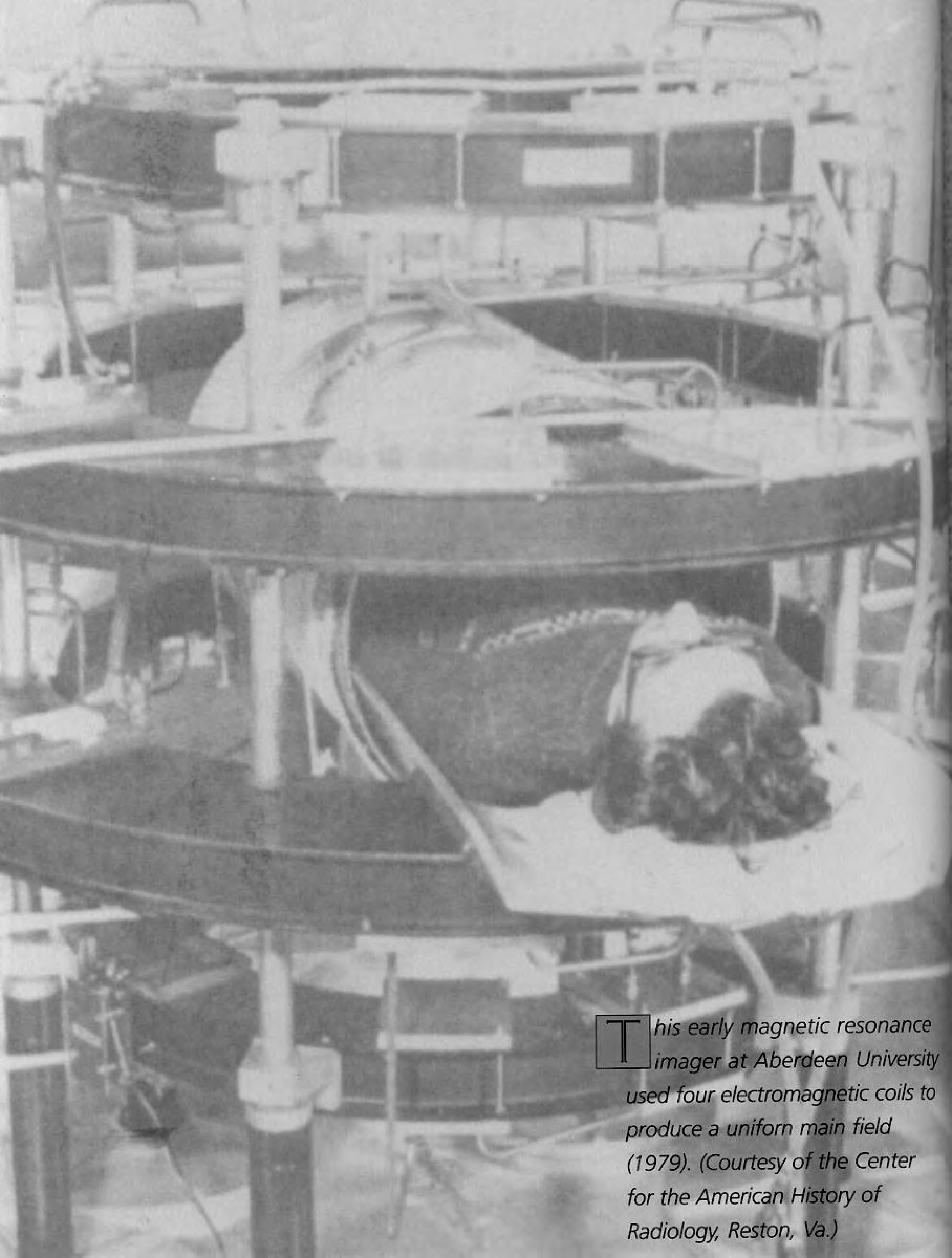


This early magnetic resonance imager at Aberdeen University used four electromagnetic coils to produce a uniforn main field (1979). (Courtesy of the Center for the American History of Radiology, Reston, Va.)

