed gas (usually xenon at up to 30 atm pressure). A high voltage is applied to tungsten septa between chambers to collect ions produced by the radiation. These detectors have excellent stability and a large dynamic range; however, they generally have a lower quantum efficiency than solid-state detectors.

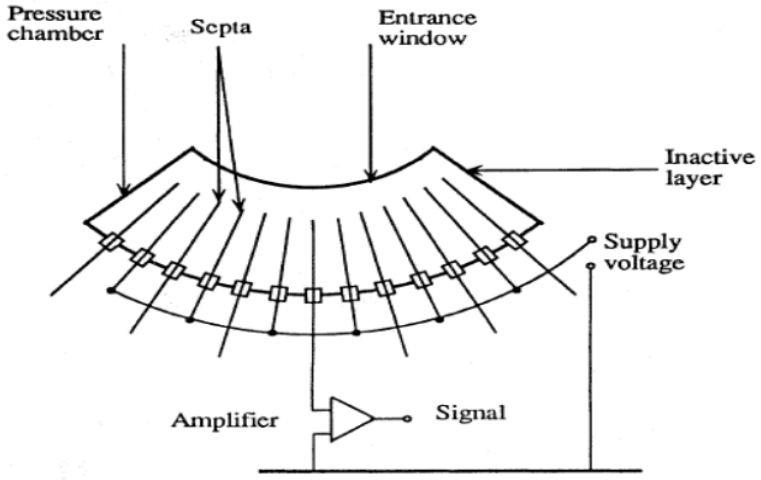

Figure 13 Gas ionization detector arrays consist of high-pressure gas in multiple chambers separated by thin septa. A voltage is applied between alternating septa. The septa also act as electrodes and collect the ions created by the radiation, converting them into an electrical signal.

Data-Acquisition System

The transmitted fraction It /Io in the above equation through an obese patient can be less than 10–4. Thus it is the task of the data-acquisition system (DAS) to accurately measure It over a dynamic range of more than 104 , encode the results into digital values, and transmit the values to the system computer for reconstruction. Some manufacturers use the approach illustrated in Fig. 14, consisting of precision preamplifiers, current-to-voltage converters, analog integrators, multiplexers, and analog-to-digital converters. Alternatively, some manufacturers use the preamplifier to control a synchronous voltage-to-frequency converter (SVFC), replacing the need for the integrators, multiplexers, and analog-to-digital converters [Brunnett, et al., 1990]. The logarithmic conversion required in Eq. (62.2) is performed with either an analog logarithmic amplifier or a digital lookup table, depending on the manufacturer.

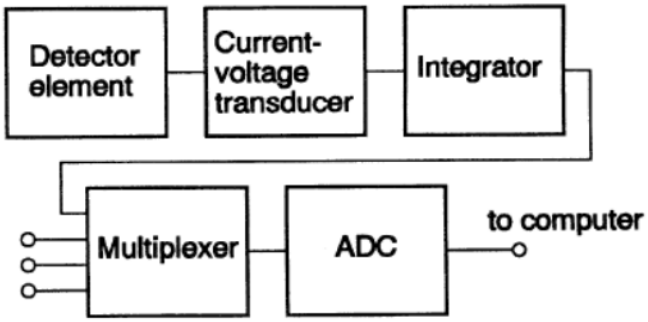

Figure 14 The data-acquisition system converts the electrical signal produced by each detector to a digital value for the computer.

Sustained data transfer rates to the computer are as high as 10 Mbytes/s for some scanners. This can be accomplished with a direct connection for systems having a fixed detector array. However, third-generation slip-ring systems must use more sophisticated techniques. At least one manufacturer uses optical transmitters on the rotating gantry to send data to fixed optical receivers [Siemens, 1989]. Computer System Various computer systems are used by manufacturers to control system hardware, acquire the projection data, and reconstruct, display, and manipulate the tomographic images. A typical system is illustrated in Fig. 15, which uses 12 independent processors connected by a 40-Mbyte/s multibus. Multiple custom array processors are used to achieve a combined computational speed of 200 MFLOPS (million floating-point operations per second) and a reconstruction time of approximately 5 s to produce an image on a 1024 × 1024 pixel display. A simplified UNIX operating system is used to provide a

multitasking, multiuser environment to coordinate tasks. Patient Dose Considerations The patient dose resulting from CT examinations is generally specified in terms of the CT dose index (CTDI) [Felmlee et al., 1989; Rothenberg and Pentlow, 1992], which includes the dose contribution from radiation scattered from nearby slices. A summary of CTDI values, as specified by four manufacturers, is given in Table 1.

