# 2.
# NMR—Historical and Technical Background

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It is not possible to provide either a comprehensive historical profile of nuclear magnetic resonance (NMR) or a detailed technical explanation of the NMR phenomenon within the scope of this document. In order to fully appreciate the excitement about the implications of being able to produce hydrogen or other atomic images using NMR, however, it is essential that the reader have some historical and technical background. The following sections attempt to provide that background. The first section discusses the historical development of NMR. The second section provides basic technical background about NMR and NMR imaging, including a description of the technical components used in NMR imaging systems. The final section introduces the types of magnets used in NMR imaging. Appendix A contains additional technical information.

## HISTORICAL BACKGROUND

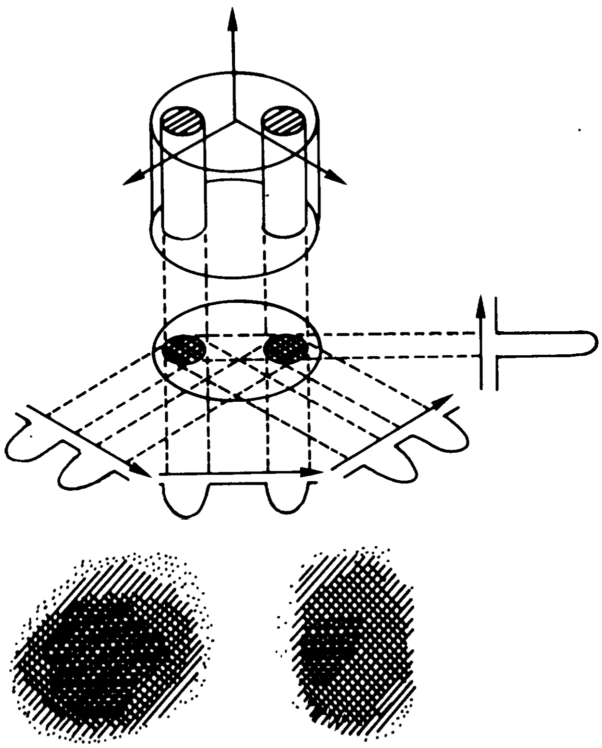
The existence of the phenomenon of nuclear magnetic resonance was predicted by a Dutch physicist, Gorter, in 1936. Gorter sought, unsuccessfully, to demonstrate the NMR phenomenon in lithium fluoride. A decade later, in 1946, two American scientists, Felix Bloch and Edward Purcell, working independently, simultaneously discovered and demonstrated the existence of NMR. Bloch's observations were made with studies of water at Stanford; Purcell's with studies of paraffin wax at Harvard. The two were jointly awarded the Nobel Prize for Physics in 1952. Since then chemists and physicists worldwide have routinely employed uniform magnetic fields in what can now be considered "conventional NMR spectroscopy" to study the molecular structure and dynamics of small homogeneous specimens (8). The NMR imaging techniques that have evolved over the past decade derive in large part from the *25* years of experience that had been accumulated prior to 1973 in the application of NMR spectroscopic techniques to the study of solids and liquids.

The establishment of a magnetic field gradient (a magnetic field that increases or decreases in strength in a given direction along a sample) across a sample was the key to going from spectroscopy to spatially encoding the information that forms the basis of NMR tomographic imaging. Although magnetic field gradients had been employed by scientists since the 1950s in studies of molecular diffusion in liquids *(78),* phase separation (separation of homogeneous but physically distinct portions of matter) in helium solutions (199), and methods of information storage (7), it was not until 1971 that Paul Lauterbur working at the State University of New York (SUNY) at Stony Brook conceived of the idea of manipulating magnetic field gradients to obtain a two-dimensional NMR image (116).[1] In his now classic experiment in which the first NMR image was produced, Lauterbur rotated magnetic field gradients (changed magnetic field gradients) in a technique he called zeugmatography to reconstruct a two-dimensional image of two tubes of water (115) (see fig. 1). In discussing the implications of his results, Lauterbur recognized the potential applicability of his technique to the imaging of soft tissue structures and malignant growths in vivo (115).[2]

[1]Lauterbur was aware of the studies performed by Damadian (42) and Hollis (93), which demonstrated that excised tumors manifested prolonged NMR relaxation times. Recognizing that it might be tremendously beneficial to be able to make such measurements in vivo, Lauterbur worked to develop a technique in which NMR could be used to produce images (116).

