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A Comparative Analysis of the Accuracy of the Technetium-99m Pertechnetate Brain Scan: Followup of 1000 Patients

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The radioisotope brain scan is now well-established as an invaluable diagnostic tool in the delineation of intracranial lesions. The accuracy of the test has been established in a number of large series (1,2,3,4). It is a nearly ideal screening study because of the simplicity of performance, the minimal morbidity and risk to the patient, the ability to actually visualize the lesion, and the accuracy of the test. Brain scanning has progressed along two lines: the development of better scanning equipment and the development of more suitable radiopharmaceuticals. The majority of the earlier studies were accomplished with ^{131}I-labeled human serum albumin. The introduction of ^{203}Hg labeled chlormerodrin by Bender and Blau and the subsequent development of ^{197}Hg labeled chlormerodrin has seen these radiopharmaceuticals almost completely replace radioiodinated albumin as the agent of choice for brain scanning.

The introduction of short half-life (six hour) ^{99m}Technetium by Harper in brain scanning (5) and its availability even at distant laboratories, through the use of ^{99}Mo-^{99m}Tc generators developed by Brookhaven National Laboratory (Richards), have established another major agent for brain scanning. The following report details the results of follow-up on the first 1000 patients scanned at this institution with ^{99m}Tc pertechnetate for localization of intracranial lesions.

MATERIALS AND METHODS

From July, 1964, through August, 1965, a total of 1000 patients were scanned for intracranial lesions with ^{99m}Tc pertechnetate in the Nuclear Medicine Section of the North Carolina Baptist Hospital, Winston-Salem, N. C.

In this retrospective study, the patient's hospital chart was reviewed at least six months after completion of the brain scan. Naturally this procedure is no guarantee that an occasional false negative might have been missed, for no

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active follow-up was attempted, other than the survey of the hospital charts. Hopefully, the majority of intracranial lesions missed by the initial hospital workup have become apparent clinically by this time (a period of six months to one year) and confirmed by other tests and surgery.

The excellent physical properties (half life of six hours and near ideal scanning energy of the 140 keV with no associated beta emission) have been adequately described in detail by other authors (5,6,7). The pertechnetate in the TcO_4^- form of ^{99m}Tc is obtained by the elution of a ^{99}Molybdenum-^{99m}Technetium generator with 15 ml of normal saline. (The half life of the parent ^{99}Mo is 67 hours). Although now commercially available, the majority of our generators were obtained from Brookhaven National Laboratory. Our method of preparation of the ^{99m}Tc pertechnetate is as listed in Table I. Each elution is assayed, checked for radiocontaminants, autoclaved and checked (after the fact) for sterility. The technique is fast, accurate, and easily accomplished by a technician. The initial 380 patients received 10 millicurie oral doses using a technique previously described (8). The remaining patients were injected intravenously (65μc/lb) in order to obtain consistent high count rates. The radiation dose to the patient with ^{99m}Tc pertechnetate is well-documented (9). The estimated total body dose is 120 mr per 10 mc of ^{99m}Tc. Lugol's solution will reduce the radiation dose to the thyroid, whereas perchlorate will reduce the dose to the thyroid and the stomach (6).

