Appendix B.— Research and Development of CT and Other Diagnostic Imaging Technologies

The computed tomography (CT) scanner was developed with little involvement of U.S. Government research agencies. Nonetheless, Federal support for R&D of the CT scanner has been substantial in the past. It is clear that this support has decreased significantly and steadily in the past few years (23,110). Meanwhile, private industry has assumed an increasing share of further basic R&D of CT scanners.

The National Institutes of Health (NIH) has been the major source of Federal funding for R&D of CT. Of the Institutes, the National Cancer Institute (NCI) has been the most active, supporting an estimated total of over $4 million in CT-related research projects *over* the past several years. The last major project funded by NIH (NCI) concerned with developing technological improvements in CT scanners, however, terminated in April **1978:** This extramurally supported research yielded the fixed-detector geometry type scanner developed by the American Science and Engineering Co. (AS&E) (1 10).

Currently, most CT-related research funded by NIH is concerned with new and improved uses of CT scanners and/or applications of CT scanning. The funding levels of current projects, however, are much more modest than those of earlier projects concerned with basic R&D of CT itself. More importantly, NIH resources currently being allocated to CT pale in comparison to NIH moneys being allocated to the R&D of other imaging technologies.

For example, NIH is currently supporting basic R&D of the dynamic spatial reconstructor (DSR) imaging system; positron emission transaxial tomography (PETT); and zeugmatography, or the application of principles of nuclear magnetic resonance (NMR) to imaging techniques, In addition, ultrasound (which much preceded CT historically) continues to be researched at NIH for improvements in the technology itself, as well as for new and improved applications.

Theoretically, the imaging capabilities of some of these new technologies exceed those of CT. Some of these technologies may also be safer than CT, because they do not use ionizing radiation. Given these advantages, the development of these technologies and their eventual emergence into clinical use could play a decisive role in the future of CT scanning. One trait that the new technologies (in particular) have in common with CT that might dampen this potential effect, however, is their costliness. In some cases, their estimated cost not only rivals, but exceeds, that of the most advanced CT equipment currently available.

Consequently, these emerging technologies will soon face many of the Federal policies established in the wake of the introduction, diffusion, and widespread use of CT scanners. Just how these expensive —but nonetheless, miraculous—technologies will fare when they encounter Federal policies toward the evaluation, diffusion, and reimbursement of new high-cost technologies will be interesting indeed. The field of diagnostic imaging is already a large and expensive one, as shown in tables B-1 and B-2.

Table B-1–Overview of Diagnostic Imaging in the United States (1977 and 1980)

	Number of hospitals with capability	Number of procedures (millions) 1977	Number of procedures (millions) 1980	Costs (millions) 1977	Costs (millions) 1980
Diagnostic X-ray.	7,000[a]	158[b]	171[b]	$5,300[b]	$7,600[c]
CT scanning	1,OOOC	1-1.4[c]	3.4[c]	$300[d]	$875[cd]
Nuclear medicine.	3,300[e]	8.2[f]	11.1[b]	$800[f]	$1 ,250[b]
Ultrasound	All	Approximately 4[g]		na	$360[g]

[a]This is the approximate number of hospitals in the United States It is assumed that all have such equipment
[b]Estimates of Bureau of Radiological Health 186) The diagnostic X-ray figures Include dental X-ray
[c]OTA estimates
[d]This figure is partially offset by reductions in other diagnostic procedures Estimates are presented in OTA's 1978 CT report 11291
[e]American Hospital Association *Hospital Statistics 1978 Edition* (Chicago, Ill 1978)
[f]L Russell Technology *in Hospitals* (1461 Russell s 1975 estimates are extrapolated to 1977
[g]No reliable figures are available The State of New York survey of Rochester N Y if projected nationally, would Indicate 76 million procedures in hospitals alone (29) Sources in the Bureau of Radiological Health cite Informal estimates of 1 4 mill ion procedures in 1979 excluding obstetrical use (a large component), but also indicate that that estimate seems too low Ultra sound use is growing rapidly The Stanford Research Institute estimates 12 m illion to 14 million procedures in 1979 growing to over 125 million in 199011 63)

NOTE Estimates *are* approximate for illustration only The Bureau of Radiological Health is presently beginning a survey of 125 hospitals to determine the rates of use of diagnostic X ray, ultrasound, and nuclear medicine This study wi l give much more conclusive figures than those shown above

Table B-2.-Sales of Diagnostic Imaging Equipment in the United States, by Year (1977-83)

	Sales (millions of dollars)						
	1974	1975	1976	1977	1981	1982	1983
Diagnostic X-ray.	$265'	$300[b]	$230[b]	$280[b]	$375[b]		—.
CT scanning	—	100[b]	12ob	160[b]	2 0 0[b]		
Nuclear medicine.	40 [c]	—	—	100[d]	—	$127[d]	—.
Ultrasound	65a	—	—	160[e]	—	269[f]	$490[e]

NOTE The validity of the sales figures IS not known They are undoubtedly rough They are included here as general indicators only The Stanford Research Institute estimates expenditures for diagnostic imaging equipment, supplies, accessories, and maintenance of $2 billion in 1978, rising to almost $65 billion in 1990 (163)

SOURCES
[a]*Electrical News* Mar 29, 1976, p 59
[b]*Electronic,* Jan 5, 1978, P 148
[c]*Predi* 88, May 1531973, P 24
[d]*Electric Business,* May 1979, P 66
[e]*,l* E/cc *Eng,* November 1979, P 14
[f]*Inst* Tech April 1978, P. 18

Basic and Applied Research on CT

Current CT Scanners

Since the publication of the 1978 OTA report on CT scanners (129), the technical capabilities of CT scanners have increased as new models have been developed. This increase has expanded the potential usefulness of these scanners. The new scanners offer technically improved image resolution, largely by virtue of reduced scanning times and the consequent minimization of problems associated with patient motion. The scan times of the most recent CT scanners are less than 5 seconds for a single cross-section image. The most recent scanners are capable of achieving image resolution of as little as 0.61 mm (see table B-3).

The scanners listed in table B-3 were developed privately with the exception of the AS&E scanner. AS&E received considerable Federal support from NCI of NIH ending in April 1978 (22). AS&E, however, only sold a few of the new scanners. In January 1978, Pfizer, Inc., made an agreement with AS&E to purchase the rights to market and produce the scanner. Using the AS&E gantry, Pfizer made certain technical modifications (primarily in the electronic computer of the scanner) and now markets a hybrid of the AS&E scanner known as the 0450 Pfizer/AS&E scanner. The scanner has a price tag of approximately **$650,000** to **$700,000.** According to the Food and Drug Administration (FDA), 13 of these scanners were reported to be sold in the United States between June 1978 and 1979 (95).

