EFFICACY AND SAFETY

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EFFICACY AND SAFETY

The development and diffusion of CT scanners occurred without formal and detailed proof of their safety and efficacy. Until June 1975, only 13 clinical papers had been published on head scanning, but almost 100 scanners had been installed (121). Nonetheless, by 1977, efficacy and safety have been more thoroughly assessed for CT scanning than for many other medical technologies at a similar stage of development and use (346). The evidence has not come from well-designed, prospective clinical trials, but, as is typical for medical technologies, it has been obtained from [illegible] clinical experience.

Although less evidence is available for body scanning than head scanning, studies have found CT scanning reliable and accurate. Accurate diagnoses of a variety of medical problems can be made with CT scanning, and as a result, it has partially replaced the use of some other neurodiagnostic technologies. The impact of CT scanning on therapy or on the patient's health has not been studied thoroughly. For both head and body scanning, exposure to X-rays and the use of contrast material pose risks to patients. As yet, the extent of that risk is unknown.

The Bureau of Medical Devices of the Food and Drug Administration (FDA) administers the Medical Device Amendments of 1976 (P.L. 94-295), which require the demonstration of safety and efficacy of medical devices, including CT scanners. In addition, the Bureau of Radiological Health of FDA has the statutory responsibility to protect the public from exposure to ionizing radiation. These two Bureaus will cooperate in developing performance standards for CT scanners. These performance standards are expected to be technical and not concerned with therapeutic impact or patient health (except in preventing radiation risk). No Federal agency has the formal responsibility for developing the information on efficacy and safety necessary to make decisions in such programs as health planning, [illegible], and medical care reimbursement.

THE ISSUE OF EFFICACY

Efficacy is defined as the potential benefit to individuals in a defined population from a medical technology applied for a given medical problem under ideal conditions of use. Efficacy is an abstract concept projecting the results that a technology might achieve. According to this definition, the efficacy of a medical technology can be determined only by examining information about four aspects of that technology:

(I) the benefit individuals receive and the probability of benefit,

(2) the population benefiting from the technology,

(3) the medical problem affected, and

(4) the conditions of use under which the technology is found to be beneficial. Technologies may be beneficial only when used in a certain manner. For example, dosages can affect the outcome of using drugs, and skill of the surgeon is important in surgery. For diagnostic technologies, conditions of use include findings from the history and physical examination indicating that use of the technology is appropriate.

Thus, efficacy is more than a simple consideration of potential benefits. No technology is beneficial in the absolute; it is beneficial only when used in an appropriate manner—for a defined population, for given medical problems, and under certain conditions of use. Well-designed studies of efficacy consider all of these factors.

The term *benefit* refers to the usefulness or value of the technology. For preventive technologies, it refers to the potential for preventing disease. For therapeutic technologies, it refers to the potential to improve the health of a patient. But for diagnostic technologies, the situation is more complicated.

Defining the efficacy of a diagnostic technology, such as the CT scanner, is particularly complex because the technology itself cannot directly affect the physical health of patients. Questions arise about how to judge the efficacy of a diagnostic technology. Is efficacy limited to considerations of the capability of the technology to aid in diagnosis? Does efficacy depend on the ability of that technology to replace another diagnostic technology? Does efficacy of a diagnostic technology depend on whether the diagnosis led to appropriate treatment? In some instances, appropriate treatment may be no treatment, such as for incurable medical problems or the identification of no medical problem at all. Or does the efficacy of a diagnostic technology depend on the availability of an efficacious therapy?

Several formulations of efficacy for diagnostic technologies have been developed. Fineberg and his coworkers have formulated efficacy of diagnostic technologies in terms of five levels **(167):**

(1) Technical capability—Does the device perform reliably and deliver accurate information ?

(2) Diagnostic accuracy—Does use of the device permit accurate diagnoses to be made?

(3) Diagnostic impact—Does use of the device replace other diagnostic procedures, including exploratory surgery and biopsy?

(4) Therapeutic impact—Do results obtained from the device affect planning and delivery of therapy?

(5) Patient outcome-Does use of the device contribute to improved health of the patient?

In a study sponsored by the American College of Radiology, an alternative approach to the assessment of efficacy of diagnostic technologies has been proposed:

Efficacy-l, the information content of the procedure; Efficacy-z, the use of the diagnostic information in prescribing treatment or in gathering more information; and Efficacy-3, the expected value of diagnostic information to the health of the patient **(335, 336).**

Assessment of the efficacy of diagnostic technologies is often limited to levels 1 and 2 of the Fineberg formulation as they are the easiest to perform. Levels 3 and 4 are more difficult to assess, but feasible. These four levels are primarily concerned with medical care processes. Patient outcome (level 5) is much more difficult and time-consuming to determine since followup of patients over time is required (33.5). Present policy and current practice have emphasized assessment of the accuracy of diagnosis, with little concern for effect upon therapy or outcome. Thus, few diagnostic technologies have been evaluated from these points of view.

