3.

Introduction to Digital Subtraction Angiography

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Digital subtraction angiography (DSA) is a new radiographic technology used in diagnosing vascular disease. DSA is employed to obtain images of arteries in various parts of the body and is highly effective in contrasting arterial structures with their surrounding bone and soft tissue (3). DSA has proven especially useful in the identification of vascular abnormalities, including occlusions, stenoses, ulcerated plaques, and aneurysms (21,58,107).

The potential importance of DSA in the diagnosis of cerebrovascular disease is suggested by Reuter's (87) observation that as much as one-quarter of the combined volume of neuroradiology and angiography services in some medical centers is now directed toward evaluating carotid and cerebral atherosclerosis, including stroke. The Cooperative Study of Transient Ischemic Attacks (TIAs) (102) reported an average of 5.4 definite TIAs per 100 acute beds per year in the participating medical centers. Estimates of the use of arteriography procedures for these hospitalized patients range between *87* and *97* percent *(23).* DSA will either supplement or replace a large portion of the arteriographic procedures.

TECHNOLOGICAL DEVELOPMENT

The development of DSA was a result of the research of medical physics groups at the University of Wisconsin, the University of Arizona, and the Kinderklinik in Kiel, West Germany during the early *1970s (21,58,74).* Fundamental advances in intravenous arteriography, which had been intermittently used since the 1930s, were made possible by the introduction of cesium iodine image intensifiers and advances in digital electronic methods of storing and manipulating information (21). By 1978, the feasibility of DSA for human subjects was demonstrated, and prototype commercial DSA systems were introduced in 1980 at the Universities of Arizona and Wisconsin, the Cleveland Clinic, and South Bay Hospital in Redondo Beach, California *(57,58,74).* There are now nearly *20* manufacturers of DSA systems and many more in the process of developing new systems **(18).**

The size of the market for DSA equipment is somewhat difficult to estimate because of the uncertain future of demonstrated uses of DSA in coronary angiography. A spokesperson for one of the major manufacturers of DSA equipment shared two projections of investment banking firms for all types of DSA units for the period from 1982 through 1986. One firm projected total sales of 5,160 units, while the other firm projected sales of 9,800 units for the same period. There were estimated to be about 600 DSA units of all types in operational status as of January 1983.

CONTEMPORARY METHODS AND CLINICAL APPLICATIONS

With respect to cerebrovascular diagnostic studies, both intravenous and intra-arterial DSA have been employed. However, in this case study the notation "DSA" is used to signify intravenous applications only. The focus is limited to intravenous DSA, because it is the method employed in the evaluation of the extracranial circulation, especially the carotid arteries, in most cases.[1]

[1]As of October 1983, when this case study was submitted to OTA for final editing.

