BRAIN SCANNING WITH MERCURY

Theory, Technique and Accuracy of the Method

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Radioisotopic Encephalography is now a standard tool of the clinician and neurosurgeon. Its accuracy compares favorably with other diagnostic procedures and, for certain types of lesions and of localizations, it is probably the method of choice. Radioisotopic scanning has been applied to the diagnosis and localization of brain lesions since 1950. However the method had not gained widespread acceptance until 1959. The present popularity of the method was prompted by the availability of scanners of very high sensitivity and of more efficient radioisotopic tracers. Brain tumors can be visualized with arsenic 72, copper 64, radioiodionated serum albumin I-131 (henceforth referred to as Risa I-131), mercury 203 and mercury 197. The brain tumor uptake is dependent upon the breakdown of the blood-brain barrier, the tumor cell type, the rate of metabolism of the tumor cells and the molecular size of the compound. With the exception of the work of Sweet and Brownell at the Massachusetts General Hospital in Boston with the positron emitters, arsenic 72 and copper 64, the brain scanning until 1959 was almost exclusively performed with Risa I-131. The positron technique has not found wide acceptance due to the relatively low sensitivity of the method and to the fact that the positron scanner cannot be used for other scanning procedures. In 1960 McAfee and Taxdal at the Johns Hopkins Hospital in Baltimore, Maryland using Risa 131 demonstrated 70 per cent of all intracranial tumors. They pointed out the advantage of brain scanning over cerebral angiography and air studies and stressed the complete freedom from complication in this method. Furthermore they recognized that the position and extent of intracranial tumors are usually portrayed accurately because the tumor bed itself is visualized. A further substantial improvement in brain scanning was obtained with the introduction of radioactive mercuhydrin (Hg 203) in 1959. This isotope was studied

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extensively by Blau and Bender at the Rosewell Park Memorial Institute in Buffalo New York. These authors studied comparatively Risa 131 and mercury 203 and found that in using mercury 203 scans were easier to interpret and more accurate. Most of the recent literature on this subject concurs with their conclusions. The advantages of mercury over iodine is due the fact that mercury 203 has a single gamma ray emission at 28.000 electron volts (.28 MEV) and that unlike Risa I–131, has a very short biological half life. The resultant low body background permits earlier scans with good results 45 minutes to one hour after the injection of the isotope. Neohydrin and its closely related mercurial diuretics are excreted in a two segment curve with about 50 per cent of the dose excreted in the first eight hours and the remainder at a rate according to a biological half life of three days. However approximately ten percent of the dose remains in kidneys and is eliminated slowly with a biological half life of 28 days. The irradiation to the kidney is presently the only drawback of mercury 203 as a scanning agent. The kidney exposure however, can be reduced by a factor of three by injecting non–radioactive mercuhydrin the night before the scanning as a kidney blocking agent. With the introduction of mercury 197, which has a very short half life, we will be able in the foreseeable future to reduce kidney irradiation by a factor of 100.

Method

In order to obtain brain scans of good diagnostic quality the physician should use a well standardized technique. We emphasize three main points:

