

# VASCULAR CHARACTERIZATION OF BRAIN LESIONS BY RAPID SEQUENTIAL CRANIAL SCINTIPHOTOGRAPHY

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Radioisotopic imaging has been shown to be a sensitive and safe means of detecting and localizing intracranial lesions. Isotope encephalography alone will detect approximately the same percentage (75–90%) of space-occupying lesions as either pneumoencephalography or cranial arteriography (1–11) and it is not associated with the morbidity and mortality of these latter procedures (12,13).

Radioisotopic imaging of intracranial pathology with standard techniques depends upon focal pooling of a radiopharmaceutical as a result of alterations of the blood-brain barrier. The substances that have been most commonly used— $^{131}\text{I}$ -albumin,  $^{203}\text{Hg}$  and  $^{197}\text{Hg}$ -chlormerodrin and  $^{99\text{m}}\text{Tc}$ -pertechnetate—normally do not cross the blood-brain barrier appreciably. Although the time to perform this standard procedure has been reduced by using  $^{99\text{m}}\text{Tc}$  and rapid rectilinear scanners or scintillation cameras (11,14–20), little information is gained about the etiology of a detected abnormality.

Because most focal intracranial lesions are the result of vascular disease or have an abnormal vascular component, the arteriographic characterization of the vascular nature of these lesions has aided greatly in diagnosis and management (21,22). In the investigation of strokes, however, arteriography is abnormal in only about 50% of the cases (23). The use of a near-ideal nuclide such as  $^{99\text{m}}\text{Tc}$  with an Anger-type scintillation camera permits the visualization and anatomic delineation of a number of vascular structures. This is accomplished by performing rapid-sequential scintiphography while the  $^{99\text{m}}\text{Tc}$ -pertechnetate bolus traverses these structures (19,24–29). The present study demonstrates the applicability of such an approach to the rapid, safe assessment of cerebral vascular disease and vascular characterization of intracranial lesions.

## METHODS AND MATERIALS

These studies were performed on patients who were referred to the Nuclear Medicine Section, Clinical Laboratories, San Francisco General Hospital for radioisotope imaging of suspected intracranial pathology.

Some of the patients received 250 mg of sodium perchlorate approximately 12 and 2 hr prior to study in an attempt to decrease choroid plexus uptake of  $^{99\text{m}}\text{Tc}$ -pertechnetate.

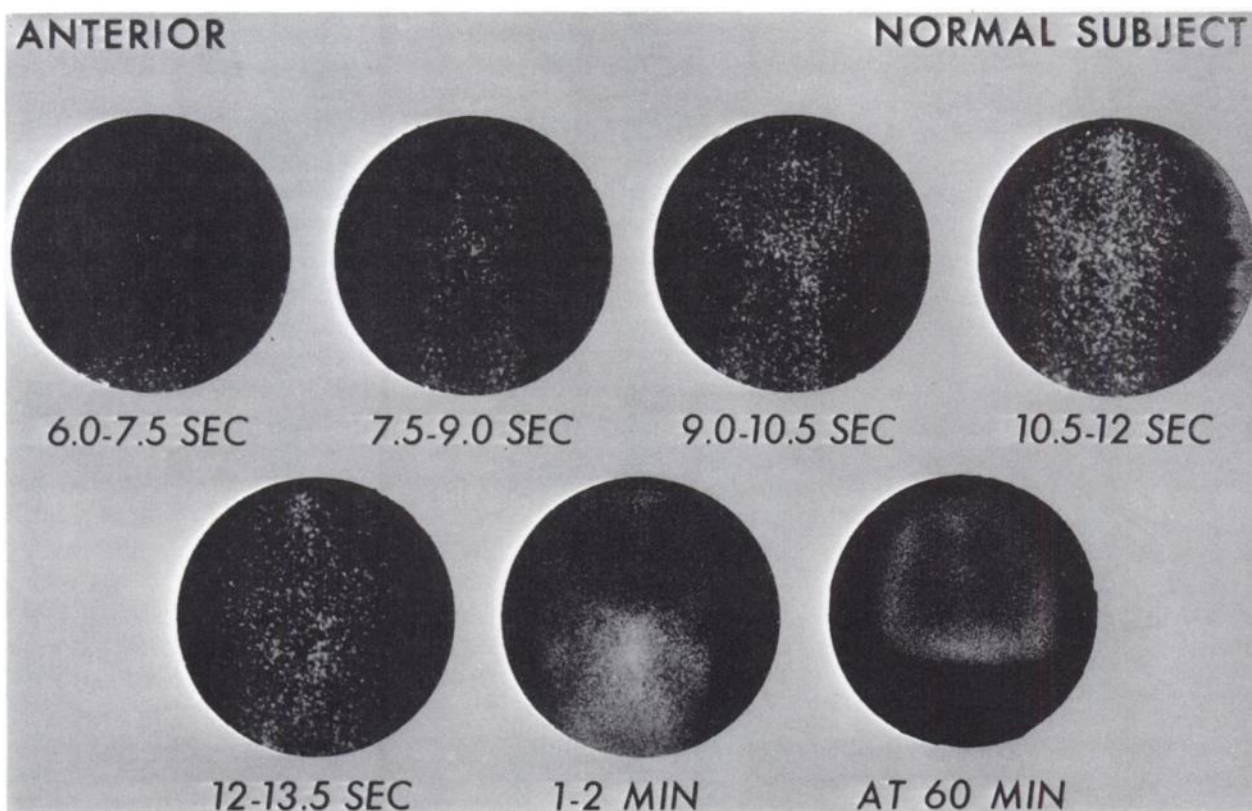
Cranial scintiphographs were obtained using an Anger-type scintillation camera with a 3-in. collimator. All scintiphography, including the sequential vascular filling studies, was accomplished by manual operation of the Pho-Gamma Scintillation camera, Model 6401\* without special attachments. The instrument was set for the  $^{99\text{m}}\text{Tc}$  photopeak with an image intensity of 10. The ratemeter was set at a maximum response with a 0.5-sec time constant. The scaler was preset at 1.5 sec with the display in the preset mode. A pack of standard Polaroid film, 3,000 speed/type 107, was inserted, and the slide of the film back was retracted.

