CEREBROVASCULAR PERMEABILITY STUDIES IN CEREBRAL NEOPLASMS AND VASCULAR LESIONS: OPTIMAL DOSE-TO-SCAN INTERVAL FOR PERTECHNETATE BRAIN SCANNING

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The suggested time intervals between injecting $^{99m}$Tc-pertechnetate and scanning the brain have varied from 10 to 60 min (1–6). Because of the apparent lack of agreement about the optimum scanning time, we have performed a series of brain scans at different intervals, digitized them and analyzed them in different ways.

MATERIALS AND METHODS

Selection of subjects. Patients with brain tumors and one with an arteriovenous anomaly (hereafter included in the tumor classification) who were referred for brain scanning were chosen for this study. At subsequent operations all the patients were found to have one of a variety of pathologic processes. There were six males and five females with ages ranging from 8 to 66 years.

Scanning dose. All patients were injected with 5–6 mCi of $^{99m}$Tc-pertechnetate ($T_{1/2}$, 6-hr; gamma emission, 140 keV). This radionuclide was assayed and injected 60–90 min after elution from a $^{99}$Mo ($T_{1/2}$, 67 hr) column. The total amount of $^{99m}$Tc in millicuries from the initial elution depends on the activity of the generator, and the activity from subsequent elutions depends on the time interval between elutions.

The generator was prepared with nonpyrogenic material and was sterilized by autoclaving; the 25 ml of eluted $^{99m}$Tc was collected in a sterile vial. Assay of the $^{99m}$Tc was then carried out with an ionization chamber that was double checked with a $^{57}$Co standard every 2 or 3 days. The $^{99m}$Tc yield was 50–70%. As a final precaution, each batch was checked microbiologically.

Scanning procedure. All patients were scanned with a modified Picker Magnascanner that has a 3-in. NaI(Tl) crystal and a 19-hole collimator. Scan speeds varied from 75 to 90 cm/min with a line spacing of 0.45 cm. In the lateral projection, cathode-ray voltage was set by placing the probe over the superior aspect of the frontal eminence. In the anteroposterior projection the probe was placed over the lateral margin of the frontal eminence. In the posteroanterior projection the lateral margin of the parieto-occipital area was used. The counting rate at these sites ranged from 4,500 to 6,500 cpm, varying with the time interval after injection (usually, the counting rate was approximately 13,500 cpm immediately after injection). When a range setting of 10,000 was used, the counting-rate range differential was set at 40%. The pulse-height analyzer was set to straddle the 140-keV $^{99m}$Tc peak with a 60-keV window.

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In addition to recording the usual photoscan and dot scan we also computer-processed each scan. Signals from the pulse-height analyzer were fed into the digitizing magnetic 8-channel tape-recording unit described previously (7) along with horizontal and vertical position signals (x and y address). The tapes were fed into an IBM 7040 digital computer and processed (8-10). Various counting rates over the scan matrix were assigned different characters of type. Matrices were printed life-size. Type symbols were chosen to afford the easiest visual recognition of the areas to be analyzed. Along with each typed scan, the following information was recorded: scan date, collimator, time after injection, start time of scan, organ and view, isotope, patient number, magnification factor and scan speed.

All printed scans were registered against tracings from magnification-free roentgenograms made by the method of Lewall and Tauxe (11).

Scanning intervals. The views which showed the lesion most clearly were scanned two to nine times at intervals after injections indicated in Table 1.

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**FIG. 1.** Top is right lateral photoscan of patient with frontal lobe meningioma registered against tracing made from magnification-free roentgenograms. Middle is same photoscan registered against diagram defining various areas: a, tumor; b, nontumor; c, vascular; d, torcula and e, posterior fossa. Bottom is digitized scan in which various characters represent various counting rates, each representing 5% of maximum counting rates.

**FIG. 2.** Decay-corrected counts at various times after injection over various areas of scan of patient with astrocytoma.

**FIG. 3.** Tumor-to-nontumor and tumor-to-vascular count ratios (in patients with astrocytoma, meningioma or vascular lesion) at various times after injection.
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Data analyses. By superimposing films and dot readouts, body landmarks and roentgenographic information was transferred onto the computer plots. Various areas of each scan matrix were chosen and delineated for analysis, including tumor, nontumor, vascular, posterior fossa and torcula (Fig. 1).

Counting rates were summed in each of these areas and expressed as counts per minute per character. Ratios of these various counting levels were derived and plotted against elapsed time after injection.

Readability. To assess readability, 10 physicians who were experienced in reading scans were asked to analyze the test scans. To the group of scans reported here an additional 10 positive and 10 negative scans were added, and the entire collection was shuffled. All identifying information was concealed. The viewers were asked to categorize each scan as (1) definitely positive, (2) probably positive, (3) probably negative or (4) definitely negative. They were asked to locate all areas called positive, and these were checked for accuracy. For additional assessment of the posterior fossa, the viewers were asked specifically to interpret this region on each scan as (1) definitely negative, (2) definitely positive or (3) indeterminate.

