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Cranial Scintigraphy: Value of Adding Emission Computed Tomographic Sections to Conventional Pertechnetate Images (512 Cases).

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A prospective trial was carried out to assess the contribution made by a radionuclide transverse-section view to conventional radionuclide scans of the brain. Each set of scans was reported by two independent teams of observers, but only one team viewed the tomographic section. An abnormality rating was used to decide whether a set of scans was positive or normal. The reports for 512 patients were analyzed and compared with the final independent diagnosis. Greater accuracy of diganosis *with* the section view was significant at the 0.1% level; the results showed that failure to detect tumors was almost halved while there was a 16% improvement for the detection of infarcts. Abnormality ratings were also used to plot ROC curves and rating curves; these showed that the addition of the tomographic view increased markedly the proportion of true positives without any increase in the proportion of false-positive reports.

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The principles of radionuclide emission tomography, first described by Kuhl et al. (*1*), have been applied for more than 7 yr in this department using the Aberdeen Section Scanner (*2*). Although the diagnostic advantages from the extra information provided by the transverse-section view, or tomogram, in addition to the conventional views, had been evident for some time in the daily reporting sessions, it was felt that an objective and quantitative evaluation was necessary.

A retrospective pilot study on a small number of selected patients (*3*) gave promising results. This paper reports the results of a prospective trial in which the evaluation was part of the routine daily reporting session and was extended to include a much larger number of patients.

MATERIALS AND METHODS

This prospective trial began in November 1976. All examinations were performed on the Aberdeen Section Scanner 1 hr after the injection of 10 mCi Tc-99m as pertechnetate. At least one transverse-section scan was performed, in addition to the four conventional views, for each patient. The scanner has two detectors, which produce opposite conventional views simultaneously. To obtain the transverse-section view, the detectors were rotated through 180° around the chosen plane, performing a single scan line at each angular interval of 6°.

The image of the distribution of radionuclide in the selected plane was reconstructed from the data collected during these 30 passes (*4,5*). The 30 measured emission profiles, each consisting of 64 line integrals, were sequentially convolved with a 31-point spatial filter (*6*). This filter is designed to reduce reconstruction artifacts due to overshoot or ringing, near regions of high reconstructed gradients. In the frequency domain it is effectively a conventional ramp filter with a cutoff frequency of f_n subjected to a Hanning window of $\frac{1}{2}[1 + \cos(\pi f/f_n)]$, for $|f| < f_n$, and subsequently transformed into the spatial domain. In our situation f_n is 0.8 cycles/cm.

The convolved profiles were back-projected onto a 64 × 64 image matrix using the principle of integral allocation to the nearest image cell. The reconstructed image

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thus obtained was linearly interpolated to a 128 × 128 matrix. Image display characteristics were standardized using a $\sqrt{8}$ sigma statistical scale (*7*), referenced to the arithmetic mean of the whole image space. This formulation of the base-line in the case of a typical brain image effectively removes projection artifacts, observable as a "star" pattern in the outer regions of the image.

Other methods of reconstruction—using larger filters, precise geometry proportional projection, and iterative techniques—were investigated but not found to produce significantly different images, probably due to the signal:noise ratio of the emission profiles. There was, however, a significant difference in computing times, ranging from 2 min for the simplest convolution method using conventional techniques, to 2 hr for the iterative method. The former technique was chosen for the duration of the trial.

Absorption correction was not attempted for the following reasons.

1. Normal brain tissue shows little activity in the central region, and the existence of a lesion in this area should be easily identifiable without attenuation correction. When one is differentiating between a small lesion and the outer rim of activity, attenuation correction will have little *diagnostic* effect.

2. No information was required on the actual concentration of radionuclide within the brain.

3. Simple absorption correction, relying on the estimation of the chord length through the physical object under investigation, makes assumptions concerning the distribution of activity and the self-attenuation along each line integral. It can be applied effectively to trunk scanning (*4,5*) but is less likely to approach the true physical situation in head scanning.