After an in-dwelling Teflon needle (No. 18)† was inserted into an antecubital vein, the patient's head and neck were positioned relative to the detector for the desired view—anterior, posterior, or lateral. The arm was positioned to achieve unobstructed venous return and to place the needle slightly anterior to the level of the right atrium. The patient then received a rapid bolus injection of approximately 10 mc  $^{99\text{m}}\text{Tc}$ -pertechnetate through a three-way stop-

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**FIG. 1.** Anterior-view rapid-sequential and 1-hr cranial scintiphotography after intravenous bolus injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate into normal subject. See text for description.

cock attached to the Teflon needle. The  $^{99m}\text{Tc}$  bolus, usually comprising less than 5 ml, was immediately flushed with a bolus injection of 10 ml of heparinized saline from a syringe attached to the second port of the stopcock. This second injection reduces "tail-ing" of the isotope bolus. The count button was depressed when the pertechnetate bolus was injected. The operator exposed the first film to approximately 2,000 scintillations accumulated during several 1.5-sec intervals. This initial exposure is usually taken during the initial 4.5–7.5 sec after injection, allowing for the variable delay of the isotope bolus as it passes through the veins, heart, lungs and aorta before entering the neck and head. The first exposure was immediately followed by seven sequential 1.5-sec scintiphotos ending approximately 15–20 sec after injection. Each of the 1.5-sec scintiphotos is composed of 2,000–4,000 scintillations.

A fresh film pack was then inserted, the intensity decreased to approximately 6 and the display set in the manual mode. From 1 to 6 min after injection, 1-min anterior, posterior and bilateral scintiphotos were taken. For the conventional detection of blood-brain-barrier abnormalities, these views and supplementary views, if necessary, were performed

again at 60 min after injection using standard cranial scintiphotographic techniques.

#### RESULTS

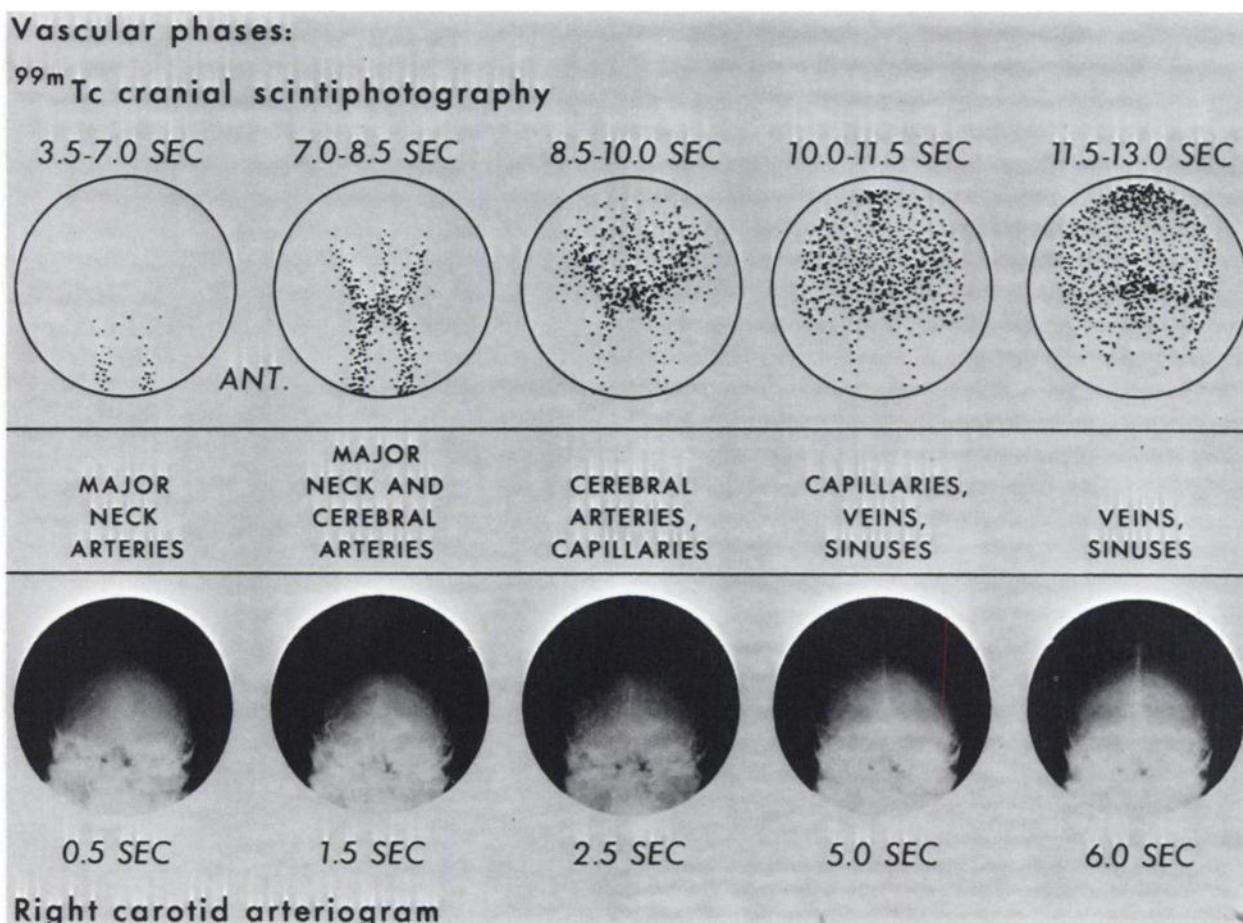
An anterior-view rapid sequential and 1-hr cranial scintiphotographic study of a normal subject is shown in Fig. 1. The scintiphoto, taken at 6.0–7.5 sec after injection, shows minimal early filling of the major neck arteries. At 7.5–9.0 sec these major arteries and their confluence at the circle of Willis are visualized. In addition, early filling is noted in the region of the anterior and middle cerebral arteries. At 9.0–10.5 sec the filling of these arteries has increased, associated with a diffuse (capillary) distribution of activity through the cerebral hemispheres. At 10.5–12.0 sec this diffuse distribution of activity becomes more intense, and the superior sagittal sinus is now well visualized. At 12.0–13.5 sec most of the bolus has passed through the capillary bed, and a relatively small amount of radioactivity remains in the venous structures. During 1–2 min, at a time approaching vascular equilibration of the  $^{99m}\text{Tc}$ , visualized intracranial activity is limited largely to the major venous vascular structures (i.e., dural sinuses and veins). Extracranial activity is seen in the bone and overlying scalp tissue as well as in the oral-nasal mucosa and salivary glands. In the normal subject, the 1-hr scintiphoto is similar in appearance to the 1–2-min scintiphoto.

Analyses of normal anterior cerebrovascular patterns obtained in 20 subjects after bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate are summarized in Fig. 2. The mean time intervals for each vascular phase were: early filling of major neck arteries, 3.5–7.0 sec; major neck and cerebral arteries, 7.0–8.5 sec; cerebral arteries and capillaries, 8.5–10.0 sec; cerebral capillaries and early venous filling 10.0–11.5 sec; and venous filling 11.5–13.0 sec. The timing of these vascular phases is in close correspondence with those obtained by carotid cerebral angiography (Fig. 2) after allowance is made for the 4–5-sec delay of the intravenous isotope bolus before reaching the major neck arteries.