EVIDENCE OF EFFICACY OF CT SCANNERS*

Efficacy cannot be measured directly, although evidence about it can be obtained from controlled clinical trials or from clinical experience. Such evidence allows judgments to be made about efficacy, judgments that may change as additional evidence accumulates. Efficacy has been more thoroughly assessed for CT scanners than for many other medical technologies at a similar stage of development and use. The available evidence has not come from well-designed, prospective clinical trials, but as is typical for medical technologies, it has been obtained from analyses of clinical experience. The results of these clinical studies are presented without necessarily endorsing the manner in which they were obtained.

Head Scanning

Technical Capability

Engineers and medical personnel find that head scanners perform reliably and deliver accurate information (44,125,129,338,382,386,405,406). Most of the technical problems and malfunctions that plagued early CT scanners have been eliminated (129,405,406). New installations often experience considerable "down-time," but most malfunctions can be corrected by hospital staff. Protocols and equipment for evaluating both the technical capabilities and performance of CT scanners have been designed **(25,191,338).**

While CT scanners usually function well and produce reliable images, their technical capabilities do have limitations. Objects are not always resolved if smaller than about 1 centimeter in diameter, or if their density differs only slightly from that of surrounding tissue (16,129,247,40.5,406). Because of the arrangement of sources and detectors in some machines, parts of sections being scanned may not be imaged at all or may be dually imaged (193). As a result of limitations in the imaging procedures, artifactual lines or patterns appear near areas of very high density or

* Conclusions in this section are based on a literature review carried out during May 1977. According to recent reviews, however, the conclusions remain valid. The interested reader should refer to Abrams, H, and McNeil, B. "Medical Implications of Computed Tomography ('CT Scanning')" *New Eng. J. Med.* 298:255 and **310,** 1978.

contrast, such as implanted ventricular shunts or surgical clips, or the skull **(108,129,191,386,405,406). Any** motion of the patient during scanning may also cause artifacts **(15,16,225,236,386,405,406),** but this problem is more serious for body than for head scanning.

Diagnostic Capability

(1) Diagnostic Accuracy. CT scanning has been used in diagnosing nearly all neurological disorders associated with an abnormality in or near the brain **(15-23, 39-41, 44-53, 55-58, 62, 74-76, 83, 87-88, 90, 92-94, 97-101, 103, 108, 124-130, 138-143, 154-156, 160, 162, 170-171, 173, 183, 192, 202-204, 210-212, 223-225, 230-231, 239, 248-249, 251-252, 255, 267-269, 271, 274, 276, 278-279, 284-289, 291-294, 308, 310, 312, 314, 318, 320, 326-330, 333-334, 343, 347, 353-354, 356-361, 368-372, 385-386, 388, 393-394, 397, 400, 405-407, 410-412, 420, 426-429, 432, 439, 441-442, 447,451, 458-460, 472, 478, 482, 488-489, 492, 516-518, 520, 522, 536-537, 539-543).** CT head scanning can reveal lesions in the brain itself, in the meninges (lining that surrounds the brain), and in the orbit (bony socket of the eye).

In a head scan, lesions are detected by abnormalities in the density or shape of the brain (125,236,237,386). A decrease in density (that is, a decreased ability of some part of the brain to absorb energy from X-rays) may indicate edema, an infarct, or a fluid-filled cyst. An increase in density suggests a tumor, hemorrhage, fibrosis, calcification or hemorrhagic infarct. An asymmetric image suggests mass lesions such as tumors. Large changes in shape, such as enlarged ventricles and dilated subarachnoid spaces, are suggestive of hydrocephalus or atrophy (see figure 5).

Many reports have attempted to assess the diagnostic accuracy of CT head scanning. Some results of these studies are summarized in table 2. In most of the studies, accurate diagnoses were obtained for 80 to 100 percent of the patients; greater than 90-percent accuracy was reported for about two-thirds of the patient groups.

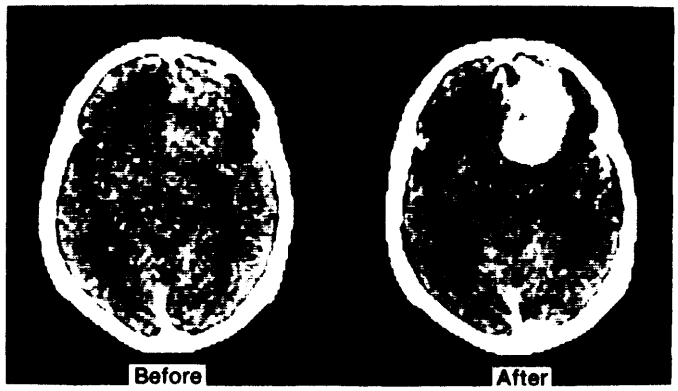
(2) *Contrast Enhancement and Diagnostic Capacity.* **In** about **60** percent of CT head examinations, and in more than 50 percent of all CT examinations, patients have contrast material injected into their bloodstreams. This percentage has increased over time **(240,241).** These patients are usually scanned both before and after the injection. The use of contrast material is often time consuming, adds sizably to the cost and price of CT scanning (see chapter 6), and exposes the patient to some risk. Although radiologists believe that these drawbacks are outweighed by the additional diagnostic information obtained, the empirical evidence is less convincing. Many lesions can be seen better on contrast-enhanced than on unenhanced scans, and information is gained about the nature of the lesion **(21,119,135,303,386)** (figure 9). On the other hand, in two large studies of the efficacy of contrast enhancement, injection of contrast material revealed lesions invisible on unenhanced scans in only 2 to **5** percent of all patients **(44,119).**