RESULTS

Decay-corrected counts over various areas of a scan of a patient with an astrocytoma are shown in Fig. 2. After an initial slight increase after injection, all counts were observed to decrease, the vascular phase starting from the highest level and decreasing the fastest.
Tumor-to-nontumor and tumor-to-vascular count ratios are shown in Fig. 3. Tumor-to-nontumor count ratios generally increased with time in the meningioma group but remained relatively constant in the astrocytoma group. In the predominantly vascular group (hemangioblastoma and arteriovenous malformation), count ratios decreased significantly with time and, in the latter case, increased again. At the nadir of the tumor-to-vascular count ratio (0.88 in this case) the scan was reported as negative by all observers (Fig. 4). This did not coincide with the nadir of the tumor-to-nontumor count ratio.

Tumor-to-vascular count ratios among the meningioma patients also increased; in the astrocytoma group they tended to remain flatter, and they decreased or remained constant in the vascular group.

Results of readability tests for accuracy are given in Fig. 5. Among the scans diagnosed “definitely positive” and “probably positive,” the astrocytoma group was diagnosed accurately in nearly 90% of the decisions by 3 hr after injection. The meningioma group was diagnosed accurately by 3 hr after injection, and the vascular group by 2–3 hr.

In the posterior fossa group (Fig. 6), accurate diagnoses increased from low values up to 100% at the third hour. Wrong answers decreased to 0 by 90 min and indeterminate answers decreased from 100% at 45 min to 0 at 3 hr.

**DISCUSSION**

Our results indicate that 3 hr after 99mTc-per-technetate injection is the optimal time for scanning for brain lesions such as meningiomas, astrocytomas, vascular lesions and hemangioblastomas. This is supported by the fact that at this time and afterward our panel reported an increased number of accurate diagnoses, no inaccurate diagnoses and relatively few indeterminate diagnoses.

At least three factors seem to influence scan diagnosticians in their decision-making process: (1) tumor-to-nontumor count ratio, (2) tumor-to-vascular count ratio and (3) site of the tumor. In our series, the tumor-to-nontumor count ratio was greater than 1.26 in all cases. In some cases the scans were accurately diagnosed 100% of the time at this ratio, but in other cases, even with a higher ratio, scans were frequently diagnosed inaccurately. This inaccurate evaluation seemed to be related to the location of the lesion within the brain. For example, a sphenoid ridge meningioma (Fig. 7) was frequently diagnosed inaccurately in spite of a relatively high tumor-to-nontumor count ratio because of its proximity to the high extracerebral uptake.
Fig. 7. Photoscans of patient with sphenoid ridge meningioma registered against tracings of magnification-free roentgenograms. Lesion was frequently misdiagnosed in spite of high tumor-to-nontumor count ratios, probably because of its proximity to high uptake in extracerebral areas. (From Ref. 11 by permission of the publisher.)

At approximately the same ratios as those associated with accurate diagnoses in the meningioma and vascular cases, diagnosis of astrocytoma was sometimes incorrect. Even though a tumor-to-nontumor count ratio of 1.33 was reached by 2½ hr after injection (tumor-to-vascular count ratio at this time was 1.18) in one of these cases, the highest degree of accuracy in diagnosis was not achieved until a tumor-to-nontumor count ratio of at least 1.40 was reached. The fact that in one case (100% correctly diagnosed) the ratio had decreased to 1.26 by 4½ hr (tumor-to-vascular count ratio at this time was 1.0) indicated that factors other than the simple tumor-to-nontumor count ratio were manifesting themselves. This was the lowest ratio in the series associated with 100% accuracy of diagnosis. Even though all scans were performed at constant contrast settings (adjusted on our machine to optimize tumor visualization over the brain), some influences resulting from changing counting rates may also have been operative.

It is probable that tumor-to-vascular count ratios are also important in the decision-making process. Nearly all accurately diagnosed scans had ratios of at least 1.0 by the third hour. Prior to the third hour, 61% of the lesions were “colder” than vascular components of the scans.

Although our data concern a relatively small number of cases, the digitization by computer processing seems to constitute an important step toward the solution of this difficult problem, and its accuracy seems to negate some of the objections to the paucity of cases reported.

**SUMMARY**

Brain scans were performed in a series of patients at various intervals after injection of $^{99m}$Tc-pertechnetate. The optimal interval between injection and scanning seems to be at least 3 hr. Our data suggest that scanning at this time leads to the greatest accuracy in diagnosing the positive scans with the least number of false-positive and false-negative reports. A method of analyzing scintiscan data is presented. This is based on the derivation of ratios based on actual counting rates obtained from digitized computer-processed scintiscan matrices.

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