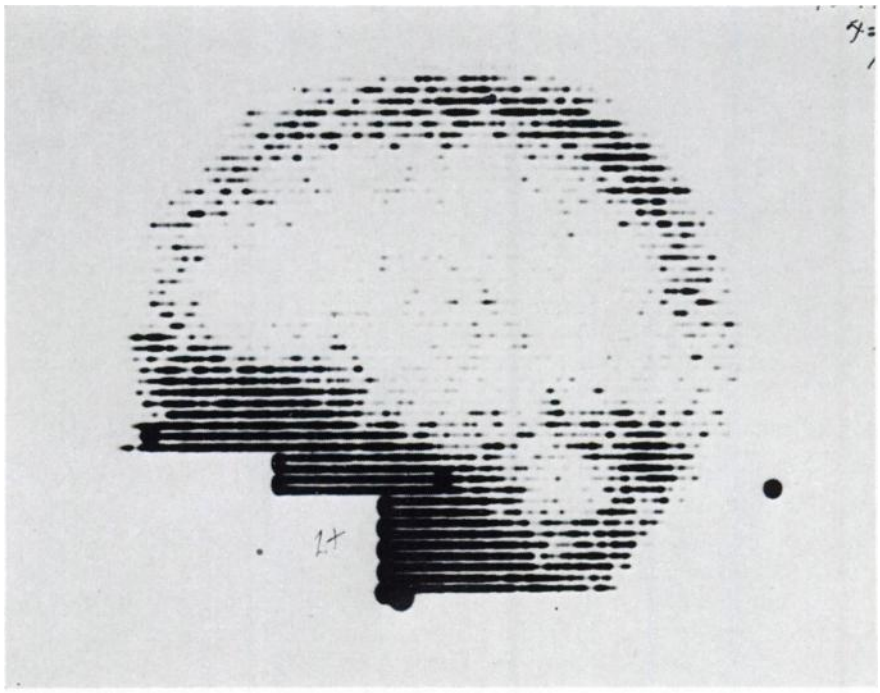

Fig. 1. Normal lateral with ^{99m}Tc pertechnetate. Note the radioactivity in the venous sinuses and the delineation of the posterior fossa.

EQUIPMENT AND TECHNIQUE

The scanners utilized in this series varied from a Picker Magnascanner with 19-hole collimator and a speed of 60cm/min to a modified Magnascanner with a maximum speed of 200 cm/min, low-energy (31-hole) collimator and a time constant of 1/50 second. The spectrometer was set at 130-160 keV. Presently, with count rates of 10,000-30,000 counts/min, the scan speed varies between 130-200 cm/min. The brain scans were started one hour after oral administration and 10 to 15 minutes after intravenous injection. Usually both laterals and either an anterior or a posterior view were obtained. For suspected subdural hematomas, all four views were routine. In cases of suspected lesions in the posterior fossa an "angled" posterior (10) was performed as a special view.

RESULTS

The distribution of the positive scans obtained in these 1000 patients is given in Table II. The results of the scan and other diagnostic studies are reported as they were interpreted at the time the test was performed. One hundred forty-eight of the scans were interpreted as positive (15%). The four cases of extracranial contamination have been discussed in detail (11). The seven false positive scans were confined primarily to our early experience and were related to problems in interpretation of the normal venous structures and the choroid plexus. Of the remaining positive scans, 75 were proven neoplasms, whereas 62 were related to non-neoplastic lesions.

Table III lists the 92 histologically proven neoplasms, together with the

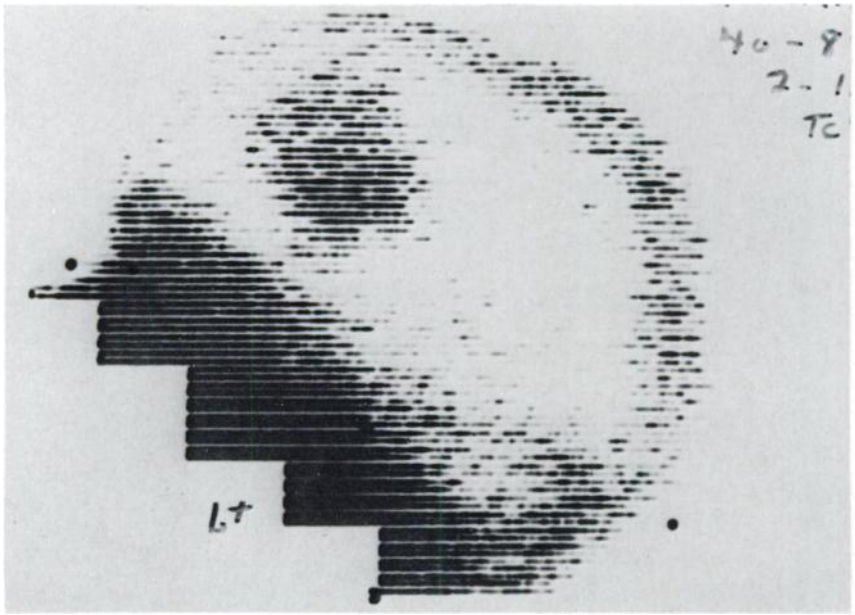

Fig. 2. Glioblastoma Multiforme.