(3) *The Validity and Reliability of CT Diagnostic Capacity.* The studies summarized in table 2 and a variety of less systematic case reports lead to the conclusion that CT scanning permits more accurate diagnosis of some types of lesions than others. Tumors in or near the brain can be diagnosed and localized quite accurately, as can a variety of cerebrovascular lesions. On the other hand, hairline fractures, small tumors, and some new infarcts are difficult to image with CT scanning. Early

Table 2.—Diagnostic Accuracy of Head Scanning: Summary of Published Studies

Diagnostic Category	Numberof Patients	Percent Accurate Diagnosis	Reference
Unclassified Neurological Disorders	800	97	44
Unclassified Neurological Disorders	53	92	228
Unclassified Neurological Disorders	450	98	487
Unclassified Neurological Disorders	75	88	344
Unclassified Neurological Disorders	641	92	90
Unclassified Neurological Disorders	109	87	4
Unclassified Neurological Disorders	79	86	244
Cerebrovascular Lesions			
hemorrhage	17	88	24
hemorrhage	13	100	90
hemorrhage	15	81	437
hemorrhage	21	100	264
nontraumatic hemorrhage	18	100	463
nontraumatic hemorrhage	100	90	213
nontraumatic hemorrhage	46	90	419
acute cerebrovascular disease	60	85	375
cerebrovascular disease	51	75	266
cerebrovascular disease	89	72	95
subdural hematoma	35	100	368
angioma	14	86	368
angioma	41	80	260
infarct	52	52	90
infarct	84	75	118
infarct ....00...	58	98	264
infarct	100	93	476
infarct (middle cerebral artery)	174	86	89
Tumor			
intracranial tumors 00	106	94	164
intracranial tumors 0	24	100	95
intracranial tumors 0	209	97	259
intracranial tumors	174	95	368
intracranial tumors 0	88	95	375
intracranial tumors	633	96	20
intracranial tumors (children)	45	89	57
intracranial tumors	114	85	90
intracranial tumors .. ..O..	35	97	4
meningioma	71	96	93
orbital lesions -mostly tumor	25	84	486
juxtasellar lesions-mostly tumor	20	100	368
pituitary adenoma	12	100	91
Atrophy	20	90	401
Abcess	22	100	356
Abcess	10	100	346
Abcess	8	88	305
Abcess	26	92	92

Figure 9.—Malignant Lymphoma in Right Frontal Region Before and After Enhancement



Source: Reproduced with permission from *Cranial Computerized Tomography*, Springer-Verlag, Berlin Heidelberg. New York, 1976, p. 88,

observations indicated that aneurysms, subdural hematomas, and small masses very near bone (such as tumors in the posterior fossa) were difficult to image **(15,16,108,129,202,405).** Other physicians, however, have reported considerable success in imaging such lesions (231,370,405,429,439).

Accuracy of CT scanning has been assessed by comparing diagnoses made through its use with those made by methods of presumably assured validity. Autopsy or surgery, which provide opportunities for rigorous confirmation, have been used in some studies. Many studies, however, rely on less exacting confirmation, such as other diagnostic tests or the subsequent course of the disease.

In a study by Messina (355, cited in 382), for example, autopsies confirmed, to some extent, diagnoses made by CT scanning in 88 percent of the patients. Only 55 percent of the diagnoses were confirmed completely, however. Partial agreement between CT scanning and autopsy results was observed in the remaining 33 percent. Many patients had multiple lesions, and when each lesion was considered separately, the accuracy of CT scanning was even lower. Only one-third of all lesions seen on autopsy were imaged by CT scanning; another third were so small that they could not possibly have been resolved; the final third, although large enough to resolve, were not seen in the CT images. It should be noted that these lesions would probably not be visualized by any other existing diagnostic technique.

Other diagnostic procedures may be more accurate than CT scanning for some diseases. A complete study of this possibility would test each procedure on each disease condition to compare true negatives, true positives, false negatives, and false positives. Such information is not yet available because few such studies have been undertaken.

Many studies include reports of early experience with CT scanners. Radiologists point out that many diagnostic failures were the result of inexperience or early equipment deficiencies. Thus the accuracy of CT scanning may be underestimated in early studies.

Several of the studies compare the simple accuracy of CT scanning and other diagnostic procedures. In general, CT scanning has been found to be more accurate

for neurological lesions than radionuclide brain scans or conventional skull X-ray films. It has been found to be at least as accurate as the risky and uncomfortable procedures of arteriography and pneumoencephalography (see below).

Diagnostic Impact

The most common neurodiagnostic procedures used before the development of CT scanning were cerebral arteriography, pneumoencephalography, radionuclide brain scanning, and skull X-ray. Others included echoencephalography, and electroencephalograph (see table 3).

(1) Arteriography or Cerebral Angiography. During arteriography, contrast material is injected into the patient's bloodstream while conventional X-ray images the blood vessels in the skull. Radiologists can recognize malformations of the blood vessels and/or infer damage to the brain itself from distortions in the vascular pattern. Arteriography requires 2 to 4 days of hospitalization (36) and exposes the patient to more radiation than a set of CT scans (443,564). Comparisons of the two procedures have found CT scanning to be at least as accurate as arteriography in revealing and pinpointing neurological lesions (21,39,45,48,62,101,180,294,388,439).

