FROM THE DEPARTMENTS OF OTOLARYNGOLOGY AND NEURORADIOLOGY, KAROLINSKA SJUKHUSET, AND THE DEPARTMENT OF RADIATION PHYSICS, KAROLINSKA INSTITUTET, S-104 01 STOCKHOLM, SWEDEN.

OBJECTIVE SYMMETRY DETECTOR METHOD FOR GAMMAENCEPHALOGRAPHY

III. Diagnosis of abnormal $^{99}Tc^{m}O_4$ distribution in the skull

M. LIND and S. LARSSON

The equipment and the physical characteristics of the symmetry detector method have been described previously (LARSSON et coll. 1975) as well as the normally obtained range of the $^{99}Tc^{m}O_4$ distribution in the skull following intravenous injection (LIND et coll. 1975). Alterations of the normal distribution of nuclides in the skull, caused for instance by brain tumours, may be detected by several methods. A single detector placed at different positions over the head was used in the first reports (MOORE 1948, MOORE et coll. 1948). Later moving scanners and stationary gamma cameras were used. These methods demand great technical, economical and personnel resources, available only in large medical centres and even so the interpretation of results is mainly subjective (BURROWS 1972).

Scintigraphic information has been digitalized and by computation related to the normal ranges of several evaluation parameters, in order to enhance the diagnostic accuracy of brain scanning (DOWSETT & PERRY 1970, POPHAM et coll. 1970, DOWSETT

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1972). However, since the normal ranges obtained were not related to the sensitivity of the evaluation parameters as described by LARSSON et coll., the detectability of an increased isotope content in different subregions of the head is not possible to estimate. The reported diagnostic accuracy, defined as successful separation of pathologic from normal cases, is thus difficult to evaluate in relation to other results reported (BURROWS).

Gamma encephalography, described inter alia by PLANIOL and MUNDIGER means estimation of the isotope distribution in the skull by determination of count rates over several stationary positions on the skull (PLANIOL 1966, MUNDIGER & ASAI 1967). The evaluation parameters of these methods included considerable errors caused mainly by poor counting statistics from small numbers of counts recorded in each position, variation in positioning of the detectors, varying levels of recorded body background, and varying reference values used for the calculation of the relative isotope distribution. These sources of variation were not very carefully analysed, nor were attempts to reduce their influence reported; furthermore, the separation of pathologic cases from normal ones was based on the subjective evaluation of several criteria, together with additional clinical information (PLANIOL, MUNDIGER & ASAI).

The purpose of the present work is to describe the choice of parameters of the symmetry detector method and a criterion with different fixed classification boundaries that makes a simple and objective separation of abnormal cases from normal ones possible in routine clinical work.

Material and Methods

Measurements of the distribution of 99m Technetium pertechnetate ($^{99}Tc^{m}O_4$) in the skull was performed using the symmetry detector method previously described (LIND et coll.). A premedication of 400 mg $KClO_4$ was given orally 30 to 60 minutes before the intravenous administration of 10 mCi $^{99}Tc^{m}O_4$. The measuring procedure started about 30 minutes after the injection of the isotope. Two NaI-detectors face to face on the same axis and shielded by collimators 30 cm in length with 3 cm × 3 cm square apertures were used and the isotope distribution was determined from measurements over 24 measuring positions, in a constant pattern, given by a positioning diagram designed to approximately suit the individual size and shape of the skull (cf. Fig. 2, LIND et coll. 1975). Values obtained were recorded on punched tape and 9 parameters per subregion were calculated, altogether 208 (LIND et coll.).

The mean values and standard deviations (SD) of all evaluation parameters of subregions of the skull, obtained from a reference group of 29 patients without known brain lesions have been described previously and were used as the basis for interpretation (LIND et coll.).

Values representing the depth dependent sensitivity of the increase-(I) and difference-(D) ratio parameters have been obtained from measurements of a skull-lesion-phantom system (LARSSON et coll.).

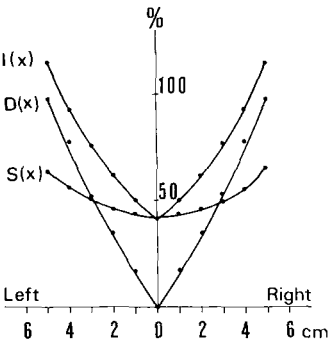

Fig. 1

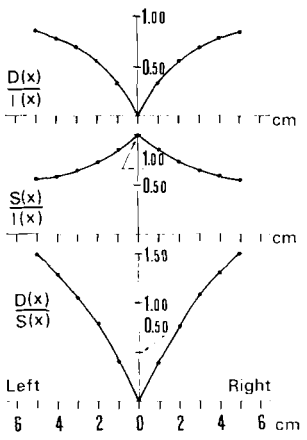

Fig.2

Fig. 1. Percentage alterations of count rate I(x) differences D(x) and sums S(x) of right and left detector values are plotted against the distance x from the median plane of the skull phantom. Tumour phantom volume: 21.3 ml. Conc. ratio: 8: 1 (LARSSON et coll.).

Fig. 2. The ratios: D(x)/I(x), S(x)/I(x) and D(x)/S(x) are plotted against the distance x from the median plane of skull phantom (LARSSON et coll.).

Five patients, one patient with a vascular malformation and four with brain tumours, later histologically verified, were examined by the symmetry detector method. The histologic examination was made as proposed by RINGERTZ (1950).