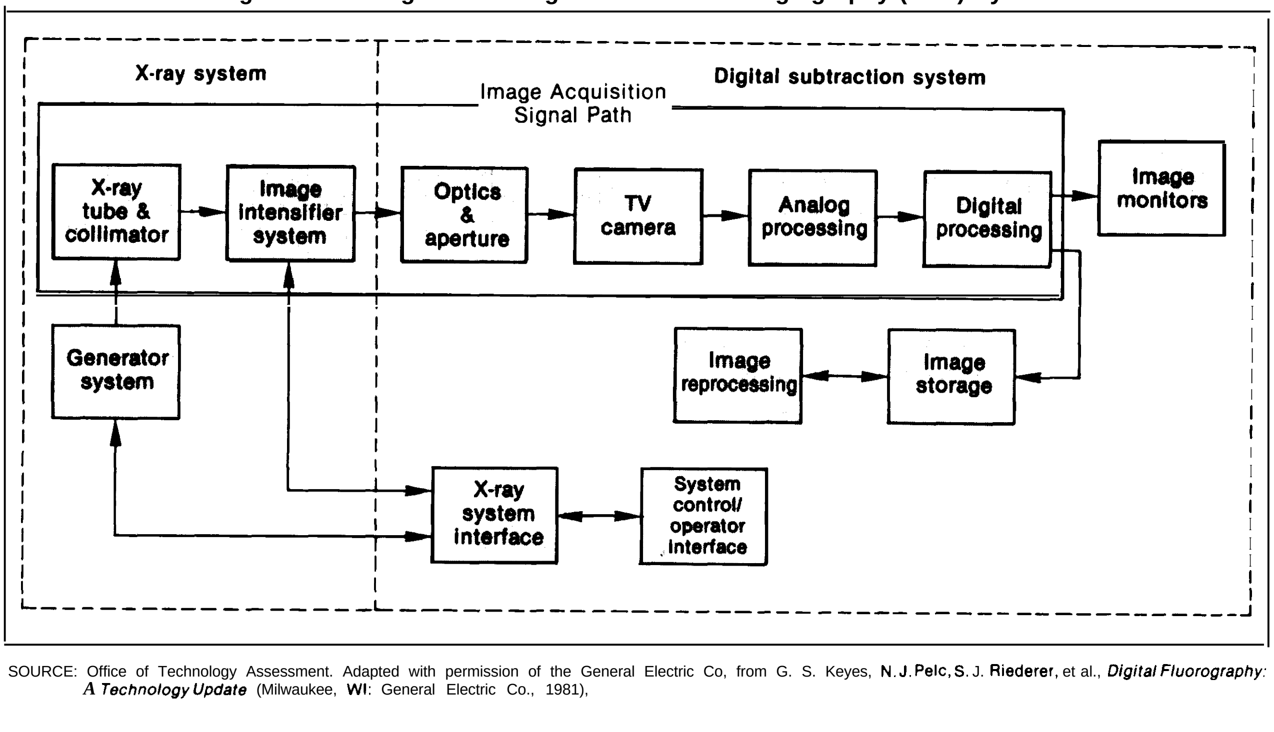
DSA systems work in the manner depicted in figure 3-1 as follows: a contrast medium is injected intravenously; X-ray detection of the contrast medium produces 1 to 30 exposures per second (before and after the injection of contrast medium); and arterial images are converted from analog to digital form and transmitted to a computer-storage complex (55). The digitalized image information makes it possible to "subtract" the precontrast images from those obtained after contrast injection so as to visualize arterial structures without direct arterial puncture and injection. The data can be recalled for viewing on a video screen, and successive images created through subtraction techniques which allow the contrast of the arterial structures to be visualized for the detection of abnormalities.

The purpose of the subtraction process used in DSA is to eliminate (or factor out) the bone and soft tissue images that would otherwise be superimposed on the artery under study **(12,58).** The serial images show changes in the contrast appearance over time (temporal subtraction) and at varying X-ray intensities (energy subtraction) **(12,57).**

Most DSA examinations require *25* to 45 minutes to perform **(63,99,112),** if there are no technical complications (e.g., difficulties with catheterization), and can be performed on an outpatient basis. This is a considerable advantage in safety and cost over most standard arteriographic examinations, which require at least overnight observation of the patient in the hospital to detect post-procedure arterial obstruction or hemorrhage **(24,33).** However, a small number of the latter have been safely performed on an ambulatory basis in recent years (45).