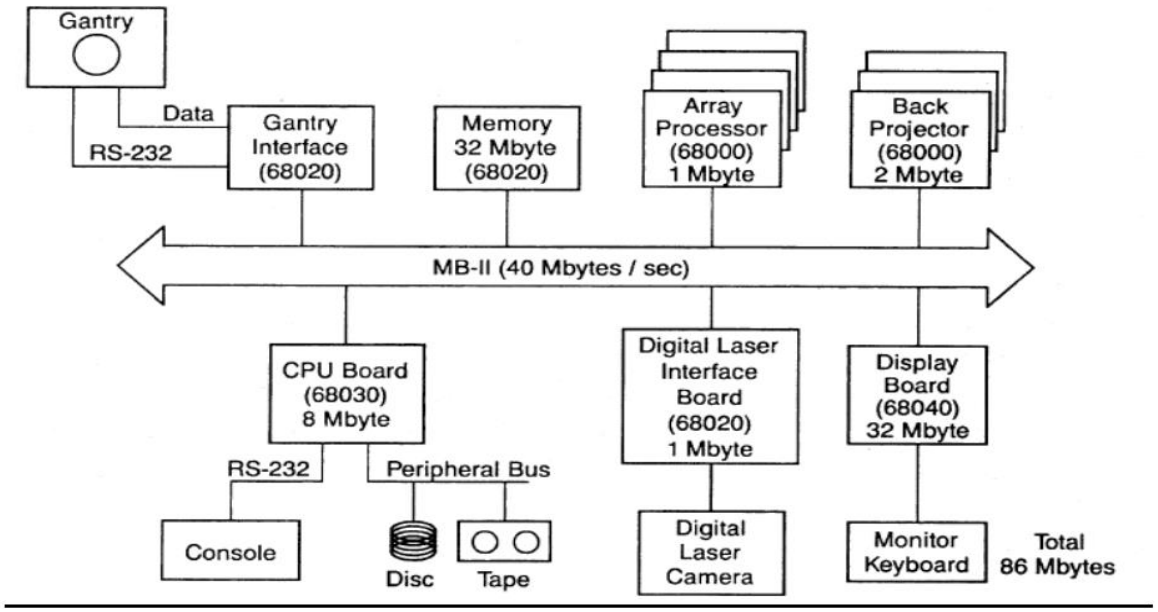

Figure 15 The computer system controls the gantry motions, acquires the x-ray transmission measurements, and reconstructs the final image. The system shown here uses 12 68000-family CPUs. (Courtesy of Picker International, Inc.)

TABLE 1 Summary of the CT Dose Index (CTDI) Values at Two Positions (Center of the Patient and Near the Skin) as Specified by Four CT Manufacturers for Standard Head and Body Scans.

Manufacturer	Detector	kVp	mA	Scan Time (s)	CTDI, center (mGy)	CTDI, skin (mGy)
A, head	Xenon	120	170	2	50	48
A, body	Xenon	120	170	2	14	25
A, head	Solid state	120	170	2	40	40
A, body	Solid state	120	170	2	11	20
B, head	Solid state	130	80	2	37	41
B, body	Solid state	130	80	2	15	34
C, head	Solid state	120	500	2	39	50
C, body	Solid state	120	290	1	12	28
D, head	Solid state	120	200	2	78	78
D, body	Solid state	120	200	2	9	16

1 s and present the reconstructed image on a 1024 × 1024 matrix display within a few seconds. The images are high-quality tomographic "maps" of the x-ray linear attenuation coefficient of the patient tissues.

Defining Terms

Absorption: Some of the incident x-ray energy is absorbed in patient tissues and hence does not contribute to the transmitted beam.

