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OBJECTIVE SYMMETRY DETECTOR METHOD FOR GAMMAENCEPHALOGRAPHY

II. Normal range

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Encephalography or cerebral angiography are not well suited for screening purposes, because they involve a certain risk, are inconvenient to the patient and also demand great economic, technical and personnel resources. There is a need for safer, simpler and more convenient methods and therefore nuclides have become important aids in the diagnosis of brain lesions, especially tumours. Radiation hazards from amounts and types of short lived nuclides, commonly used, are small (SMITH 1965, PLANIOL 1966, Swedish National Institute of Radiation Protection 1969, PAOLETTI et coll. 1969, MUNDINGER & OSTERTAG 1971, YOUNG & ROCKETT 1972).

Scanners and gamma cameras have been technically improved offering increased spatial resolution. Digital handling of data by integrated computers has become more common. Despite the development of complicated and expensive instruments, skilful subjective evaluation of results is still necessary (CHARLESTON et coll. 1964, MALLARD 1966, PAOLETTI et coll., BURROWS 1972).

Originally, one-detector methods were used in gammaencephalography and with experience a high level of diagnostic accuracy could be obtained with these methods, taking advantage of the symmetry of the skull. However, positioning of the detectors over the head created a source of variation, including different levels of body-background, difficult to control. The digital results were difficult to evaluate as they

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depend upon the subjective estimation of several different criteria (MOORE 1948, MOORE et coll. 1948, PEYTON et coll. 1952, PLANIOL 1959, 1966, WENDE 1963, VAN DER WERFF et coll. 1964, CONRAD & HORST 1966, MUNDINGER & ASAI 1967).

To avoid subjective influence, objective statistical analysis of isotope distribution measurements should be made. This demands knowledge of the normal ranges of digital parameters. The normal appearance of nuclide distribution in the skull after intravenous administration has been described by several authors (WEBBER 1965, SCHNEIDER & PRÉVOT 1966, PENNING & FRONT 1970). MUNDINGER has reported the normal distribution obtained at gammaencephalography in digital terms (MUNDINGER & ASAI); normal ranges of digitalized brain scanning data has also been published (DOWSETT & PERRY 1970, POPHAM et coll. 1970, DOWSETT 1972). However, it has been difficult to achieve reproduceable positions for measuring in relation to the size and shape of the head and to restrict the error of counting statistics to a level where it is unimportant compared to the total variance of the results.

The general purpose of this work was to develop the original gammaencephalographic methods into an objective and simple method, suitable for neurologic screening work.

This has been achieved by assessing the performance in clinical routine work of a symmetry detector method for gammaencephalography as well as the normal ranges of the $^{99}Tc^{m}O_4$ activity distribution of the skull, permitting the statistical analysis of results from clinical cases by a routine procedure. The physical characteristics of the instrument and the method have been described previously (LARSSON et coll. 1975).

Method

The use of few, clearly defined stationary measuring positions was combined with large collimator apertures. For the whole skull the number of measuring parameters was small as a result of the large apertures, thus facilitating a simple statistical analysis and an objective classification of results in clinical routine, using defined criteria.

Each examination was performed as follows:

(1) 0.4 g potassium perchlorate was administered orally (WITCOFSKI et coll. 1967, SILBERSTEIN & LEVY 1970, HARPER et coll. 1972).

(2) Between 20 and 70 min later 10 mCi technetium pertechnetate ($^{99}Tc^{m}O_4$) was injected intravenously.

(3) A 'balance test' was performed by measuring a carefully mixed solution of $^{99}Tc^{m}O_4$ in a plastic vessel (15 cm × 20 cm × 20 cm) placed between the detectors. The number of counts per minute (between 50 000 and 100 000) was recorded for 3 min before and after each examination.

(4) The patient was placed supine with the head slightly bent forward. A plastic bar fitting the root of the nose and the supraorbital arches prohibited movements of the head, using the supraorbital arches and external auditory canals as reference points. Twenty-four overlapping subregions of the skull, with square lateral projec-

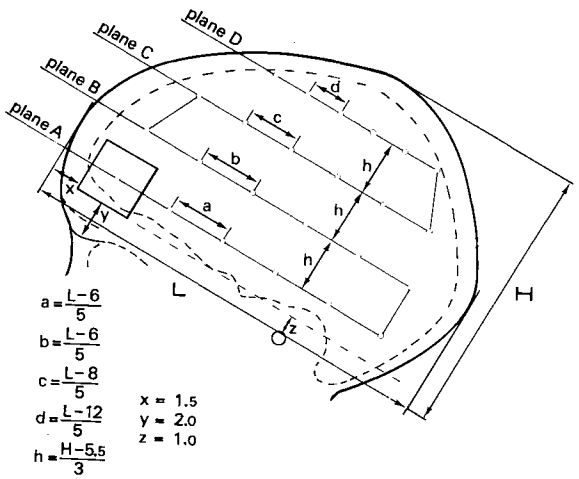

Fig. 1. The positions of the 24 measuring areas of each side of the skull are defined by circles, marking the central axis common for both collimators. Each position is identified by plane (A–D) and number (1–6). Number 1 is the most frontal and 6 the most occipital position of each plane. The aperture is indicated at position A1. The principles of the positioning diagram are given by the formulas. Position C1 is located 1 1/3 cm behind B1 and D1 is located 2 2/3 cm behind C1.

tions (30 mm × 30 mm) located in relation to the size and shape of the skull, were measured from both sides simultaneously by the movable detectors. The measuring positions were orientated in 4 parallel planes, each with 6 positions (Fig. 1).