‘In 1973, Mansfield and Grannell published a letter in which they described a method, involving magnetic field gradients, through which NMR could be used to determine spatial structure in solids (121). No mention is made in the letter, however, of a proposal to use NMR to produce images.

Figure 1.—First NMR Image



NMR image of two tubes of water

SOURCE P C Lauterbur, "Image Formation by Induced Local Interactions. Examples Employing Nuclear Magnetic Resonance," Nature 242 (5394) 190.191, Mar 16, 1973,

Remarkable progress in the quality and capabilities of NMR imaging has been made in the 10 years since Lauterbur imaged his two tubes of water. In 1974, Peter Mansfield and his colleagues at Nottingham University published the first crude NMR medical image (of a human finger) (122). Only the gross outline of the finger without any internal detail was revealed. Improved images of human fingers were produced by the same group 2 years later using a different imaging technique that relied on selective radiation[3] of the specimen in switched magnetic field gradients (123). In 1976, Damadian and colleagues, working at SUNY at Brooklyn, employed a Field Focussing Nuclear Magnetic Resonance technique (FONAR) to produce the first NMR image of a tumor in a live animal (44). A year later a human wrist was imaged (91) and the first in vivo human whole-body NMR tomographic scan (image of an individual slice) was produced (43). In the latter scan, crude by current standards, the heart, lungs, mediastinum, and descending aorta could be detected (43) (see fig. 2). In 1978a team led by Hugh Clew and Ian Young, working at English Music Industries' (EMI's) laboratories in London, produced what is believed to be the first NMR image of a human head (96) (see fig. 3). Since then considerable improvements have been made in NMR imaging of both the head and body, with no plateau in the rate of improvement in sight (see fig. 4).

[3]The radiant energy used for NMR is low-frequency, non-ionizing radiofrequency waves, not the high-frequency waves used in X-rays.

# BASIC TECHNICAL BACKGROUND

An understanding of nuclear magnetic resonance (NMR) requires a familiarity with certain natural phenomena. The first phenomenon is that all atoms, of which everything in nature is made, contain nuclei which, in turn, are made up of particles called protons and neutrons. It is these atomic nuclei to which the "N" in NMR refers.

The second natural phenomenon pertinent to an understanding of NMR is that certain nuclei, namely those that contain an odd number of protons, or an odd number of neutrons, or both, possess an intrinsic angular momentum, called "spin." Since nuclei are electrically charged, those nuclei that spin generate tiny magnetic fields. That is, they are magnetic. Only those nuclei that are magnetic, such as $^{1}$Hydrogen, $^{13}$Carbon, $^{19}$Flourine, $^{23}$Sodium, and $^{31}$Phosphorus, can be exploited in NMR experiments. It is this phenomenon of nuclear magnetism to which the "M" in NMR refers.

Supplying radiofrequency energy of the appropriate rotational frequency will excite hydrogen nuclei from a lower energy level, $E_1$, to a higher

**Figure 2.–First In Vivo Human Whole-Body NMR Scan**


SOURCE Provided by Raymond Damadien, President, FONAR Corp

level, $E_2$. If the radiofrequency energy is turned off after the nuclei have been raised into the higher energy level, the excited hydrogen nuclei drop back down to level $E_1$, i.e., they relax. In the process of relaxing, the hydrogen nuclei re-emit the energy they had initially absorbed, If this radiofrequency energy is repeatedly applied, hydrogen nuclei will oscillate, or resonate, back and forth between $E_1$ and $E_2$, alternately absorbing and emitting energy. It is this type of radiofrequency-induced resonance to which the "R" in NMR refers.