4. More analytically satisfying attenuation correction makes use of a map of assumed coefficients normalized in some manner to each individual skull shape, and must be applied to every line integral on a cell-by-cell basis. This introduces a substantially greater computing requirement, and was not attempted, both for this reason and for the lack of accurate absorption data.

The section view was given rapid appraisal, using the color TV system attached to the computer (*8*) to identify any gross artifacts caused by data anomalies (only about 1% of all section views was lost in this way) and all views were finally printed life size in color using the statistical color scale mentioned earlier. An example of the scans that were analyzed in this study is shown (only in grey scale) in Fig. 1. The level of the tomographic view was selected according to the following criteria.

1. If a definitely abnormal uptake was seen on conventional views, a tomogram was done at this level.

2. If a suspicious uptake was seen, a tomogram was done at this level to clarify its significance.

3. When the conventional views did not show any definitely abnormal or suspicious uptake, the choice of tomographic level was based on relevant clinical history.

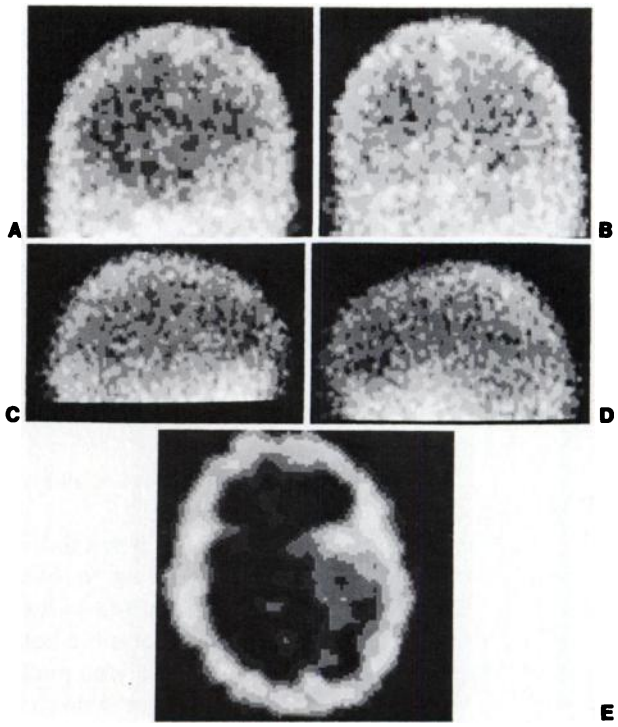


FIG. 1. Example of scintigrams used in this trial. (a) anterior, (b) posterior, (c) right lateral, (d) left lateral, and (e) tomogram at 10.5 cm from the vertex. Views were awarded abnormality ratings of 5 with tomogram and 4 without tomogram. Large cystic tumor was subsequently confirmed at operation.

4. For patients who could not be placed in any of these categories, the tomographic level was through the basal zone, where superficial activity is normally high and may mask a deep lesion.

In general, time permitted only one section view to be obtained per patient, since the full investigation, including conventional views, was normally limited to 1 hr for patient comfort and time tabling. Occasionally two sections have been performed where two notably suspicious regions were observed at different levels.

Each set of scans was reported twice, once with and once without the tomogram, by different teams of observers, each composed of one radiologist or nuclear physician and one physicist. For both reports a *pro forma* was completed so that the most important parameters could be evaluated. First, an abnormality rating, graded from 0 to 5, was given. Consistency in the allocation of abnormality ratings is essential, and the following scheme was agreed to by all observers and adhered to as rigidly as possible: rating 0—"normal"; rating 1—"probably normal," e.g., patient movement apparent, tilt and/or rotation of the head, or any technical imperfection in an otherwise normal scan; rating 2—"possibly normal," e.g., a specific area of suspicion that

could be described, but seen on only one view and frequently close to a region of normal anatomical variation (sylvian fissure, temporal muscle, choroid plexus); rating 3—"likely to be abnormal," e.g., abnormal uptake minimally identified on two views; rating 4—"probably abnormal," e.g., abnormal uptake, minimally identified on three views or clearly on two views; rating 5—"abnormal," e.g., abnormality clearly seen on at least three views. A positive report was issued to the referring physician or surgeon when the abnormality rating was 3 or more.

