Comparison of Radioactive Iodinated Serum Albumin (RISA) and Radioactive Mercury\textsuperscript{203} for Brain Scanning*


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Although many radioactive isotopes have been tried for brain scanning, the most widely used have been arsenic\textsuperscript{74} and radioactive iodine\textsuperscript{131} tagged onto serum albumin (RISA). With these agents and a variety of scanning methods satisfactory detection has been reported in 80 per cent or more of patients who subsequently proved to have intracranial tumours\textsuperscript{2,4,7,9}. But each of these radioisotopes, despite its usefulness, has certain disadvantages.

Arsenic\textsuperscript{74}, although applied successfully to brain scanning over the past 10 years, remains costly and is difficult to obtain for routine use. A high dosage is required to exploit the low percentage of emission of positrons and optimal localization is dependent upon an elaborate scanning system with matching of scans of gamma radiation and positrons.

RISA is readily available, less costly and more familiar from its common use in a variety of clinical applications. But it has two properties that also limit its value. First, in addition to the main emission of gamma rays at 360 kev (87 per cent), iodine\textsuperscript{131} gives higher-energy gamma rays at 640 kev (9 per cent) and 720 kev (3 per cent). This makes shielding of scattered radiation a difficult problem. Moreover, this high-energy gamma radiation is scattered and reduced in energy as it passes through the tissues of the head, so that some of it contributes to the main level of energy detected at 360 kev. This results in less efficient resolution and identification of the gamma radiation derived primarily from the site of the lesion.

Secondly, RISA is eliminated slowly from the body. Between 24 and 48 hrs., the most suitable period for brain scanning with this agent, about 50 per cent remains in the blood stream and about 80 per cent in the body. This offers an advantage in detecting richly vascular lesions such as angiomas, malignant gliomas and meningiomas. But, for lesions of low vascularity, the same feature operates to obscure the activity of the target by background radiation.

Neohydrin Labeled with Mercury\textsuperscript{203}

Because of these deficiencies Blau and Bender\textsuperscript{2} introduced radio-Neohydrin, an organic compound incorporating radioactive mercury\textsuperscript{203} (3-chloromercuri-2-methoxy-propl-urea). This isotope is characterized by a physical half-life of 45.8 days. A single-line emission of gamma rays eliminates the "foreign" counts coming from the scattered high-energy levels associated with RISA. The lower energy of gamma radiation at 280 kev simplifies the problem of shielding. In addition, the more rapid clearance of the radioactive mercurial compound from the body, partly because of its diuretic properties, favours an increase of the target-to-background ratio, and permits earlier scanning.

The dose of radiation to the whole body from radio-Neohydrin was calculated by Blau and Bender\textsuperscript{2} to be about 50 per cent less than that from the amount of RISA commonly employed for brain scanning. One detraction from the value of this agent, however, is the selective dosage of radiation to the kidney. Blau and Bender reported that this can be reduced by a blocking dose of nonradioactive Mercurhydrin which precedes the injection of the radio-Neohydrin.
Other approaches that may decrease the dosage to the kidney include the chemical elimination of free mercury from the Neohydrin preparation and the use of mercury\(^ {197} \) with a shorter half-life of 65 hrs. and absence of beta radiation. (See Addendum.)

Using a single extracranial detector with focusing collimation and a photo-scanning system, Blau and Bender\(^ {1,2} \) compared RISA and radioactive mercury in 100 patients. While the details of the type or verification of the intracranial lesions are not presented, they noted that radiomercury gave more readily interpretable scans in one-quarter to one-third of the cases and "in about 5 to 10 per cent a diagnosis would be made from the Neohydrin scans but not from the albumin scans." Previously, they had found localization about 85 per cent of the time in over 300 cases scanned with RISA. They concluded that radiomercury should raise this figure but noted, "The room for improvement is rather limited."\(^ {2} \)

Brinkman and others,\(^ {3} \) using radio-Neohydrin and a scanning system similar to that used by Blau and Bender, reported positive scans in two-thirds of a series of patients with verified intracranial tumours. This compares unfavourably with the rate of detection of 80 per cent or more reported by numerous authors using either RISA or arsenic\(^ {24} \), and also with that reported by Sklaroff and others\(^ {8} \) who obtained positive scans in 85 per cent of a series of 20 verified brain tumours using radiomercury.