CHAPTER NINETEEN

Magnetic Resonance Imaging

Thomas F. Meaney, M.D.

Magnetic resonance imaging is considered a special adaptation of nuclear magnetic resonance (NMR), long studied by chemists and physicists. As the field of medical NMR developed, clinical investigators, while recognizing the historical importance of the term nuclear magnetic resonance, suggested the terminology magnetic resonance imaging (MRI) as more appropriate for the imaging applications of NMR.[1,2] Gradually the term MRI has gained almost universal acceptance in the medical setting. The 1980s witnessed the introduction and dissemination of clinical MRI units, refinements in hardware and software, clinical trials, and incorporation of MRI as a standard modality in the diagnosis of many diseases. During the 1990s the role of MRI has continued to expand as new applications have emerged, often based on technological developments.

This chapter provides historical background and a brief discussion of the physical principles and technical developments. Since the physical principles of MRI differed in many respects from the educational background of most physicians and scientists, major educational programs were instituted. Human safety considerations arising from strong magnetic fields and rapid repetition of radiofrequency pulses led to restrictions on locating the magnets. Regulatory and cost considerations prompted the development of mobile units. In an effort to increase accuracy in diagnosis of certain diseases, pharmacologic agents were introduced to enhance contrast in the images, and pulse sequences were developed to visualize the vascular system without the need for exogenous contrast agents. A general discussion of clinical applications is included, and the reader is referred to other chapters where applications in specific organ systems are discussed in more detail. The current investigations of physicians and scientists to extend the field to include functional and chemical parameters provide insight into future uses of this growing technology.

Historical Background and Physical Principles

MRI was founded on the pioneering work of Felix Block and Edward Purcell and their co-workers in the field of NMR.[3,4] These two independent groups discovered NMR almost simultaneously. Their investigations, for which they received the Nobel Prize in 1952, focused on transitions of magnetic nuclei and magnetic induction in bulk matter. In the next few years, NMR was detected for most elements in the periodic table. The initial applications in physics and chemistry widened to the biological sciences, where the elements phosphorus, carbon, and hydrogen received the primary attention of investigators.

Although a detailed description of the physical principles of the NMR phenomenon is beyond the scope of this chapter, a brief discussion of its historical development is appropriate. Because of the abundance of protons in human tissues, most clinical applications for imaging rely on the hydrogen atom and its nucleus, the proton. Spinning protons (possessing small electrical charges) in magnetic moments will align with an external magnetic field and, when subjected to radiofrequency (RF) energy of a specific frequency (termed the Larmour frequency), will absorb the energy and reverse their alignment. Once excited, they may then release the absorbed energy and relax back to their original alignment. The emitted RF energy is detectable by an external receiver. Through the use of spatial encoding magnetic field gradients and subsequent Fourier transformation, digital signal data from a plane or a volume of tissue in transverse, sagittal, or coronal orientations are collected.

The concept of producing images of data derived from the NMR experiment was first advanced by Lauterbur (Fig. 19.1), who constructed an image from a set of projections.[5] He used the term *zeugmatography* to indicate that formation of an image required two irradiating fields, the exciting RF pulse and a gradient magnetic field. His efforts and refinements by others permitted spatial localization of protons as they react to external magnetic fields when excited by superimposed RF energy, reflecting the differences in hydrogen concentration and their relaxation times in tissues.

The rate at which protons relax in returning to their original state is determined by relaxation times termed, T1 (spin-lattice relaxation time or thermal relaxation time) and T2 (spin-spin or transverse relaxation time), which depend on the chemical and physical characteristics of tissues. The production of images of varying tissue contrast depends on pulse sequence strategies, which consist of timing of the application of RF and gradient fields, repetitions of the sequence (TR), and the time-to-echo delay (TE) for collecting the data, as well as other parameters that emphasize the relaxation times, T1 and T2, and the proton density of tissues or flowing blood.