DSA has a wide range of clinical applications in addition to its use in carotid artery studies. Mistretta and his colleagues (74) at the University of Wisconsin have substituted DSA for standard arteriography in the evaluation of aortic arch anomalies, aortic coarctation, and vascular bypass grafts. Digital subtraction techniques have also been used for imaging of the abdominal, cardiac, pulmonary, carotid, intracerebral, and peripheral vessels. Table 3-1 provides an overview of the range of attempted applications of DSA imaging technology reported in the literature. Be-

Figure 3-1 .—Diagram of a Digital Subtraction Angiography (DSA) System



SOURCE: Office of Technology Assessment. Adapted with permission of the General Electric Co, from G. S. Keyes, N. J. Pelc, S. J. Riederer, et al., *Digital Fluorography: A Technology Update* (Milwaukee, WI: General Electric Co., 1981),

Table 3-1 .—Attempted Applications of DSA Reported in the Literature[a]

Principal author of study	Anatomical regions studied									
	Carotid	Thoracic	Cardiac	Abdominal	Intracranial	Pulmonary	Peripheral	Aorta	Renal	Other
Weinstein, et al. (1981)[b]	X		X	X	X	X	X		X	X
Crummy, et al. (1980)	X		X				X		X	
Levy, et al. (1982)	X		X	X	X	X	X		X	
Brody, et al. (1982)	X									
Turnipseed (1982)	X		x			x	X			x
Buonocore, et al. (1981)								X	X	
Mistretta, et al. (1981)	X		X						X	X
Hillman, et al. (1981)									X	
Johnson (1982)				X			X	X	X	
Kruger, et al. (1981)	X		X							
Meaney, et al. (1980)	X	X	X	X		X	X			
Pond, et al. (1982)	X					X	X		X	
Chilcote. et al. (1981)	X									

[a]Does not necessarily imply routine clinical use at this time
[b]Full citations found in References Section

SOURCE Off Ice of Technology Assessment

cause of problems with spatial and contrast resolution, virtually all examinations of the coronary arteries, which cannot be adequately visualized with intravenous DSA at the present time, require arteriography.

Because DSA functions as both a screening procedure for at-risk or asymptomatic patients and as an evaluative procedure for reconstructive surgery (74,108), estimates of the probable volume of use based only on the latter type of use are bound to be conservative. DSA makes a unique contribution to the field of diagnostic radiology (3), serving as a bridging technique between totally noninvasive tests and conventional arteriography, at times replacing the latter. Turnipseed and his colleagues *(107)* clarified the respective uses of the techniques available to the radiologist and clinician for diagnostic imaging:

> Arteriography has played an important role in the surgical management of peripheral vascular disease because of its ability to precisely define the location and severity of arterial lesions. However, its clinical use has been limited by the risks of arterial catheterization, hospitalization cost, and poor patient acceptance. Arteriography is now commonly used to confirm a diagnosis of vascular disease and to plan appropriate surgical management in patients with symptoms and physical findings of arterial insufficiency.
>
> Because arteriography has not been practical for routine diagnostic screening, a variety of noninvasive screening tests have been developed as diagnostic aids. These noninvasive methods allow more objective evaluation of larger patient populations and are attractive because of safety, cost efficiency, patient acceptance, and the accuracy in detecting hemodynamically significant occlusive lesions. These techniques have been used primarily for diagnostic screening and postoperative assessment.
>
> Although noninvasive methods are useful, they have limited capabilities and some serious shortcomings. Many noninvasive tests are indirect and restricted by technical limitations to evaluation of isolated arterial segments. Most cannot define or distinguish minor stenosis and ulceration from normal vessels and have difficulty in assessing remote areas of the circulation (intracranial, cardiac, and visceral systems). Noninvasive equipment is expensive, often very specialized, and requires personnel with specific technical and interpretive skills **(107).**

DSA, therefore, has the potential of significantly improving the radiologist's and clinician's capabilities in diagnostic screening and postoperative assessment.

Furthermore, DSA is likely to limit the use of older noninvasive tests (e. g., periorbital ultrasonography and thermography), because of greater sensitivity and specificity for diagnostic purposes. However, the evaluation of DSA as a diagnostic technology for the study of carotid artery disease must note the increasing development and diffusion of ultrasound-based methods for diagnosing extracranial occlusive vascular dis-

ease. These technologies have developed very rapidly and newer methods are likely in the future. Because of the safety of these tests, their popularity in clinical practice is not likely to be displaced by DSA in complex or poorly understood clinical situations. However, it may be expected that, where the diagnosis of a carotid TIA seems highly likely on clinical grounds alone, the physician may select DSA as the initial diagnostic test.