To achieve standardized positioning, independent of the size of the skull, different diagrams were constructed, using the lateral projection outlines of skulls with various combinations of length and height. The length of the head and the height over the external auditory canals were measured on each patient and a corresponding diagram was chosen. A pointer indicated the actual position of the collimators and their movements on the positioning diagram placed in a plastic envelope, thus controlling the positioning of the detectors. The principle of the positioning diagram and the number identifying each position are demonstrated in Fig. 1.

Measurement I started about 30 min after the injection and lasted 30 min. The instrument was programmed for recording periods of 60 s with 15-s intervals. The intervals were used to move the detector system to the next measuring position.

Measurement II started after one hour and consisted of a second identical measuring sequence including a balance test, about 120 min after the injection of activity.

Calculation of evaluation parameters. The number of counts, N_R and N_L, obtained from each subregion in the right and left detector, respectively, was recorded on paper tape for an off-line calculation by a PDP-8 computer. All results were corrected for imbalance between the detectors from mean values of the balance test and also for the radiation decay. Each measuring value was related to two different reference values: the central mean value, C_{mv}, and the plane mean value, P_{mv}. The C_{mv} was the calculated mean number of counts registered per measuring position of the central area of the skull (B2–B5, C2–C5, right and left). The P_{mv} was the calculated mean number of counts of all measuring positions of the corresponding measuring planes

(A, B, C or D, Fig. 1). A relative conception of the distribution was thus obtained and the calculated ratios, (r) for each subregion were expressed by:

$$r_{Rp} = \frac{N_R}{P_{mv}} \cdot 100\ \% \quad r_{Lp} = \frac{N_L}{P_{mv}} \cdot 100\ \% \tag{1 a, b}$$

which were position ratios with the plane mean value as reference, and

$$r_{Rc} = \frac{N_R}{C_{mv}} \cdot 100\ \% \quad r_{Lc} = \frac{N_L}{C_{mv}} \cdot 100\ \% \tag{2 a, b}$$

position ratios with the central mean value as the reference, as indicated by the index c in the position ratios. The index p refers to the plane mean value and R and L to the right and left detector, respectively.

The percentage position ratios and their combinations, difference D and sum S were used as evaluation parameters.

$$D = (r_{Rp} - r_{Lp})\% \tag{3}$$

$$S_p = \frac{r_{Rp} + r_{Lp}}{2}\ \% \text{ and } S_c = \frac{r_{Rc} + r_{Lc}}{2}\ \% \tag{4 a, b}$$

Further, the difference between two adjacent values in the same measuring plane (N(j) − N(j − 1)), related to the most occipital of the paired values (N(j)), was used as evaluation parameter (adjacent ratio, A_R and A_L) (Fig. 1).

$$A_R = \frac{N_R(j) - N_R(j-1)}{N_R(j)} \cdot 100\%$$

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

Material. For ethical reasons nuclide was not administered to healthy volunteers. Instead patients without history or signs of neurologic disease, but subjected to radiation therapy because of carcinoma of the uterus, bladder or vulva, were used as a reference group. Hence the selection of cases was not randomized. There were no history nor signs of brain lesions (an infrequent complication of these types of cancer, RUSSELL & RUBINSTEIN 1971). However, the incidence of brain lesions could be somewhat higher in a patient group selected in this way, as compared to a group of truly normal individuals. It might thus be reasonable to presume that the normal ranges obtained in this group were wider than corresponding normal ranges of a true normal group (SCHIEFER 1972). Cytotoxic agents had not been administered. About one third of the patients originally selected refused to participate. Three patients were measured but later excluded: 2 women aged 72 and 46 years with previous mammary carcinoma and ovarian carcinoma, respectively, and one male with prostatic carcinoma. The second measurement was excluded in another three cases: in 2 of these due to failure of tape punch; the third patient refused to participate. It was for practical reasons not possible to make a careful neurologic examination of the patients in the reference group, which finally comprised 29 individuals (Fig. 2).

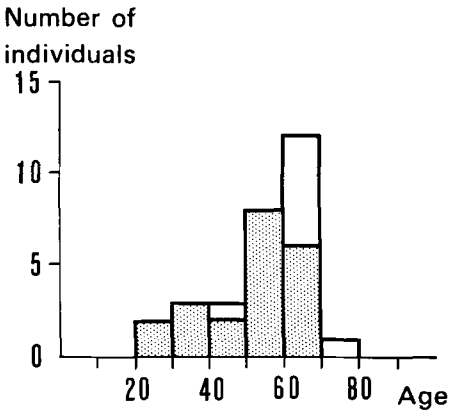

Fig. 2. Diagnoses and number of subjects. Carcinoma of the bladder 9, of the cervix 13, of the uterine body 6 and of the vulva 1. Dotted areas: females. White areas: males.