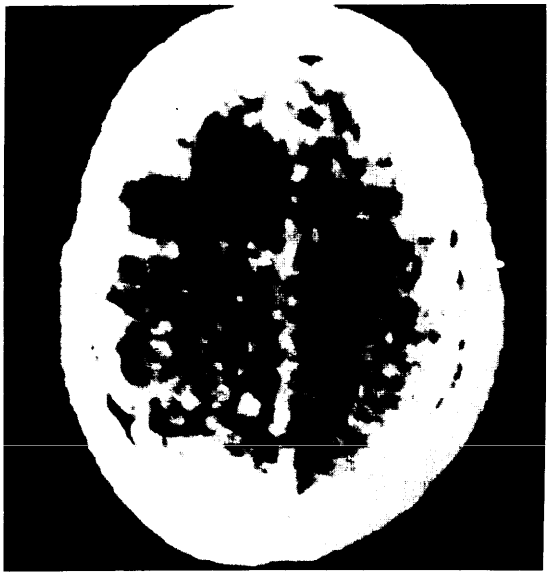
Since the NMR signals that are emitted by magnetic nuclei are extremely weak, atoms must be present in sufficient concentration in order to produce an NMR signal that is strong enough to be converted into an image exhibiting clinically useful spatial discrimination. To date, the nucleus of the hydrogen atom, which is the most prevalent in the body and has a single unpaired proton, has been most commonly exploited to produce high-quality NMR images.[4]

As Raymond Andrew has explained in his review of NMR imaging (8), NMR images are spatial representations of NMR signals. Although the signal detected in proton imaging is proportional to proton density, the image is not just a two-dimensional representation of that proton density. Rather, the signal also depends on three other parameters.

The first parameter is the velocity with which fluid is flowing through the structure being imaged, since the movement of protons in that fluid

[4]Recently, sodium and phosphorus have also been imaged in some research centers.

**F gu e 3 F s NMR mage o a Human Head**



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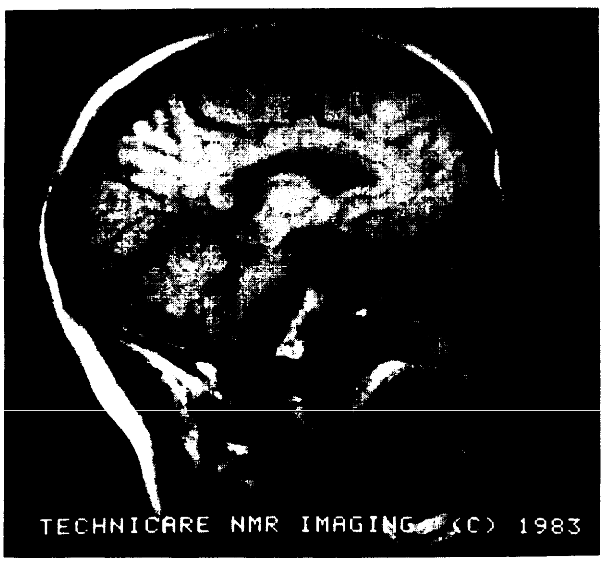
5-6 980

**F gu e 4 983 NMR mage**




h n n h gna b ng d d
Th h w pa m ha a an NMR m
g a h a a wh h nu d d
ng n NMR dy a Th a a on pa