Comparative Study of RISA and Mercury\(^ {203} \)

While the use of radio-Neohydrin appears to be having an enthusiastic reception for brain scanning, no study has yet been reported in a series of patients with verified lesions to compare the advantages of this agent quantitatively with RISA. Such a study is not done easily with a unilateral photo-scanning system in which exact registration of radioactivity is sacrificed in order to display the most suitable contrast between the local uptake and the background activity on one side of the head.

With the contour scanner,\(^ {4-6} \) however, two homologous regions on either side of the head are surveyed simultaneously. Exact rates of count are registered on the final scanning chart, so that a quantitative comparison can be made readily between the differential uptake over the lesion and the background activity of a corresponding normal region of brain on the opposite side of the head. This method also allows a direct comparison of repeated scans on the same patient at different times and with different radioisotopes.

Using this method, we have made double isotopic studies in a selected series of verified tumours. The patients were first scanned using radio-Neohydrin and then with RISA. In each instance repeated scans were carried out as soon as possible after the injection of the agent and were repeated at suitable intervals to give the values of the differential uptake over the lesion as a function of time.

The results indicate clearly that radiomercury,\(^ {205} \) tagged onto Neohydrin gives earlier and higher local uptakes as compared to radioactive iodinated serum albumin.

**Method**

Patients were given an intramuscular injection of 2 cc. of nonradioactive Mercuryhydrin on the day before scanning. Radio-Neohydrin was injected in the dosage of 10 mc. per kg. of body weight. The patients were scanned immediately and again at 3- and 6-hr. intervals. The pulse-height analyser was set to cover a range of gamma radiation between 210 and 380 Kev.

Scans with radioactive iodinated serum albumin were made several days later. The injection of 300-400 mc. of RISA was preceded by Lugol's iodine solution in a dose of 10 drops 3 times a day for 24 hrs. Scans were made immediately and at 24- and 48-hr. intervals. The window of the pulse-height analyser was set to cover a range of gamma radiation between 390 and 490 Kev.

The automatic contour-scanning device\(^ {4-6} \) consists essentially of twin matched detectors using scintillation crystals of thallium-activated sodium iodide measuring 1\(^ {\frac{3}{4}} \)\( \times \)2\( \frac{1}{2} \)". Collimation openings are 1" in diameter and 2\( \frac{1}{2} \)" in length. Each side of the head is scanned by both detectors sweeping from front to back and reversing in 9 concentric parasagittal arcs beginning along the midline. The detectors remain approximately perpendicular to the surface of the head. This scanning pattern, which is a departure from the usual rectilinear
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pattern, was selected on neurosurgical grounds to give comparative counts from symmetrical regions of the head which are uniform in regard to volume of brain tissue as well as to the ratio of brain to scalp and skull. Local variations in uptake caused by temporal muscles or longitudinal sinus, which can be troublesome in unilateral rectilinear scanning, are thus balanced out.

Registration of radioactive counts appears on a single semicircular scanning chart. Because of the crossed-axis position of the detectors, the chart indicates whether the lesion is superficial or deep.

The background count and differential uptake are registered exactly. Each arc of the scanning pattern is indicated by a double row of dots and each dot represents a number of counts, usually 100 to 200 in number, as selected. The differences of counts are recorded similarly, each dash referring to a difference of 40 counts over the right side and each inverted 'V' referring to 40 counts from the left side. From the scanning chart it is then possible to obtain the percentage of local uptake over the lesion as compared to background activity over the corresponding normal region of brain on the opposite side. Each chart, for purposes of orientation and illustration, is placed on a conventional outline drawing of the head. At the time of scanning, the positions of the inion and glabella are measured carefully and recorded.

The scan is completed in 30 min. This is less than half the time required in rectilinear scanning in which anteroposterior and one or more lateral surveys are necessary. This short time of scanning allows for repeated scans even with the fairly rapid fall off in blood levels characteristic of radiomercy.

Results

Meningioma. In double isotopic studies on 4 patients with verified meningiomas, radio-Neohydrin gave a much higher differential uptake over the site of the tumour than did RISA (Fig. 1). Even on initial scans, completed within 45 min. of injection of Neohydrin, detection of the lesion was already possible since the local uptake was then the same or somewhat higher than with RISA at 24 hrs. after injection. On repeated scans carried out at 3 and 6 hrs., Neohydrin gave a percentage uptake which was about twice that obtained with RISA at 24 hrs. (Fig. 2). Conversely, at 6 hrs. the level of tumour uptake with RISA was much less than that with Neohydrin (Fig. 3).