1. Individual settings of the scanner for each patient and for each projection.

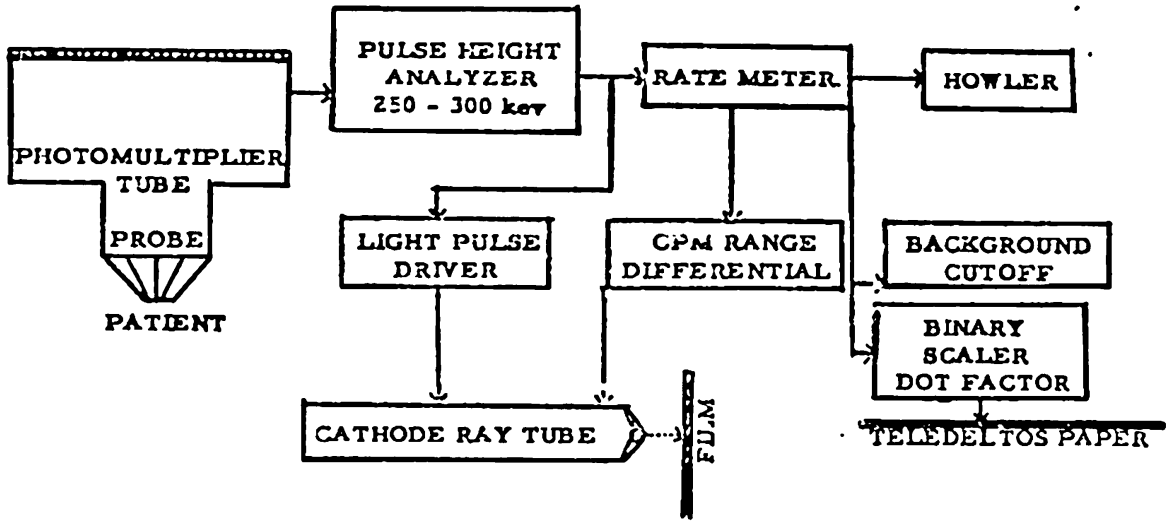
2. Uniform timing between injection of the isotope and scanning procedure.

3. Injection of a proportionate amount of radioisotope (mercuhydrin 203) calculated in relation to the patients' ideal body weight.

We do not recommend a "cook book" setting of the scanner as suggested by some manufacturers of scanners and by some independent publications. We find that the settings which may be correct for an AP projection performed one hour after injection of the isotope are definitely not adequate for PA or lateral projections performed two or three hours later. Scans performed with a "cook book" method are of different technical quality and variable target/non–target ratio. This fact adds an

unnecessary burden to a correct interpretation and should be avoided. The basic principles of the scanning procedure are relatively simple to understand.

DIAGRAM OF SCANNER SET FOR BRAIN SCANS WITH MERCURIAL [illegible]



All scanners have a scintillation crystal mounted in a heavily shielded probe. This probe is mounted on a beam driven by an electrical motor. The motor drives the probe to and fro at a speed that can be set at any point between one and 60 cm. per minute. Perpendicular to the transverse motion, the probe moves backward or forward at a line spacing rate which can be set from one to 10 mm.

During the action of the scanner the gamma rays coming from the patient under the geometrical field of the probe penetrate the sodium iodide crystal loosing their energy into it and causing a scintillation of light. This light is picked up by the photomultiplier tube and its energy is multiplied to equal the original pulse. The pulse then is conveyed to the pulse height analyzer set to a window matching the main photopeak of the isotope being employed. In this process only the selected energy peak of the isotope being used will pass through the pulse height analyzer while the unwanted pulses are rejected. The pulse thus produced activates the pulse driver which turns on the cathode ray tube for a preset fraction of time varying from one to 100 microseconds and exposes an x-ray film. The same pulse is also counted by the binary scaler and activates the dot scan system and the audio rate meter whose pitch will change with the different counting rates.

In our Institution we routinely block the kidney with 1 to 2 cc of a non-radioactive mercurial diuratic the night before the scan. The follow-

ing morning radioactive neohydrin is given i. v. in the amount of 10 microcuries per kilogram of ideal body weight. The scan is started one hour later. In order to properly set the scanning procedure the skull is hand scanned for areas of increased uptake and also in order to determine how much higher the brain background is over the background obtained with the probe pointing away from the patient. As background setting an average between these two values is selected adjusting the cathode ray voltage so that at background level the film will be barely fogged. At this point by adjusting the cpm range control the voltage which corresponds to optimal blackness of the film is set in correspondence of the area with maximum count rate which is normally found in correspondence of the nose. The dot scanning portion of the system is then set as it is completely independent of the photoscanning circuit. The output pulses pass through the binary scaler and are reduced to a level suitable for thermoelectric printing. This is controlled by a dot factor adjustment which is set in function of scan speed to maximum count rate. In brain scanning we usually set it to produce one dot for every 4 to 8 impulses counted. Finally the background cutoff is set so that it will start printing counts about 100 to 200 volts above the background voltage of the photorecorder. This brings both the dot scan and photoscan into phase and records clearly only significant information within the brain scan area.