'The term 'generation" is often applied to describe the type of scanner The first scanners to be developed all used a similar approach, and have often been labeled ' first generatior ,' The primary meaning of the phrase was to indicate that that type of scanner was the first to be developed, However, there is an Inevitable impres: ion conveyed that the 'second generation" is superior to the ' first genera t ion. ' For this reason, OTA, in consultation with the manufacturers, has accepted labels that are more descriptive and not as misleading. In particular, this was done because what has been called the 'fourth generation' " scanner is not superior to the "third generation" scanner according to both the National Electrical Manufacturers Association and the Bureau of Radiological Health of the Food and Drug Administration. The columns in table B-3 are in order of development, with those scanners sometimes called "third generation' and "fourth genera tion" together in the column labeled "rota e-only.

The Dynamic Spatial Reconstructor

Development of the DSR imaging system at the Mayo Clinic is currently receiving substantial NIH support (23). The DSR system adds the critical dimension to computerized tomography that is necessary for accurate imaging of moving organ systems (such as the heart and lung) and for studies of three-dimensional anatomy and circulatory dynamics in all regions of the body (88). These capabilities are dependent on the development of high-speed electronic data processing and digital computing techniques which is an integral part of the R&D of the DSR system (23).

Developers of the DSR system do not believe that it represents an extension of previous CT scanning principles and logic. They are reluctant to call it an advanced CT scanner (67). The DSR system does use X-ray (as does CT): But whereas CT is capable of producing only a 2-mm thick cross-section at a scan time of just a few seconds, the DSR when completed will be able to scan up to 240 l-mm thick cross-sections in 11 msec, repeat the complete scan procedure at intervals of 1/60th of a second, and reconstruct the entire three-dimensional volume of a whole organ, as well as dynamic changes in shape and dimension of moving structures (88). The principle components of the system are shown in the illustration below (see figure B-l). The DSR is described as follows (88):

> . . . A set of 28 rotating-anode X-ray sources, independently controlled, is arranged around a semicircle whose radius is 143 cm. Abutting this arrangement is another semicircle that contains 28 independently controlled image intensifiers and image isocon cam-

Table B-3.—Typesand Models of CT Scanners(1980)

	Rotate and translate, dual detector	Rotate and translate, multiple detector	Rotate only
	4-6 min scan time Single pencil beam X-ray source 2 detectors	20 see-2 min scan time 2 or more pencil beams or single fan beam X-ray source 3-60 detectors	Under 5 sec scan time Single fan beam X-ray source Hundreds of contiguous detectors
Motion of gantry:	Source and detectors traverse gantry in parallel, gantry rotates through small angle, process repeats,	Sources and detectors traverse gantry in parallel, taking more readings and rotating through larger angle than dual detector.	Rotation motion only. In some models, source and detectors move together; in other models only source moves.
Scanners no longer available commercially in the United States as new equipment	EM I Mark I General Electric Neuroscan CT/N PfIzer0100 Siemens Siretom	Elscint 850 EM I CT 1010 EM I CT 5005 EM I CT 7020 Ohio-Nuclear 25 Ohio-Nuclear 50 Ohio-Nuclear 50FS Picker TR-120 Philips Tomoscan 200 Syntex System 60 Syntex System 90 Toshiba TCT-10A	AS&E 500 Artronix 1100 Artronix 1120 EM I 6000 EM I 7070 Searle Pho/Trax 4000 Siemens Somatom I Varian V-360
Current models		CGR ND 8000 Elscint 905 Hitachi CT-W Ohio-Nuclear 100 Omni Medical 4001 Pfizer 0200FS Toshiba TCT-30	General Electric CT/T 7800 General Electric CT/T 8000 General Electric CT/T 8800 Ohio-Nuclear 2005 Ohio-Nuclear 2010 Ohio-Nuclear 2020 Omni Medical Pfizer 0450 Philips Tomoscan 300 Picker Synerview 300 Picker Synerview 600 Siemens Somatom II Toshiba TCT-60A
Scanners-announced but not yet available commercially			CGR CR 10000 Philips Tomoscan 310

SOURCE National Electrical Manufacturers Association 1980

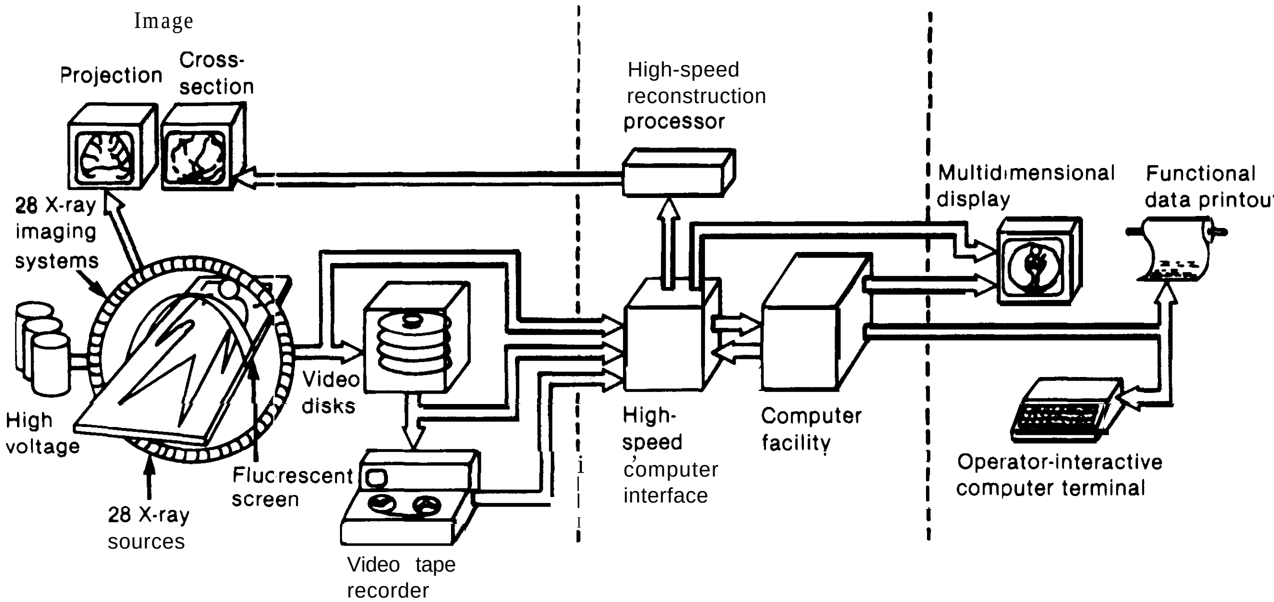
eras. These two semicircles make up one circle of equipment. Inside the circle is a 30 cm-wide flourescent screen, bent to form a semicircle with a 58-cm radius. The 28 image intensifiers and image cameras produce 28 images on the flourescent screen .