Investigators pursued studies to determine the applications of NMR to human pathology. Some of these studies demonstrated that phosphorus spectroscopy could reveal the metabolism of normal and diseased muscle.[6,7] Proton imaging, at first *in vitro* and later *in vivo*, quickly followed.[8,9]

The Fonar Corporation introduced the first commercial unit, designed by Raymond Damadian, at the meeting of the American Roentgen Ray Society in June 1980. Six other commercial companies presented works-in-progress the following year. Commercial units were produced by Picker, Diasonics, Technicare, General Electric, and Siemens, with Philips, Toshiba, Elscint, Hitachi, Resonex, and others quickly following.

While the basic principles of NMR differ significantly from computed tomography (CT), the extensive research

Fig. 19.1 Paul Lauterbur. (Author's collection)

MRI is based on physical principles completely different from Röntgen rays (X rays). X rays passing through the body are absorbed by tissues and objects to varying degrees to produce an image on film or other receptor. In MRI, the image results from the magnetic alignment of the hydrogen protons when subjected to an external magnetic field and the resultant change in their magnetic moment when influenced by a radiofrequency pulse. A radiofrequency signal is given off and detected by a radio wave receiver. Because of the ability of the equipment and the operator to vary the many technical factors, the appearance of the resultant images is almost unlimited. It is this potential that is responsible for the widespread early acceptance of the technology and which sustains its continued development and applications to medical diagnosis.

Today MR data is combined into three-dimensional data sets which can be displayed to give the impression of a solid object. Here MR data and flow data are used to show different views of a tumor and blood vessels in a pediatric patient. (Courtesy of Stephen Balter, Ph.D.)

by Hounsfield (in CT) and the subsequent refinements in instrumentation and image reconstruction techniques helped accelerate the production of clinically relevant systems for NMR.[10] The radiologic community quickly focused on image quality, comparing MR with CT images in various organs and body regions. Measurement of the relaxation values, T1 and T2, initially created hopes that such measurements might be disease-specific, even for differentiation of benign and malignant tumors as had been reported for *in vitro* studies.[11] Values of T1 and T2 for normal and pathological tissues were accumulated in experimental models at a variety of field strengths.[12,13] Several early clinical reports of MRI included the relaxation values for the normal and abnormal tissues in the image. As experience grew, however, it became obvious that there was significant overlap between benign and malignant pathologies, and such numerical assignments were of minimal value in clinical diagnosis.[14]

Technical Developments

Magnets

Early investigators of biological applications worked with magnets of small bore and limited field strength. Even so, instruments (magnets) like those of the Oxford Instrument Company allowed insertion of the human arm and leg into the unit, and images and NMR spectra were obtained for phosphorus, carbon, and hydrogen. (Note: Oxford Instrument Company produced magnets only and never produced a clinical system.) *In vivo* images of extremity tumors were obtained on these units.[15] These efforts prompted the development of magnets with larger apertures and uniform fields to permit insertion of other areas of the human body including the head and, later, the entire human torso (Fig. 19.2). The dependence of high-quality spectra on the strength of the external magnetic field limited clinical spectroscopy studies as well. Small-bore magnets with relatively high fields were constructed, but they could not accommodate body parts larger than an extremity or the head. Two types of magnets were constructed for whole body scanning.

Several types of magnets were considered for use in MRI.[16] Although permanent and iron-core magnets were the simplest, their use in human imaging was limited by the size of the magnet required to accept the human torso and provide field strength above 0.5 tesla. Researchers initially investigated air-core resistive magnets.[17] This technology continues to be used today by a small segment of the market. These magnets can produce fields up to 0.2 gauss but require high power levels to drive the magnet and water cooling to maintain a stable field. The capital costs of air-core resistive magnets of relatively low field strength are low compared with those of superconductive magnets. Before 1982 there were no superconductive magnets with adequate bore to accept the human torso for clinical MRI. Superconductive magnets of small bore were available for chemical and physical research.

