Intravenous Angiography Using Digital Video Subtraction: Intravenous Cervicocerebrovascular Angiography

The clinical application of intravenous angiography to study the cervicocerebrovascular system using the digital video subtraction system described in a companion article is reported. About 0.75 ml/kg of a standard 76% iodine contrast solution is injected into an antecubital vein using a power injector. Then 15–20 exposures of the head and neck region at a 1/sec rate are made on the image intensifier. The images are recorded by a high performance video system and the output signal is digitized for subsequent computer manipulation. The subtraction images of these vessels produced by the computer show the vessels clearly, even though they contain very low concentrations of contrast media. Standard exposure factors of 75–80 kVp, 9–10 msec at 800–1,000 mA are used. Clinically pertinent features of the data alteration and flow through the system and the step-by-step computer procedures used to achieve and analyze the various forms of subtracted images are described.

Five experimental and clinical cases demonstrate appropriate applications to cervicocerebrovascular disease: (1) evaluating the effects of surgical and medical therapy on atherosclerosis; (2) providing a screening angiographic test for patients with asymptomatic bruits and/or positive noninvasive studies; (3) evaluating patients who have significant generalized vascular disease either precluding or presenting hazardous contraindications to transarterial catheterization; (4) evaluating significantly aged patients in whom standard angiography has higher risk; and (5) evaluating currently asymptomatic patients who are medically at higher risk for developing atherosclerotic lesions. Numerous examples of the various types of image manipulations are presented: (1) linear subtraction; (2) logarithmic subtraction; (3) alterations of electronic contrast enhancement (map slope); (4) the usefulness of a series of angiographic images; and (5) the importance of multiple projections with this technique.

Intravenous angiography has added to the armamentarium of the neuroradiologist for evaluation of atherosclerotic disease [1–3]. Until development of a satisfactory intravenous angiographic technique, there was no safe method of visualizing and screening the entire cervicocerebrovascular system without intraarterial angiography. Although selective transarterial angiography will continue to play a major role in the detailed radiographic demonstration of cervical and intracranial lesions, it is not appropriately used as a screening test of these vessels. Because it has a small, but essentially irreducible morbidity even in skilled hands, it is a test with inappropriately high risk for use in neurologically asymptomatic patients. This morbidity increases significantly in elderly patients. Intravenous angiography provides an alternative method of visualizing vessels in patients in whom either a screening examination is desired or in whom catheter techniques are contraindicated or unachievable.

With the system described in our companion paper [4], we are achieving clinically diagnostic images of the cervical arteries and their proximal intracranial segments. We can use these images to make clinical decisions regarding operative versus nonoperative care in about 80% of cases. On several intravenous angiograms, questionably positive findings were confirmed with intraarterial angiography.
In this article, the techniques of the procedure and five representative clinical cases are described to illustrate the quality of images currently being produced. These also demonstrate some of the types of computer manipulations of the digitized images currently available.

We are currently using this intravenous angiographic technique primarily for the study of cervical arterial atherosclerosis. There are many additional cervical and intracranial vascular problems to which this technique can be applied as the resolution and capability of this system improve.

**Electronic Computer System**

Radiographic visualization of cervical and cerebral vessels has previously required direct, intraarterial injection of contrast material into or near the vessel being studied. This is because contrast material concentrations of less than 5%-6% are not radiographically visible even when subtraction techniques are used. Previous attempts at intravenous angiography of these vessels failed primarily because of the inability to achieve adequate intraarterial contrast concentrations.

Our digital, video subtraction system [4] allows visualization of cervical and proximal intracranial vessels containing an extraordinarily low concentration of contrast medium (down to 2%-3%). A 40%-50% intraarterial concentration is required in standard angiography to produce images of equal contrast.

Although each part of the system is vital to its overall performance, several parts have special significance. The television tube has a signal-to-noise ratio of 1,000:1, which is far superior to a conventional x-ray video system. This produces an output video signal with very low electronically induced noise to degrade the image. It also has a linear response that permits accurate density subtraction.