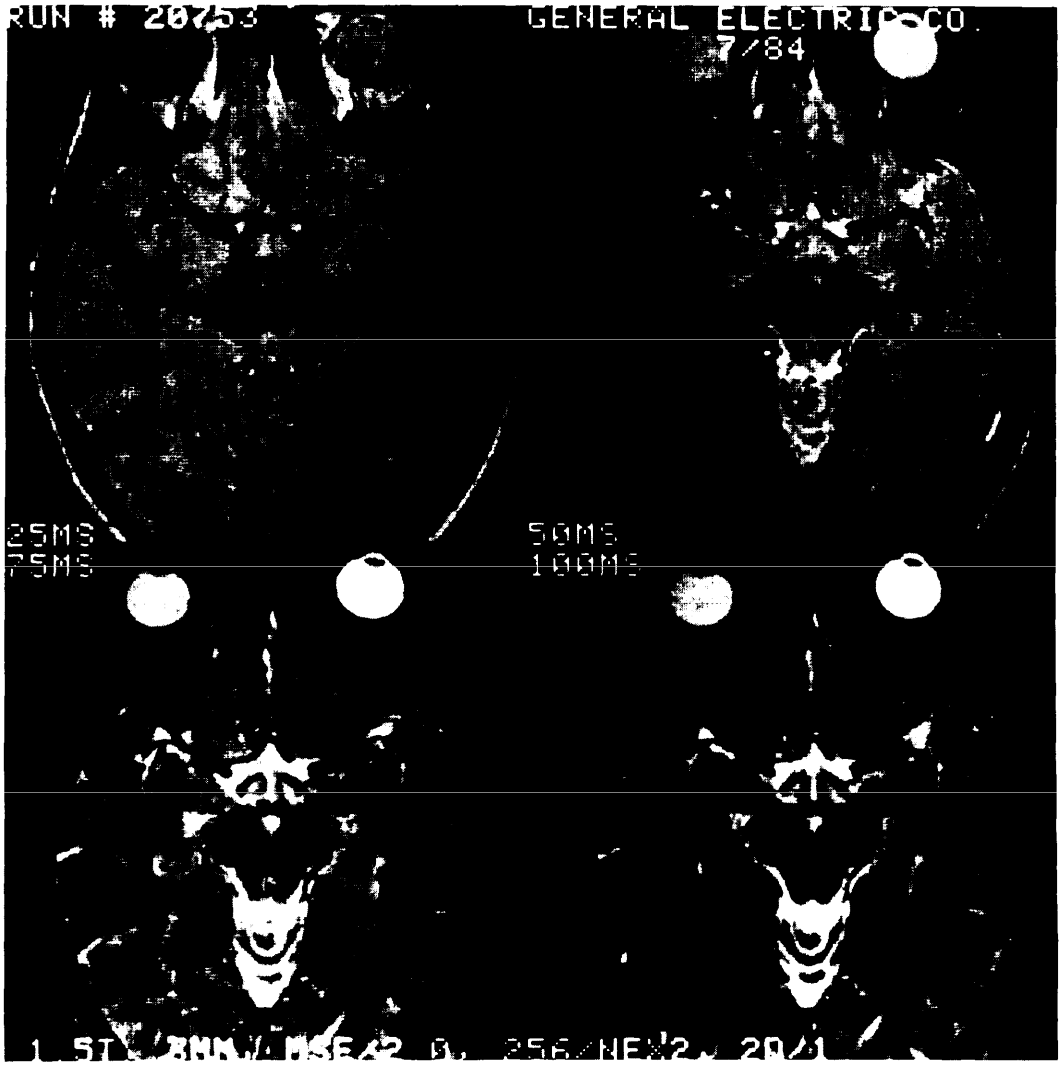
rameter, called the "spin-lattice" relaxation time, or $T_1$, is a time constant that reflects the rate at which excited protons exchange energy with the surrounding environment. The other, called "spin-spin" relaxation time, or $T_2$, is a time constant that reflects the rate of loss of coherence (the rate at which protons stop rotating in phase with each other) due to the local magnetic fields of adjacent nuclei. Naturally occurring variations in relaxation times may have biomedical significance.

The extent to which any single NMR image reflects each of these four parameters (proton density, flow, $T_1$, and $T_2$) depends on the particular radiofrequency pulse sequence employed to excite the protons in a region being imaged (see app. A). Thus, there is no such thing as a unique NMR "picture" of any region of the body. Rather, as is illustrated in figure 5, NMR images of a single region vary depending on the pulse sequence used to produce them.

NMR images thus are fundamentally different from computed tomographic (CT) X-ray images. Whereas the latter rely on the linear attenuation of ionizing X-radiation to produce images that reflect differences in the electron density and specific gravity of adjacent tissues, NMR images are formed without use of ionizing radiation and reflect fundamental physiochemical differences between adjacent tissues. It is from the belief that enormous clinical benefits might be derived from obtaining information at a nuclear level through NMR, that the excitement about and investment in NMR have arisen.