, . . The entire assembly—X-ray sources, flourescent screen, and video camera chains—is mounted on a cylindrical gantry, which is rotated at 90 degrees per second about a horizontal axis. Each X-ray source is pulsed on sequentially to irradiate the patient for 350 seconds. Simultaneously, the image intensifier and video camera for each X-ray source are activated to record the image on the flourescent screen. The heavy reliance on image intensification lowers, in effect, the X-ray dosage to levels no greater than those now employed for X-ray for X-ray procedures in general medical practice .

The DSR system, somewhat reduced for funding reasons, is currently being tested on animals on a limited basis. Researchers estimate it will be at least 2 to 3 years before it will be used to scan the first patient. At this time, it is being developed for medical research purposes, and not wit h an eye towards mass clinical application (67). The system will cost about $5 million, and might cost $3 million in mass production (34). The ultimate use of the multimillion dollar DSR system in the practice of medicine is viewed as a tertiary, or even a Quarternary tool, with perhaps 5 to 10 serving the entire country (67,83).

NIH has been the primary supporter of R&D of the DSR imaging system. The National Heart, Lung, and Blood Institute (NHLBI) has been the major source of

Figure B-1 .—Principal Components of the DSR Imaging System



SOURCE :IEEE *Spectrum,* January 1979, p 77

funding for this project since one of the major objectives is to permit accurate measurement of the structure and function of the diseased and normal heart (144). NHLBI support totals about $2 million over the past few years for development of the imaging device itself. Development of the high-speed computer system necessary to the device has been supported by the Division of Research and Resources (DRR) of NIH, which has spent about $1 million during fiscal years 1978 and 1979 (23).

Research on Applications of CT

It is difficult to compile an inclusive listing of projects related to the applications and uses of CT scanning at NIH. First, since such projects are organized by disease and organs as the Institutes are, identification of CT-related research is difficult. Secondly, even when such projects can be identified, it is difficult to determine the proportion of moneys that should be apportioned to research on CT. Without a formal survey of the Institutes, therefore, precise estimates of such projects and their funding levels are unavailable. Consequently, the projects discussed below are meant only to indicate the kinds of ongoing research being supported by NIH, Similarly, the accompanying dollar figures are provided as a rough estimate of current Federal investments in this type of CT-related research project.

Formerly the major NIH backer of research (on CT scanning, NCI spent only approximately **$75,000** in fiscal year 1979 on research for scanner development (11), In addition, however, NCI spent approximately $400,000 in that year for CT-related studies with such objectives as developing better contrast agents and new algorithms for diagnostic use to reduce radiation exposure (110). Also, in that year, NHLBI supported some extramural research grants involving the use of CT scanners in diagnostic methods for particular cardiac diseases (110), DRR, a major funding source of the DSR imaging system discussed **above,** also supported about 15 projects involving the use of CT scanners through its biomedical research support program: These few projects, however, are very modest totaling approximately $65,000 in fiscal year 1979. In addition to this research, about 3,000 patients per year are scanned in the NIH Clinical Center. Most of these represent patients who are on protocols requiring a CT scan (110).

The major project at NIH related to the application of CT is funded by the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS). In fiscal year 1979, the Institute funded a $500,000 project investigating the use of CT scanning in the diagnosis of head trauma (110). The Institute also had supported about $50,000 in intramural research projects related to the use of computed head tomography for diagnosis of diseases particularly relevant to it, such as brain tumor (110).

In conclusion, although there are still many initiatives at NIH related to applied, as opposed to basic, research on CT scanners and scanning, the cumulative resources devoted to these activities do not begin to approach the levels of funding for the ongoing development of the DSR system, for example. At this time, the Federal Government is not a significant contributor to R&D of CT scanners and scanning: Its time has come and gone. Instead, Federal support of biomedical R&D is concentrated on new imaging technologies.

Emerging Imaging Technologies

There are a number of new technologies and technological applications in the imaging field that hold great promise for medical research and eventual clinical application. These will not be covered in detail. However, there are two new technologies that are particularly exciting and at the same time raise many of the same policy issues characteristics of CT scanners. These are PETT and zeugmatography, or the application of principles of NMR to imaging techniques. Various Institutes at NIH are supporting R&D of both of these imaging techniques, and there is considerable private (worldwide) R&D investment being made in them as well.

There are now only a few PETT and NMR scanners throughout the world, and these so far have been limited to experimental clinical use (with human patients). However, the unique capabilities and attributes of these two imaging techniques have generated a great deal of excitement in the medical research community, and the possibilities for clinical application have sparked even greater enthusiasm for these technologies. Speculation regarding their role in clinical practice, associated operational costs, and commercial viability has already captured the attention of the media (83,96). One reason for excitement is that these two technologies may provide the means to image tissue function, whereas present CT and ultrasound techniques provide the means to image tissue structure.

The excitement, enthusiasm, and speculation surrounding these technologies has also drawn the attention of the Office of Health Regulation of the Health Care Financing Administration (HCFA), and the National Center for Health Care Technology (NCHCT) of DHHS (143). For example, NCHCT is preparing an overview paper on NMR that reviews the efficacy, diffusion, and utilization questions surrounding the introduction of new medical devices (73). It appears that PETT and NMR have already been flagged by these two Federal agencies, and that if and when they are ready to be introduced into medical practice, these technologies will undoubtedly be subjected to Federal policies toward the evaluation, diffusion, use, and reimbursement of high-cost medical technologies—many of which were formulated around the CT scanner.[2]

Positron Emission Transaxial Tomography

PETT is the latest of several radionuclide imaging systems belonging to the family of nuclear medicine techniques. Although ionizing radiation is used in PETT, the technology differs significantly from CT in principle and in capability. A PETT scanner may be briefly described as ". . . a large, computer-controlled tomography unit that maps the distribution of positron-emitting pharmaceuticals in order to construct detailed images of organ metabolism, physiology, and function" (96).