In 1982, driven by the search for improved signal quality and thus shorter time required for patient examinations, superconductive magnets of incrementally higher field strengths, for example 0.5 to 2.0 tesla, were produced. Image quality and thus spatial resolution depend largely on the signal-to-noise ratio which is directly related to field strength or, on signal averaging, which is clinically related to scan time. Superconductivity is based on the principle that some metals and alloys lose resistance to current flow when cooled to near absolute zero. They require the use of wire windings of alloys of niobium and titanium within cryostats containing liquid helium surrounded by a thermal blanket of liquid nitrogen. There was strong debate on the merits of the superconductive magnets because of expense. Not only were the capital costs for these higher field magnets greater, but the cryogens, nitrogen, and expensive helium required regular replenishment. The higher fields associated with superconductive systems added to the problems of magnet siting. By 1984, however, it was clear that the advantages of these units outweighed their disadvantages, and this type of magnet now dominates the market (Figs. 19.3a and b).[18]

Universal acceptance of an optimal field strength within limits of human safety remains elusive, as advocates continue to debate the merits of a particular type of mag-

◄ **Fig. 19.2 First large bore superconductive 1.5 tesla magnet. Oxford Instrument Co. The patient table is not shown in the photograph. (Author's collection)**

Fig. 19.3 Improvement in image quality. Two different patients with Chiari I malformation. a. 1985 image made at 0.6 tesla. b. 1991 image at 1.5 tesla. (Courtesy, Division of Radiology, Cleveland Clinic Foundation)

net and field strength for general and specific applications (Fig. 19.4).

Radiofrequency Coils

In human MRI applications, the signal is usually transmitted and collected by large receiver coils surrounding the bore of the magnet. In an effort to improve the signal-to-noise ratio and resolution in the image, so-called surface coils were developed for use close to the surface of the body.[19,20] Some are designed to both transmit and receive the RF pulse, while others use the built-in body coil as a transmitter and the surface coil as a receiver. Some of these coils are designed for specific body regions such as the joints, spine, and brain, and some for intraluminal positioning in the vascular system and transrectal for prostate or transvaginal for urethral imaging. Excellent detail has been obtained in anatomical areas near the body surface even though the field of view is reduced and the signal falls off as the distance from the coil increases. Subsequent designs have incorporated the use of multichannel receiver (also known as phased array) coils, which impose additional hardware and software constraints on the system.[21]

Gradients

Critical to imaging of the human body is the time required for acquisition of data. To allow for adequate ratio of signal to noise, data must be collected over time. During this period, respiratory, cardiovascular, and patient motion degrade the images to variable degrees, depending on the body part being examined. Because the magnitude of motion is less in the head and extremities than in the chest and abdomen, early workers concentrated on the study of these organs.

The wide range of technical factors employed in production of MR images described previously were exploited in the search for new pulse sequences to improve the quality of images and to reduce examination times.[22] To indicate variations in the sequences, many were described using acronyms, such as GRASS, FLASH, or FISP. In large measure these innovations were (and continue to be) dependent on the performance of gradient hardware and ingenious new techniques in data collection and image reconstruction. Newer

Fig. 19.4 Open architecture design of a 0.2 tesla resistive magnet (Siemens Magnetom) which provides ready access to the patient and serves to reduce claustrophobia. (Author's collection)

scanners offer active and passive gradient shielding for eddy current compensation, even in the presence of ever shorter gradient ramp-times and higher gradient peaks, i.e. echoplanar imaging (EPI). As a result, imaging times for certain applications have decreased to less than a second, while other applications can be accomplished within a breath-holding period. These developments and others paved the way for imaging of the cardiovascular system.

Contrast Materials

In an effort to further improve image contrast, particularly of pathological tissues, a variety of magnetopharmaceuticals were proposed, and a few have been implemented. These paramagnetic agents function by altering local magnetic environments.[23] The gadolinium ion, in the form of gadolinium-DTPA (Gd-DTPA) administered intravenously, was found to enhance proton relaxation and has proved particularly useful in the brain, where it serves as a marker of an abnormal blood brain barrier. Administered orally, Gd-DPTA was found useful in labeling the bowel in abdominal and pelvic examinations. Other agents were proposed for specific areas such as the hepatobiliary and reticuloendothelial system, and studies of clinical safety and efficacy continue. The high cost of clinically approved contrast agents (e.g. Gd-DPTA) raised the overall cost of the examination, and the benefits in diagnostic accuracy had to be weighed against the added expense.