Except for the addition of a computer and a system for producing a magnetic field gradient, the basic components used in modern day NMR imaging devices (see figs. 6 and 7) are qualitatively similar to those employed in the first NMR experiments performed by Bloch and Purcell in 1946. These components include: 1) a *magnet* whose aperture or bore (diameter) is large enough to enclose the structure being imaged (the magnet is used to produce a highly uniform magnetic field around the structure being imaged); 2) a set of *gradient cods* to impose the magnetic field gra-

**Figure 5.—An NMR Image (3 mm slice) of a Normal Head From an Axial View With Changes in Pulse Sequence**



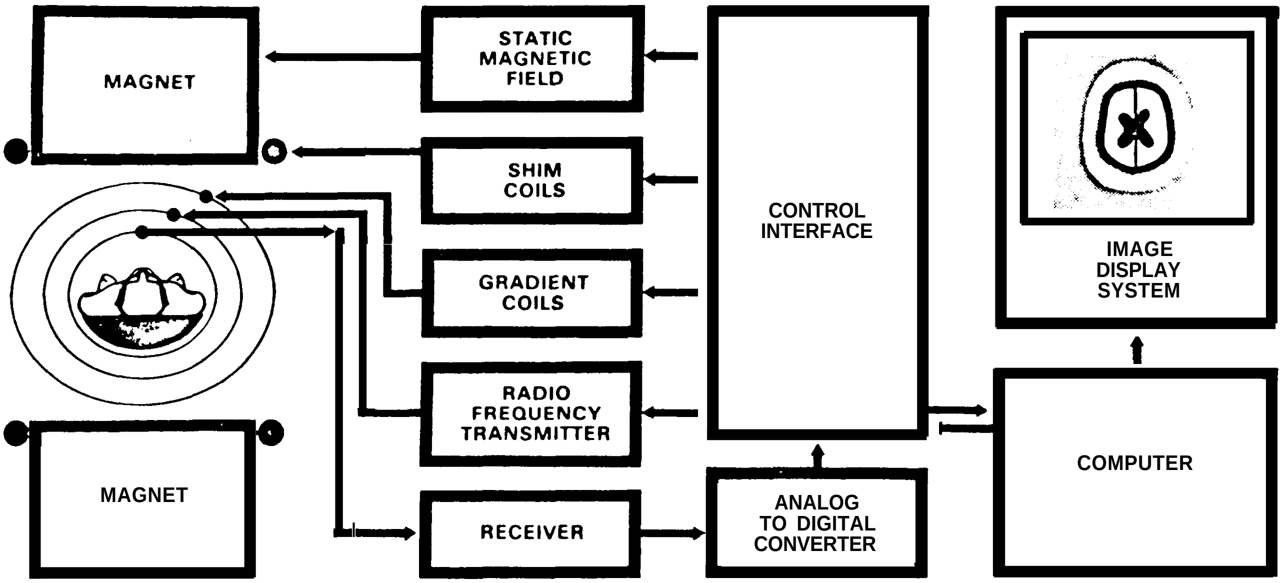

SOURCE General Electric Co , 1984

client required to provide the system with spatial discrimination; 3) a *radiofrequency transmitter* to produce radiowaves that excite the nuclei being imaged; 4) a *radiofrequency receiver* to detect the radiofrequencies being emitted by excited nuclei during the process of relaxation; 5) a *computer* to control instrument operation and to reconstruct and store the image produced from the NMR frequency signals being detected; and 6) a display system.

## MAGNETS

Although small-bore magnets had been employed in conventional NMR spectroscopy for many years, it was not until interest in NMR imaging emerged in the 1970s that magnets with bores large enough to accommodate a human being were designed and built. Much of the recent research and development on magnets for NMR imaging and in vivo spectroscopy has been funded

**Figure 6.—Schematic Diagram of NMR Scanner Instrumentation**




SOURCE: C L Partain, R. R. Price, J, A, Patton, et al. "Nuclear Magnetic Resonance Imaging," in Radiological Society of North America, Inc., 1984, figure 11, p 13. (Courtesy of C. L. Partain).

in part by the NMR imaging industry and carried out by magnet manufacturers. The design of magnets manufactured specifically for NMR imaging, however, is still in an early stage of evolution, with improvements likely to be made as interest intensifies.