Evaluation parameters. The normal ranges of the evaluation parameters are given by LIND et coll. The number of counts N_R and N_L obtained from the right and left detector of each subregion respectively were related to two different reference values, P_{mv} and C_{mv}. P_{mv}, the plane mean value, is the calculated mean value of all 12 measuring values from the six subregions of one plane (A, B, C or D). C_{mv}, the central mean value, is the calculated mean of the 16 measuring values, obtained from the central subregions (B2–B5, C2–C5) (cf. Fig. 2, LIND et coll. 1975).

The relations r_p, obtained for each subregion j, were defined as position ratios according to:

$$r_{Rp}(j) = \frac{N_R(j)}{P_{mv}} 100\%, \; r_{Lp}(j) = \frac{N_L(j)}{P_{mv}} 100\% \qquad (1\,a, b)$$

with the plane mean value, P_{mv}, as the reference, as indicated by index p. The indices R and L refer to the right and left position of the subregion.

The corresponding position ratios, r_c (j), with the central mean value, C_{mv}, as the reference (indicated by index c) were expressed:

$$r_{Rc}(j) = \frac{N_R(j)}{C_{mv}} 100\%, \; r_{Lc}(j) = \frac{N_L(j)}{C_{mv}} 100\% \qquad (2\,a, b)$$

The difference between the two position ratios r_{Rp} and r_{Lp}, (with the P_{mv} as the reference), was calculated for each subregion and defined as the difference parameter D:

$$D(j) = (r_{Rp}(j) - r_{Lp}(j))\,\% \qquad (3)$$

The sum parameters S_p and S_c were defined as the mean of r_{Lp} and r_{Rp} (reference value $= P_{mv}$), and the mean of r_{Lc} and r_{Rc} (reference value $= C_{mv}$), respectively.

$$S_p(j) = 1/2(r_{Rp}(j) + r_{Lp}(j))\,\% \tag{4a}$$

$$S_c(j) = 1/2(r_{Rc}(j)) + r_{Lc}(j)\,\% \tag{4b}$$

Finally, the adjacent parameters A were defined as the relative difference between one subregion ($N_R(j)$) and the adjacent frontal subregion ($N_R(j-1)$) of the same plane.

$$A_R = \frac{N_R(j) - N_R(j-1)}{N_R(j)}\,100\% \tag{5a}$$

$$A_L = \frac{N_L(j) - N_L(j-1)}{N_L(j)}\,100\% \tag{5b}$$

Detectability properties of the position ratio, sum and difference parameters. The need of the three different evaluation parameters (position ratio r_p, sum S_p and difference D) could be demonstrated by a comparison of the detectability properties of the parameters at different depths in a subregion.

The detectability, δ, defined as the smallest effect of interest (for instance the increase of isotope content in a subregion) which can be detected with a significance, corresponding to q standard deviations

$$\delta = \frac{q\sigma}{S} \tag{6}$$

where S is the sensitivity (true mean number of parameter units obtained per unit of the defined effect of interest) and σ the normal standard deviation (SD) of the parameter (LARSSON et coll.).

The depth dependent sensitivity functions S_I, S_D and S_S of the increase ratio I, difference ratio D and sum ratio S, were defined from measurements on a phantom system (LARSSON et coll.), and assumed to be valid also for the evaluation parameters defined for clinical measurements (position ratio r_p, difference D and sum S_p). The normal standard deviations σ_p, σ_D and σ_S of the latter parameters were calculated from results of the reference group (LIND et coll.). Hence, the detectability of an abnormal accumulation of $^{99}Tc^mO_4$ could be expressed for each evaluation parameter as a function of the location x in the subregion j according to eq. (6).