MRI Safety

As powerful large-bore magnets (up to 5 tesla for human use) developed, concerns about mechanical and biological safety grew. The attractive force of the magnetic field on ferromagnetic objects in the vicinity of the field posed dangers to both patients and workers from potential projectiles. Physical environments free of ferromagnetic materials were created to reduce these dangers. Some installations used metal detectors as a precautionary measure. The mechanical dangers extended to ferromagnetic objects within patients when they were placed in the external field. Extensive studies were conducted on various materials that might be encountered within patients, such as metallic sutures, metal implants, and aneurysm clips that might move or twist in the magnetic field.[24]

Potential biological effects were identified relating to the static magnetic field, the time-varying gradient fields, and RF heating effects.[25,26,27] Most investigators agreed that static magnetic fields of the strength used clinically posed no substantial harmful effects, but the rapid time-varying magnetic fields used in gradients switching raised concerns about induced currents. Power deposition from RF magnetic fields associated with the RF transmitter coil can cause heating within the body. Physiologic effects of induced currents such as cardiac arrhythmias, nerve and muscle stimulation, visual disturbances (magnetophosphenes), and bone healing were investigated. The Bureau of Radiological Health of the United States Food and Drug Administration (FDA) subsequently established guidelines for human examinations.[28]

Patients with cardiac pacemakers were found to be at serious risk if placed within or in proximity to the static field, because the sensitivity of pacemakers to magnetic fields may cause them to malfunction. In addition, pacemakers have conductive leads that may contain ferromagnetic components. Implanted neuro-stimulators, cochlear implants, foreign metallic fragments in the eye, and some intracranial aneurysm clips remain contraindications. Pregnancy is considered a relative contraindication, especially in the first trimester. Even though scientific documentation of possible complications has not been conclusively identified, investigators voluntarily refrain from examining pregnant women.

Site Considerations

Safety considerations and optimum performance of MRI units have dictated restrictions on the physical location of units, particularly for higher field units. The magnet can affect its immediate environment, and the environment can affect the MRI system and the process of imaging. In clinical environments such as hospitals, the size of the magnet itself and the presence of large iron structures initially precluded the location of early nonshielded units in most existing radiology departments. It was also important to limit the field to an area where personnel and magnetically sensitive equipment might be affected. Because RF receivers had to be shielded from external signals from radio, television, computers, and other sources, RF barriers, consisting of aluminum or copper plates or mesh, had to be constructed around the MRI rooms. Later units have incorporated features such as self-shielding of the magnetic fringe field and barriers to external RF, allowing greater versatility in physical placement.

Mobile Magnetic Resonance Imaging

Cost itself has precluded dispersion of MRI technology to locations where the volume of examinations would be insufficient to justify the capital purchase and operating expenses. The cost of the systems ranges from about a million dollars for units employing resistive magnets to several million dollars for superconductive magnets. The helium used in cryostats of superconductive magnets represents a significant operating expense and is not readily available in many areas.

As a result, mobile MRI units with the magnet and supporting equipment have been placed in large trailers, which can be moved by road to several separate sites a week. Initially, lower-field resistive magnets were used, but the shielding problems associated with high-field superconductive magnets have now largely been overcome, allowing mobile high-field systems as well.

Cost and Function

To increase the number of patients who could be examined, operating hours had to be extended and examination times reduced. Installations that traditionally functioned on an eight-hour day, five-day-week schedule extended times to include nights and weekends and experimented with subtle and gross alterations in the pulse sequences to permit shorter examination times. Magnet design, RF pulse generation, and gradient coils were technically refined. Ultimately, early clinical test sites and those purchasers of initial systems were confronted with the possibility of performing patient research on units that were either outmoded or lacking in some of the newer developments. Adoption and diffusion of MRI was slowed by governmental regulation and reimbursement restrictions.