Results

The $^{99}Tc^{m}O_4$ distribution in the skull was measured in a total of 48 positions, 24 on each side of the skull. The value of each position was related to a central mean value, C_{mv}, and a plane mean value, P_{mv}, in order to obtain an idea of the relative distribution, allowing comparison between individuals. The position ratios r_{Rp}, and r_{Lp}, obtained from the same region, were compared with each other by the evaluation parameter D, describing the side difference of the skull. The sum and adjacent ratios (S, A) of each region, also comparable between individuals, were calculated, and altogether 208 parameters were obtained, dependent on each other to a varying extent. Hence each region was analysed by 9 parameters. The mean values and standard deviations (SD) of the reference group were calculated for each parameter, giving the interindividual variation (between individuals). The intra-individual variation (within individuals) of each parameter was approximated from the values of the first and second measurement and expressed in SD, thus including variation caused by the method and variation caused by different time intervals between the $^{99}Tc^{m}O_4$ injection and measurement (Fig. 3). Generally between 6 000 and 12 000 counts were recorded in each position.

The results of measurement II were in agreement with the results of measurement I and therefore only the latter are presented in detail.

Position ratio parameters. (1) Per cent of the central mean value C_{mv}. The calculated r_{Rc} and r_{Lc} values from measurement I of the reference group are displayed in Table 1 and Fig. 3, where the obtained mean values and their inter-individual SD values are plotted, corresponding to a vertex projection of the skull, giving profile-diagrams for each measuring plane.

The inter-individual SD of the r_c parameters varied between different positions and were higher in marginal positions, i.e. in plane A, D and the positions B1, B6, C1 and C6 than in centrally located positions (Fig. 3, Table 1).

(2) Per cent of the plane mean value P_{mv}. Position ratios, r_{Lp} and r_{Rp}, calculated from the results of measurement I of the reference group are presented in Table 2.

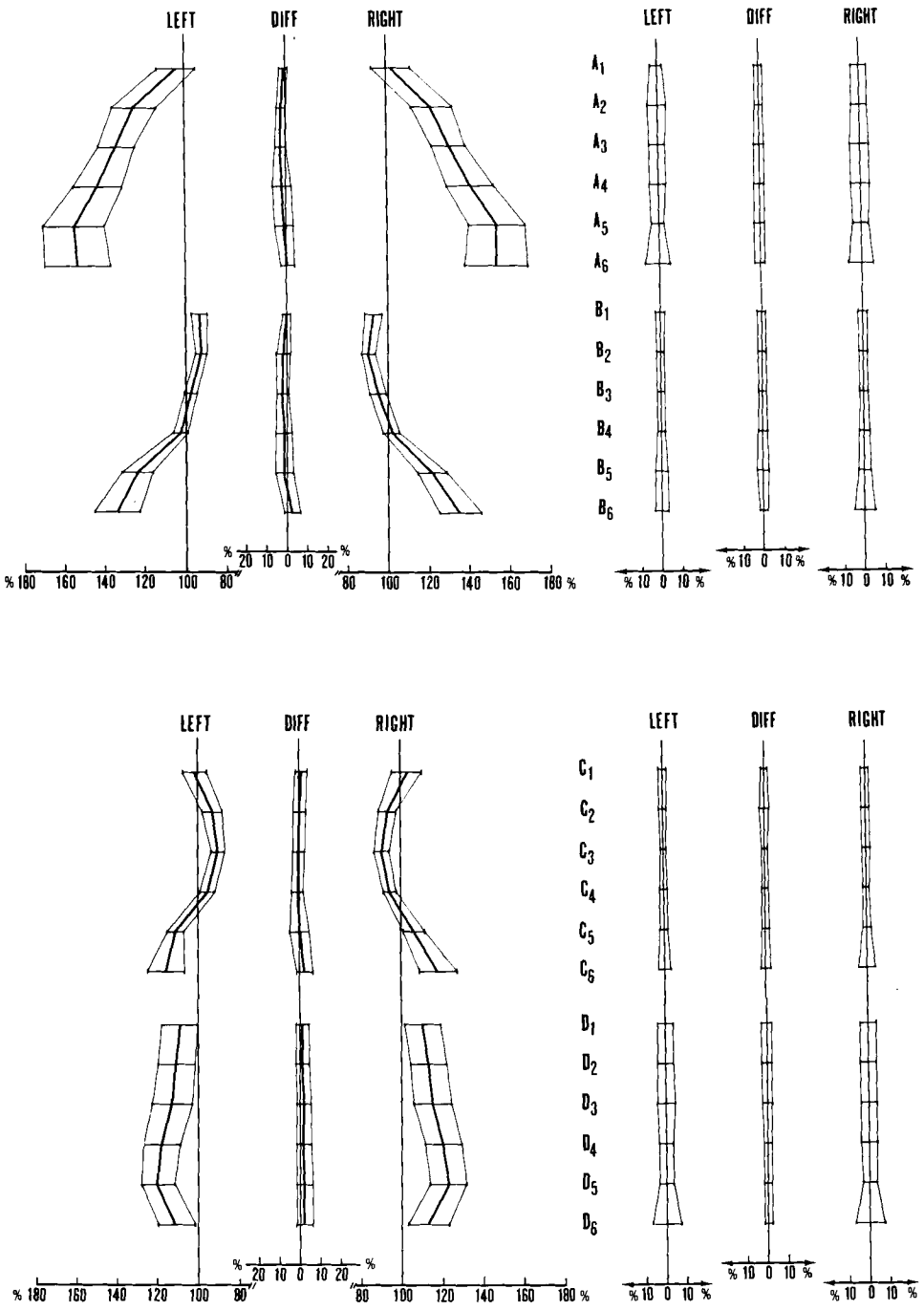

Fig. 3. Mean values $\pm$SD of r_c and D of measurement I are calculated for each position and indicated to the left; corresponding intra-individual SD-values are indicated to the right.