$$\delta_p(j, x) = \frac{q \cdot \sigma_p(j)}{S_I(x)} \tag{7a}$$

$$\delta_D(j, x) = \frac{q \cdot \sigma_D(j)}{S_D(x)} \tag{7b}$$

$$\delta_S(j, x) = \frac{q \cdot \sigma_S(j)}{S_S(x)} \tag{7c}$$

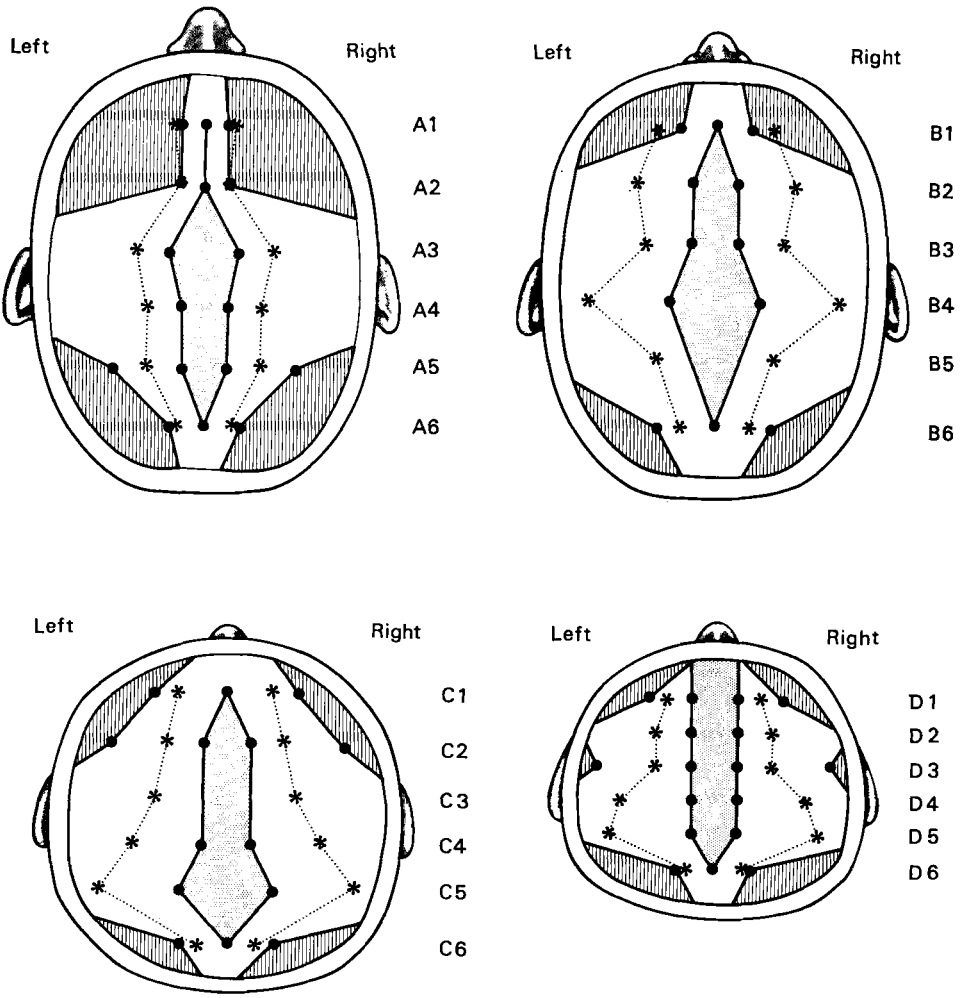

Fig. 3. Pathologic accumulation of $^{99}Tc^{m}O_4$ located in the lateral areas (hatched) were estimated to give the most significant deviations from the normal mean values in D parameters. Correspondingly the central area (dotted) should give highest significance of pathologic accumulation in S_p parameters and the white areas in r_p parameters. The punctuate line encircles a central area where pathologic accumulation was estimated to give higher significance in S_p parameters than in D parameters. Planes A to D illustrated.

By setting $\delta_p(j,x)=\delta_D(j,x)=\delta_S(j,x)$, three equations (8 a, b, c) are obtained and their solutions, regarding the depth location variable x, are each defining the depth x_0 where two of the parameters have the same detectability.

$$\delta_p(j,x)=\delta_D(j,x)=\frac{q\cdot\sigma_p(j)}{S_I(x)}=\frac{q\cdot\sigma_D(j)}{S_D(x)}\quad\frac{S_D(x)}{S_I(x)}=\frac{\sigma_D(j)}{\sigma_p(j)} \tag{8a}$$

Position	r_{Lc}	r_{Rc}	S_c
A1	6.89	2.97	5.19
B1	26.38	9.84	18.80
B2	7.31	5.89	7.73
C1	3.04	0.97	2.01
C4	2.23	- 2.28	- 2.62
D5	- 2.04	- 1.82	- 2.00

Position	r_{Lp}	D	r_{Rp}	S_p
A1	5.21	- 8.36	1.52	3.45
A4	- 2.76	1.13	- 1.12	- 2.03
B1	17.81	-15.88	5.79	12.20
B2	2.82	- 1.76	1.28	2.40
B3	- 2.89	0.32	- 1.78	- 2.80
B4	- 5.21	0.89	- 4.59	- 5.74
B5	- 3.19	- 0.32	- 4.23	- 4.70
B6	- 2.16	0.09	- 2.44	- 2.38
C1	4.91	- 4.08	1.73	3.36
C4	- 2.00	- 0.12	- 1.71	- 2.13

Position	A_L	A_R
A2	- 5.34	- 1.72
A4	- 2.64	- 2.21
B2	- 8.43	- 4.61
B3	- 6.45	- 3.14
B4	- 2.84	- 2.79
C2	- 1.95	- 0.28
C3	- 3.19	- 2.54
D6	- 1.30	- 0.48

Fig. 4. Printout of results from Case 4 by the PDP-8 computer.

$$\delta_p(j, x) = \delta_S(j, x) = \frac{q \cdot \sigma_p(j)}{S_I(x)} = \frac{q \cdot \sigma_S(j)}{S_S(x)} \quad \frac{S_S(x)}{S_I(x)} = \frac{\sigma_S(j)}{\sigma_p(j)} \tag{8 b}$$

$$\delta_D(j, x) = \delta_S(j, x) = \frac{q \cdot \sigma_D(j)}{S_D(x)} = \frac{q \cdot \sigma_S(j)}{S_S(j)} \quad \frac{S_D(x)}{S_S(x)} = \frac{\sigma_D(j)}{\sigma_S(j)} \tag{8 c}$$

$S_I(x)$, $S_D(x)$ and $S_S(x)$ can be represented by the corresponding I(x), D(x) and S(x), ratio-functions obtained from phantom measurements (Fig. 1). To solve eq. (8 a, b, c) the ratios between these functions, independent of tumour volume (V_t) and concentration ratio (c_0), were calculated and plotted as functions of x (Fig. 2). The corresponding constant ratios between the standard deviations of the evaluation parameters were also calculated for each subregion j. The values of x_0 were obtained from comparison between these constant ratios and the ratios given in Fig. 2.

As only one of the right and left parts of each subregion was considered in each equation (8 a, b, c), the values of x_0 obtained, are between 0 and d, where d is the distance from the median plane to the right or left side of the skull ($0 \leq x_0 \leq d$). Hence, considering only one of the right or left halves of the skull, the monotonously increasing functions and the monotonously decreasing function in Fig. 2 offer only one or none solution of each equation (8 a, b, c). If a solution exists, one of the two evaluation parameters in the ratios (Fig. 2) has a higher degree of detectability for accumulations of $^{99}Tc^mO_4$ located at depths $x < x_0$, and the other for accumulations located at depths $x > x_0$. As an example the difference parameter has a higher detectability of accumulations of $^{99}Tc^mO_4$ located lateral to the relevant x_0 and the corresponding sum-parameter has a higher detectability of accumulations located medial to x_0 (Figs 2, 3).