Anode: A tungsten bombarded by a beam of electrons to produce x-rays. In all but one fifth-generation system, the anode rotates to distribute the resulting heat around the perimeter. The anode heat-storage capacity and maximum cooling rate often limit the maximum scanning rates of CT systems.

Attenuation: The total decrease in the intensity of the primary x-ray beam as it passes through the patient, resulting from both scatter and absorption processes. It is characterized by the linear attenuation coefficient.

Computed tomography (CT): A computerized method of producing x-ray tomographic images. Previous names for the same thing include *computerized tomographic imaging, computerized axial tomography (CAT), computer-assisted tomography (CAT),* and *reconstructive tomography (RT).*

Control console: The control console is used by the CT operator to control the scanning operations, image reconstruction, and image display.

Cormack, Dr. Allan MacLeod: A physicist who developed mathematical techniques required in the reconstruction of tomographic images. Dr. Cormack shared the Nobel Prize in Medicine and Physiology with Dr. G. N. Hounsfield in 1979 [Cormack, 1980].

Data-acquisition system (DAS): Interfaces the x-ray detectors to the system computer and may consist of a preamplifier, integrator, multiplexer, logarithmic amplifier, and analog-to-digital converter.

Detector array: An array of individual detector elements. The number of detector elements varies between a few hundred and 4800, depending on the acquisition geometry and manufacturer. Each detector element functions independently of the others.

Fan beam: The x-ray beam is generated at the focal spot and so diverges as it passes through the patient to the detector array. The thickness of the beam is generally selectable between 1.0 and 10 mm and defines the slice thickness.

Focal spot: The region of the anode where x-rays are generated.

Focused septa: Thin metal plates between detector elements which are aligned with the focal spot so that the primary beam passes unattenuated to the detector elements, while scattered x-rays which normally travel in an altered direction are blocked.

Gantry: The largest component of the CT installation, containing the x-ray tube, collimators, detector array, DAS, other control electronics, and the mechanical components required for the scanning motions.

Helical scanning: The scanning motions in which the x-ray tube rotates continuously around the patient while the patient is continuously translated through the fan beam. The focal spot therefore traces a helix around the patient. Projection data are obtained which allow the reconstruction of multiple contiguous images. This operation is sometimes called *spiral, volume,* or *three-dimensional* CT scanning.

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Hounsfield, Dr. Godfrey Newbold: An engineer who developed the first practical CT instrument in 1971. Dr. Hounsfield received the McRobert Award in 1972 and shared the Nobel Prize in Medicine and Physiology with Dr. A. M. Cormack in 1979 for this invention [Hounsfield, 1980].
Image plane: The plane through the patient that is imaged. In practice, this plane (also called a *slice*) has a selectable thickness between 1.0 and 10 mm centered on the image plane.
Pencil beam: A narrow, well-collimated beam of x-rays.
Projection data: The set of transmission measurements used to reconstruct the image.
Reconstruct: The mathematical operation of generating the tomographic image from the projection data.
Scan time: The time required to acquire the projection data for one image, typically 1.0 s.
Scattered radiation: Radiation that is removed from the primary beam by a scattering process. This radiation is not absorbed but continues along a path in an altered direction.
Slice: See Image plane.
Spiral scanning: See Helical scanning.
Three-dimensional imaging: See Helical scanning.
Tomography: A technique of imaging a cross-sectional slice.
Volume CT: See Helical scanning.
X-ray detector: A device that absorbs radiation and converts some or all of the absorbed energy into a small electrical signal.

X-ray linear attenuation coefficient μ: Expresses the relative rate of attenuation of a radiation beam as it passes through a material. The value of μ depends on the density and atomic number of the material and on the x-ray energy. The units of μ are cm^{-1}.
X-ray source: The device that generates the x-ray beam. All CT scanners are rotating-anode bremsstrahlung x-ray tubes except one-fifth generation system, which uses a unique scanned electron beam and a strip anode.
X-ray transmission: The fraction of the x-ray beam intensity that is transmitted through the patient without being scattered or absorbed. It is equal to I_t/I_o in Eq. , can be determined by measuring the beam intensity both with (I_t) and without (I_o) the patient present, and is expressed as a fraction. As a rule of thumb, n^2 independent transmission measurements are required to reconstruct an image with an $n \times n$ sized pixel matrix.