The digitization to 8 bits (2^8) of the TV signal means that the TV picture, at this point, is changed to 262,144 words of digital information (512 TV lines, each broken into 512 discrete digital units), each of which has an electronic contrast range of ± 256 units (2^8) of displayed density. Therefore, further degradation of the signal is impossible, since it is in discrete, digital form as it moves through the rest of the system.

This totally digitized image is then essentially rebuilt, line by line, into an image in the digital image store in 0.03 sec and transferred to the computer. There, a large number of very rapid manipulations can be performed on this digitized image. Image processing capabilities currently include: (1) linear (binary) subtraction; (2) log subtraction; (3) contrast slope and position manipulations; (4) edge enhancement; (5) image smoothing; (6) digital filtering; (7) signal averaging; (8) reference image movement; and (9) image addition.

When all digitized images are in the computer, any one can be requested for subtraction (or any processing) by a simple, single letter command on a standard computer address alphanumeric terminal. The requested image begins to be displayed virtually instantaneously and requires 2–5 sec to be completely displayed. Subsequent manipulations are also obtained by single letter command and are displayed at the same rate. Therefore, during the clinical studies, the subtraction images can be viewed immediately after each injection and decisions regarding the necessity of additional injections and projections can be made promptly.

**Materials and Methods**

**Clinical Technique**

Most of our current studies are performed on outpatients. They must be well hydrated and without food intake for 2 hr before the examination. No pain or sedative medication is given or has been required. The study is done with the patient in the supine position, usually using either a right or left posterior oblique projection for the cervical vessels. After about 0.1 ml of 1% intradermal lidocaine, a 6.4 cm 16 gauge "angiocath"-type catheter is introduced into either a right or left antecubital vein. Dextrose solution (D5/W) is then slowly infused into this catheter before and between contrast injections. We prefer using the arm contralateral to the side of primary clinical interest, since there is rarely reflux of contrast material into the external or internal jugular venous systems, which interferes with obtaining a "clean" scout or reference image. However, this is not critical, as successful examinations have also been obtained ipsilateral to the side of injection even when reflux has occurred.

Numerous animal experiments (see fig. 1) demonstrated that about 0.75 ml/kg of contrast material provided very satisfactory visualization of cervical vessels with low background noise levels. For this reason, we currently use 0.70–0.75 ml of a standard 76% iodine contrast/kg of body weight. This is delivered using a standard power injector at a rate of 20 ml/sec for 2.0–3.5 sec (depending on patient’s weight). The contrast material is injected with the patient’s arm elevated to facilitate the central and intrathoracic flow. Two or three injections are usually required to obtain a complete and diagnostic set of studies.

Just before injection, the patient is hyperventilated and asked to hold his breath in midexpiration phase (if possible) for 15–20 sec. If the patient cannot do this, we find that quiet, shallow, respiration produces the least movement. Each patient has been questioned and has specifically denied the presence of any pain at or near the site of contrast injection using these volumes and rate of injection.

Using a 1.2 mm focal spot at a tube-intensifier distance of 78.7 cm and a neck-intensifier distance of 22.9 cm, a magnification of about 1.4 is achieved. Currently, we are using exposure factors of 75–80 kVp, 9–10 msec at 800–1,000 mA. Exposure rate is 1 frame/sec for 15–20 sec starting 2–4 sec after completion of the intravenous injection. Arrival time of the contrast material in the cervical vessels is 7–14 sec, depending on the patient’s cardiac status; therefore, a rather long exposure sequence is required. We hope to diminish the length of this sequence as our experience increases. As stated above, after each set of exposures, the subtracted images are reviewed and the requirement for additional projections is determined.

At the completion of the study, the intravenous catheter is removed. The patient is either returned to the ward or sent home with instructions only to force fluids in the 24 hr after the procedure and to only report to us or to his physician if he notes inordinately diminished urine output. The average study currently takes about 45 min to 1 hr. We anticipate reducing this time by at least one-half with continuing refinements in equipment, setup procedures, programs, and system standardization.
Fig. 1.—Canine cervical arteries. (See text for details of technique.) A, Reference image just before contrast reached cervical vessels. B, Low concentration of contrast in arteries not visible on "radiographic-type" image. C, Linear subtracted image obtained by electronically subtracting digital values of each point on reference image from post-injection image (B). No electronic contrast enhancement. D, Digital-electronic-enhanced image. Significant augmentation of intravascular low-level contrast. Slope of 8 means values of displayed contrast are 8 times more than contrast actually in dog’s arteries. E, Linear subtracted, digital contrast-enhanced image. Region of surgically-produced stenosis low in left common carotid artery (arrow). F, Conventional subtracted radiograph from transfemoral arch aortogram. Stenosis (arrow).