After the introduction of CT scanning in several institutions, the number of arteriograms performed decreased by 15 to 34 percent **(46,157,296,382,443).** While a 15 to 20 percent decrease is the most frequently quoted range (36,46,48, 262,264,296,382,582), a O to 5 percent increase has also been recorded (45,80). However, arteriograms were increasing in number in the late 1960's and early 1970's, and CT scanning may have halted this upward trend (45). CT scanning is most often used as an alternative to arteriography in emergency situations and on new admissions **(261,** 350,382,405,439). However, arteriography is still considered to be superior to CT scanning for delineating the vascular structure of the brain (38,45,264,41 2) and will continue to be used in some situations (264).

(2) *Pneumonencephalography.* In this procedure air is injected into the spinal canal where it moves upward into the ventricles of the brain and shows up on conventional X-ray films. Distortions in the ventricular space indicate space-filling lesions in the brain. Some risks of morbidity and a rare fatality are associated with this procedure, especially for certain groups of patients, such as the elderly. In addition, pneumoencephalography requires 4 to 10 days of hospitalization (36,264) and may expose the patient to more radiation than CT scanning (564). Clinical studies have shown that CT scanning and pneumoencephalography frequently provide diagnostic information of approximately equal accuracy (21,44,48,180,181 ,439).

The use of pneumoencephalography decreased by 20 to 75 percent in several institutions upon the introduction of CT scanning (36,45,50,82,138,140,157, 262,296,382,538,545,582). Because of its costliness in terms of resources and risks to patients' health, however, pneumoencephalography has never been a frequently used procedure. In fact, its use started to decline even before CT scanning was an available alternative (264,382). Although indispensable for identifying certain classes of tumors (62), use of pneumoencephalography continues to decline. It will probably become more restricted to neurological referral centers where medical personnel with the proper expertise are available (264).

(3) *Radionuclide Brain Scanning (RNS).* Radioisotopic material is injected into the bloodstream, and the head is scanned by a camera that can detect and record the

Table 3.—Comparison of CT Head Scanning With Other Neurodiagnostic Procedures[a]

Procedure	Diagnostic Accuracy[b]	Approximate Annual Numbers of Procedures in United States, 1976	Safety Compared to CT Scanning	Usable On Outpatients	Estimated Effect of CT Scanning on Utilization
CT Scanning	High-generally 80-900/o	855,400-987,000		Yes	
Arteriography	Similar to CT	1 00,000-350,000'	Riskier	No	-20% to 0[d]
Pneumoencephalography	Similar to CT	25,000-50,000'	Riskier	No	-40% to -750/0'
Radionuclide scanning	Inferior to CT	2,000,000	Similar	Yes	-90% to +15%
Skull X-ray	Used for purposes different from CT; inferior when compared	4,000,000'	Similar	Yes	Little or no effect

[a] Estimates of Office of Technology Assessment unless noted.

[b] Numbers given in this column are not strictly comparable. Arteriography is often used after diagnosis of a brain tumor, for example, to demonstrate its extent and vascularity. Arteriography and pneumoencephalog raphy are seldom used with stroke. Nonetheless, based on published studies, the comparisons are basically valid.

[c] Low figure is from reference 425. High figure is from reference 265.

[d] Reference 47 reported -20 percent and reference 82 reported + 0.05 percent.

[e] Figures are for 1973 and 1975. In 1976, CT head scanning had a great impact on the number of pneumoencephalograms performed, and estimates for 1976 are not available. Low figure is for 1975 (425). High figure is a national projection of a 1973 survey in southeastern Pennsylvania (582).

[f] Reference 47 reported -40 percent and reference 296 reported -75 percent.

[g] Reference 296 reported +15 percent and reference 383 reported -90 percent.

[h] Figure is for 1970 (504). The number of diagnostic X-rays rose approximately 4 percent a year from 1964 to 1970, so the number is probably larger now.

radioactivity. Areas with abnormal concentrations of radioactivity are presumed to be diseased. RNS is not considered to be a dangerous diagnostic procedure and is performed on outpatients. CT scanning has been shown to be superior to RNS in several studies of diagnostic accuracy of specific conditions (4,21,39,44,48,103,140, 180,293,295,380,382,388,393,439). Other investigators, however, have found that the two procedures produce anatomical information of approximately equivalent accuracy. RNS also gives information on the functioning of the brain and its blood supply (62,98,360).

Although a large study is underway (425) that attempts to determine the comparability of the two procedures, the change in the use of RNS after the introduction of CT scanning has varied substantially from one institution to another. The highest range shows a decline in the use of RNS by **50 to 90** percent **(46,50,382,545,582). At the other** extreme, the change in the use of RNS has ranged from a 15-percent increase to a 35-percent decrease (82,157,264,295). While some radiologists have stated a preference for CT scanning over RNS (48,140,141,380), others believe that, since the two procedures may yield different types of information, they should be used in a complementary fashion (62,76,360,382,412).