In the PETT scanning procedure, radioactive isotopes of elements such as oxygen, carbon, fluorine, and nitrogen are administered to the patient, usually by injection, but also sometimes by inhalation. This is in contrast to the manner in which CT scanners (and conventional X-ray techniques) expose the patient to ionizing radiation by means of an external X-ray tube. The radionuclides are administered as metabolically active compounds, such as glucose, or as naturally occurring compounds, such as carbon monoxide, which may be used as tracers. The images produced by PETT scanners are based largely on the detection of the distribution of the radioactivity through body tissue. Reconstructed images produced by PETT scanners, therefore, may reflect compartmentalized localization, flow, or biochemical and metabolic activity, whereas CT scanners basically detect and display anatomical structure, although the use of iodinated contrast media may give significant functional information. The difference in information presented in a comparable cross-section of the brain produced by these two technologies is illustrated by the fact that while CT scans of a cadaver and a live human would show a similar image, a PETT scan of a cadaver would show a relatively blank screen image in comparison to the scan of a live human, since due to lack of flow, the radioactive material would not have been transported (143).

[2]The memorandum from the Office of Health Regulation in HCFA suggests that local health systems agencies and State health planning and development agencies be alerted to the impending introduction of these two technologies as well (143).

Ter-Pogossian and his coworkers (175) have recently described PETT as follows:

> In this technique a chemical compound with the desired biological activity is labeled with a radioactive isotope that decays by emitting a positron, or positive electron. The emitted positron almost immediately combines with an electron, and the two are mutually annihilated with the emission of two gamma rays. The two gamma rays fly off in very nearly opposite directions, penetrate the surrounding tissue and are recorded outside the subject by a circular array of detectors. A mathematical algorithm applied by computer rapidly reconstructs the spatial distribution of the radioactivity within the subject for a selected plane and displays the resulting image on a cathode-ray screen . . . . With suitable interpretation PETT images can provide a noninvasive, regional assessment of many biochemical processes that are essential to the functioning of the organ that is being visualized.

NIH investment in the basic R&D of the use of positrons for imaging which led to PETT has been considerable, amounting to almost $9 million in grants to one research center alone over an 18-year period (143). Significant support of PETT continues and is projected for the next few years. For example, NINCDS initiated a series of new PETT projects in 1979. In the first year of support, the Institute spent $5.9 million in grants to establish five university-based neurology centers of research around the country and the construction of a positron emission tomography scanning instrument in each (151). Continued grant support for these centers is projected for the next 3 years. The Institute's interest in PETT stems from the expectation that PETT will enable physiological research of cerebral metabolism just as CT enabled research of cerebral vascular anatomy and flow (151). Thus, the purpose of research on PETT by the Institute has been to understand normal brain biochemistry and metabolic disorders and to study the effects of lack of oxygen, various pharmaceuticals, trauma, and varieties of stress on neural tissue (151).

There are probably more than 20 experimental positron emission scanning devices in the world at this time, half of which are located in the United States at 10 different locations: At least three more PETT devices are scheduled for installation (all at U.S. locations); these are also to be used for experimental purposes (143).[3] In addition to the investigation of brain functions PETT scanning is also being used for a variety of other research purposes, most of which are related to heart and lung functions (96). The strategy in research is to administer different positron-emitting chemicals which respond to different metabolic pathways in the target organ. By measuring the behavior of these chemicals at various times, information concerning the function of the organ can be obtained. For example, red cells "labeled" with the positron emitting carbon-n monoxide will show the blood distribution in the heart. Clearly, the number of positron-emitting radiopharmaceuticals and biological pathways that can be paired for study presents an almost infinite number of permutations. This potential suggests that PETT will play an important role in research in both organ physiciology, and in basic physiological research (96).

The estimated cost of a PETT scanner and its associated equipment (i. e., a cyclotron or linear accelerator for the preparation of positron-emitting isotopes, and the computer software and hardware systems necessary for imaging) is from $1.35 million (143) to $1.94 million (7).[4] Such a high cost suggests that the use of PETT scanners might be restricted to research purposes, since the cost would be prohibitive to all but the most major institutions. Nevertheless, the potential of PETT technology for clinical application and use has been recognized by manufacturers of medical equipment, and it is reported that at least a few have undertaken feasibility studies for marketing PETT scanners (143).

Nuclear Magnetic Resonance Tomography

Although the principles of NMR were discovered by atomic physicists at least 30 years ago, and have been incorporated in the techniques of NMR spectroscopy developed and used by chemists in analytical chemistry almost since that time, NMR tomography, or zeugmatography, has only been under development for the past several years (96). Since 1973, when Paul C. Lauterbur of State University of New York (SUNY) at Stony Brook first demonstrated a means for reconstructing an image in two (and even three) dimensions based on NMR signals, zeugmatography has been the most rapidly expanding application of NMR in medicine (76).[5] A variety of

[3] As of August 1980, PETT scanners are located at Washington University (2), Massachusetts General Hospital (2), UCLA, University of Miami's Brookhaven Laboratories, University of Pennsylvania, University of Chicago, Oak Ridge National Laboratory, Sloan Kettering Institute for Cancer Research, and the National Institutes of Health (7). The University of Michigan, Johns Hopkins University, and Houston are reported to have ordered PETT devices also (143).

[4] Almost half of the total estimate of $1.35 million is represented by the estimated cost of cyclotron at $600,000. The computer systems necessary for Imaging represent another $250,000, and the PETT scanner itself, approximately S500,000 (143)

[5] Examples of ongoing research on NMR at various Institutes and divisions at NIH were presented at a science writers' seminar on NMR held on Apr 23, 1980. These included. studies of the structure and mobility of DNA and proteins by NMR techniques, NMR studies of sickle cell in the intact red blood cell, and NMR studies of the molecular structure of collagen. These Intramural projects were in addition to the presentation of the project involving production of two- and three-dimensional images by NMR tomographic methods and a discussion of their potential diagnostic applications by Dr. Hoult (122),

techniques have been developed by numerous researchers in Europe and the United States since the first experiment by Lauterbur. While it remains to be seen which method(s) will gain acceptance, the technology is ready to be clinically evaluated.

Since 1973, zeugmatography has made significant advances in the clarity of computer-generated images of the body (143). It is estimated that approximately 200 individuals have been subjects of NMR scans (79). Theoretically, the resolution potential of zeugmatography is much greater than X-ray, nuclear, or ultrasound imaging techniques (for reasons which will be shown below) (77). However, this potential is not the sole—or even the major—reason for the excitement surrounding NMR tomography. Rather, the excitement stems from the fact that NMR does not use ionizing radiation (either X-ray or gamma-ray), is not "stopped" by bone, and most importantly, can yield metabolic information with appropriate adjustments (77). The relatively greater potential capabilities of NMR tomography in comparison to other imaging technologies (including PETT) implies tremendous potential for application to a wide range of diagnostic and treatment monitoring functions. However, the effects of the magnetic fields used in NMR are unknown. Although NMR may be safer than X-ray, it is much too soon to know for certain.