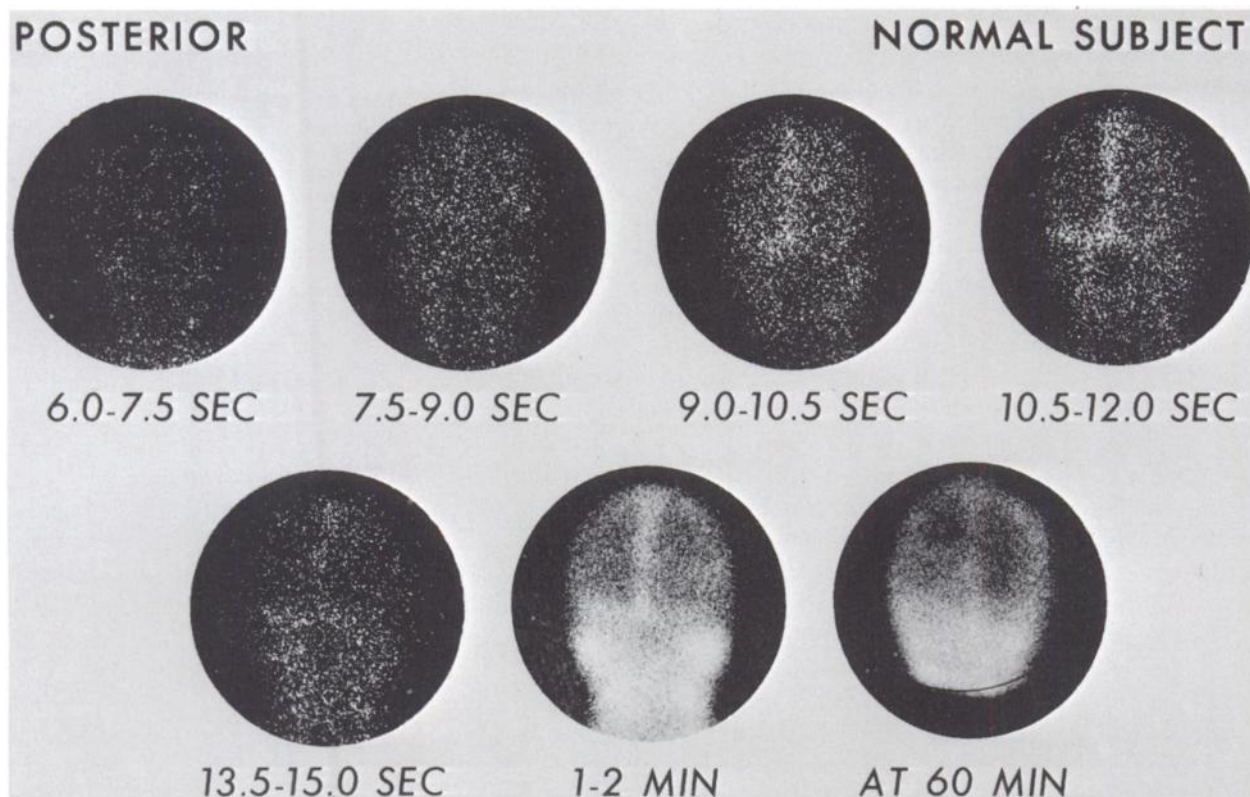
A posterior-view, rapid sequential and 1-hr cranial scintiphotographic study of a normal subject is shown in Fig. 3. The first scintiphoto (6.0–7.5 sec) shows filling of the major neck arteries and early filling of cerebral arteries. The next scintiphoto (7.5–9.0 sec) shows further filling of cerebral arteries and diffuse distribution of activity in capillaries. As noted in this representative study, the delineation of major cerebral arteries in posterior view was usually poorer than in anterior view (Fig. 1). At 9.0–10.5 sec the diffuse distribution of ac-

tivity has increased, and the initial filling of the sagittal sinus is noted. At 10.5–12.0 sec, further increase in activity is noted in the sagittal sinus coupled with filling of the lateral sinuses. This venous phase is associated with a decrease in the diffuse cerebral activity. By 13.5–15.0 sec, a major portion of the bolus has already passed through the head. At 1–2 min, the sagittal and lateral sinuses are prominent. Some extracranial activity is seen in the bone, overlying scalp tissue, oral-nasal mucosa and salivary glands. In the normal subject, the 60-min scintiphoto is similar in appearance to the 1–2-min scintiphoto except for a relative decrease in prominence of the dural sinuses. Analyses of normal posterior cerebrovascular patterns obtained in 13 subjects after bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate are summarized in Fig. 4. The mean time intervals for each vascular phase were: early filling of major neck arteries, 4.5–6.0 sec; major neck and cerebral arteries, 6.0–7.5 sec; cerebral arteries and

**FIG. 2.** Analyses of normal anterior cerebral vascular patterns obtained after intravenous bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate. Time intervals are means obtained in 20 subjects. Patterns are compared with typical right carotid arteriogram.







**FIG. 3.** Posterior-view rapid-sequential and 1-hr cranial scintiphotography after intravenous bolus injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate into normal subject. See text for description.

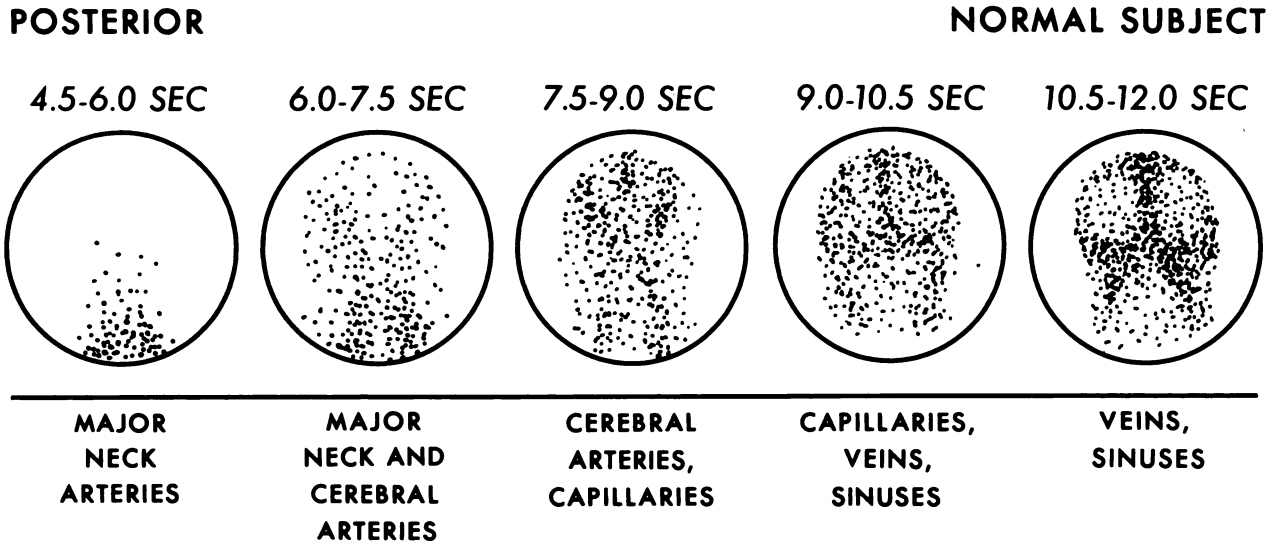
capillary filling, 7.5–9.0 sec; capillaries and early venous phase, 9.0–10.5 sec; and venous phase, 10.5–12.0 sec. The various vascular phases on anterior view occurred approximately 1 sec after visualization of the corresponding phase on posterior view (Figs. 2 and 4).