There are four main characteristics of magnets used in NMR scanners with which one should have some familiarity: magnet type, field strength, bore size, and homogeneity of field.[5]

## Magnet Type

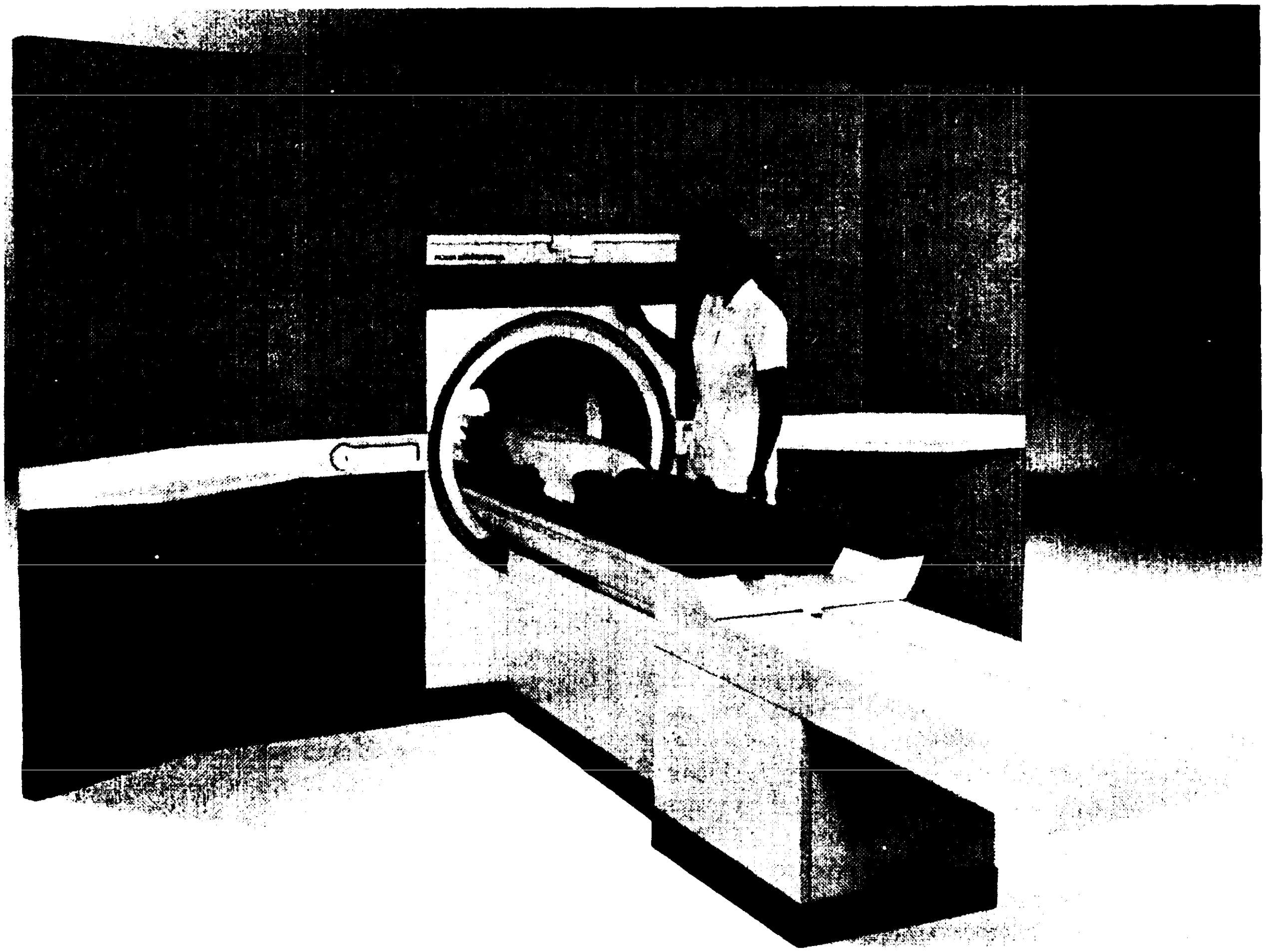
Two different classes of magnets can be used to produce the static magnetic field employed in an NMR scanner: electromagnets (either resistive or superconductive) or permanent magnets. Resistive magnets use electric current carried by copper or aluminum wire to create a magnetic field. Because copper and aluminum offer resistance to the flow of electric current, power must be supplied to force current through the wire. Energy supplied to power the system is lost as heat, requiring employment of a cooling system (usually cold water). Resistive magnets are comparatively light and inexpensive, and, because they can be shipped in parts, the costs of installing them are comparatively less than that for superconductive magnets. Resistive magnets do have high power requirements (50 to 100 kilowatts) resulting in operating costs of about $20,000 per year (6), however, and field strength is limited by cooling considerations to about 0.15 tesla[6] (126).