(4) *Echoencephalography.* This procedure applies ultrasound technology to neurological diagnosis. Ultrasound waves are directed at the head, and their reflections are detected and analyzed to find distortions in the shape of the brain. Echoencephalography is a safe and noninvasive procedure that can be performed on outpatients.

The accuracy of CT scanning and that of echoencephalography have not been compared systematically. The two procedures are not designed to yield exactly the same information. However, the Mayo Clinic, the only institution in this country to publish observed changes in the use of echoencephalography after the introduction of CT scanning, reported a decrease of 40 to 50 percent (50).

(5) *Skull Films or Skull Series,* A skull series involves a set of four or five conventional X-ray films taken according to a standardized protocol. CT scanning provides more accurate diagnostic information than a skull series for certain conditions (180,343,439). Skull films, however, are often used to detect abnormalities of the bone, such as fractures, which are difficult to image with CT. Also, skull films are accepted as a standard screening procedure for patients with general neurological symptoms. Medicolegal factors reinforce this use (61). CT scanning has had a small impact on the use of skull films because skull X-rays are usually performed prior to CT head scanning. Some radiologists have suggested that this practice is unnecessary (270).

(6) *Electroencephalography (EEG).* Electroencephalograph records the electrical activity of the brain through leads taped or pasted to the scalp. A noninvasive and safe procedure, it is widely used in diagnosing epilepsy. Because EEG provides different diagnostic information from CT scanning, its use has been little affected by CT scanning **(39,30,296).**

(7) *Exploratory Surgery.* One study examined the actual impact of CT scanning on neurosurgical procedures following head trauma. Before CT scanning, exploratory surgery often followed head injuries to ensure that life-threatening damage had not occurred and to correct such damage if found. A London hospital found a sharp reduction in the need for such surgery following introduction of CT scanning (21). In the year before introduction of the CT scanner, 33 percent of patients had such

surgery; in the year following introduction of the CT scanner, only 2 percent had such surgery. However, no attempt was made to ensure that the two groups of patients were comparable.

Therapeutic Impact

To date, only one study has attempted to assess the impact of CT head scanning on the planning of therapy. The study covered 194 patients; physicians were interviewed before and after their patients were scanned. Treatment plans were altered for 19 percent of the patients. This figure dropped to 15 percent when counting only those for whom improvement in outcome was possible (i. e., those who did not die soon). Changes included ordering new treatment, abandoning previous therapy plans and increased precision of already planned therapy, such as surgery or radiotherapy (167).

The only known study to examine the actual impact on neurosurgical procedures is summarized in the section above under exploratory surgery (21). A similar study examined groups of patients with stroke before and after introduction of CT scanning. No differences in therapy were found (313).

Patient Outcome

Better diagnosis does not necessarily lead to improved treatment and improved health. An extensive study of radionuclide scanning, for example, indicated that its application has little or no effect on patient outcome in cases of neurological abnormality **(185).** Nuclide scans are often used to diagnose diseases for which no definitive therapy is available; the same situation also applies to CT scanning, as discussed in chapter 5. In the one study of outcome, patients with head trauma who entered a hospital before installation of a CT scanner were compared with those admitted afterwards (21). No difference in mortality between the two groups was observed. However, as noted above, no attempt was made to ensure that the two groups of patients were comparable. More complete studies, or studies using less drastic indicators of health (such as morbidity or decreased worry, instead of mortality), have not yet been reported. However, simply reducing the use of dangerous diagnostic and therapeutic procedures can help improve the outcomes of patients.

Body Scanning

Technical Capability

The technical capabilities and limitations of body scanners are generally similar to those of head scanners (see below), Changes in density or shape are used to indicate abnormalities in both body and head scans, The major difference is that patient motion poses particular problems for body scanning. The normal, rhythmic motions of breathing, heartbeat, and intestinal contraction can all cause artifacts and may result in images of unacceptable technical quality (9,10). For this reason, the heart and intestine cannot be satisfactorily imaged (157). Whether new, faster machines will be able to overcome problems of motion is not yet fully known.

Diagnostic Accuracy

Reports on the diagnostic accuracy of body scanning have recently been published; their results are summarized in table 4. Evidence has been reported that CT scanning can image tumors in the liver, pancreas, kidney, pelvic, and retroperitoneal space that are invisible on conventional X-ray films (6,8,9,95,159,217,465,474,477,526). CT scanning can also differentiate obstructive from nonobstructive jaundice, a distinction that has important implications for therapy planning **(6,7,8,159),** and it can reveal abscesses **(215)** and aortic aneurysms **(38).** Although preliminary and limited in scope, these studies indicate that CT scanning can accurately diagnose mass lesions and other conditions in several organs of the abdomen. Diagnostic accuracy in other areas of the body such as the lung and heart has not been demonstrated.