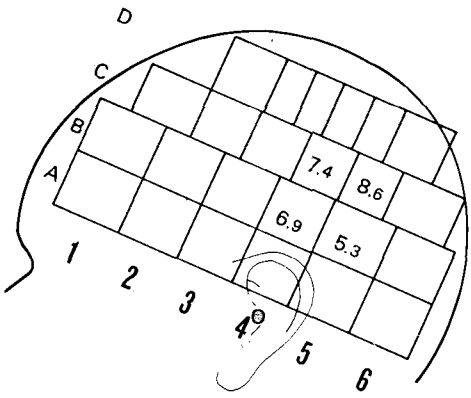

Fig. 5

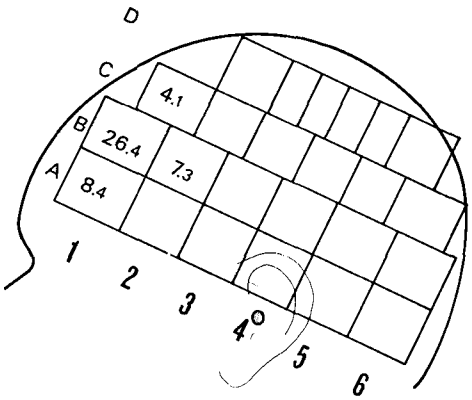

Fig. 6

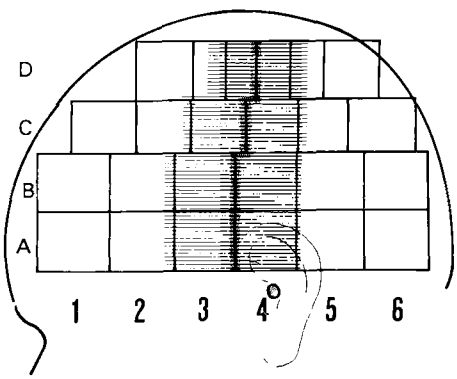

Fig. 7

Fig. 5. Case 5. Areas with evaluation parameters deviating more than 3 SD.

Fig. 6. Case 4. Areas with evaluation parameters deviating more than 3 SD.

Fig. 7. The border between the anterior and posterior groups of measuring areas is marked by the heavy line. An intermediate group is marked by the hatched area, which overlaps the border.

The advantage of using adjacent values and different reference values is illustrated by exemplification.

Criteria and classification. The measuring values of one individual were compared to the normal range estimated from the reference group (LIND et coll.). Deviations from the mean values of each evaluation parameter were given in number of SD and the separation of abnormal from normal $^{99}Tc^{m}O_4$ distributions in the skull was determined from the parameter giving the maximum deviation (SD_{max}).

All negative deviations from the normal were excluded, except in difference parameters, in which negative values arbitrarily indicated increased count rates on the left side, and in adjacent parameters (AV) in which negative deviations indicated a higher value in the more frontal of two regions (LIND et coll.).

To save time in routine clinical work, only parameters deviating more than 2 SD were printed out by the computer (Fig. 4). To make clinical interpretation easier, positions which had a deviation of the evaluation parameters larger than 3 SD

Table 1

The parameters used in measuring the whole skull are marked by +. [1]. *A1, A2, A6, B1, B6, C1, C6 D1 and D6 were excluded.* [2]. *A3, A4, A5, B2, B3, B4, B5, C3, C4, C5, D2, D4 and D5 were excluded*

	r_c	r_p	A	S_c	S_p	D
208 parameters						
A1–A6	+	+	+	+	+	+
B1–B6	+	+	+	+	+	+
C1–C6	+	+	+	+	+	+
D1–D6	+	+	+	+	+	+
123 parameters						
A1–A6	–	+	+	–	+[1]	+[2]
B1–B6	–	+	+	–	+[1]	+[2]
C1–C6	–	+	+	–	+[1]	+[2]
D1–D6	–	+	+	–	+[1]	+[2]
75 parameters						
A1–A6	–	+	–	–	+[1]	+[2]
B1–B6	–	+	–	–	+[1]	+[2]
C1–C6	–	+	–	–	+[1]	+[2]
D1–D6	–	+	–	–	+[1]	+[2]

from the normal mean were indicated on a lateral projection of the head by the actual maximal deviation in number of SD (Figs 5, 6).

The value of SD_{max} was calculated for each individual included in the reference group, using 208 parameters (Table 1).

The same procedure was repeated using 123 and 75 parameters, respectively (Table 1).

In order to take a smaller number of parameters into consideration the skull was also divided into six areas (Fig. 7). The different areas were supposed to correspond approximately to the frontal, temporal + parietal and occipital + posterior fossa regions, respectively. The maximal deviation, expressed in the number of SD in any of the parameters of each area, was calculated for each individual of the reference group.

Results

Each subregion was divided into several parts in regard to the type of parameter expected to offer the highest significance in the detection of a small tumour activity (Fig. 3): (1) Central part, where sum parameters on average will give the highest significance in measuring a tumour activity, (2) lateral parts, where the difference parameters on average will give the highest significance, (3) intermediate parts, where the position ratio parameters on average will give the highest significance.