Of the large and growing number of noninvasive tests, ultrasound imaging has proved to be the most versatile and reliable in clinical practice. A combination of B-mode real-time imaging, with a Doppler scanning device (often called "duplex scanning"), has become increasingly prevalent. Using this method, an image of the carotid vessel is obtained with the B-scan, and then the blood flow pattern at a given anatomic location is determined with the Doppler signal. This method is advantageous in noninvasive diagnosis in skilled hands, but it takes considerable experience for an operator to become sufficiently expert in the use of this tool to produce reliable and reproducible information of clinical value. However, in part because these techniques have proved popular with practicing clinicians, and in part because they are affordable in office-based practice, industry is likely to respond to the demand for this technology with more accurate and more easily performed duplex scanning in the near future.

By way of comparison, the indirect noninvasive tests (e.g., periorbital ultrasonography), which monitor the cerebral and orbital circulations beyond (downstream from) a carotid lesion, have been shown in most practice settings to have a lower sensitivity and specificity than DSA and/or arteriography and are employed much less frequently at this time than was the case only a few years ago. This trend is likely to be accentuated in the coming years.

As described above, DSA is also likely to limit the use of, or substitute for, arteriography under many clinical circumstances. In addition, it will be employed in situations where arteriography is inapplicable, thus increasing the total volume of arterial examinations. For example, some patients for whom arteriography is risky—such as elderly patients, who are at greater risk for stroke from cerebral arteriography--can have their carotid arteries examined easily and with reduced risk of complication using DSA. Also, DSA may be performed repeatedly on the same individual in order to monitor postoperative or therapeutic progress, without significant morbidity and with good patient compliance. The comparative advantages of DSA and standard arteriography have been summarized in table 3-2.

It is clear that DSA examinations are not **a** simple substitute for arteriograms. Instead, for those conditions for which DSA and arteriography are both applicable, the lower radiation and complication rates of DSA, the outpatient site of testing, the reduced time required for the procedure, and patient acceptance **(83,112)** may result in a use rate of DSA many times greater than that of arteriography. In addition, DSA may be used as a substitute for or a supplement to other noninvasive tests. Two studies of DSA cost effectiveness estimate that for patients with suspected TIAs, clinicians order DSA examinations (where this technology is available) at approximately twice the current rate of arteriographic studies (24,33). However, at present there are no empirical bases for future estimates of DSA utilization.

Table 3.2.—Comparative Advantages of DSA and Conventional Arteriography

Advantages of DSA	Advantages of standard arteriography
Decreased morbidity	Increased spatial resolution[a]
Decreased patient discomfort	Feasibility of selective injections
Decreased hospitalization time	Less degradation of patient motion
Decreased procedure time	Visualization of smaller blood vessels
Decreased film cost	
Increased contrast resolution[b]	
Usefulness in patients with limited arterial access	
Lower cost per examination	

[a] *Spatial resolution:* extent to which radiographic image makes it possible to detect and distinguish anatomically contiguous structures.
[b] *Contrast resolution:* extent to which computer can detect subtle differences in amount of contrast medium present

SOURCE: M. F. Steighorst, C. M. Strother, C. A. Mistretta, et al., "Digital Subtraction Angiography: A Clinical Overview," *Applied Radiology* 10(6):45-49, 1931.

CLINICAL EFFICACY AND EFFECTIVENESS OF DSA

The claimed advantages and disadvantages of DSA derive, in large part, from the efficacy and safety of the technology. A substantial volume of evidence regarding the efficacy and safety of DSA is now available through clinical testing of DSA in several medical centers.

