Technical Papers

A Computational Procedure for the Isotope Method of Brain Tumor Localization[1]

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G. E. Moore's original technique (*1*) for brain tumor localization by means of radioactive isotopes depends for accuracy very largely on the skill and experience of the individual investigator. To reduce this element of subjectivity to a minimum, we have developed what we believe to be a more objective analytical method which is giving us promising results. Thus far, we have examined 80 cases by this method; we feel, however, that the number is too small to allow statistical interpretation.

Better instruments are now being developed, but the work reported here was done with the following instrumentation: two bismuth-wall Geiger tubes—at first a long tube, 1 in. in diameter (RCL Mark 1, Model 12), and lately a shorter tube 1½ in. in diameter (RCL Mark 1, Model 13). The tubes were mounted in lead collimators 14 mm thick, and fixed in the cylindrical holes so that the resulting angle of collimation is about 30° (this is the angle between the axis and a direction of 50% sensitivity for a small source). The collimated tube is supported by a flexible dental x-ray arm. A standard decimal counting unit with automatic reset and preset time is used. The patient, when capable of sitting, is placed in a barber's chair provided with head and chin rests. Tagged material[2] (DIF or IHSA) is administered to the patient by intravenous injection.

The rate of elimination of radioactive substances from the brain is different for each part of the brain, and the empirically obtained correction factors used till now are inaccurate. The present method disregards the individual elimination differences from point to point and considers only artificial averages which we derive by taking two readings for each point, equally removed in time from the beginning and end of the total examination time. In practice, we use the 32 standard points developed by the original investigators (*1–3*). We take our first measurement over the glabella and then over the remaining 31 points of the skull until we reach the occipital midline point (I, PF-6, PF-4, PF-3, PF-5, F-7 F-5 . . . . . V, 0-3, 0-5, VI), these points describing a spiral; from here we repeat all measurements in retrograde sequence. In this way we have 2 counts for each point, each taken more or less equally spaced before and after the middle of the whole measuring period. Finally, we sum the 2 counts for each point, this figure becoming our value for the following computations.

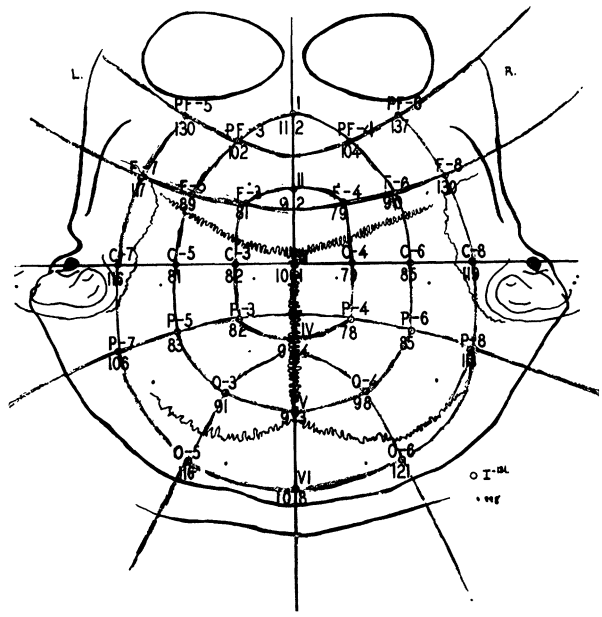

FIG. 1. Spread-out map of skull surface. The 32 measurement points are shown with their standard designations used in isotope localization techniques, and their percentage activity (D^*) for the average normal skull.

By averaging data on 13 patients without organic brain lesion, we obtained an average pattern for the normal head. In order to obtain comparability to the normal skull pattern, we convert the absolute values of our counts to percentage values. We take the arithmetic average of our 32 values, and then express each individual value in percentage of this average. With each patient to be examined, we compare the individual results to the normal pattern and determine the following values:

C_H and C_L = pair of counting rates at 2 symmetrical points on the skull. H and L as subscripts stand, respectively, for the higher and lower counts. (Counts per unit time using any convenient unit of time.)

$A = 100\ (C_H - C_L)/C_L$ = observed asymmetry in counting rates, expressed as percentage of C_L.

$\overline{C}$ = average counting rate over the skull = average of all the Cs.

$D = 100\ (C/\overline{C})$ = percentage activity at each point.

$E = D - D^*$ = excess activity expressed in percentage (excess % activity). * Normal skull pattern.

$F = E_H - E_L$ = asymmetry in excess percentage activity (corrected asymmetry).

We have constructed a new map of the head which gives in a plane an approximate visualization of the three-dimensional relationship of the whole head (Fig.

[1] This work was started while the senior author was on an Isadore Abrahamson Neurological Fellowship, and is being continued under a research grant and fellowship from the Damon Runyon Memorial Fund for Cancer Research, Inc.