Hounsfield, who was awarded the Nobel prize for his work in CT scanning, described the principles of NMR as follows (80):

> When hydrogen protons are placed in a magnetic field they will precess (or "wobble") around the field direction just as a spinning top precesses around its vertical gravitational field. This precession occurs at a definite frequency, known as the Larmor frequency, and is proportional to the magnetic field intensity.
>
> The usual NMR procedure for imaging is to apply a strong magnetic field along the body to be studied. After a short period of time, the nuclei will align with their magnetic moments along the field. A radio frequency tuned to the precession frequency of the hydrogen nucleus is then applied at right angles to the main field by means of a set of coils at the side of the body, This causes some of the hydrogen nuclei to precess—all keeping in step. After the radio receiver field has been switched off, the nuclei will continue to precess in phase, generating a similar radio frequency which can be picked up in receiver coils placed at the side of the body, these signals detect the water content of the body. It will take some time for the precession to die away, as the nuclei again realign themselves with the magnetic field. The measurement of this time is important as it gives us some information about the nature of the tissue under investigation.

This knowledge immediately suggests the comparison of recovery times of hydrogen atoms in healthy versus diseased tissue. In early 1971, Raymond Damadian at SUNY Downstate Medical Center in Brooklyn published research suggesting that the NMR signal from the water in tumor cells differed from that in normal cells, the signal from cancerous cells being much longer than that from normal cells (96). The possibilities of a noninvasive, highly sensitive diagnostic tool based on chemical information at a cellular level were obvious.

In 1973, these subtle differences in chemical information in human tissue were displayed in the first NMR tomographic pictures, published by Paul C. Lauterbur. Lauterbur realized that by changing the direction of the magnetic field (in which the patient, or portion of the patient is placed) gradient, and repeating the experiment at a variety of orientations (i.e., taking projections at many different angles, and then reconstructing them by computer), it was possible to picture the subject in two (and potentially) three dimensions (77).[6] Lauterbur named this technique "zeugmatography" (from the Greek "joining together") based on the underlying physics whereby the magnetic field gradient joins together frequency and spatial information (77). Although a variety of NMR tomographic techniques are currently being pursued, all are based on the phenomenon of resonance of hydrogen atoms in body tissue. The outcome is a reconstructed image of an organ or whole body cross-section which appears on a screen (143). Differences in body tissue are thus detected by their intrinsic chemical differences, rather than by their density or absorpability of X-rays as in CT scanning, or by tracing administered positron-emitting isotopes as in PETT scanning.

Perhaps the most exciting potential of NMR, however, is the potential for metabolic studies that will be realized over the longer term. The dimension of metabolic information is already represented in NMR images. Eventually, it may be possible to "zoom in" on part of an organ, such as the ventricle of the heart or hemisphere of the brain, to obtain metabolic information in that specific region (79). In these extended capabilities, one may envision the imaging of metabolic information that would be comparable to that currently obtainable only by biopsy. It is the combination of metabolic information (not intrinsically available in any other imaging technique) with the image that makes the NMR technique potentially so powerful.

Hoult (79) has described one potential application, a scan of a baby's head for hydrocephalus or intracranial bleeding. NMR could locate a particular artery, measure the blood flow in that artery, and

[6] The techniques of projection and reconstruction associated with tomography are similar to those first developed for the CT scanner (96).

then check that the oxygen uptake of a hemisphere is adequate. All of this would be done totally noninvasively, and perhaps without risk to the infant (77). In the Biomedical Engineering and Instrumentation Branch of the Division of Research Services at NIH, such an experiment is under way. The imaging system developed at NIH has been almost entirely built within the Branch (apart from the computer required). The crux of this particular NMR tomographic system is a novel magnet design that has two movable hemispherical windings which can generate powerful transverse magnetic field gradients (78). Construction of the magnet was near completion in May 1980. Initially the equipment will be used with phantoms and animals to obtain experience and verify safety. Imaging of human subjects is to begin in spring 1981 (approximately). Eventually, the NIH system will be used to scan premature neonates in a series of experiments. It is hoped that the NMR instrument will provide a major imaging facility at NIH for diagnosis and repeated observation of diseases to which NMR is particularly suited (77).

Besides these capabilities, the final and immediate advantage of NMR over other imaging techniques is that it may be safer because it does not use ionizing radiation (79). However, there are real and potential hazards from strong magnetic fields, especially with pulsed or alternating polarity fields, and resulting induction currents (101). Although some have proposed that NMR is particularly well suited for use with infants and fetuses of pregnant women, FDA spokesmen urge caution in applying it to infants or pregnant women (86).

Meanwhile, the expectations based on the capabilities and attributes of NMR have attracted the intense interest of researchers throughout the world. University and research centers developing NMR scanning techniques include Nottingham, London, and Oxford Universities in England, and SUNY at Stony Brook, SUNY at Downstate New York Medical Center, the University of California at Berkeley, the University of Illinois, and Johns Hopkins University in the United States (143).[7] Damadian, who is affiliated with Downstate has formed his own company, FONAR Corp. and plans to place an instrument in a diagnostic center in Cleveland, Ohio, for clinical evaluation (101).

In addition, there is substantial private investment currently being made in R&D that will translate the principles of NMR tomography into devices that may be commercially marketed. In the United States, Pfizer has a scanner at the University of California in San Francisco (143). Johnson & Johnson (Technicare), General Electric, and Intermagnetics are also reportedly involved in the commercial development of NMR scanners (79,101). In Europe, there are four companies known to be developing NMR scanners. These are: EMI, Ltd. (United Kingdom), Brouker West Germany), Siemens (West Germany), and Philips (Holland) (143). The intense involvement of these companies attests to their expectations regarding the potential marketability of NMR techniques. The estimated cost of an NMR for whole-body scanning is about $500,000, but with the addition of computer equipment necessary to provide the imaging capability of the scanner, total costs would approach $750,000 (101,143) .

Interestingly, EMI, Ltd. (now Thorn EMI), which pioneered the R&D of the CT scanner, is actively involved in NMR (80,101). Both EMI and Nottingham University have recently produced images of body sections using NMR. These models have been the basis for research by several of the U.S. manufacturers (143). In May 1980, EMI installed its prototype NMR scanner in Hammersmith General Hospital in London with the purpose of evaluating the device under conditions of hospital use (79). It is conjectured that EMI will begin manufacturing and marketing this device in the near future (143).