MRI:

Magnetic resonance imaging (MRI), **nuclear magnetic resonance imaging (NMRI)**, or **magnetic resonance tomography (MRT)** is a medical imaging technique used in radiology to visualize detailed internal structures. MRI makes use of the property of nuclear magnetic resonance (NMR) to image nuclei of atoms inside the body.

An MRI machine uses a powerful magnetic field to align the magnetization of some atomic nuclei in the body, and radio frequency fields to systematically alter the alignment of this magnetization. This causes the nuclei to produce a rotating magnetic field detectable by the scanner—and this information is recorded to construct an image of the scanned area of the body.[1]:36 Magnetic field gradients cause nuclei at different locations to rotate at different speeds. By using gradients in different directions 2D images or 3D volumes can be obtained in any arbitrary orientation.

MRI provides good contrast between the different soft tissues of the body, which makes it especially useful in imaging the brain, muscles, the heart, and cancers compared with other medical imaging techniques such as computed tomography (CT) or X-rays. Unlike CT scans or traditional X-rays, MRI does not use ionizing radiation.

How MRI works

The body is largely composed of water molecules. Each water molecule has two hydrogen nuclei or protons. When a person is inside the powerful magnetic field of the scanner, the average magnetic moment of many protons becomes aligned with the direction of the field. A radio frequency transmitter is briefly turned on, producing a varying electromagnetic field. This electromagnetic field has just the right frequency, known as the resonance frequency, to be absorbed and flip the spin of the protons in the magnetic field. After the electromagnetic field is turned off, the spins of the protons return to thermodynamic equilibrium and the bulk magnetization becomes re-aligned with the static magnetic field. During this relaxation, a radio frequency signal is generated, which can be measured with receiver coils.

Information about the origin of the signal in 3D space can be learned by applying additional magnetic fields during the scan. These fields, generated by passing electric currents through gradient coils, make the magnetic field strength vary depending on the position within the magnet. Because this makes the frequency of the released radio signal also dependent on its origin in a predictable manner, the distribution of protons in the body can be mathematically recovered from the signal, typically by the use of the inverse Fourier transform.

Protons in different tissues return to their equilibrium state at different relaxation rates. Different tissue variables, including spin density, T_1 and T_2 relaxation times, and flow and spectral shifts can be used to construct images.[2] By changing the settings on the scanner, this effect is used to create contrast between different types of body tissue or between other properties, as in fMRI and diffusion MRI.

MRI contrast agents may be injected intravenously to enhance the appearance of blood vessels, tumors or inflammation. Contrast agents may also be directly injected into a joint in the case of arthrograms, MRI images of joints. Unlike CT, MRI uses no ionizing radiation and is generally a very safe procedure. Nonetheless the strong magnetic fields and radio pulses can affect metal implants, including cochlear implants and cardiac pacemakers. In the case of cochlear implants, the US FDA has approved some implants for MRI compatibility. In the case of cardiac pacemakers, the results can sometimes be lethal,[3] so patients with such implants are generally not eligible for MRI.

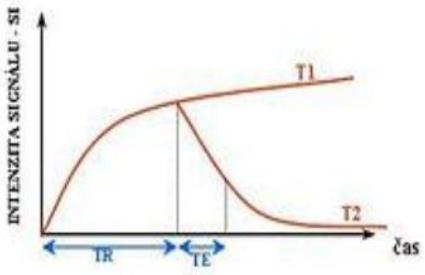
Since the gradient coils are within the bore of the scanner, there are large forces between them and the main field coils, producing most of the noise that is heard during operation. Without efforts to damp this noise, it can approach 130 decibels (dB) with strong fields [4] (see also the subsection on acoustic noise).

MRI is used to image every part of the body, and is particularly useful for tissues with many hydrogen nuclei and little density contrast, such as the brain, muscle, connective tissue and most tumors.

Applications

In clinical practice, MRI is used to distinguish pathologic tissue (such as a brain tumor) from normal tissue. One advantage of an MRI scan is that it is harmless to the patient. It uses strong magnetic fields and non-ionizing radiation in the radio frequency range, unlike CT scans and traditional X-rays, which both use ionizing radiation.