The points of reference are marked on the teledeltos paper. In AP view we use the tip of the nose, the bridge of the nose and the pupil. In the lateral view we use the ear canal and the corner of the eye on the side facing the scanning probe. These points are marked and eventually are recorded on the film by superimposing it on the simultaneously obtained teledeltos scan. During the performance of the scanning procedure the settings are rechecked and generally changed to compensate for the diminished activity present in the brain at the time the subsequent projections are being taken. A properly set scan should be jet black over the nose, slightly gray over the normal brain tissue and should present a light gray appearance outlining the skull. Tumor or intracranial lesions appear gray to jet black depending on how well they take up the neohydrin.

Interpretation of the Results

The reliability of the radioisotopic encephalography is dependent upon technically accurate scans. We feel that if one had to mark the scan with a crayon to identify the outline of the head the scan is too light and all the information has not been recorded. This is in our opinion probably the main reason for a small but disturbing incidence of false negative results reported in some papers. It is our impression that the

technique or proper background adjustment is the primary reason why, to the best of our knowledge, we have not had thus far a false negative in our statistics. Another important point to be considered is the position of the patient. The head of the patient should be in a very accurate plane perpendicular to the scanning probe. We found that the use of sand bags is inadequate for proper immobilization of the patient and we are now using exclusively vacuum air bags which are far more comfortable to the patient and give a much greater degree of immobilization. For the interpretation and analysis of the scan we take into consideration the following facts:

A. We do not consider an AP projection sufficient for screening negative scans. We have often found AP projections presenting no evidence of localized activity in patients with posterior lesions in which lateral and PA projections were strongly positive and diagnostic.

B. We feel that it is very important to remember that areas of low target/non-target activity indicates often low grade and possibly curable tumors. These are the types of lesions indeed that we wouldn't want to miss. A critical analysis of the scan is important. On occasion the examiner may have to step back and look at the films at an angle to notice fine differences of uptake. Once an area of localized uptake, present in at least three successive passes of the probe is detected, it should be matched with the other projections and only considered of diagnostic or of suspicious significance if present in a corresponding position in more than one projection.

C. When examining lateral projections we draw an ideal line from slightly above the bridge of the nose to the auricular canal. There should be normally no activity above this line. Any activity above this line is suspicious and should be correlated with the opposite side scan and with the AP projection. By concentrating his attention on this difficult area the examiner will not miss pituitary, pineal and orbital lesions which could easily be mistaken as part of the normal activity of the paranasal and ethmoidal regions.

D. In the scanning procedure we examine first an AP projection and decide which first lateral to perform basing our opinion on whatever minimal difference between left and right side may be present. In a completely negative AP we select the lateral side most likely to be affected on the basis of the clinical history or patient's symptoms. In all scans presenting posterior activity a PA scan is also performed for proper localization. We try whenever possible to avoid being influenced by the clinician or by the clinical history or by the symptoms of the patient. We believe that the scan should be interpreted in a completely objective way to avoid the danger of over-reading or over-diagnosing.

The examiner should be well aware of the fact that activity present in any projection may be originating from the bone of the skull. We have observed that in many cases regenerating bone or bone affected by metastatic tumor picks up the isotope. Marginal to bone flaps there is activity even many months after surgery and this should not be confused with recurrence of the disease. However by proper evaluation of perpendicular projections the activity is usually localized in the bone when this is the case. In our experience, finally, the following patterns are of diagnostic importance:

1. A diffuse salt and pepper effect often seen in post arteriography or post pneumoencephalography scans. Similar, but more pronounced, salt and pepper effect is seen in encephalitis and in leucoencephalitis of the type associated with generalized metastatic tumor.