A left-lateral view, rapid sequential and 1-hr cranial scintiphotographic study of a normal subject is shown in Fig. 5. The vascular phases noted in this study were similar to those seen on anterior and posterior views (Figs. 1–4). Two definite columns of activity are noted in the neck region on the first three scintiphotos. The column of activity which is posterior and extends into the cranium is formed mainly by the internal carotid and vertebral arteries. The anterior column of activity that extends to the lower face region represents the external carotid artery and its major branches.

A rapid sequential and 1-hr cranial scintiphotographic study performed pre-operatively in a patient with a right frontoparietal meningioma is shown in Fig. 6. The patient, a 58-year-old male, presented with bizarre behavior. A right carotid arteriogram revealed a 9-cm well-circumscribed mass lesion in the right frontoparietal area causing displacement of all the adjacent vessels of both the middle and anterior cerebral groups. A “tumor blush” in addition to some abnormal draining veins within the mass was noted. At craniotomy, a mass was noted in the right frontoparietal region which was subsequently

shown to be a meningioma. Anterior-view scintiphotography was performed during the rapid sequential portion of the study. At 6.0–7.5 sec, during the phase of neck and cerebral artery filling, an area of excessive filling is noted in the right cerebral hemisphere. Further increase in activity noted in this area during 7.5–9.0 sec is followed by a subsequent decrease in activity during 9.0–10.5 sec. A general decrease in diffuse (capillary) activity and initial visualization of the sagittal sinus is also noted during this time interval. At 6–7 min, a well-circumscribed area of increased activity is noted in the right cerebral hemisphere. This area corresponds to that area of excessive early filling (“arterial blush”) noted in the earlier scintiphotos. The relatively increased intensity of this area, as compared to normal vascular structures, indicates that considerable leakage of  $^{99m}\text{Tc}$  across the blood-brain barrier has already occurred. A further increase in activity in this area due to the blood-brain-barrier defect is noted in the 1-hr scintiphotos where the lesion is accurately localized by multiple views to the right frontoparietal region.

A rapid sequential and 1-hr cranial scintiphotographic study in a patient with an acute right middle cerebral artery thrombosis is shown in Fig. 7. The patient, a 62-year-old female, was admitted because



**FIG. 4.** Analyses of normal posterior cerebral vascular patterns obtained after bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate. Time intervals are means obtained in 13 subjects.

of the acute onset of left hemiparesis. Pertinent findings included weakness of face, arm and leg on the left and a left extensor plantar response. Lumbar puncture revealed only a slight increase of cerebrospinal fluid protein, 60-mg/100 ml. During 6 weeks in the hospital, strength progressively returned to the left side of her body. Anterior, rapid sequential and 1-hr cranial scintiphotography was first performed 1 week after the onset of symptoms. Decreased vascular filling of the right cerebral hemisphere is noted during the arterial and capillary phases as shown in the 7.5-9.0-sec, 9.0-10.5-sec and 10.5-12.0-sec scintiphotos. During the venous phase (12.0-13.5 sec) and the phase of vascular equilibration (1-2 min) no asymmetry or abnormality of the distribution of activity is noted. However, at 60 min, some increased activity is now noted in the area of the right cerebral hemisphere that formerly demonstrated decreased vascular filling. A right-lateral scintiphoto localizes this abnormality to that parietal region. Repeat 1-hr cranial scintiphotography was performed 2 weeks after the initial study and demonstrated a marked increase in the blood-brain-barrier abnormality previously noted (Fig. 7).

A rapid sequential and 1-hr study in a patient with a right-posterior parietal subdural hematoma is shown in Fig. 8. The patient, a 70-year-old male, presented with left hemiparesis and increasing headaches for 4 weeks after a vague history of head trauma. After a large chronic subdural hematoma was evacuated from the right-posterior parietal region, the patient's neurologic symptoms and findings

cleared. Anterior-view rapid sequential and 1-hr cranial scintiphotography was performed just prior to surgery. Decreased vascular filling of the right cerebral hemisphere is noted throughout the entire rapid sequence, including the 1-2-min vascular equilibration scintiphoto. At 1 hr, an area of increased activity is well localized to the right-posterior parietal region by multiple-view scintiphotography (Fig. 8). This area of blood-brain-barrier abnormality is noted to occur on the side in which decreased blood flow was previously demonstrated.

A rapid sequential and 1-hr study in another patient with a subdural hematoma is shown in Fig. 9. The patient, a 39-year-old male chronic alcoholic, was admitted because of recent head trauma and grand mal seizures. Right carotid arteriography revealed an avascular extracerebral space in the right parietal region with an associated midline shift of the anterior cerebral artery and internal cerebral vein. A subdural hematoma was evacuated from the right-posterior region. Throughout the entire rapid sequence of posterior-view scintiphotography, decreased vascular filling of activity is noted in a portion of the right cerebral hemisphere. Decreased activity is noted in the same area of the right cerebral hemisphere at 1-2 min during the phase of vascular equilibration of the injected radioactivity. However, unlike the findings in the first patient with subdural hematoma (Fig. 8), no area of increased activity (blood-brain-barrier abnormality) corresponding to the defect in blood flow was demonstrated at 1 hr. (Fig. 9).