While CT provides good spatial resolution (the ability to distinguish two separate structures an arbitrarily small distance from each other), MRI provides comparable resolution with far better contrast resolution (the ability to distinguish the differences between two arbitrarily similar but not identical tissues). The basis of this ability is the complex library of *pulse sequences* that the modern medical MRI scanner includes, each of which is optimized to provide *image contrast* based on the chemical sensitivity of MRI.



Effects of TR and TE on MR signal.

For example, with particular values of the *echo time* (T_E) and the *repetition time* (T_R), which are basic parameters of image acquisition, a sequence takes on the property of T_2-weighting. On a T_2-weighted scan, water- and fluid-containing tissues are bright (most modern T_2 sequences are actually *fast* T_2 sequences) and fat-containing tissues are dark. The reverse is true for T_1-weighted images. Damaged tissue tends to develop edema, which makes a T_2-weighted sequence sensitive for pathology, and generally able to distinguish pathologic tissue from normal tissue. With the addition of an additional radio frequency pulse and additional manipulation of the magnetic gradients, a T_2-weighted sequence can be converted to a **FLAIR** sequence, in which free water is now dark, but edematous tissues remain bright. This sequence in particular is currently the most sensitive way to evaluate the brain for demyelinating diseases, such as multiple sclerosis.

The typical MRI examination consists of 5–20 sequences, each of which are chosen to provide a particular type of information about the subject tissues. This information is then synthesized by the interpreting physician.

Basic MRI scans

T_1-weighted MRI

T_1-weighted scans refer to a set of standard scans that depict differences in the spin-lattice (or T_1) relaxation time of various tissues within the body. T_1 weighted images can be acquired using either spin-echo or gradient-echo sequences. T_1-weighted contrast can be increased with the application of an inversion recovery RF pulse. Gradient-echo based T_1-weighted sequences can be acquired very rapidly because of their ability to use short inter-pulse repetition times (T_R). T_1-weighted sequences are often collected before and after infusion of T_1-shortening MRI contrast agents. In the brain T_1-weighted scans provide appreciable contrast between gray and white matter. In the body, T_1 weighted scans work well for differentiating fat from water - with water appearing darker and fat brighter.[24]

T_2-weighted MRI

T_2-weighted scans are another basic type. Like the T_1-weighted scan, fat is differentiated from water - but in this case fat shows darker, and water lighter. For example, in the case of cerebral and spinal study, the CSF (cerebrospinal fluid) will be lighter in T_2-weighted images. These scans are therefore particularly well suited to imaging edema, with long T_E and long T_R. Because the spin echo sequence is less susceptible to inhomogeneities in the magnetic field, these images have long been a clinical workhorse.

T^*_2-weighted MRI

T^*_2 (pronounced "T 2 star") weighted scans use a gradient echo (GRE) sequence, with long T_E and long T_R. The gradient echo sequence used does not have the extra refocusing pulse used in spin echo so it is subject to additional losses above the normal T_2 decay (referred to as T_2'), these taken together are called T^*_2. This also makes it more prone to susceptibility losses at air/tissue boundaries, but can increase contrast for certain types of tissue, such as venous blood.

Spin density weighted MRI

Spin density, also called proton density, weighted scans try to have no contrast from either T_2 or T_1 decay, the only signal change coming from differences in the amount of available spins

(hydrogen nuclei in water). It uses a spin echo or sometimes a gradient echo sequence, with short T_E and long T_R.

Specialized MRI scans

Diffusion MRI

Diffusion MRI measures the diffusion of water molecules in biological tissues.[25] In an isotropic medium (inside a glass of water for example), water molecules naturally move randomly according to turbulence and Brownian motion. In biological tissues however, where the Reynolds number is low enough for flows to be laminar, the diffusion may be anisotropic. For example, a molecule inside the axon of a neuron has a low probability of crossing the myelin membrane. Therefore the molecule moves principally along the axis of the neural fiber. If it is known that molecules in a particular voxel diffuse principally in one direction, the assumption can be made that the majority of the fibers in this area are going parallel to that direction.