Table 1

Mean values, inter-individual and intra-individual SD values of r_c from measurement I

Position	r_{Rc}			r_{Lc}		
	Mean	Inter-individual SD	Intra-individual SD	Mean	Inter-individual SD	Intra-individual SD
A1	102.0	9.4	3.9	103.8	9.5	3.3
A2	122.4	10.4	4.3	124.8	10.7	4.6
A3	130.1	8.4	4.8	133.8	9.2	4.3
A4	140.4	11.7	4.6	143.0	11.8	3.8
A5	154.1	14.2	4.1	155.5	14.9	3.1
A6	154.5	15.5	6.2	153.2	16.2	6.4
B1	93.1	4.4	2.2	93.0	4.2	1.9
B2	89.9	2.8	1.6	91.8	3.3	1.4
B3	94.7	3.9	1.9	96.7	3.2	1.6
B4	101.6	3.9	2.4	103.0	3.7	1.7
B5	121.8	6.9	3.1	123.1	7.3	3.0
B6	136.3	10.6	4.5	133.2	10.9	3.7
C1	103.0	6.7	2.2	102.0	5.9	2.1
C2	93.2	4.5	2.2	92.8	4.7	1.7
C3	89.8	3.4	1.6	90.2	3.4	1.6
C4	94.4	3.0	1.8	95.1	3.4	1.9
C5	110.9	4.8	1.8	111.1	4.4	2.0
C6	118.4	9.2	3.6	115.6	9.1	3.2
D1	110.1	9.4	4.1	109.1	9.2	4.0
D2	113.0	9.2	4.1	111.5	9.4	3.8
D3	115.1	9.2	4.3	113.1	10.0	4.6
D4	119.8	9.3	4.1	118.2	9.2	3.4
D5	122.7	8.8	3.6	120.3	7.9	3.3
D6	113.5	10.2	7.0	110.8	9.2	6.7

The obtained inter-individual SD values of the r_p varied between 2.7 and 8.4 per cent and were especially in plane A and D less than the corresponding SD values of the r_c parameters, 2.8 to 16.2 per cent (Tables 1, 2). The lower standard deviations were to a certain extent, but not completely, explained by the difference in magnitude between C_{mv} and the different P_{mv}.

Difference parameter. The calculated mean values, inter-individual and intra-individual standard deviations of parameter D, calculated from the results of measurement I of the reference group, are tabulated in Table 4. The calculated mean value of D varied between -2.7 and $+2.9$ per cent in all subregions (Fig. 3).

The inter-individual SD values of D were always of the same order as or less (SD = 2.0 % to 4.8 %) than the standard deviations of the corresponding r_c and r_p

Table 2

Mean values, inter-individual and intra-individual SD values of r_p from measurement I

Position	r_{Rp}			r_{Lp}		
	Mean	Inter-individual SD	Intra-individual SD	Mean	Inter-individual SD	Intra-individual SD
A1	75.8	6.3	2.0	77.1	5.9	1.5
A2	90.8	5.3	1.7	92.6	5.0	2.1
A3	96.6	3.1	2.1	99.3	3.0	1.9
A4	104.2	5.8	3.6	106.1	5.0	3.5
A5	114.2	5.7	2.6	115.3	5.9	2.4
A6	114.5	7.1	3.4	113.5	7.5	3.8
B1	87.5	4.6	2.1	87.4	4.5	1.5
B2	84.5	3.4	1.4	86.2	3.9	1.6
B3	88.9	3.8	1.6	90.9	2.9	1.3
B4	95.4	3.2	1.8	96.7	3.0	1.6
B5	114.3	5.0	2.7	115.5	5.4	2.8
B6	127.8	7.1	3.0	124.9	7.6	2.5
C1	101.6	5.3	1.6	100.6	4.4	1.6
C2	92.0	3.6	1.5	91.5	3.8	1.4
C3	88.6	3.4	1.2	89.0	3.3	1.3
C4	93.1	2.7	1.9	93.8	3.2	1.7
C5	109.4	4.0	2.2	109.6	3.4	2.1
C6	116.8	8.2	3.0	114.1	8.4	2.5
D1	95.9	5.5	2.8	95.0	4.8	2.6
D2	98.4	3.6	1.9	97.0	4.0	2.1
D3	100.2	3.4	2.7	98.5	4.9	3.0
D4	104.3	2.7	2.6	103.0	4.4	2.4
D5	107.0	3.9	1.7	104.9	3.1	1.5
D6	99.0	8.4	5.4	96.8	7.8	5.3

parameters (SD = 2.8 % to 16.2 %). This decrease was largest in the marginal positions of the skull base plane A and top plane D and in the marginal positions B1, B6, C1, and C6 (Fig. 3, Tables 1, 2, 4).

Sum parameter. The parameters S_c and S_p calculated from results of measurement I of the reference group, are tabulated in Table 5. The inter-individual SD of these sums were generally smaller than the corresponding SD values of r_c and r_p (Tables 1, 2, 5).