Educational Needs

The fundamental differences between the physics of MRI and X rays posed educational problems for radiologists and radiological physicists. The density differences of tissues imaged by X rays were well understood and taught, but MRI was based on physical principles not previously taught or learned by most clinical users. Moreover, in the early years only the most knowledgeable investigators understood the effects of various pulse sequences used for optimal imaging of normal and diseased tissues and organs.

Clinical investigators undertook major educational efforts with visitors to their sites. Some investigators migrated to new locations and took on both teaching and developmental roles. New sites in academic institutions provided learning opportunities for faculty, residents, and visitors. Fortunately, most clinicians had experience with the transverse orientation of CT, which eased the transition, although the image contrast produced by MRI was usually quite different. Major national and international radiological societies and commercial vendors offered courses in the new modality, including MRI physics and clinical imaging. New professional societies, including the Society for Magnetic Resonance in Medicine and the Society of Magnetic Resonance Imaging (later merged), were formed with the specific purpose of providing educational opportunities and offering forums for investigators to present the results of their efforts. The body of practicing radiologists rapidly gained expertise, and academic faculty incorporated MRI into their teaching of radiological residents and fellows.

Regulatory Issues

Concern over the high cost of capital and operating expenses has prompted government agencies in many countries to regulate acquisition, diffusion, and indications for the use of MR technology.

In the United States several government agencies regulate medical devices. The FDA's Bureau of Radiological Health and Center for Devices and Radiological Health are the main participants at the federal level. Other regulations were implemented by state agencies. The CT era saw the implementation of the process of certificates of need (CON), under which potential users were required to demonstrate the safety and efficacy of a technology or medical procedure, its expected use in a local or regional area, the need for new or additional sites, the health care cost impact, and many other parameters. In many areas the CON regulation was adopted for MRI and, with other regulatory and legislative decrees, proved a major impediment to the diffusion of the new technology. As with CT, such rules restricted patients' access to cost-saving, and often life-saving, diagnostic examinations.

Paradoxically, the rules also stimulated the acquisition of units in outpatient clinics and offices beyond the range of government authority, which was generally limited to hospitals. In 1984 the government implemented a prospective payment system for hospitals, which further encouraged outpatient examinations.

The American College of Radiology created a commission on magnetic resonance and assembled a resource group of knowledgeable scientists and diagnostic radiologists who were leaders and innovators in MRI. In 1985 Medicare approved reimbursement for MRI examinations of the head and neck and a few applications in imaging the spine, pelvis, and pericardium. In 1987 the National Institutes of Health convened a consensus conference which reported favorably on the utility of MRI.[29] As the technique gained recognition in the diagnosis of musculoskeletal pathology, coverage was broadened to include soft tissue masses, bone tumors, and ischemic necroses, and extended to other organ systems as diagnostic efficacy was demonstrated.