The recent development of diffusion tensor imaging (DTI)[7] enables diffusion to be measured in multiple directions and the fractional anisotropy in each direction to be calculated for each voxel. This enables researchers to make brain maps of fiber directions to examine the connectivity of different regions in the brain (using tractography) or to examine areas of neural degeneration and demyelination in diseases like Multiple Sclerosis.

Another application of diffusion MRI is diffusion-weighted imaging (DWI). Following an ischemic stroke, DWI is highly sensitive to the changes occurring in the lesion.[26] It is speculated that increases in restriction (barriers) to water diffusion, as a result of cytotoxic edema (cellular swelling), is responsible for the increase in signal on a DWI scan. The DWI enhancement appears within 5–10 minutes of the onset of stroke symptoms (as compared with computed tomography, which often does not detect changes of acute infarct for up to 4–6 hours) and remains for up to two weeks. Coupled with imaging of cerebral perfusion, researchers can highlight regions of "perfusion/diffusion mismatch" that may indicate regions capable of salvage by reperfusion therapy.

Like many other specialized applications, this technique is usually coupled with a fast image acquisition sequence, such as echo planar imaging sequence.

Magnetization transfer MRI

Magnetization transfer (MT) refers to the transfer of longitudinal magnetization from free water protons to hydration water protons in NMR and MRI.

In magnetic resonance imaging of molecular solutions, such as protein solutions, two types of water molecules, free (bulk) and hydration (bound), are found. Free water protons have faster average rotational frequency and hence less fixed water molecules that may cause local field inhomogeneity. Because of this uniformity, most free water protons have resonance frequency lying narrowly around the normal proton resonance frequency of 63 MHz (at 1.5 teslas). This also results in slower transverse magnetization dephasing and hence longer T_2. Conversely, hydration water molecules are slowed down by interaction with solute molecules and hence create field inhomogeneities that lead to wider resonance frequency spectrum.

In free liquids, protons, which may be viewed classically as small magnetic dipoles, exhibit translational and rotational motions. These moving dipoles disturb the surrounding magnetic field however on long enough time-scales (which may be nanoseconds) the average field caused by the motion of protons is zero. This is known as “motional averaging” or narrowing and is characteristic of protons moving freely in liquid. On the other hand, protons bound to macromolecules, such as proteins, tend to have a fixed orientation and so the average magnetic field in close proximity to such structures does not average to zero. The result is a spatial pattern in the magnetic field that gives rise to a residual dipolar coupling (range of precession frequencies) for the protons experiencing the magnetic field. The wide frequency distribution appears as a broad spectrum that may be several kHz wide. The net signal from these protons disappears very quickly, in inverse proportion to the width, due to the loss of coherence of the spins, i.e. T2 relaxation. Due to exchange mechanisms, such as spin transfer or proton chemical exchange, the (incoherent) spins bound to the macromolecules continually switch places with (coherent) spins in the bulk media and establish a dynamic equilibrium.

Magnetization transfer: Although there is no measurable signal from the bound spins, or the bound spins that exchange into the bulk media, their longitudinal magnetization is preserved and may recover only via the relatively slow process of T1 relaxation. If the longitudinal magnetization of just the bound spins can be altered, then the effect can be measured in the spins of the bulk media due to the exchange processes. The magnetization transfer sequence applies RF saturation at a frequency that is far off resonance for the narrow line of bulk water but still on resonance for the bound protons with a spectral linewidth of kHz. This causes saturation of the bound spins which exchange into the bulk water, resulting in a loss of longitudinal magnetization and hence signal decrease in the bulk water. This provides an indirect measure of

macromolecular content in tissue. Implementation of magnetization transfer involves choosing suitable frequency offsets and pulse shapes to saturate the bound spins sufficiently strongly, within the safety limits of specific absorption rate for RF irradiation.