Image Analysis

A number of clinical studies have been obtained using the technique described above. Analysis of the images of each series begins by selecting the best reference image obtained just before the appearance of contrast material in the cervical vessels. It is then subtracted from each of the remaining images of the study. The subtraction of each sequential image takes about 3 sec. By this method, the images with the best arterial visualization are selected. These images are then subjected to variations in electronic contrast enhancement and may have some additional image manipulations performed on them (e.g., log subtractions, contrast slope and position manipulations, and, occasionally, edge enhancement). These manipulated images are then stored on the video disc recorder for subsequent display, review, and photography.

The data and graphic section on the lower left of each image (figs. 3–5) shows patient identification data, a description of the type of subtraction done (linear versus log), and a graphic display of the "map" or the slope and position of the electronic enhancement used on that individual image. The abscissa represents the...
digital value of the electronic contrast material actually present and the ordinate represents the digital value of the electronic contrast enhancement that is displayed. The numerical value after slope refers to the ratio of electronic contrast enhancement displayed/electronic contrast material actually present. The numbers at the bottom of the "map" graph describe the range of numbers contained between the bottom and top parts of the steep part of the map. Varying the slope gradient (steepness) is analogous to changing the window width in CT. A steep slope is equivalent to a narrow CT window setting and produces a high contrast image. Changing the position of this steep part of the map (moving it to the left or to the right) is analogous to changing the position of the center of the CT window. In this system, the slope position and the slope steepness are independent manipulations.

Representative Case Reports

The following cases demonstrate some images achieved with the system and techniques described above and show the results of applying different methods of subtraction and digital image processing.

Case 1

A 32-kg greyhound had a 24 ml bolus of 76% contrast material hand-injected into a foreleg vein (volume equals about 0.75 ml/kg). (All images were photographed directly from the current 512-line television video display.) The first image (fig. 1A) is the reference or scout image and was obtained before the arrival of contrast material in the cervical vessels. The arterial phase (fig. 1B) shows the contrast material in the arteries that is not seen on this standard radiographic-type image. To achieve a standard linear subtraction (fig. 1C), the digital densities of each point on the reference image are directly subtracted from those on the postcontrast image being studied (fig. 1B). As the densities being subtracted are perfectly numerically balanced, the resultant subtraction is the same as a "second order"-type subtraction done on standard radiographs. The only remaining density is that of the minimal contrast enhancement within the vessels. On the map, the slope is 1 (or 45°), indicating there has been no electronic contrast enhancement or manipulation. Figure 1D demonstrates the significant augmentation of the low-level contrast enhancement within the vessels when the images are displayed with digital-electronic enhancement, as evidenced by the steep slope shown in the map. A relatively steep slope of 8 means the digital value of the output electronic contrast is 8 times the input electronic contrast values.

Using a 1 ml/kg intravenous contrast injection in this same dog, the lower cervical region was studied. One of the linear subtracted, digital contrast-enhanced images (fig. 1E) clearly shows a region of stenosis in the left common carotid artery. This stenosis had been surgically produced in the laboratory. The accompanying image (fig. 1F) is a subtracted radiograph from a transtemporal aortogram using conventional radiography. This stenosis is as easily visualized on the intravenous angiographic study as it is on the standard radiographic intraarterial aortogram. However, the intravenous an-
Fig. 3.—Case 3, 68-year-old presurgical patient with suspected stenosis or occlusion in left internal carotid system. Right posterior oblique position, standard amount of intravenous contrast. A, Linear, mapped subtraction of cervical vessels. Left and right internal and external carotid arteries well visualized and normal. Parts of vessels superimposed over bone not well seen. B, Log-type, mapped subtraction. Significantly improved visibility of vessels superimposed over bone. Left internal carotid artery entirely normal up to cavernous segment with no stenosis or minor atheromatous irregularity. a = left common carotid artery; b = left internal carotid artery; c = left external carotid artery; d = left vertebral artery; e = right vertebral artery; f = basilar artery; g = right internal carotid artery; h = right external carotid artery. C–F, Progressively increased electronic contrast enhancement (slope). Slope of C = 1, D = 3.49, E = 7.12, and F = 11.43. Single, computer manipulation produces substantially improved visibility of arteries.