The rest of the parameters considered in the *pro forma* included position, shape and size of the lesion, intensity of the uptake, and final probable diagnosis (for further details see reference (*3*)). To avoid bias, a team of observers reported alternate scans with and without the tomographic views. Head scans from 628 patients were reported in this way between 1 November 1976 and 31 August 1977.

RESULTS

A final diagnosis was established for 512 of the 628 patients who entered the trial. The allocation of a case to the abnormal group was based on one or more of the following criteria: postmortem, operative findings, biopsy, other radiological procedures, plus a strong clinical history. A case was classified as normal if the patient had at least a 6-mo period free from relevant symptoms following completion of the brain scan. On this basis there were 372 proven normals and 140 confirmed abnormals, of which 124 were intracranial and 16 were skull lesions.

The abnormality rating given with and without tomogram was compared with the final diagnosis for each patient. The results are presented in two ways.

1. To facilitate analysis of the data, reports given abnormality ratings of 0, 1, and 2 were regarded as negative and reports given ratings of 3, 4, and 5 as positive. This corresponds to the somewhat arbitrary decision the reporting team (Consultant in Nuclear Medicine/Radiologist/Medical Physicist) must make when reporting to colleagues, and is referred to as a simplified analysis.

2. The weakness of this approach is that it imposes an absolute but arbitrary boundary between abnormality ratings of 2 and 3. We chose this boundary to correspond with that adopted in everyday clinical practice, but to provide a fuller analysis that takes account of all abnormality ratings, ROC curves and rating curves were also prepared.

Simplified analysis of abnormality ratings. Scans were classified into three groups as shown in Table 1. In the first group there were 386 cases for which both reports, with and without the tomogram, were in the negative range. The second group contains 79 cases in which both reports were in the positive range. The third group contains 47 cases in which the reports disagreed—one in the negative range and the other in the positive. In this simplified analysis, the addition of the tomogram obviously did not make any difference in reporting in either the first or the second group, since with or without the tomogram, both reports were finally classified positive, or both negative.

TABLE 1. CLASSIFICATION OF REPORTS FOR ALL PATIENTS FOLLOWED-UP

Both reports negative (0, 1, 2)	386
Both reports positive (3, 4, 5)	79
Reports different	47
Total	512

TABLE 2. ANALYSIS OF 47 CASES IN WHICH REPORTS BASED ON ABNORMALITY RATINGS DISAGREED

Actual reports	True positive	True negative	Total
Correct with tomogram	27	9	36
Correct without tomogram	6	5	11
Total	33	14	47

TABLE 3. ANALYSIS OF ABNORMALITY RATING REPORTS FOR 124 PATIENTS WITH CONFIRMED INTRACEREBRAL LESIONS

	True positive	False negative	Sensitivity
With tomogram	93	31	93/124 (75%)
Without tomogram	76	48	76/124 (61%)

However, for the third group in which the reports disagreed, Table 2 shows that of the 47 cases, 27 of the 33 true positives were correctly identified when the tomogram was available. The other 14 cases were true negative, and nine were correctly identified when they were reported with the tomogram. Overall, the with-tomogram report was correct 36 times and incorrect only 11 times.

Three hundred seventy-two of the 512 patients were proven normals, and the specificity for detecting a normal case was 99% (367/372) with the tomogram and 98% (363/372) without. This specificity is high and the difference between the two percentages is negligible.

There were 140 confirmed abnormals, of which 124 were intracerebral and 16 were skull lesions. Analysis of the 124 intracerebral lesions (Table 3) shows that 75%

TABLE 4. ANALYSIS OF ABNORMALITY RATING REPORTS FOR 50 PATIENTS WITH CONFIRMED BRAIN TUMORS

	True positive	False negative	Sensitivity
With tomogram	44	6	44/50 (88%)
Without tomogram	39	11	39/50 (78%)

TABLE 5. ANALYSIS OF ABNORMALITY RATING REPORTS FOR 59 PATIENTS WITH CONFIRMED INFARCTS (RECENT AND OLD)