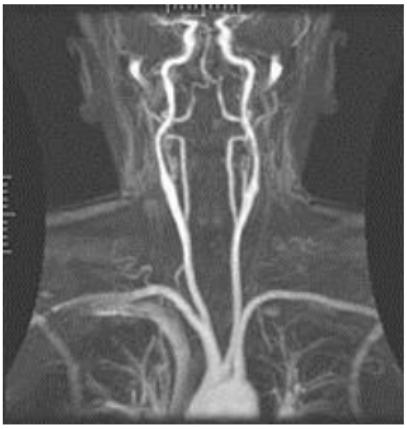
T1rho MRI

T1ρ (T1rho): Molecules have a kinetic energy that is a function of the temperature and is expressed as translational and rotational motions, and by collisions between molecules. The moving dipoles disturb the magnetic field but are often extremely rapid so that the average effect over a long time-scale may be zero. However, depending on the time-scale, the interactions between the dipoles do not always average away. At the slowest extreme the interaction time is effectively infinite and occurs where there are large, stationary field disturbances (e.g. a metallic implant). In this case the loss of coherence is described as a "static dephasing". T2* is a measure of the loss of coherence in an ensemble of spins that include all interactions (including static dephasing). T2 is a measure of the loss of coherence that excludes static dephasing, using an RF pulse to reverse the slowest types of dipolar interaction. There is in fact a continuum of interaction time-scales in a given biological sample and the properties of the refocusing RF pulse can be tuned to refocus more than just static dephasing. In general, the rate of decay of an ensemble of spins is a function of the interaction times and also the power of the RF pulse. This type of decay, occurring under the influence of RF, is known as T1ρ. It is similar to T2 decay but with some slower dipolar interactions refocused as well as the static interactions, hence $T1\rho \geq T2$.[27]

Fluid attenuated inversion recovery (FLAIR)

Fluid Attenuated Inversion Recovery (FLAIR)[28] is an inversion-recovery pulse sequence used to null signal from fluids. For example, it can be used in brain imaging to suppress cerebrospinal fluid (CSF) so as to bring out the periventricular hyperintense lesions, such as multiple sclerosis (MS) plaques. By carefully choosing the inversion time TI (the time between the inversion and excitation pulses), the signal from any particular tissue can be suppressed.

Magnetic resonance angiography

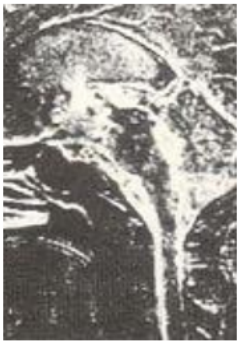


Magnetic resonance angiography (MRA) generates pictures of the arteries to evaluate them for stenosis (abnormal narrowing) or aneurysms (vessel wall dilatations, at risk of rupture). MRA is often used to evaluate the arteries of the neck and brain, the thoracic and abdominal aorta, the renal arteries, and the legs (called a "run-off"). A variety of techniques can be used to generate the pictures, such as administration of a paramagnetic contrast agent (gadolinium) or using a technique known as "flow-related enhancement" (e.g. 2D and 3D time-of-flight sequences), where most of the signal on an image is due to blood that recently moved into that plane, see also FLASH MRI. Techniques involving phase accumulation (known as phase contrast angiography) can also be used to generate flow velocity maps easily and accurately. Magnetic resonance venography (MRV) is a similar procedure that is used to image veins. In this method, the tissue is now excited inferiorly, while signal is gathered in the plane immediately superior to the

Magnetic resonance gated intracranial CSF dynamics (MR-GILD)

Magnetic resonance gated intracranial cerebrospinal fluid (CSF) or liquor dynamics (MR-GILD) technique is an MR sequence based on bipolar gradient pulse used to demonstrate CSF pulsatile flow in ventricles, cisterns, aqueduct of Sylvius and entire intracranial CSF pathway. It is a method for analyzing CSF circulatory system dynamics in patients with CSF obstructive lesions such as normal pressure hydrocephalus. It also allows visualization of both arterial and venous pulsatile blood flow in vessels without use of contrast agents.[30][31]

Diastolic time data acquisition (DTDA). Systolic time data acquisition (STDA).