2. In AP projection, activity diffuse to one hemisphere with counterlateral hemisphere completely negative is suggestive of subdural hetoma. This finding should be correlated with a lateral projection which in the case of subdural hematoma reveals no localized activity, but only diffuse salt and pepper effect.

3. CVA are oftentimes of difficult interpretation as they may appear as areas of localized activity similar to that produced by tumors. In many cases however a differential diagnosis is possible since CVA presents often irregular margins of activity with uneven concentration of the isotope within the area itself. There is, furthermore, poor correlation in shape and size between the lateral and AP or PA projections.

4. Occasionally a metastatic tumor may display vague and diffuse activity at the beginning of the symptoms. This will eventually localize in a more definite pattern if a repeat examination is performed within a few weeks.

Conclusion

In summing up our experience and the conclusions of various workers in the field we find that brain scanning is a major breakthrough as localizing agent for intracranial expanding lesions. Cerebral scanning has a very definite place in the evaluation of cranial tumors and should be part of the routine investigation when brain tumor is suspected. Scan should always be performed as the first procedure to avoid positive results due to post arteriographic or pneumoencephalographic artefacts.

Brinkman and others at the University of Michigan Hospital in 1961 offered corroborative evidence of the value of mercury 203 in bran scanning. They said that "when the scan is unequivocally positive, and though neurological findings are minimal, we are willing to operate without

further contrast studies, should the symptoms and accessibility of the tumor warrant such a procedure." Some may agree with this statement, some may disagree. One fact remains clear: the neurologist and the neurosurgeon now join the group of medical people who can benefit from the use of isotopes in their diagnostic procedures.

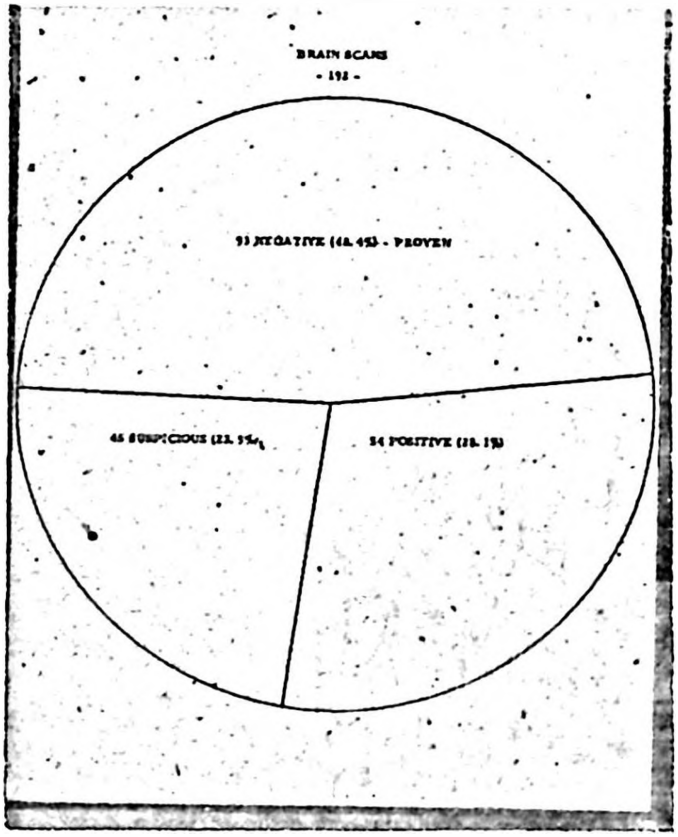


Figure 1. Distribution of brain scans obtained from April, 1962 to September 1964.