	True positive	False negative	Sensitivity
With tomogram	37	22	37/59 (63%)
Without tomogram	29	30	29/59 (49%)

TABLE 6. ANALYSIS OF ABNORMALITY RATING REPORTS FOR 16 PATIENTS WITH CONFIRMED EXTRACEREBRAL LESIONS

	True positive	False negative	Sensitivity
With tomogram	14	2	14/16
Without tomogram	7	9	7/16

(93/124) were detected with the tomogram and only 61% (76/124) without it. Tumors (50) and infarcts (59) account for most of these cases, the remainder being five A-V anomalies, one aneurysm, two subarachnoid hemorrhages, four intracerebral hemorrhages, one encephalitis, and two subdural hematomas. For tumors, there was considerable improvement in reporting sensitivity when the tomographic view was added. Referring to Table 4, 88% of the tumors in our series (44/50) were detected with help from the tomogram and 78% (39/50) without it.

There was also considerable improvement for the 59 infarcts in the series (Table 5): 63% (37/59) were detected when the tomographic view was available and only 49% (29/59) when it was not. If eight old infarcts or scars are excluded and only recent infarcts, where the diagnosis is really relevant for patient management, are considered, the sensitivity of detection was 73% (37/51) with the added tomogram and 57% (29/51) without.

During the course of the main investigation, 16 extracerebal lesions were detected, and these results have been included for completeness. They also show a useful contribution from the addition of the tomogram, since 14 lesions were identified with the tomogram but only seven were identified without it (Table 6).

Fuller analysis of the abnormality ratings. Here the object was to find out in more detail how the abnormality rating varied between the two reports, and this was done first by constructing ROC curves (receiver operating characteristics), one with and one without the tomograms. One point on each ROC curve can be obtained by assuming that all scans with an abnormality rating of one or more are positive. The numbers of true-positive and false-positive responses are found on the basis of this criterion, and the figures are expressed as percentages of the total numbers in the true-positive group and the true-negative group, respectively. An abnormality rating of two or more is then taken to indicate a positive response, and the procedure is repeated to obtain another point on each curve.

Table 7 shows how the results were tabulated, and Fig. 2 shows the final overall ROC curves. A significant increase in "true-positive response" was obtained at all "false-positive response" levels when the tomogram was included with the conventional views.

To find out more about the reasons for this improvement, rating curves were prepared. Consider the 140 confirmed abnormal cases. First, assume that all scans are positive, whatever their abnormality rating. This, of course, gives 100% positives and this value is entered against an abnormality rating of 0 (see Table 7 and Fig. 3). Next assume that scans are positive only if the abnormality rating is 1 or higher. The incidence of true positives falls to 86.5% with the tomogram and to 80% without it. If only scans with an abnormality rating of 2 or higher are assumed positive, the true positives fall to 80% with tomogram and 68% without tomogram, and so on. At each abnormality rating the "with-tomogram" curve is higher, showing more successful identification of true positives. The curves are closer at abnormality rating 5, and this agrees with the prediction that when a lesion is obvious, the section view contributes very little to its detection.

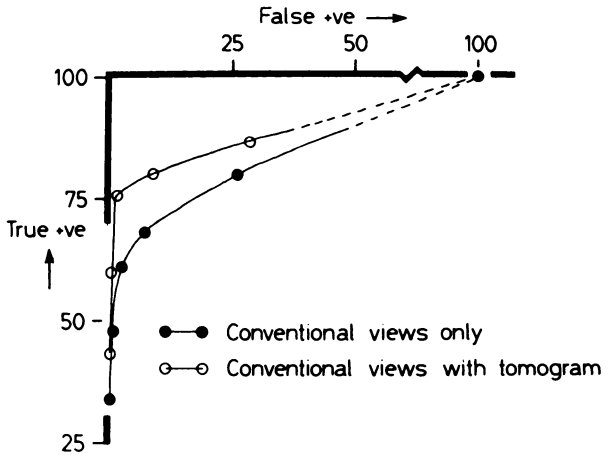


FIG. 2. Overall results demonstrated as ROC curves. Scales are percentages.