Table 4.—Diagnostic Accuracy of Body Scanning: Summary of Initial Results

Area Scanned (lesions detected)	Number of Patients	Percent Accurate Diagnoses	Reference
Abdominal abscess	22	90	215
Aorta (aneurysms)	32	100	38
Bile duct (dilation, obstruction)	8	88	8
Bile duct (dilation, obstruction)	17	100	474
Extraperitoneum (mostly tumors)	13	100	474
Kidney (cyst and tumor)	18	94	474
Liver (mostly tumors)	31	94	474
Liver (mostly tumors and cirrhosis)	61	74	8
Pancreas (mostly tumors)	37	83	474
Pancreas (tumors)	25	92	216
Pancreas (tumors)	26	84	321
Pelvis (mostly tumors)	14	100	474
Spinal cord (syringomyelia)	9	78	134

Diagnostic Impact

Little information is available on the impact of CT body scanning on other diagnostic procedures. Preliminary results from a study conducted at the Massachusetts General Hospital indicate that when used in "high payoff areas" of the body, such as the liver, pancreas, and kidneys, body scanning can have considerable impact on diagnostic methods used. In 94 patients, **27** percent were spared surgery by the findings of CT scanners (533). No other studies of diagnostic impact are yet available. With the large number of organ systems that can be evaluated and the large number of alternative diagnostic tests that can be used, it will be some time before this area is understood.

Therapeutic Impact

Radiologists have suggested several ways in which information obtained from body scanning might be useful in the planning and delivery of therapy (157,

158,316,317,465,493). In patients with jaundice, for example, CT scanning may reveal whether the bile ducts are obstructed. If so, surgery may be needed; unobstructed ducts suggest a diagnosis of hepatitis, which can be treated nonsurgically. In cases of suspected tumor, CT scanning may reveal spread of the tumor, and thus differentiate patients who might benefit from surgery from those for whom it would be futile.

As mentioned above, one study found surgery was averted for 27 percent of patients. That study also found that treatment plans were changed for about 19 percent of patients scanned (533).

Patient Outcome

No analyses of available data examine the impact of body scans on improved health of patients. But simply averting dangerous therapeutic or exploratory procedures such as surgery can be expected to improve patient outcome.

SAFETY OF CT SCANNERS

The potential benefits of CT scanning must be weighed against its risks. Safety, like efficacy, can be assessed by well-designed clinical trials or by studies of clinical experience. Determinations of safety of a medical technology examine the four factors specified above for efficacy: potential risk, population at risk, medical problem, and conditions of use for minimum risk,

Like other radiological devices, CT scanners emit X-rays, a form of potentially dangerous ionizing radiation that can cause cancer, leukemia, and genetic changes. Early reports indicated that the EMI head scanner exposed a patient to about 1 to **2.5** roentgens (R), * less than other neurodiagnostic techniques using X-ray (see table 5) (189,190,338,397,564). Recent articles, however, indicate a higher radiation exposure (521). Horsley and Peters examined the question of scattered radiation from adjacent scans and found that with 3 scans, the peak exposure with the EMI head scanner is 4 to 5 roentgens (240). Newer systems used in certain areas of the body produce a higher exposure. The Bureau of Radiological Health of FDA has stated that machines in use give a patient a dose of radiation as high as 30 rads (503). A recently published article reported a dose as high as 31 rads from use of the Ohio Nuclear prototype head scanner and **16** rads from the Ohio Nuclear production model head scanner when used at slow speed **(521).** If scans were performed and then repeated after contrast injection, these figures could double. The number of sections scanned is proportional to dose and is variable depending on physician judgment. Furthermore, higher radiation makes the image clearer, and on many machines a radiologist can increase the radiation dose by a simple adjustment of a switch. For example, at normal speed the dose to the back of the head from six "scan pairs" with an Ohio Nuclear head scanner is 7.7 rads, which increases to 15 rads with scanning at slow speed (521).

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* A roentgen (R) is a quantity of radiation measured in air. A rad is the unit for absorbed dose of radiation. A rem is the quantity of ionizing radiation such that the energy imparted to a biological system has the same biological effectiveness as an absorbed dose of 1 rad of X-radiation. As the terms are used in this paragraph, the amounts are essentially equal.

Table 5.—Radiation Exposures From Use of Some Common Neurodiagnostic Procedures[a]

	No. of Roentgens
CT Head Scan (EMI) (3 slices)	1-4.5 R
Skull Series (4 films)	1.2 R
Pneumoencephalogram (8 films)	2.8 R
Cerebral Angiogram (24 films)	10.7 R

[a] Radiation exposure from CT scan derived from references 190,240,338, and 397, Other radiation exposures are based on the 1970 National X-ray Exposure Study (503). Numbers of films are for typical community hospitals, Institutions that specialize in neurodiagnosis or that see more complicated problems often do two or three times the number of films shown (135).

A specific risk cannot be attributed to these amounts of radiation because systematic information on the effect of life-long, low-dose irradiation is simply not available (373). The National Research Council estimated the risk as follows: "If such rates (taken from studies of people with known exposure to radiation) . . . are assumed to apply generally, then exposure of the U.S. population of about **200** million persons to an additional 0.1 rem during one year . . . could be expected ultimately to cause 1,350 to 3,300 deaths *annually,* provided that the effect of a given increment of dose did not persist beyond 25 years after exposure" (373). This kind of reasoning has led to rather low limits of allowable exposure to radiation (260,375). A prominent textbook sums up this way: "It is therefore prudent to adopt the working principle that radiation exposure be kept to the lowest practical amount" (42).

Reaction to contrast material is another risk. In practice, mortality from such injections ranges from 1 death in 13,000 examinations to 1 death in 50,000 examinations. This rate may be compared to a rate of approximately 1 in 1,500 cases in angiographic examinations (5).