Banta and Behney (8) define technological *efficacy* as "the probability of benefit to individuals in a defined population from a medical technology applied for a given medical problem under *ideal* conditions of use" (emphasis added). *Effectiveness* is the probability of benefit under *average* conditions of use. The literature to date on DSA generally addresses clinical efficacy and safety, not effectiveness. Most studies have been conducted in institutions engaged in clinical research under carefully monitored conditions (21). An exception is the experience documented at Scottsdale Memorial Hospital in Arizona (63). It is not clear whether experimental and early clinical data from academic medical centers, such as the Universities of Wisconsin and Arizona—each with several years of pioneering experience in DSA use—can be employed reliably to predict the effectiveness and safety of DSA by radiologists and clinicians in community hospitals, clinics, and group practices and the resulting patterns of DSA use.

Measurement of the efficacy of DSA is multidimensional, as depicted in table 3-3 (adapted from Fryback [38]), because benefits can be discerned at the levels of: 1) physical image; 2) the detection, accuracy, and sensitivity of tests; 3) diagnostic decisionmaking; 4) therapeutic decisionmaking (or "management efficacy"); 5) patient outcome; and 6) social utility (38). Implicit in this scheme is the belief that increasing diagnostic accuracy is not an end in itself, but rather an instrumental value. The overall efficacy of DSA, then, lies in its contributions to better patient outcomes and ultimately to improved social welfare (31,38),

Most of the clinical evaluations of DSA have taken place at levels 1 and 2 of the Fryback model, namely, with a focus on image quality or on diagnostic sensitivity, specificity, and accuracy. "Sensitivity" may be defined as the proportion of positive tests in all patients with disease; "specificity" is the proportion of all negative tests in patients without disease; and "accuracy" is the ratio of correct diagnoses to all diagnoses.

Investigations of the efficacy of DSA have not yet concentrated on the effects of DSA throughout the medical care system. The literature generally does not address differences in physician diagnosis, selection of treatment alternatives, patient outcomes, or social welfare attributable to DSA. The majority of studies consider the accuracy of DSA for diagnosis in comparison to other diagnostic techniques, usually conventional

Table 3-3.—Levels At Which Diagnostic Technologies May Be Assessed

Level of the measurement	Typical output measures
Level 1: Image efficacy	quality of image resolution
Level 2: Image and observer efficacy	percentage yield of abnormal cases; percentage correct diagnoses; sensitivity; specificity
Level 3: Diagnostic efficacy	change in order of clinician's diagnostic considerations
Level 4: Management efficacy (therapeutic decisionmaking)	percentage change in therapeutic protocol; percentage change to appropriate therapy
Level 5: Patient outcome efficacy	survival rates; percentage cures; morbidity measures; reduced worry of patient and family
Level 6: Societal efficacy (or utility)	dollars added to GNP; age-adjusted survival rates

SOURCE: Off Ice of Technology Assessment, Adapted from D G. Fry back, "A Conceptual Model for Output Measures in Cost. Effectiveness Evaluation of Diagnostic Imaging, " paper presented at the Symposium International de Evaluation Cout-Efficacite en Neuroradiologie, Bordeaux, France, May 14-15, 1982.

arteriography. For images of good diagnostic quality (approximately *85* percent), the sensitivity (95 percent), specificity (99 percent), and accuracy (97 percent) of DSA appear to be very good (19,112).

in general, the principal reason for inadequate visual resolution is movement of the patient during the scan procedure. The quality of images can be affected by swallowing, breathing, peristalsis (movement of esophagus), or other physical motions, depending on the vessels to be visualized (112). Other causes of failure are inadequate venous access, leakage of dye, and faulty injection.