#### DISCUSSION

Visualization of vascular structures and organs has been performed in humans by rapid sequential scintiphotography after peripheral venous bolus in-

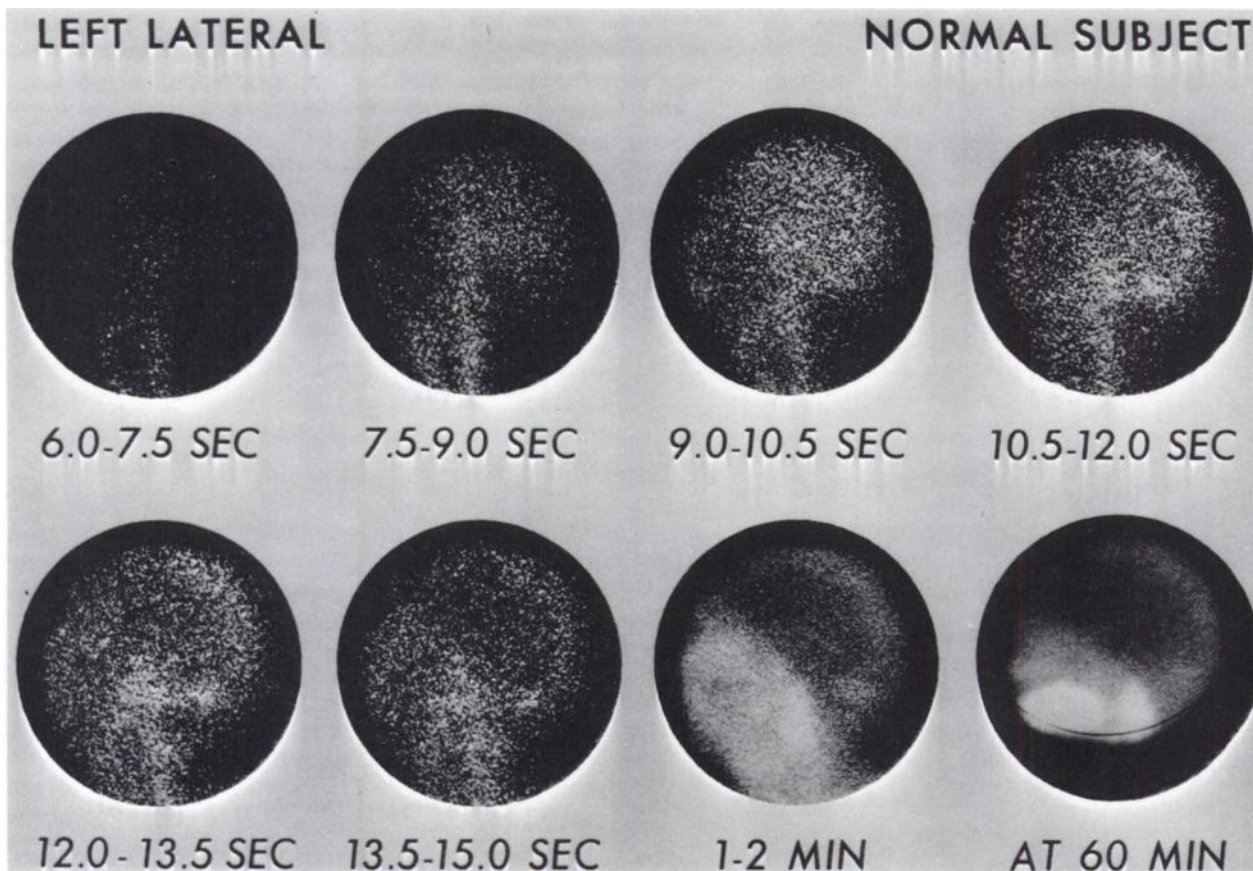
jection of  $^{99m}\text{Tc}$ -pertechnetate (19,24-29). The almost ideal properties of  $^{99m}\text{Tc}$  (30) allowing for large doses of administered radioactivity, and the ability of the Anger-type scintillation camera to obtain simultaneous isotope localization in relatively large areas (31), have made these studies possible in humans. The fact that free pertechnetate ion leaves the blood rapidly because of diffusion into extravascular fluid and clearance (15) does not invalidate this approach which involves the taking of scintiphotographs during the initial passage of a bolus of radioisotope through the vessels and/or organ in question. The purpose of this study was to apply this approach to the assessment of cerebral vascular disease and the vascular characterization of intracranial lesions.

It is readily apparent that one is able to image and distinguish the various normal phases of cranial vascular filling and emptying by rapid-sequential scintiphotography at 1.5-sec intervals after intravenous bolus injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate (Figs. 1-5). With this technique, the expected normal vascular phases were imaged in a predictable

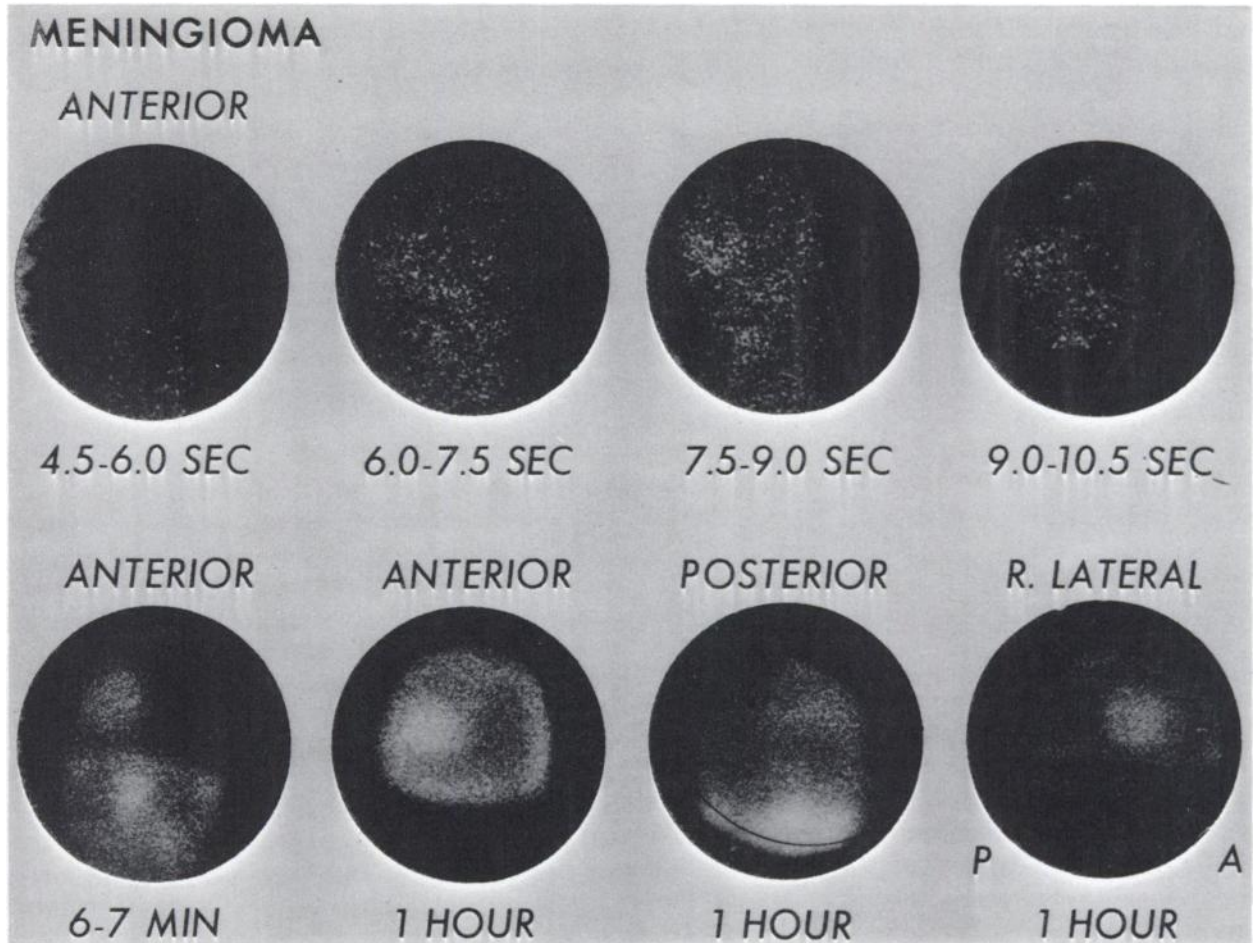
sequence (Figs. 2-4). These phases, which included major neck arteries, neck and cerebral arteries, cerebral arteries and capillaries, capillaries and venous structures and venous structures were somewhat more clearly defined on anterior view (Figs. 1, 3, 5). The timing of these phases was in close correspondence with that obtained by direct carotid arteriography after appropriate allowance is made for the delay of appearance of the intravenous isotope bolus (Fig. 2). Resolution of vascular structures and phases is inferior to that obtained by carotid arteriography, mainly because of the limited number of scintillations (2,000-4,000) per 1.5-sec interval and the elongation of the  $^{99m}\text{Tc}$  bolus by its passage through the heart and lungs. While increasing the exposure for each sequential scintiphotograph would result in an increased number of scintillations per image, it would tend to decrease the resolution of each of the vascular phases. Although these isotope images cannot yet match the detailed delineation of arteries and veins obtained by carotid arteriography, the visualization of the diffuse capillary distribution of radioactivity allows for the assessment of vascular perfusion of brain tissue. Such a capillary-perfusion phase is usually not visualized by conventional carotid arteriography.