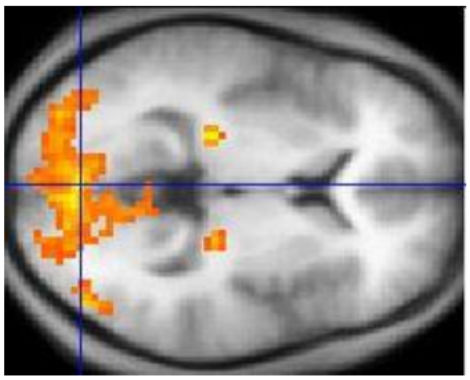


Magnetic resonance spectroscopy

Magnetic resonance spectroscopy (MRS) is used to measure the levels of different metabolites in body tissues. The MR signal produces a spectrum of resonances that correspond to different molecular arrangements of the isotope being "excited". This signature is used to diagnose certain metabolic disorders, especially those affecting the brain,[32] and to provide information on tumor metabolism.[33]

Magnetic resonance spectroscopic imaging (MRSI) combines both spectroscopic and imaging methods to produce spatially localized spectra from within the sample or patient. The spatial resolution is much lower (limited by the available SNR), but the spectra in each voxel contains information about many metabolites. Because the available signal is used to encode spatial and spectral information, MRSI requires high SNR achievable only at higher field strengths (3 T and above).

Functional MRI



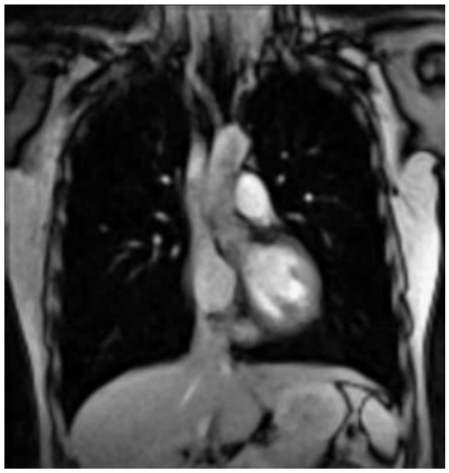
A fMRI scan showing regions of activation in orange, including the primary visual cortex (V1, BA17).

NEUROSCIENCE

Functional MRI (fMRI) measures signal changes in the brain that are due to changing neural activity. The brain is scanned at low resolution but at a rapid rate (typically once every 2–3 seconds). Increases in neural activity cause changes in the MR signal via T^*_2 changes;[34] this mechanism is referred to as the BOLD (blood-oxygen-level dependent) effect. Increased neural activity causes an increased demand for oxygen, and the vascular system actually overcompensates for this, increasing the amount of oxygenated hemoglobin relative to deoxygenated hemoglobin. Because deoxygenated hemoglobin attenuates the MR signal, the vascular response leads to a signal increase that is related to the neural activity. The precise nature of the relationship between neural activity and the BOLD signal is a subject of current research. The BOLD effect also allows for the generation of high resolution 3D maps of the venous vasculature within neural tissue.

While BOLD signal is the most common method employed for neuroscience studies in human subjects, the flexible nature of MR imaging provides means to sensitize the signal to other aspects of the blood supply. Alternative techniques employ arterial spin labeling (ASL) or weight the MRI signal by cerebral blood flow (CBF) and cerebral blood volume (CBV). The CBV method requires injection of a class of MRI contrast agents that are now in human clinical trials. Because this method has been shown to be far more sensitive than the BOLD technique in preclinical studies, it may potentially expand the role of fMRI in clinical applications. The CBF method provides more quantitative information than the BOLD signal, albeit at a significant loss of detection sensitivity.

Real-time MRI



Real-time MRI refers to the continuous monitoring (“filming”) of moving objects in real time. While many different strategies have been developed over the past two decades, a recent development reported a real-time MRI technique based on radial FLASH and iterative reconstruction that yields a temporal resolution of 20 to 30 milliseconds for images with an in-plane resolution of 1.5 to 2.0 mm. The new method promises to add important information about diseases of the joints and the heart. In many cases MRI examinations may become easier and more comfortable for patients.

Interventional MRI

The lack of harmful effects on the patient and the operator make MRI well-suited for "interventional radiology", where the images produced by a MRI scanner are used to guide minimally invasive procedures. Of course, such procedures must be done without *any* ferromagnetic instruments.

A specialized growing subset of interventional MRI is that of intraoperative MRI in which the MRI is used in the surgical process. Some specialized MRI systems have been developed that allow imaging concurrent with the surgical procedure. More typical, however, is that the surgical procedure is temporarily interrupted so that MR images can be acquired to verify the success of the procedure or guide subsequent surgical work.