Glioblastoma Multiforme. Similar findings were noted in 4 patients with glioblastoma

Fig. 1. Double radioisotopic studies with curves of repeated scanning values in meningiomas.
Demonstrated, for example, by the scans in Fig. 3 where the total background counts (noted in the legends on the drawings) are of similar numerical order. But the differences in the local uptakes, 80 per cent and 20 per cent, are striking.

With both types of tumours, the repeated scans indicate that the differential uptake over the site of tumour rapidly increases to an optimal level at about 3 hrs. after the injection of radio-Neohydrin. At 6 hrs., the differential uptake over meningiomas increased further in 3 cases, but was slightly lower in a fourth case, and the same in another instance (Fig. 6).

In 7 patients with glioblastoma multiforme in whom a second and third scan were made with Neohydrin, the percentage local uptake was higher in 4 and slightly lower in 3 on the third as compared to the second scan (Fig. 7).

These findings indicate that the best time for scanning is 3 hrs. after the injection of Neohydrin, although tumours with a high percentage of local uptake can be detected even on the immediate scan and may give an increased percentage of local uptake in some instances after the interval of 3 hrs.

From the plots of the values of the local uptakes with Neohydrin, it is evident that the average tumour-brain ratio tends to be higher for meningiomas than for glioblastomas. Maximal uptakes exceeding 100 per cent at 3 hrs. were recorded only over 2 meningiomas. But the values for the 3 other

Comment

It should be noted that the difference in uptake is expressed in the charts as a percentage increase of counts over the site of the tumour as compared to the counts from a homologous region of the head on the opposite side. The initial higher dose of radio-Neohydrin, aside from ensuring a statistically useful rate of count, thus has no bearing on the percentage value of local uptake. This is
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meningiomas fall within the same range as those for glioblastoma. Even with repeated scanning, therefore, no distinction in any individual case could be made on the basis of percentage uptake as to which type of tumour might be present.

Further studies with more selective radio-isotopes and improved instrumentation may provide means of making a more specific distinction between different types of lesions. But at present such a specificity even between two such widely different neoplasms as meningioma and glioblastoma, seem, except for certain instances, quite uncertain.

Fig. 5. (Above) Scan of glioblastoma multiforme with Neohydrin at 3 hrs. showing a local differential uptake of 100 per cent. (Below) Scan on the same patient with RISA at 28 hrs. showing a local differential uptake of 45 per cent.

It should be remembered, of course, that many non-neoplastic lesions, such as abscess, tuberculoma, subdural hematoma, intracerebral hematoma, cerebral infarct, and angioma, give a positive uptake and make any precise differentiation of the nature of the lesion on the basis of the pattern of the scan still further unlikely.

In a smaller number of double isotopic studies on the low-grade gliomas and metastatic carcinomas the earlier and higher uptake of Neohydrin as compared to RISA was also found.

Conclusion

1. Quantitative comparison of radio-Neohydrin and radioactive iodinated serum albumin has been made using an automatic contour brain scanner.

2. With this method, exact registration of radioactive counts gives a value for the percentage of differential uptake over the lesion as compared to the background activity of a normal region of brain of the opposite side of the head.

3. In a selected series of patients with meningiomas or glioblastoma multiforme, radioactive Neohydrin gave a differential uptake over the tumour of double that obtained with RISA.

4. Triple scans after a single injection of radio-Neohydrin have shown that the optimal time for scanning with this agent is about 3 hrs.
5. The highest percentage of differential uptake appeared over certain meningiomas. With this exception, no distinction from Neohydrin scans could be made between meningiomas and glioblastomas on the basis of either a percentage of differential uptake or the value of percentage of uptake on repeated scans at intervals.

6. Although the pattern of the scan and the anatomical site of the local uptake often may be correlated with the patient’s clinical findings to provide a useful guide as to the nature of the lesion, the nonspecificity of radioisotope uptake is emphasized. We would caution against using a single scan as a means of distinguishing between a neoplasm and a cerebral vascular lesion.

Addendum

Since submitting the above report, a further double tracer study in 15 patients with verified gliomas, metastatic neoplasms, subdural haematomas and infarcts has shown that Neohydrin-mercury\(^{197}\) gives uptakes as early and as high as Neohydrin-mercury\(^{208}\), with the distinct advantage that calculated dosage of radiation to the kidney is reduced to a very low level of less than 1 per cent of that from mercury\(^{208}\).

References