Intracranial lesions associated with increased vas-

**FIG. 5.** Left lateral rapid-sequential and 1-hr cranial scintiphotography after bolus intravenous injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate into a normal subject. See text for description.







**FIG. 6.** Rapid-sequential and 1-hr cranial scintiphotography after bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate into patient with meningioma located in right frontoparietal region. See text.

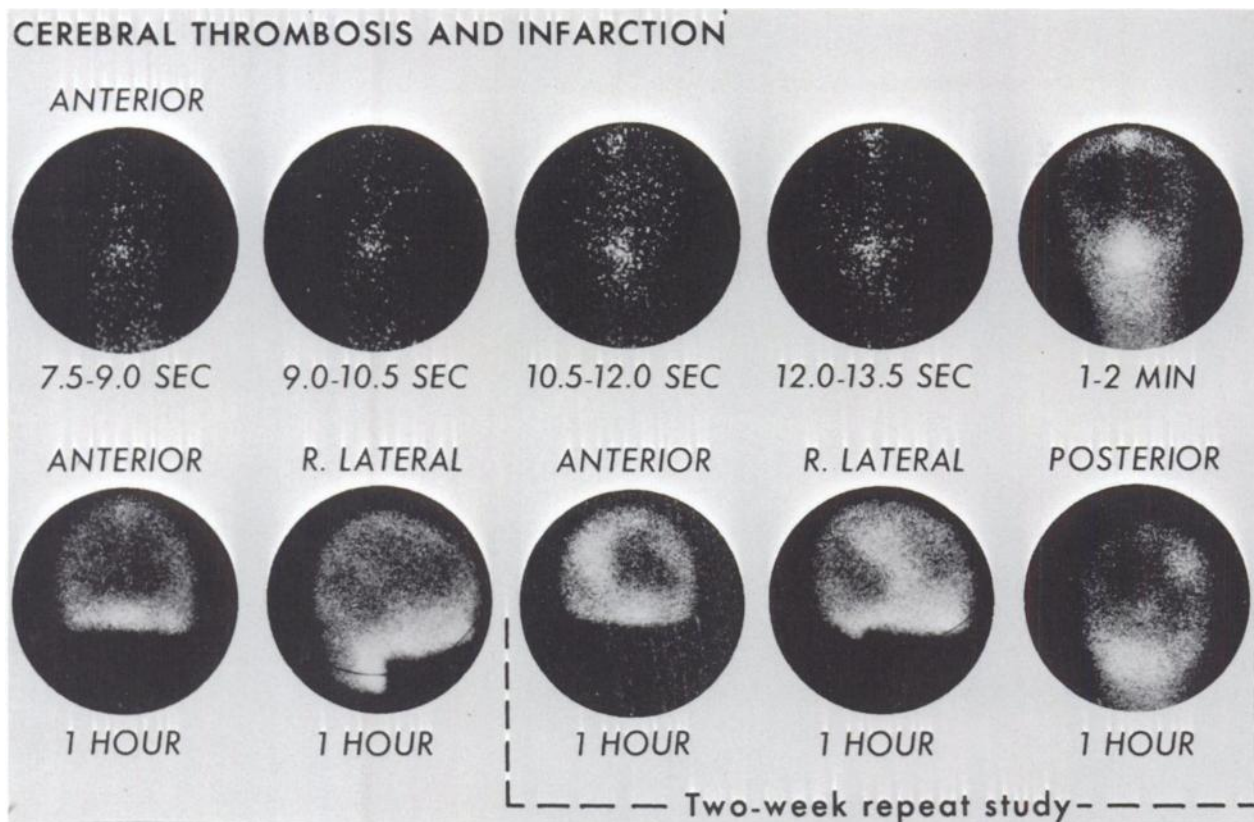
cularity and blood flow are readily delineated and characterized by this rapid scintiphotographic technique (Fig. 6). Such lesions usually demonstrate early rapid filling followed by a phase of partial and sometimes delayed venous emptying as the isotope bolus passes through the head (Fig. 6). Because of the marked abnormality of blood-brain barrier associated with the lesion shown in Fig. 6, scintiphotography alone at 6 min would not allow for the vascular characterization of this lesion.

The ability of this technique to visualize the diffuse capillary perfusion of brain tissue (Figs. 1, 3, 5) affords a sensitive means of detection of areas of decreased blood flow. This ability to detect and characterize relatively avascular lesions is clearly demonstrated in the studies of the patient with cerebral artery thrombosis and infarction (Fig. 7) and the two patients with subdural hematoma (Figs. 8, 9).