Adjacent ratio parameters. The results of measurement I of the reference group, calculated according to eq. 5 a, b are presented in Table 3. Each value obtained in this way gave information about the difference between two adjacent values. The

Table 3

Mean values, inter-individual and intra-individual SD values of A from measurement I

Position	A_R			A_L		
	Mean	Inter-individual SD	Intra-individual SD	Mean	Inter-individual SD	Intra-individual SD
A1	—	—	—	—	—	—
A2	+20.1	5.4	2.5	+20.4	5.2	2.7
A3	+ 6.6	6.1	2.2	+ 7.4	5.8	1.8
A4	+ 7.9	5.1	4.5	+ 6.9	4.9	4.9
A5	+ 9.8	6.1	3.0	+ 8.7	5.3	2.8
A6	+ 0.4	6.7	4.4	− 1.4	6.4	4.2
B1	—	—	—	—	—	—
B2	− 3.2	5.1	2.4	− 1.2	5.0	2.0
B3	+ 5.3	3.8	2.6	+ 5.5	3.9	2.7
B4	+ 7.4	3.7	2.7	+ 6.6	4.2	2.2
B5	+19.9	5.6	2.3	+19.5	5.6	2.9
B6	+12.0	7.7	4.3	+ 8.4	8.6	3.8
C1	—	—	—	—	—	—
C2	− 9.3	4.2	1.7	− 9.0	3.8	1.7
C3	− 3.6	3.3	1.7	− 2.7	3.3	1.9
C4	+ 5.2	3.2	2.4	+ 5.5	2.8	1.8
C5	+17.6	5.2	2.5	+16.9	4.8	2.5
C6	+ 6.8	7.6	4.1	+ 4.2	7.8	3.6
D1	—	—	—	—	—	—
D2	+ 2.8	5.4	3.8	+ 2.4	6.1	3.4
D3	+ 1.9	2.8	1.9	+ 1.5	2.8	1.7
D4	+ 4.1	2.6	2.0	+ 4.7	3.1	2.5
D5	+ 2.6	4.3	2.8	+ 1.9	4.3	3.0
D6	− 7.4	6.7	4.9	− 7.7	6.9	4.7

inter-individual SD values were of about the same sizes as the standard deviations of the r_p parameters and consequently less than SD of the r_c parameters (Tables 1, 2, 3).

The intra-individual standard deviations of all parameters were in all subregions less than the corresponding inter-individual standard deviations, and generally about 50 per cent less (exception: SD of D in subregion A1). The intra-individual standard deviations of D parameters were in almost all positions less than the intra-individual standard deviations of the corresponding r_c and r_p parameters (Fig. 3, Tables 1 to 5).

Discussion

The necessary limitations of the measuring time and the amount of nuclide administered, restricted the amount of information available. The purpose of avoiding

Table 4

Mean values, inter-individual and intra-individual SD values of D from measurement I

Position	D		
	Mean	Inter-individual SD	Intra-individual SD
A1	−1.3	2.0	2.2
A2	−1.8	2.2	1.6
A3	−2.7	3.0	2.4
A4	−1.9	4.8	2.4
A5	−1.0	4.6	2.5
A6	+1.0	3.5	2.2
B1	+0.1	2.0	1.6
B2	−1.7	3.8	1.7
B3	−1.9	3.2	1.6
B4	−1.3	3.9	2.6
B5	−1.2	4.6	3.1
B6	+2.9	4.3	2.2
C1	+1.0	3.3	1.6
C2	+0.5	3.0	1.9
C3	−0.4	3.3	1.7
C4	−0.7	3.2	1.4
C5	−0.1	4.6	2.0
C6	+2.7	4.3	2.3
D1	+0.9	3.6	2.5
D2	+1.4	3.5	2.2
D3	+1.8	3.5	2.3
D4	+1.3	4.0	2.1
D5	+2.1	4.0	1.8
D6	+2.3	4.1	2.1

both complicated equipment and subjective evaluation of results made the use of gamma cameras or brain scanners impossible. Counting statistic errors and variation of counting efficiency and positioning of measuring areas, as well as the error caused by a varying body-background were difficult to restrict. They tend to decrease the significance of a pathologic deviation outside the biologic normal range of the nuclide distribution in the skull.

Statistical analysis of brain scans and gamma camera images includes an error caused by difficulties in getting reproduceable measuring areas in relation to the skull, and the performance demands complicated computation (POPHAM et coll.

1970). Besides, the gamma camera has an inhomogeneous sensitivity over the viewing field at best of about ± 10 per cent that can be compensated for only by computer correction to obtain reliable results (MALLARD 1972, SPECTOR et coll. 1972, BROOKEMAN 1973).

The results obtained by the gammaencephalographic technique of PLANIOL includes an error caused by varying body-background in the measurement perpendicular to the surface of the skull. Variation in positioning as well as in direction of the detector was involved and therefore a reproduceable measuring procedure was difficult to obtain. Side differences were also difficult to reproduce because only one detector was used. In each position only about 300 to 500 counts were registered which have a considerable counting statistic error of about 6 to 8 per cent of the position value in difference parameters, which should be compared to the values in Tables 1 to 5 (PLANIOL 1959, 1966).

MUNDINGER did not relate the measuring position to the size of the head and side differences were not calculated from simultaneous measurements by two symmetrically located detectors of each subregion. The total skull was not completely covered and the different sources of variation and the physical characteristics of the method were not discussed in detail (MUNDINGER & ASAI).