Another risk stems from general anesthesia. Although CT scanning usually can be performed with the patient awake, some children and confused, uncooperative patients often must be sedated or anesthetized to ensure an adequate scan (3,300). Such anesthesia carries some risk (166).

FEDERAL POLICIES CONCERNING EFFICACY AND SAFETY

Developing information on efficacy and safety involves identifying technologies to be studied; conducting the appropriate evaluations; and synthesizing the results of those evaluations, clinical experience, and other relevant information. Synthesis may be of many types. Examples of synthesis include informal collection and interpretation of existing information, analyses of gaps in current information, and policy judgments based on clinical knowledge but often extrapolating from that knowledge. The judgments or other synthesized information may then be disseminated to the organizations and individuals in need of it.

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Food and Drug Administration (FDA)

Medical Devices Legislation

The Food and Drug Administration requires studies to be conducted by private industry prior to marketing certain medical devices and also synthesizes the results of such studies. The safety of medical devices first became subject to Federal regulation in 1938. However, it was not until **1976** that the Medical Device Amendments gave FDA the authority to require that manufacturers prove the safety *and* effectiveness* of medical devices prior to marketing.

The Amendments require FDA to classify all existing medical devices into one of three categories: Class I—General controls: medical devices for which general controls are sufficient to provide that the device is safe and effective or that the device is not used in the support or sustaining of human life, or for a use that is of substantial importance in preventing impairment of human health and does not present a potential unreasonable risk of illness or injury; Class II—Performance standards: devices for which Class I controls are not adequate and for which sufficient information exists to set performance standards that will ensure safety and effectiveness; and Class III—Premarket approval: devices for which Class I and Class II controls are not adequate to ensure that the device is safe and effective, and which are used in supporting or sustaining human life, or for a use which is of substantial importance in preventing impairment of human health, and which present potential unreasonable risk of illness or injury. New devices, or devices introduced into use after May **28, 1976,** that are not of the same type and are not substantially equivalent to those on the market on May **28, 1976,** will automatically be placed in premarket approval category (Class III) and cannot be commercially marketed until either an application is approved or the device is reclassified into performance standards (Class II) or general controls (Class 1) categories.

According to the law, the safety and effectiveness of Class III devices are to be determined:

(a) with respect to the persons for whose use the device is represented or intended,

(b) with respect to the conditions of use prescribed, recommended, or suggested in the labeling of the device, and

(c) weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from such use.

The law continues

> the effectiveness of a device is to be determined, in accordance with regulations promulgated by the Secretary (of HEW), on the basis of well-controlled investigations, including clinical investigations where appropriate, by experts qualified by training and experience to evaluate the effectiveness of the device, from which investigations it can fairly and responsibly be concluded by qualified experts that the device will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling of the device.

The Bureau of Medical Devices has begun implementing the Amendments by

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* The language of the Act uses the term "effectiveness" instead of "efficacy."

appointing advisory panels to make recommendations as to which class each device belongs. The Neurology Panel and the Radiology Panel have recommended classifying existing CT scanners as Class II, but in September 1977, classification was not completed. Such a classification means that the CT scanner will be subject to performance standards of a technical nature, a point further discussed below. (Such panels are made up largely of the professionals who use the device in question, in this case radiologists, and who may have some vested interest.) New CT scanners that FDA determines to be similar to existing ones will be placed in the same class (i. e., Class 11). Any development that represents a radical departure in nature or operation from existing models could be placed in Class 111 requiring premarket approval.

Radiation Protection

The Food and Drug Administration also has statutory responsibility for protecting the public from radiation exposure from electronic devices such as X-ray machines. Its Bureau of Radiological Health develops and enforces standards to ensure minimal radiation exposure from X-ray devices. CT scanners have been subject to general radiation safety standards since the first one was installed. In 1974, specific guidelines were developed for their regulation.

Because the Bureau of Radiological Health has had experience with the CT scanner already, it will have the responsibility for developing performance standards for both safety and efficacy. * The Bureau of Radiological Health and the Bureau of Medical Devices have developed an inter-Bureau agreement to ensure cooperation in this effort. The Bureau of Radiological Health established a CT task force in 1970 that is presently considering the necessity for performance standards concerning efficacy.

The National Institutes of Health (NIH)

NIH supports basic and applied research and technology development. Initial human trials and then larger clinical trials are often stages in the research and development process. A little more than 5 percent of the NIH budget is allocated to clinical trials. The results of these investigations sometimes provide information about the safety and efficacy of technologies. However, NIH has no statutory mandate to conduct studies related to efficacy and safety.

NIH is using CT scanning in its intramural program and supporting extramural research studies involving its use. Extramurally, about 100 NIH-funded projects involve CT scanning, with the largest single group in cancer research. Several of these studies will provide more definitive information than is now available on the diagnostic accuracy of CT scanning. These studies are not, however, designed to examine efficacy in terms of its effect on therapy decisions or on the health of patients.

NIH has established a mechanism to develop and disseminate information on efficacy and has titled this mechanism “evolution of a consensus. ” During 1976, NIH applied this new process using outside experts to the problem of hypertension and its treatment. In September 1977, the second consensus process considered screening

* The legislation uses the term “effectiveness,” but the Bureau of Medical Devices considers efficacy and effectiveness to be synonymous,

for breast cancer. This mechanism may be a way of developing recommendations on efficacy for the use of other Federal programs, the public, and medical practitioners.