Clinical Applications

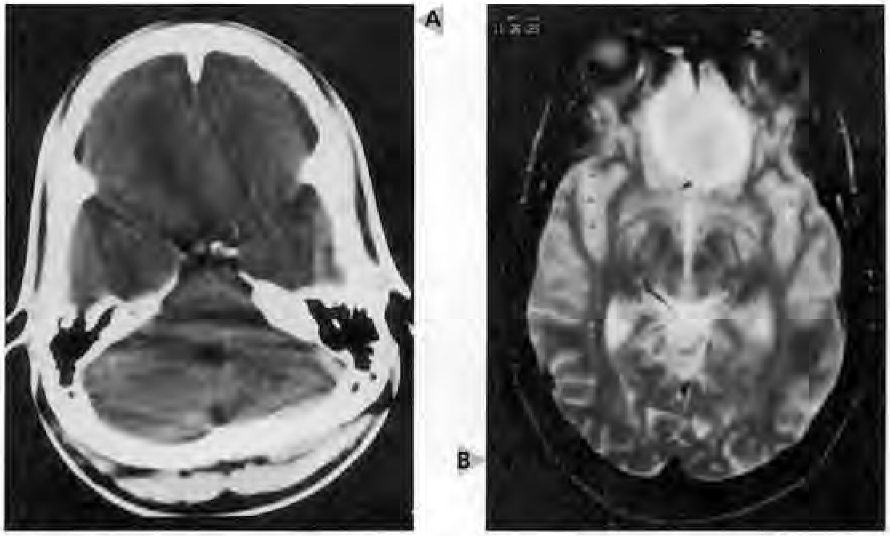
Magnetic Resonance Imaging

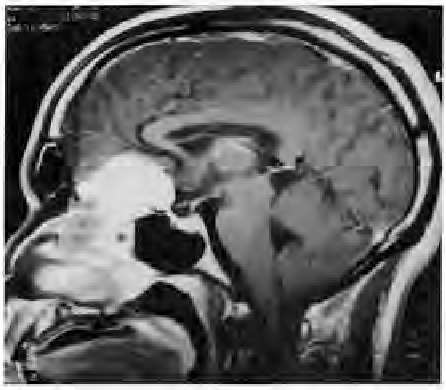
Because the clinical applications of MRI in multiple organ systems are described in other chapters of this text, this section addresses only a few examples.

The first reports of clinical human use of MRI were published in 1981. Hammersmith Hospital in London took the lead role in clinical research, quickly followed by programs at the Massachusetts General Hospital and the University of California, San Francisco. The first site dedicated primarily to clinical use was constructed in 1983 at the Cleveland Clinic Foundation.[30]

Initially, because of technical considerations at the time and the improved contrast of MRI compared with CT, interest was directed to MRI of the brain.[31] The early air-core resistive magnets and superconductive systems were constructed with apertures sufficient to accommodate the head and to provide relatively high signal-to-noise ratios in areas of the body where physiological motion was minimal during long data acquisition times. In contrast to CT, MRI directly provided images of transverse, sagittal, and coronal slices or any arbitrary orientation of the slices (Figs. 19.5.a, b, and c). These orientations in the brain provided more meaningful anatomic images for display of many diseases than did directly acquired CT images in transverse orientation. Initially, the greater sensitivity of MRI delineated the plaques of multiple sclerosis, a disease difficult to identify in

Fig. 19.5 Images from a patient with a sub-frontal meningioma. a. Basilar view CT appears virtually normal. b. Comparative view MRI, T2 weighted, made at 1.5 tesla, clearly demonstrates the large tumor. c. Sagittal view MRI, T1 weighted, 1.5 tesla showing the meningioma in the sub-frontal region. (Courtesy, Division of Radiology, Cleveland Clinic Foundation)





early stages by other modalities.[31] This success raised expectations that other diseases similarly difficult to diagnose by other imaging methods might be identified. The early clinical MRI literature abounded with reports of small series of patients with diverse disease processes who underwent MRI with interesting results and varying claims of efficacy.[32, 33]

As larger-bore magnets were produced and surface coil technology was applied, MRI of the spine and larger body parts or regions became possible, and organs in the chest, abdomen, and pelvis became the subject of investigations. It was quickly noted, however, that patient and physiologic motion—cardiovascular, respiratory, and gastrointestinal—compromised image quality. Techniques for data collection during periods of relative quiescence of motion (so-called gating techniques) were implemented to integrate respiratory detectors and/or the electrocardiographic signals during MRI signal collection. Gating techniques thus opened the door to study of the heart for both congenital defects and acquired diseases, such as myocardial ischemia and infarction, and improved images in the chest and abdomen.

Gating techniques proved to be cumbersome and generally increased imaging time. Using techniques to reduce scan times and enhance imaging contrast, investigators modified pulse sequences and developed innovative pulse sequences under the rubric of "fast scanning."[34, 35] Standard spin-echo techniques, which lack flexibility, were augmented by echo-planar (gradient echo) imaging sequences with shorter scan times, greater patient throughput, and, in many instances, more diagnostic information.