Ultrasonography

Ultrasonography is not a new technology: Its development preceded that of CT scanners by at least 20 years and it has been used in the clinical practice of obstetrics since 1956 (59), Ultrasound has experienced a much slower developmental history than CT scanning, and it has been slower than CT to gain wider acceptance by practitioners and broader application in medical practices (153). However, there are now several indications that suggest that ultrasound is rapidly coming of age [8]

Recent improvements in ultrasound instrumentation have resulted in enhanced image quality and reliability, convenience of use, and quicker study times, all of which have heightened the appeal of ultrasound to practitioners. These emerging improvements in the technical performance of ultrasound imaging systems, however, are not the sole reason for its relatively newfound appeal. There is also increasing importance being placed on cost and safety —two attributes that have always made ultrasound appealing relative to CT scanners for some uses. Ultrasound

[7] Also in this country the Massachusetts Institute of Technology, Harvard University, and Bell Laboratories are developing NMR scanners They have not yet produced images that are comparable to those of the institutions listed in the text, however (143).

[8] Market trends indicate that ultrasound is currently the most rapidly growing market of imaging products (see table B-2)

equipment is much less expensive than any CT scanner (in terms of capital cost): The most technologically advanced, fully automated ultrasound imaging systems now commercially available still sell for about $150,000, a price that is about one-fifth that of some present generation CT scanners.[9] A real-time ultrasound scanner costs around $50,000 (174). In addition, ultrasound units are smaller than CT, require no elaborate installation, and are portable, allowing them to be used in areas such as the newborn nursery and the intensive care unit.

The second attribute of ultrasound that has always made it preferable to CT scanning (and other X-ray modalities) is that it is based on the physics of sound rather than radiation, and therefore does not impose the risks associated with ionizing radiation (136). The higher growth rates for ultrasound sales observed in 1979 data and projections through the coming decade suggest a market trend toward imaging devices that do not use X-ray (91). In part, this may reflect the heightened public awareness of the harmful effects of radiation **(91).** However, relative to CT, ultrasound has the limitation that it cannot penetrate bone and thus cannot be used to image the adult brain, and the limitation that it cannot penetrate gas, and hence cannot be used to image structures surrounded by gas- filled loops of bowel (136). It likewise has no role diagnosing disease in the lungs.

Although it is true that ultrasound is safer than CT because it does not use X-ray, more cautious observers point to the possibility that ultrasonics may involve other risks yet unknown **(86).** Until recently, ultrasound has been presumed to be harmless, and its supporters have insistently promoted it on this basis. Indeed, this assumption has been one of the primary reasons for its near-routine application in the practice of obstetrics.[10] Now, however, the possibility of risk entailed in using ultrasound is becoming the focus of considerable concern particularly because of its prevalent application in obstetrics (17). It is more realistic, and safer, to say that the risk associated with ultrasonic energy is unknown rather than nonexistent.

The principles of ultrasonics can be clarified by a discussion of one of the two types of ultrasound, pulse echo imaging (59). The key element of the ultrasound system is the transducer that changes voltage into high-frequency sound by means of a piezo-electric crystal: This crystal also has the capability of picking up reflected sound and changing it back into electricity. This electronic input is then converted into visual data. There are several formats for display, not all of which provide a two-dimensional image. The format most closely approximating the X-ray view supplied by CT scanner is that of the B-mode compound scanning method which provides a two-dimensional, cross-sectional view of a body tissue or structure (59). Its principal components include the transducer, transmitter and receiver, digital or analog processor, and display monitor. There may also be a television camera, video tape recorder, and record monitor so that image sequences of particular interest may be recorded for later analysis (88). An ultrasound imaging system is shown schematically in figure B-2.

One problem with ultrasound is that the quality and reliability of the images depends directly on the skill of the person operating the equipment. Recent refinement and automation have not yet solved that problem **(136).** In addition, some observers have attributed the rather long developmental path of ultrasound, as well as its consequent slow application and acceptance by practitioners in diagnostic capacities, to the fact that ultrasound has no "natural" constituency among the medical specialties (153). There is no medical specialty to which ultrasound is particularly germane (outside obstetrics), although it is now being applied in many: Cardiology is one specialty with rapidly expanding applications of ultrasound (150). Many other specialities including ophthalmology, pediatrics, and neurology, are now acquiring their own units, which helps explain the recent explosive growth (174).

Historically, ultrasound has received fairly large funding support from NIH. Table B-4 shows Federal investment in 1975—present levels are probably comparable. NCI has done some recent work: Two projects are currently in progress, each funded at about **$500,000** in fiscal year 1979 (153). NHLBI is also investigating the use of ultrasound diagnostic techniques in cardiology. The most active research unit for ultrasound applications at NIH is the Division of Radiology in the Clinical Center of NIH. Most of the work done in that division relates to clinical applications, but research has involved advances in instrumentation as well. New equipment is being developed in the field of real time scanning **(153).**

In spite of these past trends in development and adoption into wider use in medical practice, however, ultrasound is now being applied to a variety of medical problems outside its longstanding and now

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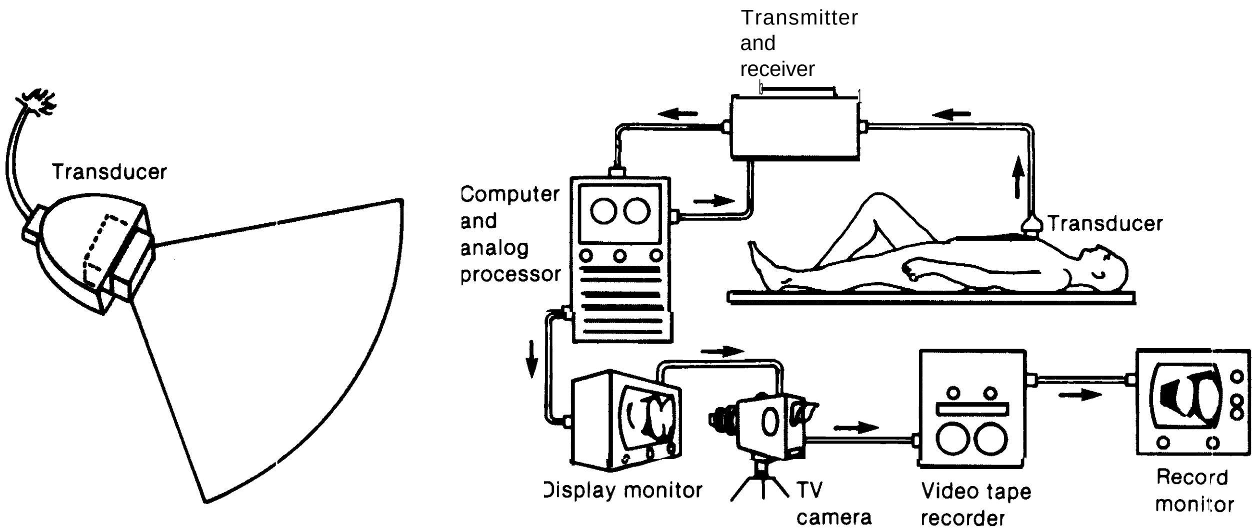
[9] This is the price of the Datason manufactured by General Electric and introduced in November 1979, which integrates the B-mode and real time scanning capabilities (123)