SHORTCOMINGS OF EFFICACY AND SAFETY POLICIES

Shortcomings in Federal policies related to efficacy and safety information occur in several areas: definition of efficacy, determination of efficacy and safety, dissemination of information, and use of the information. Use of information on efficacy and safety will be addressed in subsequent chapters.

A definition of efficacy and a discussion of some of the difficulties in applying any definition to diagnostic technologies were presented earlier in this chapter. Only FDA has been given a statutory definition of efficacy. In the FDA statutes, however, the term "effectiveness" is used rather than efficacy. According to the Food, Drug, and Cosmetic Act a medical device or drug is to be considered effective if it "will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the labeling." This effect is largely determined by the manufacturer and is not necessarily a demonstrable impact on health outcome. This statutory language results in the FDA's evaluating the efficacy of diagnostic technologies on grounds other than patient outcome. Whether patient outcome should be the standard of efficacy for diagnostic technologies is controversial. However, the lack of any generally accepted measure of "benefit" for such technologies can lead to difficulties in assessing their efficacy,

Not only is FDA the only agency that has a statutory definition, no common definition has been developed for use by all Federal programs. Some Federal agencies develop information on efficacy and safety, others disseminate the information, and still others use it to regulate various aspects of medical practice. Personnel in these programs use the term "efficacy" in various ways, to mean different things. Lack of a policy on the definition of efficacy can lead to confusion and difficulty in cooperation and communication. Judgments by one agency of the efficacy of a technology may be of little use to other agencies because different criteria are used to determine efficacy by the various agencies.

No Federal policy sets out clear responsibilities for evaluating the efficacy and safety of all classes of medical technologies—drugs, devices, and procedures. Evaluating efficacy and safety involves identifying the technologies to be studied, conducting the appropriate clinical trials, and synthesizing the results of those trials with information from clinical experience. Such synthesis can include a formal or official judgment of the efficacy and safety of a particular technology. Information on efficacy is seldom collected, organized, and made available in such a way that it can be helpful either to policy makers or medical practitioners. Presently, evaluations of efficacy for devices and drugs are performed almost exclusively by the industry that produces them, although FDA examines the design and the results of these studies for validity.

No formal mechanism exists for determining which technologies warrant eval-

uation. In particular, when the private sector has not conducted adequate studies on efficacy, no mechanism exists to identify the inadequacies and to ensure that proper studies are funded. Thus, pre-clinical and clinical studies and clinical experience are not always evaluated, and no policy exists for developing tentative positions pending availability of definitive information. Further, lack of a formal system to identify technologies to be studied often results in the needs of users of efficacy and safety information being excluded from the decision to study.

There is no formal policy, nor has any Federal agency been assigned a clear mandate, for the conduct of evaluations of efficacy and safety. More than a dozen Federal agencies conduct clinical trials, but none of the agencies do so as a result of an explicit statutory mandate. Only NIH and to a lesser extent the Veterans Administration support a substantial number of trials. In fiscal year 1975, NIH spent about $100 million dollars on approximately 750 trials. This expenditure represented about 5 percent of NIH's budget. Trials of drugs and biologics predominated; trials of devices and procedures represented only a small proportion of the total. Existing technologies received far less attention than did new or emerging ones. No clear Federal policies for identification of technologies warranting study and for conducting the appropriate evaluations exist. And no agency has been assigned the responsibility for carrying out these functions. It is also clear that the clinical trials currently conducted are not fully satisfying the needs of health planners, third-party payers, Professional Standards Review Organizations, and the practicing medical community.

Determining which technologies to study is only one contributor to the situation. Current trials often do not develop information related to each of the four factors specified by the definitions given above for efficacy and safety. Questions have also been raised about the efficacy and safety of many more technologies than can be studied with the available resources. And once the trials have been conducted, no formal mechanism exists to collect and synthesize the results of the trials, along with relevant clinical information. No agency has the responsibility (or resources) to make formal judgments of the efficacy and safety of technologies, except FDA in the case of new drugs and devices. * Medical and surgical procedures receive no systematic scrutiny.

Once information is developed, no consistent policy or agency focus exists for disseminating it to the organizations and individuals in need of it. NIH and FDA both have major activities related to dissemination, but their efforts are hampered by a number of factors. For example, FDA disseminates information related to its evaluations of the efficacy and safety of drugs and devices, but the usefulness of that data is diminished by definition-related problems. Also, NIH has been given only moderate funding for the task, and historically lacks ties to the practicing medical community and to other Federal programs, such as Medicare.

There are shortcomings in Federal policy at each of the stages in defining and evaluating efficacy and safety and in disseminating the resultant information. Moreover, the underlying problem is the absence of a consistent and explicit policy that views these stages as part of a continuous process. Evaluation depends on definition; dissemination depends on evaluation. Failure to recognize these dependencies can lead to fragmented policies relating to each of the parts.

*The FDA process is impacted by the definitional shortcomings mentioned here and from lack of funds to carry out efficacy and safety tests independent of the sponsoring industries.