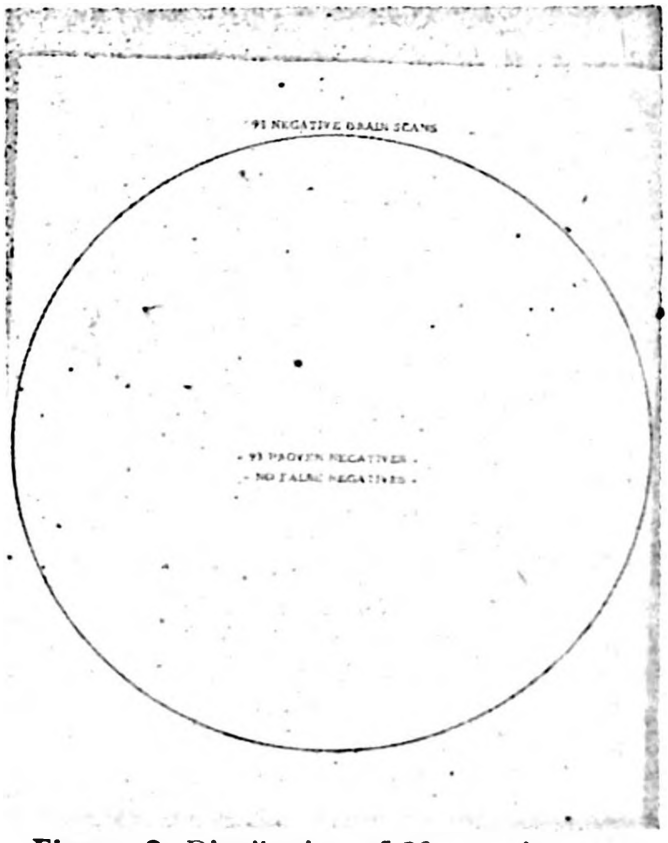


Figure 2. Distribution of 93 negative cases.

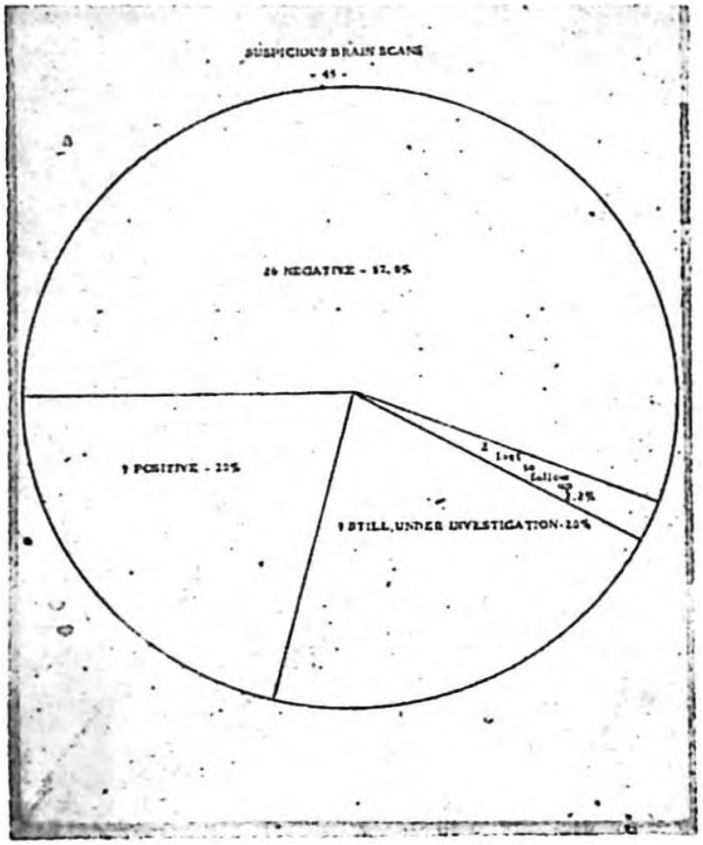


Figure 3. Distribution of 45 suspicious cases.