TABLE 7. FULL ANALYSIS OF 140 ABNORMAL CASES AND 372 NORMAL CASES IN PREPARATION FOR ROC PRESENTATION*

Abnormality rating	Conventional views without tomogram		Conventional views with tomogram	
	True positive	False positive	True positive	False positive
≥0	140 (100)	372 (100)	140 (100)	372 (100)
≥1	112 (80)	98 (26)	121 (86.5)	106 (28.5)
≥2	95 (68)	27 (7.3)	112 (80)	33 (8.9)
≥3	85 (61)	9 (2.4)	106 (76)	5 (1.3)
≥4	67 (48)	3 (0.8)	84 (60)	3 (0.8)
≥5	48 (34)	0 (0)	61 (43.5)	0 (0)

* Percentage values in parentheses.

This idea may be developed further by separating (a) those confirmed abnormal cases where the lesion was obvious (79 cases with abnormality ratings of 3 or more in both reports) and (b) those confirmed abnormals where the lesion showed inadequate tracer uptake (28 cases with abnormality ratings of 2 or less in *both* reports). The remaining 33 cases (subsequently confirmed true positives with marked disagreement between the abnormality ratings) illustrate most convincingly the true value of the section view. These patients represent only 5% of the number entering the trial, but the rating curves in Fig. 4 show that for this group successful lesion identification can be up to four times as high with the tomographic view as without it.

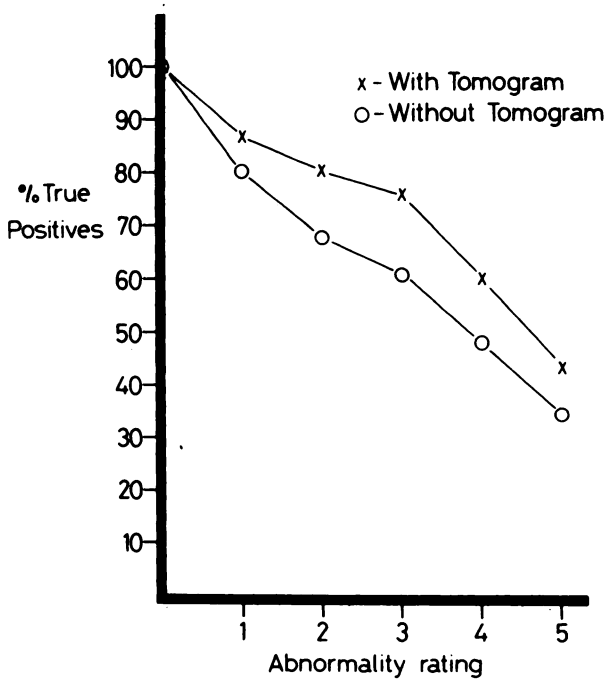


FIG. 3. Rating curves based on abnormality rating reports for 140 true abnormals.

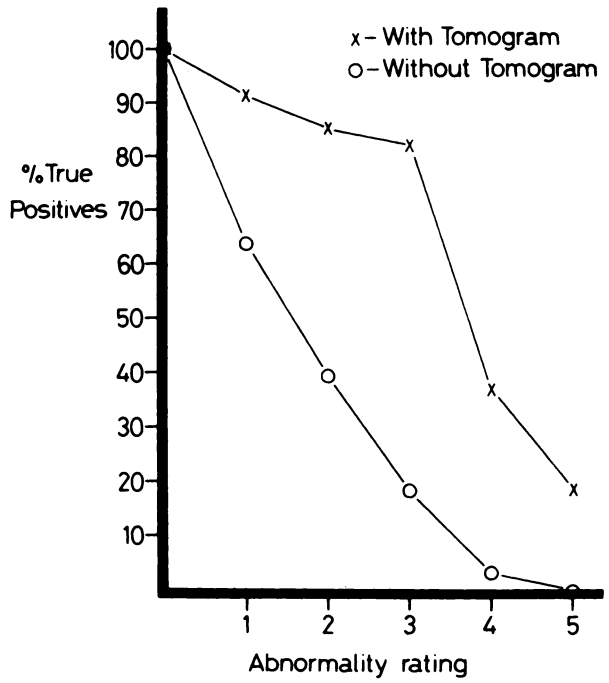
A similar approach can be applied to the 372 proved normal cases (Fig. 5). Using the same criteria, the curves will now represent the percentage of false positives as a function of abnormality rating. The curves start at 100%, by definition, for an abnormality rating of 0, but fall rapidly to about 25% at an abnormality rating of 1, and to about 10% at an abnormality rating of 2.