results of brain scanning. Twenty-one of these were metastatic and 71 were primary lesions. Thus, the ^{99m}Tc pertechnetate brain scans were positive in 81.5% (75 out of 92) of the proven neoplasms. This percentage compares quite closely with the 83% reported by Quinn (12) with pertechnetate (65 proven neoplasms) and the 79% accuracy with ^{197}Hg and ^{203}Hg chlormerodrin (720 proven neoplasms) reported in the combined data of Goodrich (4). When the data from this series is compared with that with the radiomercurials, the accuracy in all instances is closely paralleled (Table IV).

A variety of other diagnostic studies (skull films, electroencephalogram, echoencephalogram, arteriogram and ventriculogram-pneumoencephalogram) were performed on these 95 patients. However, every patient did not have all

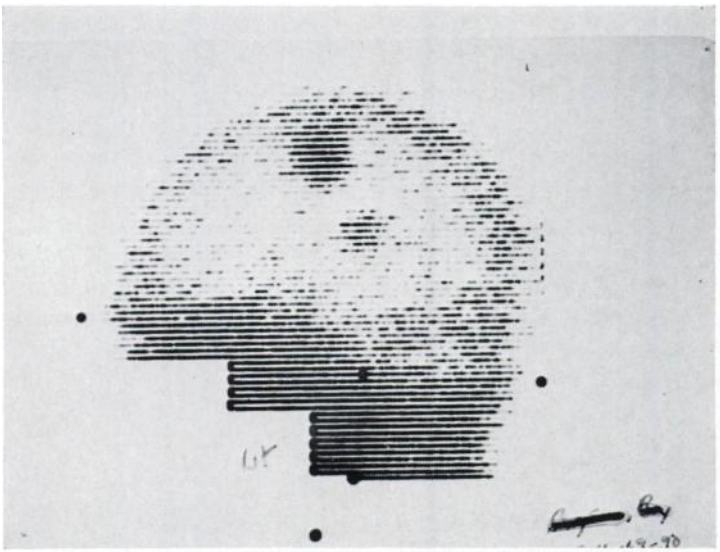

Fig. 3. Demonstration of two metastatic foci (carcinoma of the lung).

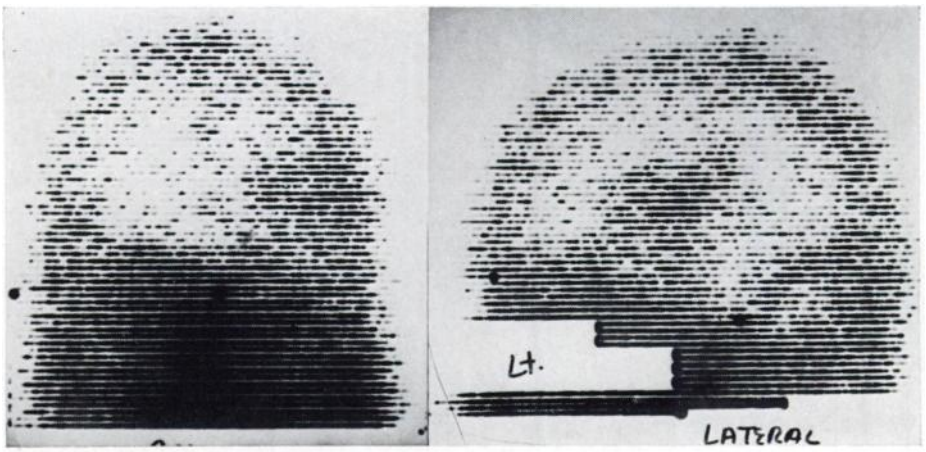

Fig. 4. Infarction of the left middle cerebral artery.

of the studies. Table V compares our results with those of two other reported series (3,4).