Generally adopted principles for premedication with 0.4 g postassium perchlorate were applied before the brain scanning with 10 mCi $^{99}Tc^{m}O_4$ was performed (HARPER et coll. 1964, 1972, MCAFFEE et coll. 1964, WITCOFSKI et coll. 1967, SILBERSTEIN & LEVY 1970). This amount of pertechnetate is reported to give a whole body dose of about 0.1 rad and after premedication with 0.4 g $KClO_4$ a critical organ dose of about 1 rad (colon, kidney, salivary glands) (SMITH, Swedish National Institute of Radiation Protection).

Several sources of variation (1—counting statistics, 2—electronic device, 3—positioning of detectors, 4—movements of the head, 5—change of $^{99}Tc^{m}O_4$ distribution with time, 6—individual size and shape of the head, 7—individual distribution of $^{99}Tc^{m}O_4$ in the skull) will be considered in detail. The intra-individual variations calculated from results obtained in measurements I and II were composed of variations according to points 1 to 5, but the inter-individual variation included all sources of variation (points 1 to 7). To exemplify the relative importance of these different sources of variation, the calculated SD values of the reference group are given in Table 6 for positions A3, A6, B3 and B6. B3 was a central position and the other marginal ones.

Clinical measurement procedure

Counting statistics. The error caused by estimation of the balance factor could be neglected, because about 150 000 to 300 000 counts were registered in each detector. The large collimator apertures permitted registration of about 6 000 to 12 000 counts in each stationary position, within a total measuring time of 30 min. The loss of precision by counting statistics in side differences was unimportant compared to

Table 5

Mean values, inter-individual and intra-individual SD values of S_c and S_p from measurement I

Position	S_c			S_p		
	Mean	Inter-individual SD	Intra-individual SD	Mean	Inter-individual SD	Intra-individual SD
A1	102.9	9.4	3.3	76.4	6.0	1.4
A2	123.6	10.5	4.3	91.7	5.0	1.8
A3	131.9	8.6	4.3	97.9	2.6	1.6
A4	141.7	11.3	3.9	105.2	4.9	3.3
A5	154.8	14.2	3.2	114.7	5.3	2.2
A6	153.9	15.6	6.1	114.0	7.1	3.4
B1	93.1	4.2	1.8	87.4	4.4	1.6
B2	90.9	2.3	1.2	85.4	3.1	1.2
B3	95.7	3.2	1.5	89.9	3.0	1.2
B4	102.3	3.1	1.6	96.1	2.4	1.1
B5	122.4	6.7	2.6	114.9	4.7	2.3
B6	134.7	10.5	3.9	126.3	7.0	2.5
C1	102.5	6.1	2.0	101.1	4.6	1.4
C2	93.0	4.4	1.7	91.7	3.4	1.1
C3	90.0	3.0	1.4	88.8	2.9	0.9
C4	94.7	2.8	1.7	93.5	2.5	1.6
C5	111.0	4.0	1.6	109.5	2.9	1.9
C6	117.0	8.9	3.2	115.4	8.1	2.5
D1	109.6	9.1	3.8	95.5	4.8	2.4
D2	112.2	9.1	3.7	97.7	3.4	1.7
D3	114.1	9.4	4.2	99.3	3.8	2.6
D4	119.0	8.9	3.6	103.7	3.1	2.3
D5	121.5	8.1	3.3	105.9	2.9	1.3
D6	112.2	9.4	6.8	97.9	7.9	5.2

the decrease in total standard deviation (Table 6). However, the diminished relative counting statistic error in sums might be of importance in central positions A3 and B3 (Table 6). It may be concluded that the error of counting statistics should not exceed about 2 per cent and that a deviation of less than 1 per cent was not relevant for most parameters compared to other sources of variation (Table 6). Regarding side differences this corresponded to between 5 000 and 20 000 registered counts in each position. PLANIOL (1966) and POPHAM et coll. (1970) have used only 300 to 1 000 recorded counts in each measuring area, thus accepting an error of counting statistics of about 8 to 4.5 per cent in side difference parameters which is high enough to influence the total variation of a normal group (PLANIOL 1966, POPHAM et coll.). The large number of counts in each position was thus essential to get the low total normal variation (BENDER & BLAU 1964).

Table 6

Four different types of estimated SD-values are compared in this table for 16 different parameters of four positions.

Parameter	Error caused by the electronic device SD %	Error caused by counting statistics SD %	Intra-individual variation SD %	Inter-individual variation SD %
r_{Rc} (A3)	Negligible	1.0	4.8	8.4
r_{Rp} (A3)	Negligible	1.0	2.1	3.1
D (A3)	Negligible	1.4	2.4	3.0
S_p (A3)	Negligible	0.7	1.6	2.6
r_{Rc} (A6)	Negligible	1.0	6.2	15.5
r_{Rp} (A6)	Negligible	1.0	3.4	7.1
D (A6)	Negligible	1.4	2.2	3.5
S_p (A6)	Negligible	0.7	3.4	7.1
r_{Rc} (B3)	Negligible	1.0	1.9	3.9
r_{Rp} (B3)	Negligible	1.4	1.6	3.2
D (B3)	Negligible	1.4	1.6	3.2
S_p (B3)	Negligible	0.7	1.2	3.0
r_{Rc} (B6)	Negligible	1.0	4.5	10.6
r_{Rp} (B6)	Negligible	1.0	3.0	7.1
D (B6)	Negligible	1.4	2.2	4.3
S_p (B6)	Negligible	0.7	2.5	7.0

Equipment. The mechanical construction offered stable positions of the movement and the error caused by instability of counting efficiency was negligible compared to the total standard deviation of results obtained (LARSSON et coll.). The use of a correction factor for imbalance between the detectors was important in order to compensate for errors in the evaluation parameters caused by variation in the counting efficiencies of the detectors from day to day (Table 6).