[2] The di-iodo^{131}-fluorescein (DIF) and iodinated human serum albumin (IHSA) were furnished by the Abbott Laboratories, North Chicago, Ill., under an allocation from the U. S. Atomic Energy Commission.

1). Such maps are used to record the observations and steps of computation. Each 15% increase of activity is arbitrarily taken as one unit and is represented as a line beginning at the point of measurement and drawn at the same angle as that of the collimated tube positioned at this point. (Increase of over 15% is considered as symptomatic of tumor.)

In the case of an increased radiation zone (characteristic of tumor), these lines, which are an index of the magnitude and the location of increased activity, intersect over the critical area. Taking into consideration the angle of collimation (30°), we can then fairly well delineate the location, shape, and size of the area of increased activity.

We have the impression, based on a few observations, that by taking into account not only the increased but also the decreased uptake values, other pathological brain processes could eventually be detected and evaluated by the method described (e.g., necrotic, ischemic areas, nontumoral lesions, etc.—processes where, probably because of circulatory or other deficiencies, the distribution of the tagged material is impeded, thus demonstrating in the involved area measurably less than normal radiation).

References

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The Solubilization of 4-Dimethylaminoazobenzene (Butter Yellow) in Serum

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Many of the carcinogenic agents, including the azo dye 4-dimethylaminoazobenzene, are fat-soluble. As a vehicle for such substances emulsions of corn oil are used with polyglycerolester as emulsifier and stabilizer. In other experiments (*1*) rats were fed with a diet containing .058–.064% of 4-dimethylaminoazobenzene. It is a well-known fact that the mode of administration of the carcinogenic agent can have a decisive influence on the result; we were therefore looking for a technique to allow solubilization of such agents in homologous serum without any denaturation of the serum proteins.

To this end thick filter paper (Munktell No. 20/150, Grycksbo, Sweden) is thoroughly soaked in a solution of 12.5 mg% 4 dimethylaminoazobenzene in a 1:1 mixture of ethanol and ether. After drying the paper contains about 4 γ of the azo compound per cm². It is cut in strips of 40 × 7 cm, and .08 ml of normal human serum is placed on the middle of each strip. We arrange the apparatus for paper electrophoresis in a deep-cooling tank, keeping a constant temperature of 2° C and giving the effect of a closed atmosphere. Within 9 hr, 5–6 mg of serum protein can be separated, when 5 v/cm and 5–6 mamp are applied. The paper is wet with veronal/veronal sodium buffer of .06 ionic strength and pH 8.9. Of the two paper strips used simultaneously, one is afterwards stained with bromphenol blue; this strip serves as a guide for cutting off the fractions from the still wet unstained strip. The protein/azocompound is eluted from the cuttings with saline (.85%), the volume of each of the solutions being brought to about 3 ml. Then the optical density of the perfectly clear solutions is read in the Beckman spectrophotometer at 420 mμ and thereupon the content of the azo compound is calculated. The eluate from a protein-free paper cutting serves as a blank.

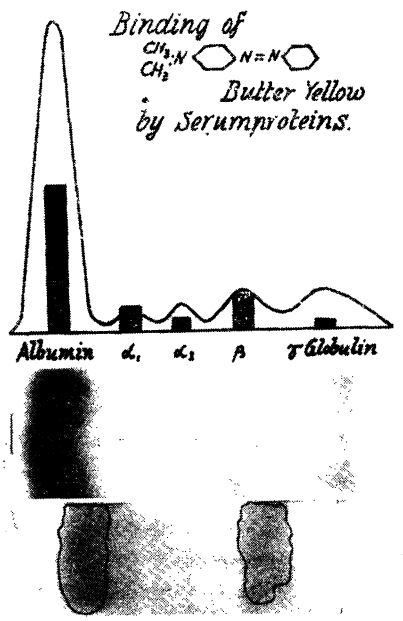

FIG. 1. Above: Serum protein fractions colored with bromophenol blue. Below: Same paper strip without coloring, showing the accumulation of butter yellow in the regions of albumin and β-globulin; blank space corresponds to site of γ-globulins.

The black columns in Fig. 1 show graphically the γ of azo compound bound to each serum protein fraction. The total of azo compound transported by this

TABLE 1

	Albumin	α_1^-	α_2^-	β	γ-Globulin
Serum fractions in rel %	63.2	4.0	7.1	9.6	16.1
Bound azo compound in γ	9.01	1.50	0.46	2.20	0.32
Bound azo compound in % of the total of transported azo compound	66	11	3	16	4
γ Azo compound/mg protein	6.7	4.2	3.0	11.0	0.9
Elution of Sudan red by isolated fractions of normal human serum protein[2] γ/mg protein	9.5		10.1	11.3	5.4