Routine views of the skull were positive in 46.9% of the neoplasms, a percentage which is somewhat higher than other reported series (Table V). The skull films were of most benefit in intrasellar lesions. Of the five meningiomas, however, none produced changes in skull findings. Metastatic lesions had positive findings in 9/19 (47%) while the combined astrocytoma-gliomas were positive in 12/39 (31%). Overton reported abnormal skull roentgenograms in only 2% of gliomas and 5% of metastatic lesions.

The accuracy of the electroencephalogram in this study (70.4%) paralleled closely the results of Overton (71%) with proven neoplasms. On the basis of the concept of normal or abnormal, these percentages are quite respectable. The EEG, however, yields abnormal patterns, such as diffusely abnormal tracings or abnormal foci distant from the neoplastic lesion. In this respect, the information is of less value than that of the brain scan.

The arteriogram correctly localized the lesion in 92.3% of our cases, whereas the pneumoencephalogram-ventriculogram was slightly more accurate (93.9%). The accuracy of these tests reflects to some extent the role of the brain scan

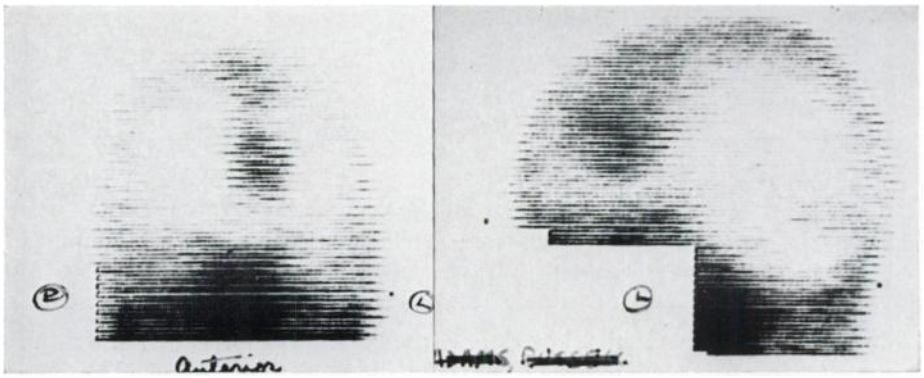

Fig. 5. Arteriovenous malformation.

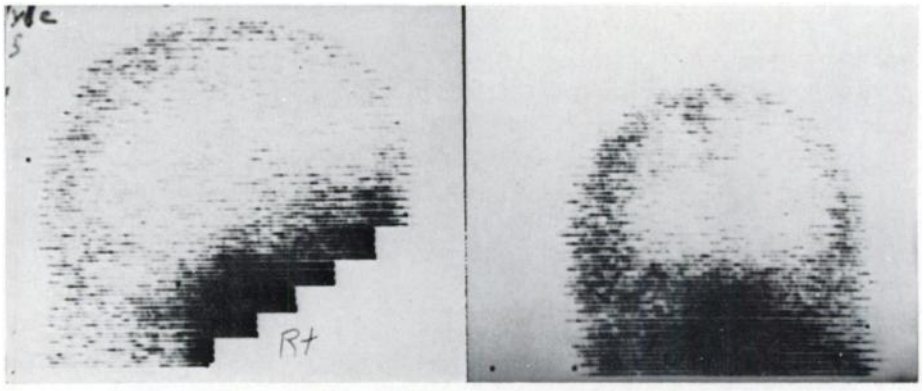

Fig. 6. Right subdural hematoma.

as a screening agent in this institution. The brain scan is very valuable in helping the physician to select the appropriate contrast study.

Although only 29 of the 92 patients with tumors had echoencephalography, the accuracy of this test (78%) for astrocytomas I and II was greater than that of the brain scan (72%). Many very large astrocytomas may not take up adequate radiopharmaceutical to be outlined by scanning, but they produce a shift in the midline. It should be pointed out that the majority of these abnormal patterns were related to a shift in the midline structures.