Positioning of detectors. The variation caused by positioning was restricted by several means. The collimators being unfocused with large apertures made a small variation in positioning less important. Influence of varying levels of body-background including stomach, thorax, thyroid and skull base activity was avoided by pulse height discrimination and by always keeping the axis of the collimators orthogonal to the median plane of the skull (PLANIOL 1966).

Involuntary movements of the head during the measuring procedure constituted an important source of variation which could be expected to be particularly relevant in neurologically diseased patients. It was thus mandatory to get a simple and convenient as well as effective fixation of the head. A plastic bar fitting the root of the nose and the supraorbital arches, was found to be a satisfactory solution in the ref-

erence cases, as demonstrated by the small intra-individual variation compared to corresponding inter-individual variation (Tables 1 to 5).

Unavoidable positioning variation was most important in marginal positions near the borders of the skull area, i.e. positions A1 to A6, D1 to D6 and B1, B6, C1 and C6. This probably explained why the obtained SD values of these positions were considerably larger than the SD values of more central positions (Fig. 3, Tables 1 to 5).

The use of the plane mean value, P_{mv}, instead of the central mean value, C_{mv}, as a reference, reduced the variation of the evaluation parameter caused by a varying distance between the measuring planes (A–C) and the skull base. Only about one third of this obtained reduction of SD values was explained by the different bases for calculation of the ratios r_p and r_c (Tables 1, 2, 6). Hence, the much lower inter-individual and intra-individual standard deviations of the r_p parameters in the skull base plane A, compared to the standard deviations of corresponding r_c values, demonstrated the advantage of using r_p as evaluation parameter (Tables 1, 2, 6). However, positions B3 and B6 were not close to the skull base and hence they did not have the corresponding reduction of SD between the r_c and r_p ratios (Table 6).

The penumbra zones of the collimators were narrow (LARSSON et coll.) and therefore the precisely opposed detectors measured almost the same region from right and left, respectively. Thus some biologic and positioning variation could be avoided in parameters based on side difference, taking advantage of the symmetry of the head which was demonstrated to be high with mean values of side differences obtained between −2.7 and +2.9 per cent. The inter-individual standard deviations of difference parameters were smaller than the SD values of corresponding r_c and r_p parameters, especially in marginal positions of the skull area as skull base plane A, top plane D and the positions B1, B6, C1 and C6 (Fig. 3). Again, this decrease of the percentage SD values of differences D was to a certain extent, but not completely, explained by the difference in magnitude between the reference values, P_{mv} and C_{mv}. Side difference in positions A6 and B6 offered a considerable reduction of SD, probably because a variation in position in relation to the border of the skull area here involved a large change of count rate, not compensated for otherwise. The effect was less important in centrally located measuring area, for instance position B3 (Tables 1, 2, 4, 6).

Side differences, measured simultaneously by carefully opposed detectors thus constituted measuring parameters with a comparatively small error caused by positioning, and they might therefore be important for the overall diagnostic accuracy of the method. Side differences cannot easily be obtained from measurements with gamma cameras or any single detector system (MOORE 1948, MOORE et coll. 1948, WENDE, PLANIOL 1966, MUNDINGER & ASAI, DOWSETT & PERRY 1970, MÜKE & SAEGER 1970).

Change of $^{99}Tc^{m}O_4$ distribution with time was included in the intra-individual variation and from the results obtained it was seen that this source of variation was of little importance between 30 and 150 min after the administration of activity. Stu-

dent's t-test was applied to the difference between the mean values of the r_c, D and S_c parameters of measurements I and II. There were no significant ($p > 0.01$) changes of the mean values of D parameters between the first and second measurements. Significant ($p < 0.01$) increases of the mean values of the r_c and S_c parameters were obtained only in position A4 and C4 (A4 + 3.5 % and C4 + 1.5 %). Significant ($p < 0.01$) decreases of the mean values of r_c or S_c parameters were obtained only in position A2, A3, B6 and D5 (A2 – 3.0 %, A3 – 3.0 %, A6 – 6.0 %, B6 – 2.5 % and D5 – 2.0 %). However, 96 parameters were regarded together and therefore about one of them should be expected to have a t-value outside the levels given by $p = 0.01$ (TAUXE & THORSEN 1969).

Individual size and shape of the head. Differences in head size was an important source of variation and was limited by the use of individualized positioning diagrams and the use of plane mean values as the bases for reference and the differences as parameters (Tables 1, 2, 4). Variation in head size and shape was compensated for in the design of the measuring procedure and not only afterwards in the calculation of the obtained results, as in statistically analysed brain scans (DOWSETT & PERRY 1970, POPHAM et coll., DOWSETT 1972). In particular, the large inter-individual variation of marginally located parameters compared to the smaller inter-individual variation of centrally located ones, indicated that a varying head shape was an important source of variation (Tables 1, 2).