The boundaries between the three parts were determined by the values of x_0 and varied between the subregions. Despite the inaccuracy of the estimation of the

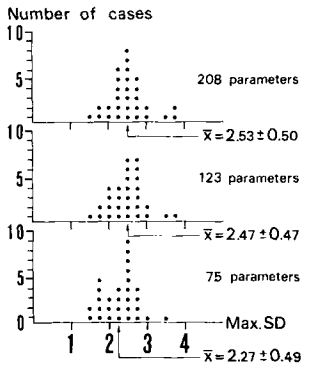

Fig. 8

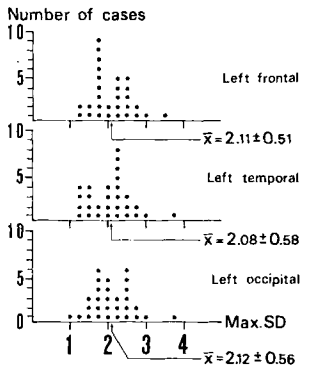

Fig. 9

Fig. 8. Normal ranges of SD_{max} of the 208-, 123- and 75-groups of parameters, which cover the whole measured skull area. obtained from the reference group.

Fig. 9. Normal ranges of SD_{max} of the left frontal, temporal and occipital groups of parameters obtained from the reference group.

values of detectability, it was concluded that all the parameters were important in clinical examinations.

Separation of laterally from centrally located accumulations of $^{99}Tc^{m}O_4$. The high depth dependence of the ratio D(x)/S(x) (Fig. 2), indicates a possibility to estimate the depth location of a $^{99}Tc^{m}O_4$ accumulation. From the solution of eq. (8 c) ($\delta_D(j, x) = (\delta_S(j, x))$ the skull volume could be divided into a central part where the sum parameters on average will give larger significance of an accumulated amount of isotope than the difference parameters and lateral parts with the opposite conditions (Fig. 3).

Normal and abnormal isotope distribution in the whole skull. The maximal deviation in number of SD in any of the used parameters (SD_{max}) was used as a criterion for separating pathologic cases from normal ones. The normal mean value of SD_{max}, calculated from the reference group (208 parameters) was large (2.53 ± 0.50 SD) which was explained by the large number of parameters, increasing the probability of getting a large deviation from the mean value in any of them. The distribution of SD_{max} among the 29 reference cases is presented in Fig. 8. From this diagram it was decided to use the following classification for the clinical examinations:

Criterion = Maximal deviation in number of SD (SD_{max}) in any of the 208 parameters used.

I	0–3.0	Definitely normal $^{99}Tc^{m}O_4$ distribution
II	3.0–3.5	Probably normal $^{99}Tc^{m}O_4$ distribution
III	3.5–4.0	Probably abnormal $^{99}Tc^{m}O_4$ distribution
IV	4.0–∞	Definitely abnormal $^{99}Tc^{m}O_4$ distribution

The number of parameters could be reduced thus offering a smaller normal mean value of SD_{max}; 123 and 75 parameters were selected to find out if relevant advantage could be made of such reduction. Sum and difference parameters of the subregions,

Position	r_{Lc}	r_{Rc}	S_c
A2	0.48	- 0.12	0.19
A6	- 2.16	- 2.69	- 2.44
B1	- 4.78	- 4.95	- 5.01
B2	0.47	- 3.85	- 2.02
B4	3.05	2.28	3.20
B6	- 1.99	- 2.65	- 2.37
C1	- 3.04	- 3.20	- 3.24
C2	- 1.45	- 2.85	- 2.26
C3	- 1.80	- 2.93	- 2.71
C6	- 3.52	- 3.80	- 3.77
D1	- 1.80	- 2.06	- 1.98
D2	- 1.45	- 2.23	- 1.88
D5	- 2.78	- 2.94	- 2.97
D6	- 4.55	- 4.39	- 4.60

Position	r_{Lp}	D	r_{Rp}	S_p
A2	2.69	- 2.41	1.51	2.13
A6	- 2.27	- 1.55	- 3.17	- 2.78
B1	- 3.42	- 1.02	- 3.77	- 3.69
B2	1.49	- 3.27	- 1.93	- 0.11
B4	5.29	- 0.60	4.21	6.08
B5	2.99	0.54	3.69	3.71
B6	- 1.96	- 1.41	- 2.96	- 2.55
C1	- 1.64	- 1.13	- 2.09	- 2.00
C2	1.05	- 2.24	- 0.73	0.20
C4	4.90	- 0.42	5.23	6.00
C5	4.42	- 0.51	3.22	4.77
C6	- 2.52	- 0.70	- 2.94	- 2.82
D2	2.02	- 1.99	0.31	1.36
D3	2.23	- 1.78	1.36	2.03
D4	2.83	- 1.45	2.45	3.10
D6	- 2.91	- 0.60	- 2.98	- 3.04

Position	A_L	A_R
A2	2.70	1.04
A3	- 2.16	- 1.08
A6	- 2.68	- 2.90
B2	5.81	2.84
B3	- 0.70	2.78
B4	2.96	3.49
B6	- 2.89	- 4.10
C2	2.95	1.93
C4	4.12	5.00
C6	- 3.81	- 4.10
D5	- 2.40	- 2.04
D6	- 3.24	- 3.20

Fig. 10. Printout of results from Case 1.

where they were not expected to offer higher detectability of lesions than corresponding position ratios, were excluded (Fig. 3). The remaining parameters are tabulated in Table 1. The mean value of the criterion used in the reference group was in this way decreased from 2.53 ± 0.50 SD to 2.47 ± 0.47 and 2.27 ± 0.49, respectively (Fig. 8).

Normal and abnormal distribution in one defined subdivision of the skull. The number of parameters used could also be reduced by regarding only a small part of the head. It is common in clinical work that symptoms and signs as well as the results of preliminary investigations indicate pathology in a limited part of the brain. To investigate this approach the head was divided into six overlapping areas (Fig. 7).