THE SAFETY (ASSOCIATED PATIENT RISKS) OF DSA

OTA defines the "safety" of a medical technology to be:

> . . . the judgment of the acceptability of relative risk in a specified situation;

while "risk" is defined as:

> . . . the probability of an adverse or untoward outcome occurring and the severity of the resultant harm to health of individuals in a defined population associated with use of a medical technology applied for a given medical problem under specified conditions for use **(8).**

Using these definitions, the safety of DSA may be measured and compared to the present methods of diagnostic imaging for vascular diseases. As noted by Patterson (81), the efficacy and safety of neurosurgical and related technologies are only estimated informally, because of measurement difficulties, different conditions of use, and the experimental nature of some technologies. This appears to be the case for DSA. There are no rigorous epidemiological or randomized clinical studies that document either the direct or indirect safety effects. This seems to be due to the fact that most clinicians are impressed with the apparent low risk of DSA relative to benefit, as compared with alternatives.

The amount of radiation from DSA is so small that clinical decisionmaking generally does not take radiation into consideration. Radiation doses for DSA reported in carotid studies are given in table 3-4. Radiation exposure varies depending on the subtraction method selected for the exam and the number of views required for diagnosis (21, 24,56).

Complications from DSA are minimal compared to standard arteriography. Both peripheral and central intravenous injections are likely to be less risky than arterial punctures required for arteriography. In particular, arteriographic procedures may cause stroke due to dislodging embolic material (19), dissecting the arterial walls, or rupturing aneurysms (54), whereas this does not occur with DSA.

A survey of radiologists at 514 hospitals showed that about 2 to 3 percent of all patients undergo-

Table 3-4.—DSA Radiation Exposure Estimates for Cerebrovascular Studies

Principal author of study	Area of study	Estimated radiation exposure per image[a]
Crummy, et al. (1980)[b]	Extracranial arteries	100-150 mR[c]
Chilcote, et al. (1981)	Carotid arteries	230 mR
Brody, et al. (1982)	Carotid arteries	130 mR
Detmer, et al. (1982)	Extracranial arteries	3.6 R[d]

[a]Number of images per study may vary considerably depending on anatomical site, operators, or Patient characteristics.
[b]Full citations found in References Section.
[c]mR . milliroentgen (1 Roentgen (R) = the unit of radiation exposure equivalent to 2.08 x 10° ion pairs in one cc. of air. The measure of radiation exposure in human tissue conventionally used is the "Rad " the absorbed dose of 100 ergs/gin of tissue. One Rad is equivalent to 1.02 Roentgen, the difference between two units of measure being considered negligible,)
[d]R . Rad. (Detmer, et al. (24), the source for data on a complete DSA study (including multiple images), note that a conventional arteriographic study would expose the patient to approximately 20 Rads of radiation.)

SOURCE: Office of Technology Assessment, ing a total of 118,591 arteriographic exams—transfemoral, transaxillary, translumbar—suffered complications which required additional therapy or prolonged the patient's hospital stay (54). These complications included 30 deaths (0.03 percent of all exams). Another study indicated that of 1,328 patients who were suspected of having TIAs and had arteriograms, 13 percent had temporary complications and 0.65 percent suffered permanent neurological complications (102). Johnson (56) concludes that:

> "(t)he complexity, expense, and a certain morbidity and mortality associated with this radiographic procedure [arteriography] compel a set of indications virtually as strict as that for surgery."

Certain complications can arise in DSA exams due to leakage of contrast medium outside the vein, venous reflux (contrast medium going into vein the wrong direction), or patient reaction to the contrast medium (21,57,108,112). Various clinical studies have documented only a small number of such problems—all were transient—of several thousand patients examined (19,21, 57,112).

The safety as well as the clinical efficacy of DSA will depend to a considerable extent on the quality of the particular equipment being used (a factor which also affects diagnostic accuracy and specificity); the compatibility of new DSA equipment with existing facilities; the techniques used; and the experience of the physicians and allied health personnel performing and interpreting these diagnostic images. Several investigators have noted some variability in imaging capabilities of DSA under different technical conditions and have evaluated the physical requirements of the imaging systems with regard to assuring high quality standards (6,67).