[10] The technology was first found to be very useful in obstetrics because of the fact that sound transmits very well through water, or fluid such as that found in the amniotic sac Its safety was assumed and later accepted based on accumulating clinical experience This application is based on the sonar principle It displays images of sections of the human body so rapidly that internal movement may be detected its main use is recording the fetal heart rate during labor

Figure B-2. -Principal Components of Real-Time B-Mode Ultrasound Imaging System



SOURCE:IEEE *Spectrum,* January 1977, p 80

Table B-4.—Federal Funding for R&Din Ultrasonic Imaging Diagnostic Instrumentation (1975)

National Bureau of Standards	$ 100,000
Department of Defense:	
Army	120,000
Navy	285,535
Energy Research and Development Administration	80,000
Department of Health, Education, and Welfare:	
Food and Drug Administration	841,459
Health Resources Administration	25,000
National Institutes of Health:	
National Cancer Institute	418,514
National Heart and Lung Institute	2,851,165
National Institute of General Medical Sciences	1,530,166
National Institute of Arthritis, Metabolic, and Digestive Diseases	118,964
National Eye Institute	439,297
National Institute of Neurological and Communicative Disorders and Stroke	379,905
Division of Research Resources	20,000
Division of Research Services	50,000
Social and Rehabilitation Service	24,851
National Aeronautics and Space Administration	360,000
National Science Foundation	818,850
Veterans Administration	20,500
Total	$8,484,206

[a]Does not include all Intramural programs, which are considerable

SOURCE: All lance for Engineering in Medicine and Biology, *Directory of Federal Programs in Medical Diagnostic Ultrasound* (Chevy Chase, Md , 1976).

near-routine use in the practice of obstetrics. Applacations of ultrasound have expanded to include studies of the brain, eyes, and various organs and structures of the abdomen (including the liver, gall bladder, spleen, pancreas, kidney, and adrenal glands), as well as fluid collections in the abdomen (147). With the emergence of these new applications, ultrasound has become the diagnostic imaging modality that is currently most often compared to CT scanning for studies of the abdomen.

Thus, ultrasound is being applied in diagnostic roles that compete with and/or complement those typically performed by CT scanners and/or other radiological diagnostic imaging modalities. Ultrasound has proved particularly popular in applications where the risks associated with ionizing radiation are especially high (as has always been the case with the use of ultrasound is obstetrics). The recently published results of a clinical trial testing the efficacy of using ultrasound for breast cancer screening for tumor,[11] for example, showed ultrasound to be able to accurately and reliably diagnose tumors of the breast when they are fairly large **(25).**

The successful application of ultrasound for breast cancer screening for tumor would be significant in that it would offer an alternative to X-ray mammography, a procedure for breast cancer screening that has been the focus of much controversy. Breast cancer screening was the topic of the first consensus development conference sponsored by NIH **(24).** Consideration of X-ray mammography, as used for screening rather than diagnosis, was an important part of that conference. The risks and potential benefits of X-ray mammography screening were such that the panel recommended routine screening for women age **50** and over, but that women between **40** and 49 years be routinely screened only if they have either a personal or family history of breast cancer, and that women under **40** years of age not be routinely screened unless they have a personal history of breast cancer **(24).**

Other potential applications of ultrasound may become increasingly important. One is carotid artery scanning to diagnose occlusion (blocking) of the artery (156). Another is the use of ultrasound to characterize tissue such as liver (155) and pancreas (154) to diagnose such diseases as pancretitis. In terms of its capability to diagnose some diseases, ultrasound is not superior to or even equal to CT: For other diseases, the two may be about equal. In those cases where the images produced by each modality can enable accurate and reliable diagnosis, and one modality involves irradiating the patient while the other does not, it stands to reason that the obvious choice would be to avoid imposing the risk associated with radiation.

It is important to stress, however, that ultrasound cannot be assumed to be harmless because no ionization occurs with the interaction of ultrasonic energy and human tissue. Rather, the associated risk is unknown and is cause for growing concern by more cautious observers **(148).** Proponents of ultrasound maintain that the risk is negligible, noting that no adverse effects attributed to ultrasound have been reported by either obstetricians or pediatricians **(59).** Proponents further substantiate this claim by pointing to the fact that the developing embryo or fetus is tremendously susceptible to traumatic influences and that such a fragile organism would be the first to manifest any ill effects. Critics argue that the absence of reported hazards does not constitute proof of safety (59). Although there have been no adequate human studies of the risk entailed in the use of obstetric practice to date, experimental laboratory studies with mice and primates have indicated a variety of problems as a direct result of using ultrasound at high levels (148).

The possibility of risk associated with intrauterine exposure to ultrasonic energy is particularly poignant given its prevalence of use in the United States (59). Virtually every large labor room in the country is equipped with ultrasound for the purposes of monitoring the fetus during labor; an application now regarded as routine practice. More recently, there has been a trend toward the routine use of ultrasound for monitoring the embryo and fetus in early stages of gestation as well (59). The current high use levels observed and expanding routine application of ultrasound may not be justified in terms of the benefits attained by the monitoring procedure **(17).**

Thus, at the same time that considerable concern is being expressed over the safety of ultrasound as applied in obstetrics, it is being more liberally applied: The controversy over risks and benefits has placed the technology at the center of a heated debate regarding its appropriate use in obstetrics. Certainly there is the potential for abuse in applying the technology. At the least, unnecessary use of ultrasound could result in unnecessary costs. But at the worst, it could result in unknown damage in a generation of children. The controversy points out, in the most dramatic way, a great need for basic information regarding the safety and efficacy of ultrasound.

The Future of CT Scanning

As recognized by the honor of the Nobel Prize bestowed on its originators in **1979,** the CT scanner undoubtedly remains a remarkable advance in diagnostic medicine. With CT technology now well beyond the phase of basic R&D to which Federal funding sources are primarily oriented, Federal funding has recently supported the R&D of new imaging technologies such as NMR, PETT, and ultrasound, the capa-

[11] These are the first clinical trials of this application of ultrasound However this equipment was marketed commercially a few years ago, and there are already at least three commercial models presently available (153)

[12] There are nine human studies but all are methodologically flawed (153).

bilities of which may exceed those of current CT scanners.