The 208-group of parameters was reduced corresponding to these subdivisions and SD_{max} in any of the reduced number of parameters of each subdivision was used as a criterion. The mean values of SD_{max} of each subdivision were calculated from the results of the reference group (Fig. 9). It was found that these mean values were

Position	r_{Lc}	r_{Rc}	S_c
B2	- 2.16	- 1.64	- 2.23
C3	2.27	4.15	3.75
C4	0.62	2.22	1.66
C6	- 0.64	0.24	- 0.22
D3	0.85	2.08	1.52
D4	0.27	1.93	1.14

Position	r_{Lp}	D	r_{Rp}	S_p
C1	- 2.23	1.95	- 0.73	- 1.49
C3	1.52	2.07	2.97	2.50
C6	- 0.83	2.08	0.11	- 0.40
D3	0.77	2.58	2.22	1.64
D4	- 0.12	2.94	2.24	1.28
D5	- 2.04	1.74	- 0.22	- 1.30

Position	A_L	A_R
B4	1.75	1.74
C3	3.10	3.99
C4	- 1.79	- 1.80

Fig. 11. Printout of results from Case 2.

reduced by about 0.5 for all subdivisions compared to the mean value of SD_{max} of the whole head. There were no relevant differences between right and left sides. The variance of SD_{max} was found to be of about the same size in all subdivisions and also of the same size when the whole head was regarded. It was therefore concluded that the boundaries of the criterion used to classify an individual $^{99}Tc^mO_4$ distribution as normal or abnormal could be decreased by 0.5 SD if, for clinical reasons, only one subdivision was regarded (Fig. 9). The classification will then be as follows:

Criterion = Maximal deviation in number of SD (SD_{max}) in any of the parameters used.

I	0–2.5	Definitely normal $^{99}Tc^mO_4$ distribution
II	2.5–3.0	Probably normal $^{99}Tc^mO_4$ distribution
III	3.0–3.5	Probably abnormal $^{99}Tc^mO_4$ distribution
IV	3.5–∞	Definitely abnormal $^{99}Tc^mO_4$ distribution

Use of plane mean value P_{mv} as the reference. Case 1 had an arteriovenous malformation in the central parts of the brain. The deviations from the normal mean of the C_{mv} group of parameters in number of SD were classified as probably normal, but the deviations of the P_{mv} group of parameters were large enough to classify the patient as definitely abnormal (Fig. 10). The region of increased activity was almost completely equivalent to that constituting the C_{mv} but not equivalent to the region of the P_{mv}. Hence, the detectability of the accumulation of $^{99}Tc^mO_4$ evaluated by the r_c and S_c parameters should be less than the detectability of the accumulation evaluated by the r_p or S_p parameters as demonstrated by the case.

The use of C_{mv} as the reference. Case 2 had a cystic tumour within the right parietal region, histologically an astrocytoma grade II. The deviations from the normal mean values of the r_p and S_p parameters in number of SD were classified as definitely

Position	r_{Lc}	r_{Rc}	S_c
B1	2.62	1.68	2.20

Position	r_{Lp}	D	r_{Rp}	S_p
A6	- 1.89	- 0.57	- 2.29	- 2.14
C4	- 0.72	- 1.16	- 2.21	- 1.67
D3	- 0.99	- 1.19	- 2.64	- 1.81
D4	- 1.38	- 0.79	- 3.38	- 2.48

Position	A_L	A_R
A2	- 3.20	- 1.74
A6	- 2.54	- 2.62
D2	- 1.83	- 2.07
D6	2.05	1.62

Fig. 12. Printout of results from Case 3.

normal (Fig. 11). However, the deviations of r_c parameter were classified as definitely abnormal. (This measurement was made 2 hours after the injection of $^{99}Tc^mO_4$ and related to the corresponding normal ranges; LIND et coll.) Probably, the region of accumulated $^{99}Tc^mO_4$ corresponded more to a P_{mv} region than to the C_{mv} region. In that case the detectability of the accumulation, evaluated by the r_p and S_p parameters can be expected to be less than the detectability of the accumulation evaluated by the r_c and S_c parameters, as demonstrated by this case.

Use of adjacent values as the reference. Case 3 had a small meningeoma close to the skull base and to the median plane, above the olfactory region. Characteristic calcifications were found at roentgen examination of the skull. The deviations from the mean of all parameters but one A parameter were classified as definitely normal. This parameter displayed a deviation that was classified as probably normal, when regarding the whole skull, but probably abnormal, when regarding the frontal region (Fig. 12). The SD values of the r_c, r_p, S_c and S_p parameters of the reference group were high in the A1 to A2 region (LIND et coll.) However, the A parameters had comparatively small normal SD values (5.2 %–5.4 %) in these positions (LIND et coll.). Hence, the detectability of an accumulation of $^{99}Tc^mO_4$ in this position, close to the median plane of the skull, might be higher in A parameters compared to the detectability of the r_c, r_p, S_c, S_p or D parameters, as demonstrated by this case.

It was hence concluded that the use of the reference values P_{mv} and C_{mv} as well as the A parameters, was important in clinical investigation, to avoid some risks of diagnostic failure.

Examples of diagnostic results. Case 4 had a low differentiated metastasis in the left frontal lobe, possibly originating from the kidney or the thyroid gland. SD_{max} was at a level far above the borders chosen (26.4 SD) (Figs 4, 6).

In case 5 a tumour, histologically an astrocytoma grade III, was present with a $SD_{max} = 8.6$, thus far above the borders chosen (Fig. 5).

Discussion

Investigation of the isotope distribution in the skull by conventional methods involves the use of several basic parameters and their combinations. The evaluation based on image interpretation is subjective and complicated, and demands great experience (MALLARD 1966, BURROWS 1972).