Despite improvements in sequences, gating, and surface coils, MRI applications in the abdomen and chest constituted a minority of examinations wherever competitive imaging modalities, such as CT and ultrasound, could provide diagnostic information at lower cost. MRI of the head, neck, spine, and musculoskeletal system, particularly the knee joints, constitute about 95 percent of all studies where the clinical advantages of MRI have been clearly demonstrated.

MR Flow Imaging

Accurate noninvasive visualization of the vascular system has long been the goal of angiography. Standard methods require the percutaneous introduction of a catheter or needle into arteries or veins and injection of iodinated contrast agents, capturing the image with X-ray techniques.

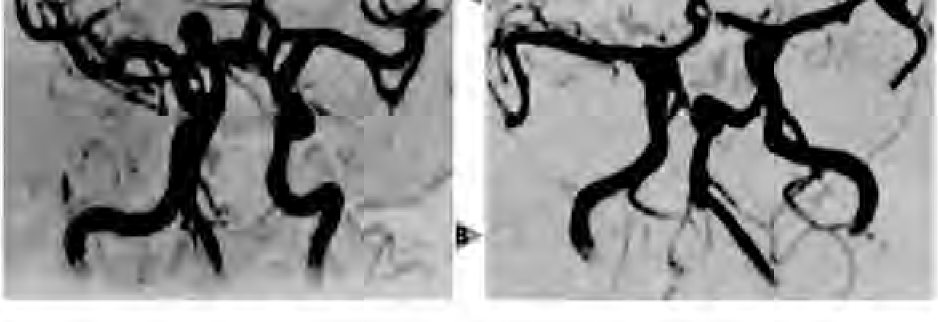
Flowing blood alters the MR signal.[36, 37] Two irradiating fields employed in pulse sequences must both affect protons in the blood to produce a signal. Unsaturated blood that enters the region of signal detection which has not absorbed RF energy results in a bright signal. The user can manipulate the pulse sequence so that flowing blood containing non-irradiated protons can be identified with high signal intensity against a background virtually devoid of signal, creating an image analogous to a digital subtraction angiogram but without the need for contrast material or the use of a catheter or needle (Figs. 19.6a and b). This technique is termed magnetic resonance angiography (MRA). Clinical applications based on these principles developed in many areas of the vascular system, notably in the extra- and intracranial vascular system.[38,39] Studies of other regions quickly followed, including the heart and coronary circulation, aorta, pulmonary circulation, and extremities.

MRA investigations of the vascular system continue to focus on overcoming two problems largely solved by invasive selective catheter angiography: a high degree of contrast between the vessel of interest and the surrounding background tissues, and overlap of adjacent blood vessels which obscure the vessel(s) of interest.

Recent Developments

Special imaging applications include diffusion-weighted imaging, which is based on the principle that image contrast is determined by the degree to which water molecules are free to move. By applying large magnetic field gradients for short periods, the MR signal can be made highly sensitive to the random molecular motions produced by diffusion. These additional parameters have been shown to demonstrate subtle pathologic changes in the brain.[40] Other advantages of improved gradient systems include the ability to perform fast scanning to measure such physiologic functions as local tissue perfusion. This has been attempted using bolus injection of susceptibility contrast agents as well as making local changes in hemoglobin oxygenation.[41,42]

As noted, MRI has been focused on the hydrogen proton. Much experimental biological work has been directed not only to hydrogen but also to other nuclei, such as phosphorus and carbon, where the production of spectra has been obtained to reflect the metabolic dynamics of these elements in relatively uniform samples of normal and diseased tissues. Extending this potential to study metabolism in the intact human requires delineating a small, clearly defined volume of human anatomy and identifying that region in an image for spectroscopic analysis.[43] Such dual applications of MRI with spectroscopy of protons and other nuclei are expected to broaden the understanding of normal and disease processes. Research has also expanded to include functional imaging using paramagnetic contrast agents and ultrafast imaging techniques in response to external stimuli.



A B

◄ **Fig. 19.6a MR angiography. No exogenous contrast material was administered to visualize the carotid arteries. b. Spin-echo images of the same patient with a basilar tip aneurysm. (Courtesy, Division of Radiology, Cleveland Clinic Foundation)**

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