This is not to suggest that the limits of the CT scanner, based on the principles of radiology and CT, have been fully realized. But continued refinements and improvements in CT technology are now more the concern of those private companies that currently have considerable vested interest in the future of CT scanning. Among the performance improvements that current CT technology may now be capable of supporting are subsecond, high-resolution, and/or three-dimensional reconstructions (64). Proponents of CT are confident regarding the continuing technical evolution of the technology through the remainder of this century (64).

Meanwhile, however, private, as well as Federal, investments in the R&D of new principles of imaging have resulted in the emerging technologies of NMR and PETT scanning. While the contribution of CT imaging to biomedical research and medicine was to provide studies of anatomical structure in a noninvasive, automated mcde, the techniques of PETT and NMR provide studies of physiology and function, and metabolism (respectively) in that same mode (151). In the case of NMR, these capabilities are particularly enticing since they are achieved via a technique that does not involve radiation exposure, either from X-ray or from the administration of radionuclides.

It is not only the new and emerging imaging techniques that are poised to present a challenge to CT scanners, but also other older techniques such as ultrasound. Continued research on ultrasound diagnostic imaging techniques has resulted in improvements in equipment and procedure that have brought about comparable diagnostic capabilities for certain conditions, as well as convenience of use for practitioners. At the same time, the appeal of diagnostic ultrasound has been enhanced as increasing emphasis has been placed on cost and safety of equipment and procedure. Diagnostic ultrasound, which is assumed to be not only safer than X-ray imaging techniques but also far less expensive even in its newest forms, can be expected to continue its competitive position in medical practice, and consequently in the commercial marketplace.

Several indicators already reflect the increasing preference and demand for less expensive, noninvasive, non-radiation-emitting modalities such as ultrasound. For example, an estimate of 1979 (worldwide) dollar volume sales in ultrasound imaging equipment indicates an increase of 40 percent over sales in 1978, while an increase of 10 percent over 1978 was estimated for CT scanner sales (48). Projections of annual growth rates from 1979 through 1982 show an extension of these trends: It is expected that sales of CT scanners will continue to increase at an annual rate of approximately 10 percent, but ultrasound is expected to show a 31-percent rate of increase per year (48). Increased utilization of ultrasound in medical practice may also be expected in the coming years based on such indicators as the papers presented at the annual meeting of the Radiological Society of North America in November 1979 (134). While the number of papers on applications of ultrasound increased from the previous year by about 15 percent, the number of papers on applications of CT decreased by about 10 percent (91). It is already predicted that the increased use of ultrasound in diagnostic capacities enabled by recent refinements in ultrasound technology will affect the future sales of CT scanners (91).

Eventually, the diagnostic imaging instrument market will be further altered by the introduction of new technologies. However, it also seems to be recognized that these new imaging techniques will be subjected to an increasingly critical and extended period of evaluation to establish efficacy, and also cost effectiveness (64). Further, primarily because of their costliness, they will come under particular scrutiny as their diffusion and widespread utilization in medical practice become imminent (143). If well-designed studies are not done of their clinical utility, two equally undesirable outcomes are possible: Rapid spread without demonstration of usefulness or concerted attempts by Government to restrict diffusion without a good basis on scientific studies on which to rely.

Expectations surrounding the introduction and use of new technologies have given rise to a certain skepticism regarding their becoming generally available (64). Some believe that the cautious environment into which expensive new diagnostic modalities such as NMR will be introduced will have a net effect of favoring continued evolutionary changes in diffused, accepted technologies and procedures— in this case CT scanners and scanning. The recent trends observed with respect to the development and use of ultrasound equipment and procedure are a pertinent example of this prediction. [13]

Ultimately, the way in which these new and improved diagnostic imaging modalities will compete with CT scanners in the marketplace will be determined by the way in which their capabilities are used

[13] Although ultrasound is not nearly as capital intensive as either CT is, or NMR is expected to be, expenditures associated with its use now rival those associated with CT because of the prevalent and frequent application of ultrasound in its current capacities. And as the diagnostic applications of ultrasound expand, these expenditures can also be expected to rise, The issue of capital costs v. the cost associated with actual utilization (that ultrasound so aptly Illustrates) is an Important one.

to complement, supplement, or replace CT scanning in medical practice. Essentially, this is tantamount to saying that the clinical efficacy of CT scanning—as well as that of emerging and improved diagnostic imaging techniques—must be evaluated. The future of CT scanning lies in determining what the potential impact of CT scanning can be and under what conditions these benefits can be attained. For example, comparisons of CT and ultrasound for abdominal diagnoses show that CT is generally the better imaging technique for corpulent patients, ultrasound the better for thinner ones (153). Since ultrasound does not require the patient to be motionless, it is also better than CT for imaging very young, elderly, and agitated patients (153). To be sure, the principles underlying each technique, as well as the attributes of the associated procedure, will aid in determining the ultimate place that each will occupy in the practice of medicine.

Until very recently, CT has been used primarily as a supercapable X-ray machine. But new applications of CT need to be explored and refined if it is to establish a legitimate position relative to other diagnostic technologies that are being, or soon will be, used in medical practice. Investigation of the use of CT in capabilities that lie beyond its traditional diagnostic role is especially important to extending and establishing the boundaries of its domain. Examples of such applications are the use of CT in the planning and delivery of radiation and chemotherapy treatment, and the monitoring of cancer patients under treatment (5,68, 75, 169). Another is its application in emergency medicine for head trauma (91). A final example is the use of CT as a guide in biopsying tumors, aspirating cysts, and draining abscesses of the brain.

Applications of CT outside conventional diagnostic roles will be important to establishing its clinical efficacy. The benefits accruing from the use of CT in therapeutic capacities (e. g., in conjunction with radiotherapy for cancer) are more readily discerned than those accruing from the use of CT in diagnostic capacities, partially because they have a more direct potential influence on health outcome (102,183,185, 186). These new applications could provide a broadened base for arguing the need for additional CT scanners. However, they have not yet been raised as a major issue in the current heated public debate surrounding the National Health Planning Guidelines. Presently, the evaluation of efficacy and cost effectiveness, the regulation of diffusion, and the financing of CT scanning are primarily based on the application of CT in its diagnostic capacities. New applications being made outside the diagnostic role in which CT was born, however, will be a critical factor in determining its future.