Two more important conclusions can be drawn from Fig. 5. First, examination of the section view in addition to the conventional views makes no difference, either good or bad, to the frequency with which false positives are reported. Second, provided scans are not reported as positive to clinical colleagues until an abnormality rating of 3 is reached (the criterion we have adopted), the incidence of false positives will be only about 2%. A more lax criterion may allow more lesions to be detected but it will also result in more false positives.

Other parameters recorded for the scans. Detailed analysis of the rest of the parameters recorded on the *pro forma* concerning features of the lesion provided no further useful information. When the lesion was detected by both teams, the features of the lesion (shape, size, position, etc.) were equally reliable in both reports. Similarly, there was no significant difference in the differential diagnosis (for example, distinguishing an infarct from a tumor) with and without tomogram. These findings are to be expected from the detailed analysis of abnormality ratings, since Fig. 4 shows that most differences arise from the almost complete failure of one team (usually reporting without tomogram) to detect the lesion at all.

DISCUSSION

In the course of routine work, a high proportion of brain scans are normal. It is necessary, therefore, to enter a large number of patients into any trial in order to obtain satisfactory statistics. In this prospective trial we



	Without Tomogram					
Abnormality rating	5	4	3	2	1	0
Number	0	1	5	7	8	12
Cumulative total	0	1	6	13	21	33
Percentage	0	3.0	18.2	39.4	63.6	100
	With Tomogram					
Abnormality rating	5	4	3	2	1	0
Number	6	6	15	1	2	3
Cumulative total	6	12	27	28	30	33
Percentage	18.2	36.4	81.8	84.9	91.0	100

FIG. 4. Rating curves based on abnormality rating reports for 33 true abnormals where reports disagreed.

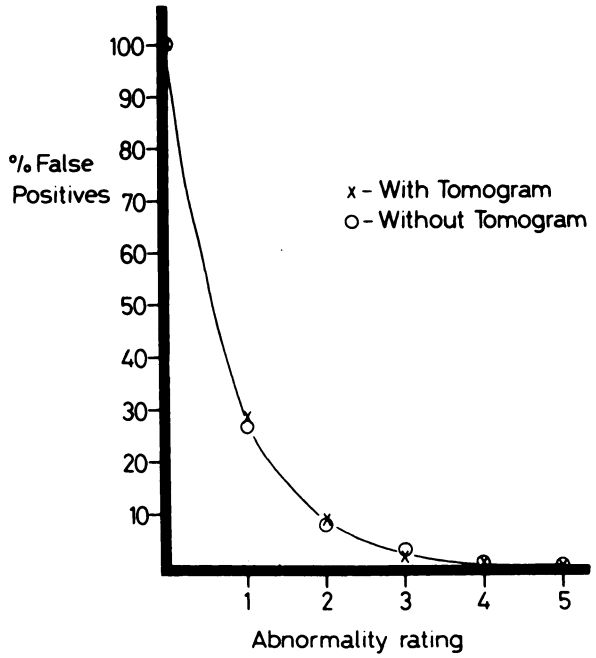


FIG. 5. Rating curves based on abnormality rating reports for 372 true normals.

entered 628 patients and they provided 140 confirmed abnormals. We also followed up 372 patients who were classified as true normals because they had at least 6 mo follow-up free from relevant symptoms.

When a simplified analysis was applied to the abnormality ratings, it showed 465 tied pairs where both reports were the same (see Table 1). Where the reports disagreed, the "with-tomogram" report was right 36 times and wrong only 11 times. Statistical analysis of these figures using a chi square test with continuity correction shows that they are significant at the 0.1% level. In other words, this distribution in favor of the "with-tomogram" report would arise by chance on a purely random basis only once in a thousand times. We conclude that the section view does result in a significant increase in the successful detection of lesions.