The intravenous angiogram is much more sensitive to minor degrees of movement compared with standard angiography. There is minimal movement of the trachea in this anesthetized dog on the intravenous angiogram.

Case 2

A 71-year-old white man had recent right cerebral hemispheric transient ischemic attacks. Previous arch angiography demonstrated a 50% stenosis at the right carotid bifurcation. Selective right carotid angiography on this admission demonstrated a 75% stenosis at the origin of the right internal carotid artery with ulceration. The patient had a right proximal internal carotid endarterectomy. On postoperative day 4, the surgeons were interested in the patency of the right internal carotid endarterectomy site, but they did not believe the clinical status warranted a repeat transfemoral angiogram so intravenous angiography was performed.

While in the left posterior oblique position, the patient was injected with 0.8 ml/kg of 76% contrast medium. Figure 2A is the reference image. Intraarterial contrast enhancement is fairly visible in the midarterial phase (fig. 2B). The standard linear subtraction image (fig. 2C) was obtained by digitally subtracting all the densities on figure 2A from those on figure 2B. Note the 45° slope of the map in the left lower corner of the image, indicating a numerical slope of 1. The results of applying electronic contrast enhancement at the cervical parts of the arteries are now well visualized (fig. 2D). There is a slight stenosis at the superior end of the endarterectomy site, probably of no clinical significance since the filling of the right internal carotid artery above this stenosis is satisfactory. A standard transarterial angiogram was not required and the patient was discharged several days later.

Case 3

A 68-year-old white man needed extensive oral-dental surgery with general anesthesia. Cardiac evaluation because of recent vague, nonspecific neurologic symptoms demonstrated moderate cardiac arrhythmias that were corrected by medical therapy. Doppler ocular sonography and ocular plethysmography (OSM/OPG), however, suggested a significant stenosis in the left internal carotid artery system. The patient and his physicians did not want to proceed with the surgery and general anesthesia without further
evaluation of the internal carotid system. However, his neurologic symptoms had cleared with medical treatment for cardiac arrhythmias and formal transarterial angiography did not seem indicated. Intra-venous angiography, however, seemed appropriate for this possible high-risk patient who had no current clinical neurologic symptoms or signs.

As the left carotid artery was of primary interest (positive left OSM/OPG studies), the intravenous angiogram was done with the patient in the right posterior oblique position using the standard amount of contrast medium delivered at a standard rate. The linear subtraction of the cervical vessels was mapped (i.e., the contrast was electronically enhanced) (fig. 3A). The cervical parts of the left and right internal and external carotid arteries are well visualized and entirely normal. However, those parts of the cervical and proximal intracranial vessels superimposed over bone are not well visualized.

To better demonstrate vascular structures that are partly superimposed over soft tissue and partly over bone, a logarithmic-type subtraction was done in which the computer program considered the logarithmic characteristics of the attenuation of x-ray by bone and soft tissue. This produces a more balanced image and improves the visibility of the vessels superimposed over bone. This is well demonstrated in figure 3B, which is a log-type subtraction film. Both carotid bifurcations and internal carotid arteries are excellently visualized up to and slightly above their petrous intracranial segments.

No abnormalities of the left internal carotid artery are evident on this study or on the several other projections. The patient went home for dinner after this outpatient procedure and the next week had general anesthesia and dental surgery without complication.

Figures 3C–3F are examples of the same logarithmic subtracted image (image 7 minus reference image 4) in which the electronic contrast enhancement (map slope) is progressively increased in steepness. They demonstrate the effect this single manipulation has on improving the visibility of arteries on the display TV image.