Although the primary application of the brain scan is the detection and localization of neoplastic lesions, it is of considerable value in the demonstration of non-neoplastic intracranial lesions. In our experience, the ^{99m}Tc brain scan has been most accurate in the demonstration of arteriovenous malformations (14 of 14) and subdural and epidural hematomas (9 of 9). The pertechnetate brain scan usually outlines the subdural hematoma as a crescent-shaped peripheral area on the anterior or posterior, but with essentially normal lateral views (Fig. 6). The brain scan is not routinely used in the acute subdural because these patients usually have immediate arteriograms, but it is of considerable benefit in the diagnosis of chronic subdural hematomas. A complete

TABLE I

METHODOLOGY OF ^{99m}Tc PREPARATION AND USAGE

Procedure	*Method*	*Reference*
Elution	15 ml of normal saline poured through ^{99}Mo-^{99m}Tc generator. Generator eluted twice daily to increase yield.	(8)
Radioassay	Ionization chamber used routinely. The ion chamber is calibrated weekly by dilution of a ^{99m}Tc elution and standardization with a scintillation well counter and a cobalt-57 source.	(7)
Radiocontamination Assay	Eluate counted with scintillation spectrometer set for 450-1000 Kev. This energy range is greater than the ^{99m}Tc gamma rays but includes the high energy contaminants (^{99}Mo, ^{103}Ru). Counted against 1 microcurie ^{137}Cs source as a standard.	(7), (13)
Sterilization	Autoclave at 260°F, 120 psi, for 15 min.	(6)
Sterility Testing	Bacterial broth culture observed daily for 7 days, cultured at 37°C.	

tabulation of the results with non-neoplastic lesions is given in Table VI. Finally it should be pointed out that one is usually unable to differentiate between neoplastic and non-neoplastic conditions from the scan pattern.

DISCUSSION

It would appear that neither pertechnetate nor the radiomercurials offer a decided advantage in over-all accuracy of the brain scan, or in the delineation of specific varieties of intracranial neoplasms. Further, it would appear that the lesions commonly missed with the radiomercurials (astrocytomas, pituitary tumors, etc.) are also missed with pertechnetate (Table IV).

Reports in the literature (14,15) have described the demonstration of lesions with ^{203}Hg chlormerodrin which were not visualized (or not visualized

TABLE II

DISTRIBUTION OF POSITIVE SCANS

Total Scans	1,000
Positive Scans	
Neoplasms	75
Non-Neoplasms	62
Extracranial Contamination	4
False Positives	7
TOTAL	148

TABLE III

SUMMARY OF BRAIN NEOPLASMS SCANNED WITH ^{99m}Tc PERTECHNETATE

Tumor	*Total*	*Positive Scans*
Astrocytoma I & II	18	13
Glioblastoma Multiforme	24	23
Meningioma	5	5
Metastatic	21	20
Pituitary	9	4
Medulloblastoma	3	3
Ependymoma	3	2
Pinealoma	2	0
Acoustic Neuroma	2	2
Angioblastoma	1	0
Papilloma Choroid Plexus	1	1
Oligodendroglioma	2	2
Epithelioma	1	0
	92	75

as well) with pertechnetate. Our experience in double scanning of patients with proven lesions with radiomercurials and pertechnetate has revealed no difference in these compounds. The pertechnetate has obvious advantages over the radiomercurials: the clean 140 Kev gamma ray is easily collimated; the radiation dose to the patient is considerably less (repeat scans to follow lesions and brain scans in children are a reality); the scan time is much reduced (5-10 minutes per view) allowing more views to be made of the brain for increased accuracy; and with the high scanning speeds, comatose and uncooperative patients can be scanned routinely (the 20-30 minutes required per view with the radiomercurials eliminated the brain scan in many of these patients). Also, we feel that with experience the radioactivity in the vascular pools is not a problem with pertechnetate. In addition, the technician seems to be able to obtain scans of better quality on a routine basis than with the radiomercurials. From the standpoint of economics, in a busy laboratory, more patients may be scanned with the same equipment at less cost per dose of radioisotope.