Four of the tumors that were detected only on the basis of the tomographic information were located in the basal zone of the brain (one in the posterior fossa, two in the middle fossa, and one in the anterior fossa). This agrees with previous reports (*9–11*) showing the value of the transverse-section view for lesions adjacent to the skull base where the activity is normally very high on standard views.

A similar explanation can be applied to some of the infarcts detected only on the tomogram. In a few important cases, an uptake that, without the tomogram, was thought to be a normal variant (ears, sylvian fissure, temporal muscle, etc.) showed as an abnormality when the tomogram was available.

As with ordinary radiological tomograms, it was found that after a lesion had been detected on the tomographic section, it could be seen in retrospect, with some difficulty, on the standard views. Similarly, we learned by experience that an apparently abnormal area on the section view, which could not be found on the conventional views even upon careful re-examination, was probably normal anatomy such as cavernous sinus, torcula, etc., appearing abnormal because we were unfamiliar with such anatomical detail on radionuclide images.

The more detailed analysis, which obviates the need for any arbitrary division of abnormality ratings, confirms the value of the section view. The ROC curves show improved diagnostic accuracy with the tomogram at all abnormality rating levels. The rating curves show that this is almost entirely due to more frequent and more confident identification of true abnormals.

Moreover, this analysis shows clearly that although a section view through a lesion that is clearly visualized on the conventional views may sometimes provide extra three-dimensional information, this is not its real merit. Rather, it is the ability to get further information about

any suspicious region, however slight the grounds for doubt. Thus, a section view should be taken through any area that looks slightly suspicious. In the majority of cases the section view will show no abnormality and simply add confidence to the "no abnormality detected" report. In a small but important number of cases, however, the suspicions are confirmed by the section view, and the lesion is successfully detected; i.e., a false negative is transformed into a true positive. Overall, the results are generally consistent with those of previous work by Kuhl and Sanders (*9*).

In sharp contrast to the pilot run (*3*), the prospective study did not show improved differential diagnosis when the tomographic view was available. We attribute this to minor differences in the design of the trial. In the pilot study, all clinical details were withheld to prevent patient identification and recall of scan details by the observer. The section view assisted differential diagnosis in this situation. In the prospective trial, all relevant clinical information was made available as part of the normal, daily reporting procedure. With the benefit of a brief clinical history, it was extremely rare to suggest the wrong cause whether the section view was seen or not, provided the lesion was detected.

Finally, a number of comments of a more technical nature are relevant. First, the accuracy of the technique would certainly be increased very slightly by repeated sections. However, for the service work which formed the basis of this paper, as opposed to research work, this was not possible with the scanner at our disposal. Second, it is important to note that the comparison did not require reference to any other imaging device. A comparison of scanners and gamma cameras carried out in this way, although highly desirable, would be meaningless because at best it would be a comparison of *one* scanner and *one* camera with no concensus or criteria for deciding which is the best scanner and which the best camera currently available. Perhaps a modern large-field gamma camera would provide accuracy equal to, or even better than, that reported here. However, it should still be possible to improve accuracy by adding the tomograms, and this is why several centers are attempting to develop useful gamma-camera tomographic devices without the need for expensive additional machinery. Finally, it is important to note that the precision of the emission brain scan, even with a tomogram, is highly dependent on the precise purpose for which it is used, ranging from 99% for identification of true normals, to 88% for tumors, 73% for recent infarcts, and down to 0% for old infarcts. Thus comparison with a different technique—for example computer-assisted transmission tomography—ideally requires large numbers of patients to be examined by both techniques. At the very least, careful attention must be given to matching the numbers of patients in a given category. For some categories we have shown that the precision of the radionuclide scan is very good. It is not the purpose of this paper to engage in a discussion of the relative merits of emission brain scanning plus tomographic section views against computer-assisted transmission tomography of the brain. However, we believe the above analysis shows that the emission brain scan, with added tomography, has an important role to play as a complementary study to computer-assisted transmission tomography for large numbers of patients referred for brain scanning.

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