The necessity of rapid sequential scintiphotography performed in these studies for the accurate detection of an area of decreased blood flow is demonstrated by the sequence shown in Fig. 7. In this study only the first three scintiphotos taken up to 12.0 sec after injection demonstrate decreased filling on the right

side. By 12.0–13.5 sec (venous) and 1–2 min (vascular equilibration) the distribution of activity is symmetrical. This need of rapid sequential scintiphotography for the definite localization of areas of decreased perfusion is also demonstrated in the study of the patient with a subdural hematoma shown in Fig. 9. Posterior scintiphotography at 1–2 min and 1 hr may be interpreted as showing either abnormally increased activity on the left side or abnormally decreased activity on the right side. The basis of this asymmetrical distribution of radioactivity is revealed by the rapid sequential study showing a decreased area of vascular filling on the right side.

Conventional radioisotope imaging of intracranial lesions depends upon the associated focal abnormalities of the blood-brain barrier. The results of this preliminary study indicate that when a blood-brain-barrier abnormality is slight (i.e., in early cerebral infarction), scintiphotography performed several minutes after injection may fail to detect the slight but definite pooling of activity that can be



**FIG. 7.** Rapid-sequential and 1-hr cranial scintiphotography after intravenous bolus injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate into patient with right cerebral vascular accident performed 1 week and 3 weeks after acute onset of left hemiplegia. See text.

shown at 1 hr (Fig. 7). In this particular case, a repeat study two weeks after the initial scintiphotography demonstrates a definite increase of the blood-brain-barrier abnormality. (Progressive increase over a period of several weeks of the blood-brain-barrier defect in patients with cerebral infarcts has been well documented (32,33). Most importantly, the performance of rapid sequential scintiphotography after bolus injection allows for the detection of intracranial lesions not yet associated with blood-brain-barrier abnormalities detectable by appropriately delayed isotopic imaging (Fig. 9). In this case, the patient had a subdural hematoma of recent onset. The results in this case can raise the possibility of detecting other lesions which may not exhibit significant abnormalities in blood-brain barrier such as chronic cystic lesions and gliomas of low-grade malignancy (4,5,10).

The advantages of this approach to the detection, localization and characterization of intracranial lesions are multiple. Most important of these advantages is the amount of useful information that can be obtained after a single antecubital intravenous injection of a standard dose of  $^{99m}\text{Tc}$ -pertechnetate. This information may include the demonstration of

blood-brain-barrier defects, the assessment of the degree of blood flow in these abnormal areas and the detection of lesions and abnormalities of perfusion not associated with detectable defects of the blood-brain barrier. The ability of this procedure to image the perfusion of brain tissue is a distinct advantage over carotid arteriography, a technique which provides excellent resolution of arteries and veins but does not allow for routine visualization of the capillary perfusion phase. This lack of routine visualization of a perfusion phase may partially account for the relatively high number of so-called normal arteriograms in patients with cerebral vascular accidents (13-23).

Rapid sequential and delayed scintiphotography is a relatively simple and fast procedure, involving 5-15 min of physician and technician time at the beginning of the study for insertion of the Teflon needle and bolus injection, and 15-20 min of technician time for performing 1-hr post-injection multiple view scintiphotography. This procedure is as safe as conventional  $^{99m}\text{Tc}$ -pertechnetate encephalography, being essentially without mortality, morbidity or risk and involving a total-body radiation exposure of 0.1 rad and gonadal exposure of 0.15 rad (15,30,34). The near complete safety of this procedure is to be compared with a combined mortality-morbidity rate of between 3 and 20% associated with cranial arteriography (12,13,35).



These favorable features allow use of this technique in children, outpatients and severely ill patients as well as a safe means of screening and selecting patients for cerebral arteriography and/or surgery. Serial studies can easily be performed to follow the course of cerebral vascular disease as well as to monitor the postoperative effects of vascular and neurosurgery. At the present time this procedure usually complements rather than replaces cranial arteriography.

This laboratory is now routinely performing 3-4 rapid sequential and delayed-cranial scintiphotographic studies per morning. More than 200 studies have been performed. Evaluation of these studies including comparison with cranial angiography and other neurodiagnostic procedures is in progress.

SUMMARY

A technique is described for the detection and vascular characterization of intracranial lesions. This technique consists of the administration of <sup>99m</sup>Tc-pertechnetate (10 mc) by antecubital intravenous

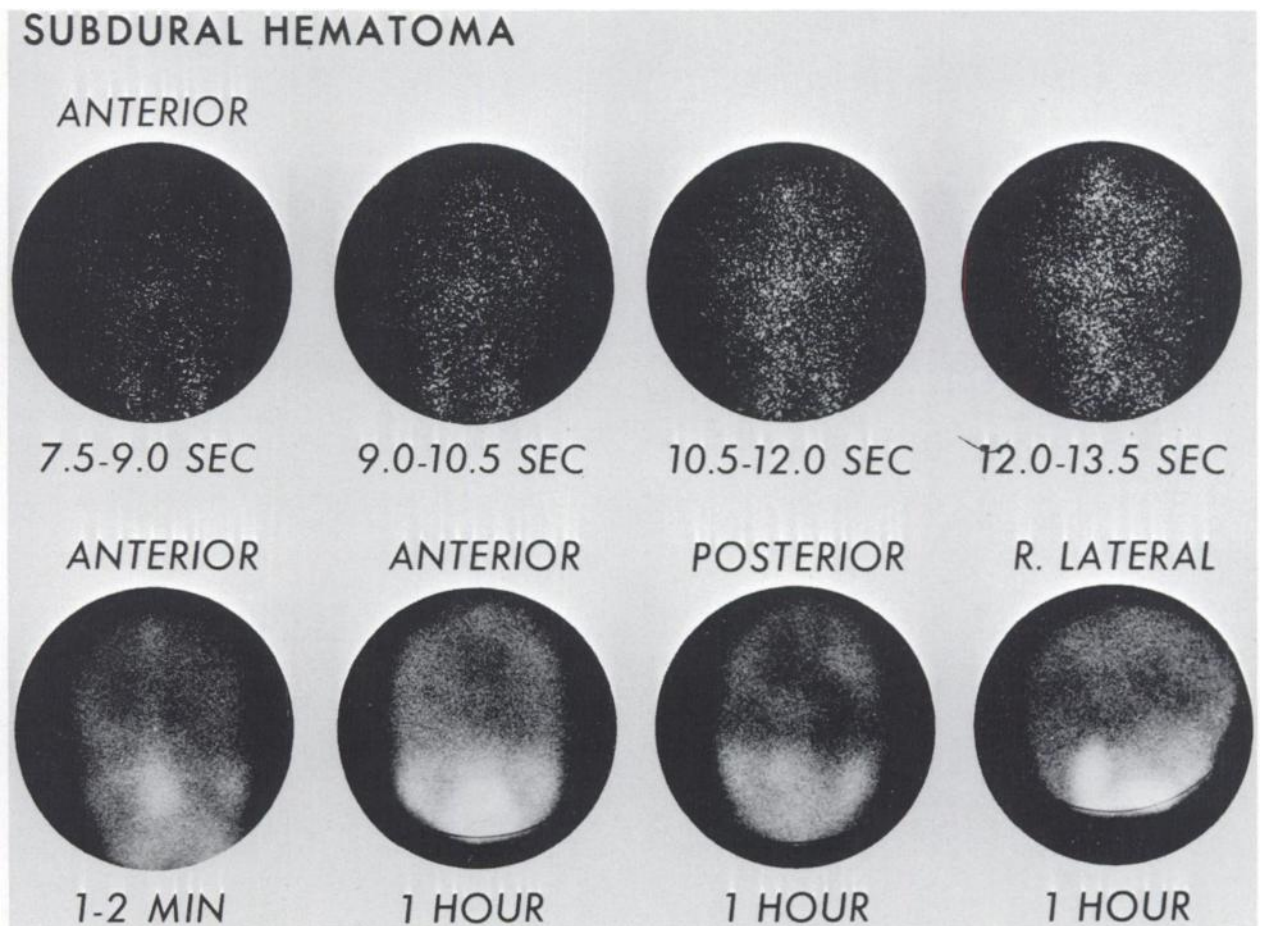
bolus injection followed by immediate rapid sequential and delayed scintiphotography using an Anger-type scintillation camera.