Long experience of a subjective method adds information to the diagnostic process, thus enhancing the diagnostic accuracy, especially if a large number of parameters with large normal variations is used, as for instance in gamma encephalography according to PLANIOL and MUNDIGER or in the interpretation of brain scans and gamma camera images (PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, POPHAM et coll., MUNDIGER & OSTERTAG 1971, DOWSETT). An evaluation of diagnostic accuracy is therefore difficult, and a strictly objective and automatic interpretation of the results should be of great value.

To obtain a strictly objective diagnosis, one defined criterion of abnormal isotope distribution with fixed classification boundaries must be chosen. It might include several parameters and also their combinations. The maximum deviation in any of the 208 defined parameters was chosen as criterion in this work.

The significance of a pathologic deviation corresponding to q standard deviations outside the normal range of a parameter could be expressed:

$$q = \frac{X_p - \bar{X}}{\sigma_X}$$

X_p = actual parameter value
$\bar{X}$ = normal mean of the parameter value
σ_X = standard deviation of X

A criterion of abnormality could be defined as the maximum q-value (SD_{max}) of any of several parameters. A large number of parameters will increase the normal mean value of SD_{max} above 0 and thus decrease the significance of a pathologically high value of SD_{max}. Thus, ideally (1) the parameters chosen should have a high sensitivity to the diagnostic problem of interest, giving large values of $(X_p - \bar{X})$, (2) their standard deviations in a normal group should be small, and (3) the number of the parameters should be small.

Variance of parameters. Each evaluation parameter was obtained by dividing a measuring value with a reference value. The variance of a parameter (σ_x^2) was thus dependent on two sources of variation, and both should be restricted in order to increase the diagnostic accuracy (DUGGAN et coll. 1964, PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, POPHAM et coll., DOWSETT). The important problem of restricting the normal variation has been discussed elsewhere (LIND et coll.).

Detectability properties of the position ratio, sum and difference parameters. Theoretical calculation and phantom experiments demonstrated that the increase ratio is

always more sensitive to added tumour phantom activities than the sum or difference parameters (LARSSON et coll.) (Fig. 1). However, according to eq. (6) the normal standard deviation of the chosen parameter in clinical measurements exert influence on detectability, and hence position ratio parameters do not always imply a higher degree of detectability than the sum and difference parameters, in spite of being more sensitive. Calculation of results from the phantom experiments correlated to results obtained from the reference group are presented in Fig. 3, which demonstrates that the sum parameters (S_p) should give the highest significance (q) for pathologic accumulations of $^{99}Tc^mO_4$ in the central regions of the skull and difference parameters (D) for accumulations in the lateral parts of the skull. Position ratios (r_p) should give the highest significance in between these central and lateral regions. Position ratios, sums and side differences were therefore all regarded as important for the diagnostic accuracy (MOORE, BASCHIERI et coll. 1965, MCALISTER 1965, POPOVIC 1965, CONRAD & HORST 1966, PLANIOL, MUNDIGER & ASAI, POPHAM et coll.).

The number of measuring parameters used and hence the spatial resolution of the symmetry detector method had to be limited in order to obtain a simply applicable diagnostic criterion, SD_{max}, with a small normal mean value, which was dependent on the size of each measuring area and on the number of reference values used. A large number of measuring parameters should increase the probability of obtaining one optimal measurement from one subregion with abnormally high isotope content (high sensitivity of the effect of interest, high value of $(X_p - \bar{X})$), but the probability of a large value among normals of SD_{max} will also increase and thus decrease the relevance of high values of SD_{max}. The 208 parameters were reduced to 123 and 75, respectively, to find out if such reductions changed the criteria boundaries between normal and abnormal favourably. The normal mean value of SD_{max} was only reduced by 0.06 and 0.27 SD, respectively, in spite of the loss of several important parameters (Fig. 8). It was therefore concluded that a reduction of parameters below 208 could not be expected to increase the diagnostic accuracy.

On the other hand, a larger number of parameters might increase the diagnostic accuracy. This, however, would interfere with the purpose of designing an uncomplicated method.

The measuring areas were generally overlapping and square, 3 cm × 3 cm, in order to obtain a good coverage of the skull. Consequently, there were 24 measuring areas of each side of the skull offering 48 measuring values. The size 3 cm × 3 cm was chosen to correspond approximately to the size of a lateral projection of a region with the effect of interest, i.e. increased amount of isotope, caused by a small brain tumour (PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, ZEIDLER et coll. 1970, BURROWS, DOWSETT).

Table 2

The maximum deviation in the C_{mv}, P_{mv} and A groups of parameters are given in number of SD for the five pathologic cases. The maximum deviation in any of all 208 parameters is marked in boldface. This maximum deviation can occur in any of the three groups of parameters. (Case 2 was measured 2 hours after injection of $^{99}Tc^{m}O_4^-$; values obtained were related to a corresponding norm alrange, (LIND *et coll.*)

Case No.	Maximal deviation of any of the parameters in the		
	r_c, S_c	r_p, S_p, D	A
1	3.2	**6.1**	5.8
2	**4.2**	3.0	4.0
3	2.6	1.2	**3.2**
4	**26.4**	17.8	8.4
5	7.9	11.3	**12.1**

Reference values: C_{mv}, P_{mv} and A. Ideally, a reference value should be unaffected by the pathologic accumulations analysed and have a negligible variation, otherwise the relation between the measuring value and the reference value may remain constant and the parameter value lie within the normal range in spite of the pathologically increased amount of isotope.