Case 4

A white man in his late 50's had severe, bilateral, lower extremity claudication. Examination demonstrated total absence of all lower and upper extremity pulses, severe, chronic obstructive pulmonary disease, and a loud right carotid bruit. He had no neurologic symptoms or findings. Noninvasive Doppler and ocular pulse studies (OSM/OPG) were positive on the right. The surgeons were unwilling to consider major aortic and lower extremity vascular reperative surgery without a carotid study. As no arm or leg vessels were available for transarterial catheterization, intravenous angiography was indicated.

The study was done with the patient in the left posterior oblique position to best demonstrate the right carotid artery. The two logarithmic subtractions with electronic contrast enhancement (figs. 4A and 4B) are separated by 2 sec. A large amount of calcium obscures visualization of the right common carotid artery bifurcation. There is a minimal filling of the right internal carotid artery (fig. 4A) but good opacification of the cervical, petrous, and cavernous parts of the left internal carotid artery. Figure 4B shows definitely more contrast enhancement in the right internal carotid artery. This indicates that the cephalad flow of contrast medium in this artery is significantly slower than that on the left, probably secondary to a high-grade stenosis in the poorly seen, proximal, right internal carotid artery.

The images on this patient have significant superimposed motion artifacts in the neck and skull secondary to the prominent accessory respiratory muscular movements associated with his severe chronic obstructive pulmonary disease. Because of his compromised pulmonary status and asymptomatic neurologic status, surgery on the right internal carotid artery was deferred until lower extremity vascular reperative surgery is clinically imperative. Repeat intravenous angiography will be done at that time to determine if the right internal carotid artery really became occluded in the interim.

Case 5

A 78-year-old man had vague “dizzy spells,” but no other neurologic symptoms or positive neurologic findings. Later, however, positive right carotid OSM/OPG studies suggested either a high-grade stenosis or occlusion of the right internal carotid artery. In a patient this old with only minor neurologic symptoms and no neurologic deficit, standard transarterial angiography has an ordinarily high risk unjustified by either symptoms or findings and intravenous angiography is appropriate.

This study was done first in a left posterior oblique position with standard technique and contrast material. A log-subtracted, mapped image of the cerebral and proximal intracranial vessels (fig. 5A) shows complete occlusion of the right internal carotid artery. To confirm this finding, repeat angiography in a right posterior
oblique projection (fig. 5B), also log-subtracted and mapped, demonstrates no visible right internal carotid artery. Right external carotid branches are seen, as are the left internal and external carotid arteries, both vertebral arteries, and the proximal basilar artery.

We concluded that this patient had asymptotically occluded his right internal carotid artery. Intravenous angiography obviated transarterial angiography and its risks in this elderly patient. It also answered the question raised by the positive right carotid OSM/OPG studies of whether this patient had an occlusion or a more dangerous, high-grade stenosis of his right internal carotid artery.

Discussion

Our goal has been to develop a noninvasive method of angiographically visualizing and screening the cervico-cebrovascular system. This was accomplished by using relatively small amounts of peripherally delivered intravenous contrast material. Development of a sophisticated, electronic, video subtraction system capable of displaying the resultant low levels of intravascular contrast agent was the first step. A low-noise video TV camera system for collecting the data is very important. Digitization of the TV image data allows diverse and high-speed manipulations of these images. After successful visualization of cervical and cerebral vessels in animals, we began to apply this technique to humans.

The test is usually done on outpatients and no hospitalization before or after the study is required unless indicated by the results. Patient acceptance has been very good. They have appreciated our attempt to avoid intraarterial catheterization and all have specifically denied any pain associated with the injection of contrast material into the antecubital veins. We have successfully attempted to keep patient manipulation and volumes of contrast medium to a minimum.

Several categories of clinical problems are specifically well addressed by intravenous angiography. Case 2 exemplifies how the effects of surgical or medical therapy for cervical atherosclerotic lesions can be evaluated by this technique. This postoperative patient with only minimal symptomatology had his endarterectomy site evaluated without using transarterial angiography. Clinical questions about the patency and configuration of the postoperative artery were answered.