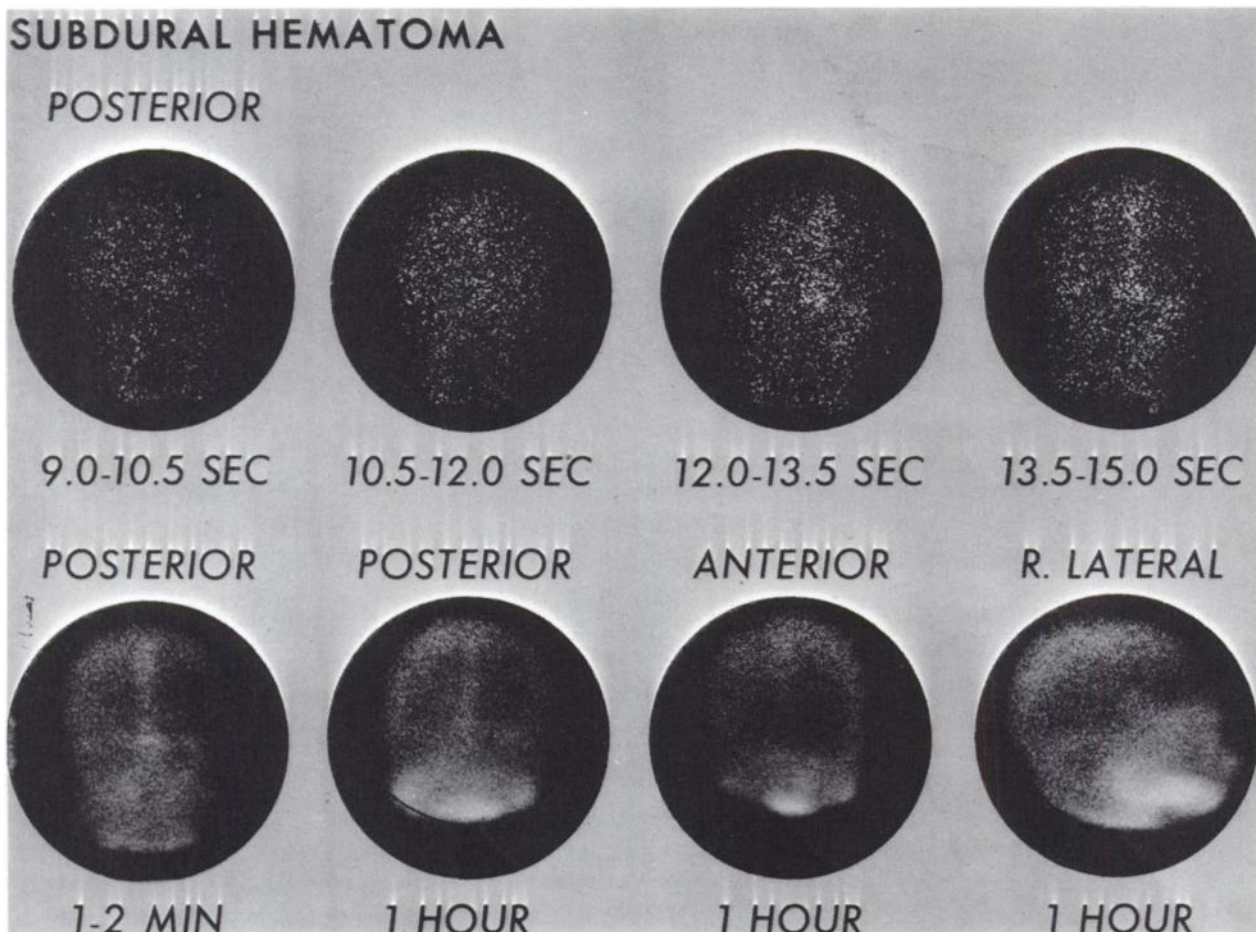
The results of multiple studies indicate that arterial capillary and venous phases can be visualized and distinguished. Analyses of these results provide mean time intervals for the various vascular phases on anterior and posterior viewing.

Representative studies from patients with a variety of intracranial lesions—primary neoplasm, cerebral infarct and subdural hematoma—are shown to demonstrate vascular and avascular lesions and their relationship to blood-brain-barrier abnormalities.

The advantages of this technique are discussed with emphasis on the great amount of relevant information obtained, the relative ease and speed of performance, patient safety and the possibility of acquiring data on the vascular characterization of intracranial lesions not obtainable by conventional brain-scanning or current methods of cerebral angiography.

**FIG. 8.** Rapid-sequential and 1-hr cranial scintiphotography after intravenous bolus injection of 10 mc <sup>99m</sup>Tc-pertechnetate into patient with right parietal subdural hematoma. See text.





**FIG. 9.** Rapid-sequential and 1-hr cranial scintiphotography after intravenous bolus injection of 10 mc  $^{99m}\text{Tc}$ -pertechnetate into patient with right posterior parietal subdural hematoma. See text.

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