C_{mv} was assumed to be more stable than a mean value of all measuring areas. which would include marginal areas with high variation. P_{mv} was for the same reason assumed to be less constant, but provided a possibility of compensating for unavoidable differences in the positioning height above the skull base plane. The adjacent parameter was used because the relation between the isotope contents in two adjacent subregions might be abnormal, even if both are within the normal range when evaluated by the r_p or r_c parameters (PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, POPHAM et coll.).

Cases 1 and 2 demonstrated areas with pathologic amounts of isotope almost covering the C_{mv} or P_{mv} regions, thus giving false negative C_{mv} or P_{mv} parameter values, respectively (Figs 10, 11).

The maximum deviation might occur in any of the C_{mv}, P_{mv} or a A groups of parameter (Table 2). This clearly demonstrates the advantage of using several reference values and therefore the C_{mv}, P_{mv} and A were used as references in this work. It is possible to use a large number of differently constructed parameters, but for reasons given previously, the use of the 208 parameters investigated was considered to be adequate.

Criteria. A theoretical calculation of the boundaries between normal and abnormal criteria values was impossible, even if the normal SD values of the parameters included were known, the degree of dependence between the parameters was un-

known. It was thus necessary to apply the chosen criterion on the reference group of cases without brain lesions, in order to obtain a basis for a rational choice of boundaries between normal and abnormal. It was also necessary to know the relative number of false positive cases, obtained with the chosen boundaries, otherwise the usefulness of the method for diagnostic screening purposes could not be evaluated (DUGGAN et coll., PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, POPHAM et coll., DOWSETT).

The distribution of the SD_{max} obtained from the reference group is presented in Fig. 8. It is seen that the classification boundaries chosen should restrict the false positive cases to a very small number. However, the parameters used were chosen after estimation of their SD values in this reference group, and thus application of the criterion to the same (selected) group will not give correct information about the normal range of the SD_{max} (PLANIOL, MUNDIGER & ASAI, POPHAM et coll.).

Often, in clinical work, only one defined subdivision of the whole brain is the possible location of a lesion. This clinical information can be combined with the measuring results, in order to increase the diagnostic accuracy by reducing the number of parameters analysed, thus decreasing the criterion boundaries between normal and abnormal. A division of the skull area into six subdivisions (Fig. 7) made a reduction of the criterion boundaries by about 0.5 SD possible (Fig. 9). This might be of special interest in attempts to exclude the existence of a pathologically increased amount of isotope in a defined brain area.

Separation of laterally located lesions from centrally located ones. Comparison between sum and difference parameters (Fig. 3) offers a possibility of estimating the depth of an abnormal source of activity. Fig. 2 clearly demonstrates the depth sensitivity of D/S.

Case examples. Cases 1 to 3 are presented to illustrate the necessity of using several types of parameters to avoid false negative classification (Figs 10–12) (PLANIOL, MUNDIGER & ASAI, DOWSETT & PERRY, POPHAM et coll.).

Case 4 demonstrates the evident, semiautomatically obtained objective diagnosis of an accumulation of $^{99}Tc^{m}O_4$ caused by a brain metastasis (Figs 4, 6).

The results in case 5 were also evident and easily interpretated; diagnosis: astrocytoma grade III (Fig. 5).

Conclusion

Knowledge of the normal ranges of parameters of the distribution of $^{99}Tc^{m}O_4$ in the skull is necessary for the separation of abnormal from normal.

Knowledge of the relative importance of different sources of variance in the evaluation parameters facilitates the limitation of the most important contributions to variance and the choice of evaluation parameters.

Knowledge of the sensitivity of each evaluation parameter related to the corre-

sponding standard deviation in a normal group makes it possible to use the conception of detectability in order to choose those parameters, that are most relevant for the detection of the effect of interest.

Hence, the choice of evaluation parameters of a diagnostic method can be made on these rational bases and objective comparison between the diagnostic accuracy obtained by different methods facilitated by use of this conception of detectability.

The uncomplicated symmetry detector method was developed on these bases. Objective and semiautomatic classification of $^{99}Tc^{m}O_4$ distributions in the skull as normal or abnormal were obtained without the need for experienced evaluation of individual results.

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SUMMARY

The objective classification of results of the previously described symmetry detector method for gamma encephalography is reported. The different evaluation parameters were chosen after comparing their detectability in different subregions of the head or as a result of findings in certain patients. The detectability was estimated from the results of phantom measurements related to the normal ranges of evaluation parameters. The borders of the classification criterion are discussed in relation to the number of evaluation parameters used.

ZUSAMMENFASSUNG

Die objektive Klassifizierung der Ergebnisse der zuvor beschriebenen symmetrischen Detektor-Methode zur Gammaencephalographie wird beschrieben. Die verschiedenen Untersuchungsparameter wurden nach dem Vergleich ihrer Nachweisbarkeit in verschiedenen Subregionen des Kopfes oder als Ergebnis von Befunden bei bestimmten Patienten gewählt. Die Grenzen der Nachweisbarkeit wurde aus Phantommessungen, die auf den normalen Bereich der Untersuchungsparameter bezogen waren, bestimmt. Die Grenzen der Klassifikations-Kriteria werden im Verhältnis zur Zahl der verwendeten Messparameter diskutiert.

RÉSUMÉ

Présentation de la classification objective des résultats de la méthode de détecteur de symétrie précédèment décrite pour la gammaencéphalographie. Les différents paramétres d'évaluation ont été choisis après avoir comparé leur détectabilité dans différentes sous-régions de la tête ou d'après le résultat des examens chez certains malades. La détectabilité a été estimée à partir des résultats de mesures sur fantôme en fonction des variations normales des paramètres d'évaluation. Les limites du critère de classification sont discutées en fonction du nombre des paramètres d'évaluation utilisés.

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