TABLE IV

A COMPARISON OF RESULTS OF BRAIN TUMOR SCANNING USING ^{99m}Tc PERTECHNETATE WITH ^{197}Hg AND ^{203}Hg CHLOROMERODIN

Tumor	*Present 99mTc*		*Combined 197Hg, 203Hg*	
Astrocytoma	(13/18)	72%	(90/135)	67%
Glioblastoma	(23/24)	96%	(128/137)	93%
Meningioma	(5/5)	100%	(105/111)	95%
Metastatic	(20/21)	95%	(159/196)	81%
Pituitary	(4/9)	44%	(17/36)	47%
Other	(10/15)	67%	(68/105)	65%
Total	(75/92)	81.5%	(567/720)	78.8%

TABLE V

A COMPARISON OF THE BRAIN SCAN WITH OTHER DIAGNOSTIC STUDIES IN THE DEMONSTRATION OF PROVEN INTRACRANIAL NEOPLASMS

Study	*Present Study*		*Overton*[3]		*Goodrich*[4]	
Brain Scan	(75/95)	81.5%	(84/100)[1]	84%	(99/118)[1]	84%
Skull Series	(39/83)	46.9%	(35/94)	37%	(45/114)	40%
EEG	(31/44)	70.4%	(54/76)	71%	(11/12)	92%
Echo	(20/29)	68.9%	—		—	
Arteriogram	(60/65)	92.3%	(64/76)	84%	(70/85)	82%
PEG-Vent	(31/33)	93.9%	(20/21)	95%	(21/25)	84%

[1] ^{197}Hg and ^{203}Hg Chlormerodrin

It should be pointed out that ^{99m}Tc pertechnetate is not without its disadvantages. The major disadvantage is the necessity of the generator; the material is not readily available (except in some localities) in a precalibrated and tested radiopharmaceutical form ready for injection. This means that the user must also assume the role of manufacturer of the material. Because of the short half-life, adequate sterility testing can only be carried out "after the fact". Using the technique described in Table I, we have administered over 2000 intravenous doses of ^{99m}Tc pertechnetate up to this time (February, 1966) with no evidence of any type of pyrogen reaction. This, however, does not rule out the possibility of such a reaction. A further complication in the use of ^{99m}Tc is the fact that the A. E. C. has not as yet made it available on its general license program.

Except for the problems of preparation and standardization, the authors believe that ^{99m}Tc pertechnetate is the current agent of choice for brain scanning.

SUMMARY AND CONCLUSIONS

A review of 1000 patients scanned with ^{99m}Tc pertechnetate for intracranial lesions produced 148 positive scans. In the series 72 out of 95 patients with proven intracranial neoplasms (81.5%) had positive scans. The distribution of these positive scans with respect to the various types of neoplasms was presented, as well as comparative analysis with ^{197}Hg and ^{203}Hg chlormerodrin brain scanning. Positive scans were obtained in a number of non-neoplastic conditions. A comparison of the accuracy of the brain scan was made to other diagnostic tests: the echoencephalogram, the electroencephalogram, skull films, the arteriogram, and the pneumoencephalogram-ventriculogram.

TABLE VI

THE DISTRIBUTION OF POSITIVE PERTECHNETATE SCANS IN NON-NEOPLASTIC CONDITIONS

Lesion	*Positive Scans*	
Arteriovenous Malformation[1]	14	(14/14)
Subdural and Epidural Hematoma[1]	9	(9/9)
Vascular Occlusion[1]	18	(18/22)
Intracerebral Hematoma[1]	8	(8/9)
Abcess	1	
Encephalitis	2	
Contusion	1	
Craniectomy Defect	5	
Subarachnoid Hemorrhage	2	
Meningitis	1	
Sturge-Weber	1	
TOTAL	62	

[1]Proven by angiography, surgery, or autopsy.

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ADDENDUM

Since preparation of this article, the A. E. C. has released sterile, sealed generators on its general license.

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