Superconductive magnets also utilize electric current to create a magnetic field, but instead of employing resistive materials such as aluminum or copper wire to carry the current, they use wire made from superconductive materials such as niobium-titanium alloys. Such alloys offer no resistance to current flow when operated at temperatures near absolute zero (126). In contrast to a resistive magnet, a superconductive magnet does not require an external source of electrical energy to sustain current flow once it has been started, as long as temperatures are maintained near absolute zero (126). Cooling of superconductive magnets is accomplished through use of liquid helium and liquid nitrogen. Helium needs to be replen-

[5] Individuals interested in more than the following brief description of these features can consult standard physics texts or reviews written about magnets used in NMR imaging systems (57,126).

[6] Magnetic field strengths are measured in units of tesla (T). 1 T = 10,000 gauss (10 kilogauss). For perspective, the magnetic field strength of the Earth is approximately half a gauss.

**Figure 7.—Modern Day NMR Imager**



SOURCE Picker International

ished approximately once per month, whereas nitrogen needs to be replenished every one to two weeks.

Manufacturers are developing systems to reduce the loss, and therefore expense, of these coolants. Considerable research, for example, is being directed at development of techniques for recycling and liquefying the helium that now boils off into the atmosphere. In the event of excessive helium boil off, a superconductive magnet can quench (i.e., lose its superconductive properties). At least a day can be required to recool the magnet, during which time the instrument is unusable (126). The primary advantage of superconductive magnets is that they can carry high current densities, enabling generation of very high magnetic field strengths (see "Field Strength" below). Superconducting magnets can also provide magnetic fields that are both highly uniform and stable, once equilibrium is established.

Probably the most serious problem associated with use of resistive or superconductive magnets for NMR imaging derives from the external magnetic fields produced by the magnets and disruptions in the magnet's magnetic field produced by ferromagnetic objects (e.g., passing vehicles or elevators) in the vicinity of the magnet. The fringe field produced by electromagnets can erase magnetic tape and disrupt pacemakers. Magnetic objects in the environment, in turn, can cause unacceptable distortions in the primary magnetic field that degrade image quality. Because of these potential distortions, expensive preventive site preparation or renovation is necessary.

Problems related to stray magnetic fields do not occur with permanent magnets (126), resulting in fewer siting problems with the installation of permanent magnets. Because permanent magnets eliminate the need for either electrical power or liquid helium, they also have the advantage of lower operating costs. Permanent magnets tend to be extremely heavy (as much as 100 tons), however, often creating a need for reinforced floors. The field strength of most currently available permanent magnets does not exceed 0.3T.

## Field Strength

The optimum field strength for proton NMR imaging is the subject of intensive research and debate. It is likely that no one field strength will be optimum for all NMR applications. Higher field strengths might be preferable to lower ones because a higher field strength increases the NMR signal/noise ratio, and increased signal to noise translates directly into improved image quality, finer spatial resolution, or reduced scan times, all other parameters being equal (21). Still at issue, however, is whether improvements in image quality achieved through increases in field strength above 0.3T will result in clinical benefits.

## Bore Size

The size of specimens that can be imaged with NMR is limited by the diameter of the magnet bore. Whole body NMR scanners therefore require magnets with an effective bore diameter sufficient to accommodate a human body. Approximately 1 to 3 percent of patients that have been imaged to date have complained of feeling claustrophobic in the magnet.

## Homogeneity of Field

Inhomogeneities in the magnetic field (lack of uniformity in magnetic field strength) can result in clinically important distortions in NMR images. As mentioned previously, both stationary and moving ferromagnetic objects can produce such inhomogeneities in the fields of resistive and superconductive magnets. Many of these problems can be minimized (albeit at significant expense) by magnetic field shimming (adjustments such as addition of special coils made to eliminate inhomogeneities in the magnetic field) and appropriate site renovations. Higher degrees of field homogeneity are required to perform $^{31}P$ spectroscopy than to perform proton imaging.