A second category of patients needing a screening-type angiographic test comprises those with asymptomatic bruits and positive noninvasive studies that may place them at higher anesthetic and surgical risk, as in case 3. This presurgical patient had a bruit and positive, noninvasive tests suggesting a significant carotid stenosis. The absence of clinical symptoms and neurologic findings were relatively contraindications to transarterial angiography making him a good candidate for intravenous angiography. It demonstrated normal carotid arteries and he and his surgeons then confidently proceeded with his anticipated general anesthesia and surgery.

A third important group for which intravenous angiography is an important alternative includes those in whom significant, generalized vascular disease either precedes or presents significant and perhaps hazardous contraindications to transarterial catheterization, such as case 4, who had no palpable femoral or axillary pulses. This patient was also neurologically asymptomatic, another reason for avoiding a transarterial study. In addition, he had such severe pulmonary disease it was questionable whether he could remain supine long enough for a complete, transarterial study. Demonstration of a probable high-grade stenosis in one carotid artery gave the surgeons information pertinent to their preoperative plans for anticipated major aorticotiaic surgery.

A fourth group of candidates for intravenous angiography comprises aged patients in whom standard transarterial catheter angiography has a higher morbidity. This is because of increased vessel wall fragility, widespread atheromatous involvement with associated pelvic and cervical vessel tortuosity, and marked intimal surface irregularities. The latter predispose to higher possibilities of embolization during catheter manipulation. If these elderly patients have minor neurologic findings or have positive noninvasive tests,
angiographic evaluation is certainly desirable but selective catheterization carries a higher risk. The demonstration in case 5 of a complete occlusion of the right internal carotid artery and a normal left internal carotid artery precluded the necessity for any further angiographic evaluation in this older patient.

One other large and important group of patients that we have not begun to evaluate comprises those currently asymptomatic patients who are at high risk for development of atherosclerotic lesions. Some examples are: (1) patients with poorly controlled or chronic hypertension; (2) patients with insulin-dependent diabetes; (3) those with significant atherosclerotic disease in other parts of the vascular system (heart, kidneys, aortoiliac system); and (4) those with metabolic problems that may predispose to atheromatous disease (hypercholesterolemia, hyperlipidemias, obesity).

Our cases have demonstrated several features of current computer data manipulation. The striking increase in visibility of those vessels superimposed over bony structures when logarithmic subtraction is applied to the images is well demonstrated in case 3 (figs. 3A and 3B). This capability is necessary for studying extracranial vessels superimposed over bone and intracranial vessels within and adjacent to the base of the skull. The advantage of obtaining sequential images similar to a standard angiographic series is demonstrated in case 4, which shows delayed flow in the right internal carotid artery. This capability will soon be improved when this system is updated to accepting and digitizing up to 30 frames/sec. The study of cervical and intracranial arteriovenous malformations should be well served with this capability. The importance of high-speed digital computer processing and display of the data is emphasized in case 5, in which the initial intravenous angiogram was processed and displayed, immediately ascertaining the need for another projection. This capability is especially important with this technique because all the cervical and intracranial vessels are simultaneously opacified, and, therefore, are frequently superimposed.

In the clinical application of this technique, we have identified three problem areas not usually encountered with intraarterial angiography. The first, mentioned above, is that of the simultaneous opacification of all cervical and intracranial vessels. Currently, we are altering the patient’s position to obtain different projections. In the first clinical unit now being installed, this study will be routinely done biplane, and stereoscopic capability is also planned. The latter will be especially important in intracranial studies. A second problem is that computer-generated subtraction techniques seem much more sensitive to skeletal and even minor soft tissue movement than standard radiographic subtraction techniques. Currently, software programs for reference image manipulation in two axes are being refined. A third problem related to the second is that any calcification in the arterial wall is in constant motion and the images presented in case 4 show how difficult this is to subtract. Other techniques, currently being developed, will be necessary to address this problem, which is a frequent associated finding in large atheromatous plaques.

Additional angiographic areas may become appropriately studied by intravenous angiography. These include postoperative evaluation of the patency and function of cervical-intracranial arterial bypasses, and follow-up studies of cervical, facial, and possibly intracranial arteriovenous malformations and tumors after surgery or transcatheter therapeutic embolization. With improved image resolution we also hope to follow intracranial aneurysms and the associated arterial spasm after subarachnoid hemorrhage, thereby avoiding repeated transarterial catheterizations.

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REFERENCES