The low spatial resolution of the method did not permit conclusive comparison between anatomic structures and the distribution pattern and its variation. Further improvements could probably be made by an even more carefully chosen measuring position related to the individual head size and shape and with the aid of roentgen monitoring. However, this would defeat the purpose of simplicity (CHEVALIER & METHLIN 1964, PLANIOL 1966, MUNDINGER & ASAI).

Individual distribution of $^{99}Tc^{m}O_4$ in the skull constituted a fundamental source of variation, that limited the theoretical possibilities of detecting a pathologic distribution of activity. The importance of varying accumulation of $^{99}Tc^{m}O_4$ in the choroid plexus was diminished by premedication with potassium perchlorate (WITCOFSKI et coll. 1967, SILBERSTEIN & LEVY 1970, HARPER et coll. 1972). A pathologic variation caused by a brain lesion should rise significantly above the normal biologic variation to be detectable. The use of large collimator aperture gave a smoothing of the normal biologic variation of the $^{99}Tc^{m}O_4$ distribution in the skull. The sizes of the aperture were chosen to correspond approximately to the projection of areas with increased amount of $^{99}Tc^{m}O_4$ caused by small brain tumours (BECK 1964, BROWNELL 1964, PLANIOL 1966, MUNDINGER & ASAI, ZEIDLER et coll. 1970, BURROWS 1972).

Inter- and intra-individual variation. From Tables 1 to 5 it is evident that the intra-individual SD was almost always about 50 per cent of corresponding inter-indi-

vidual SD values or less. It could thus be concluded that the methodologic error was small enough compared to the total variation, and further limitation of methodologic sources of variation was unnecessary, with the important exception of the shape and size of the head. On the other hand the decrease of the total normal standard deviation obtained by the use of precision equipment, large number of registered counts, individualized positioning diagrams, plane mean values as reference as well as the difference parameters was of great importance.

Adjacent ratio. A pathologic increase of activity in one position might be within the normal range of the r, D or S parameters but the difference between two adjacent positions might be significantly abnormal if the boundary between them approximately corresponds to the boundary between a pathologic and a normal area. Therefore all values were related to an adjacent value as previously described, thus offering a further type of parameter. The inter-individual SD of these parameters varied between 2.6 and 7.7 per cent and the intra-individual variation was considerably smaller (Table 3) Their influence upon the diagnostic accuracy of the method is impossible to evaluate as yet.

Clinical utility. The examination was convenient for the patient, lasted 30 min and was easily carried out by a technician. Results from patients can be correlated to the normal range presented and can automatically be evaluated statistically, thus avoiding subjective evaluation (LIND & LARSSON). The method might thus be valuable in clinical routine work even outside large medical centres, where fewer specialists are available. The diagnostic accuracy in a patient material will be the subject of a forthcoming publication (LIND).

SUMMARY

A standardized clinical examination procedure of a previously described symmetry detector method for gammaencephalography is presented and the results obtained from a reference group of subjects without known neurologic disorders are reported. The $^{99}Tc^{m}O_4$ distribution in the skull was investigated by 208 evaluation parameters obtained from measurements of 24 subregions of the skull from 48 symmetrical positions. Mean values and associated inter-individual and intra-individual standard deviations are given. Different sources of variation are discussed in relation to the results obtained. The method enables the $^{99}Tc^{m}O_4$ distribution in the skull to be objectively classified as normal or abnormal.

ZUSAMMENFASSUNG

Ein standardisiertes klinisches Untersuchungsverfahren einer zuvor beschriebenen symmetrischen Detektor-Methode zur Gammaencephalographie wird vorgestellt und über die an einer Referenzgruppe von Personen ohne bekannte neurologische Veränderungen erhaltenen Ergebnisse berichtet. Die $^{99}Tc^{m}O_4$ Verteilung im Schädel wurde durch 208 bestimmte Parameter, die von Messungen von 24 Subregionen des Schädels von 48 symmetrisch-

en Positionen erhalten worden waren, untersucht. Durchschnittswerte und zugehörige inter- und intra-individuelle Standard-Abweichungen werden gegeben. Unterschiedliche Ursachen für die Abweichung werden im Verhältnis zu den erhaltenen Ergebnissen diskutiert. Es war das Ziel, die $^{99}Tc^{m}O_4$ Verteilung im Schädel objektiv als normal oder nicht normal zu klassifizieren.

RÉSUMÉ

Présentation d'une technique d'examen standardisé basée sur une méthode de détecteur de symétrie décrite préalablement. Les auteurs présentent les résultats obtenus à partir d'un groupe témoin de malades sans troubles neurologiques connus. La distribution du $^{99}Tc^{m}O_4$ dans le crâne a été étudiée par 208 paramètres d'évaluation obtenus à partir des mesures de 24 sous-régions due crâne à partir de 48 positions symétriques. Les auteurs indiquent les valeurs moyennes et les déviations standard interindividuelle et intraindividuelle. Ils examinent différentes sources de variation en rapport avec les résultats obtenus. Le but était de permettre de classer objectivement comme normale ou comme anormale la distribution dans le crâne du $^{99}Tc^{m}O_4$.

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