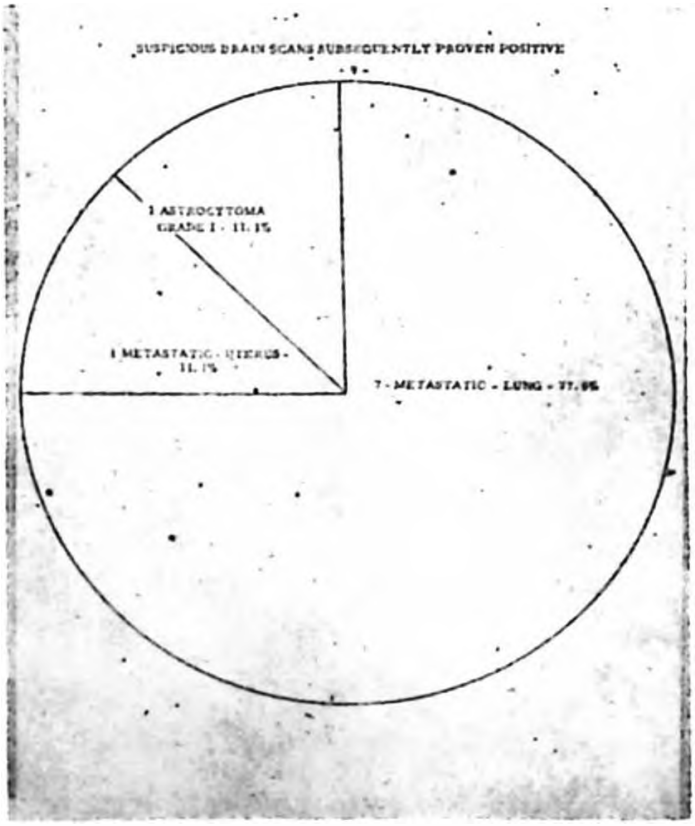


Figure 4. Suspicious cases subsequently proven positive.

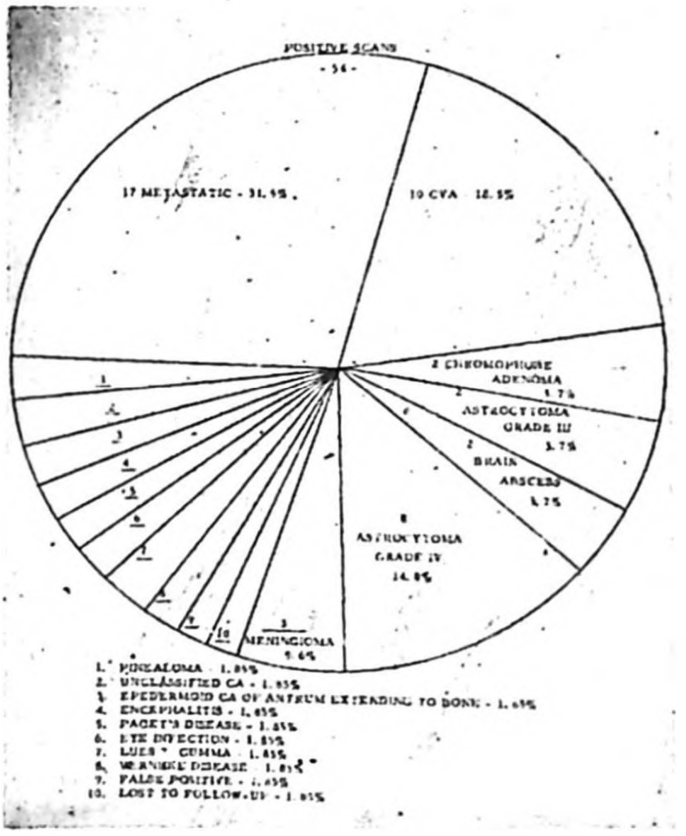


Figure 5. Distribution of 54 positive scans.

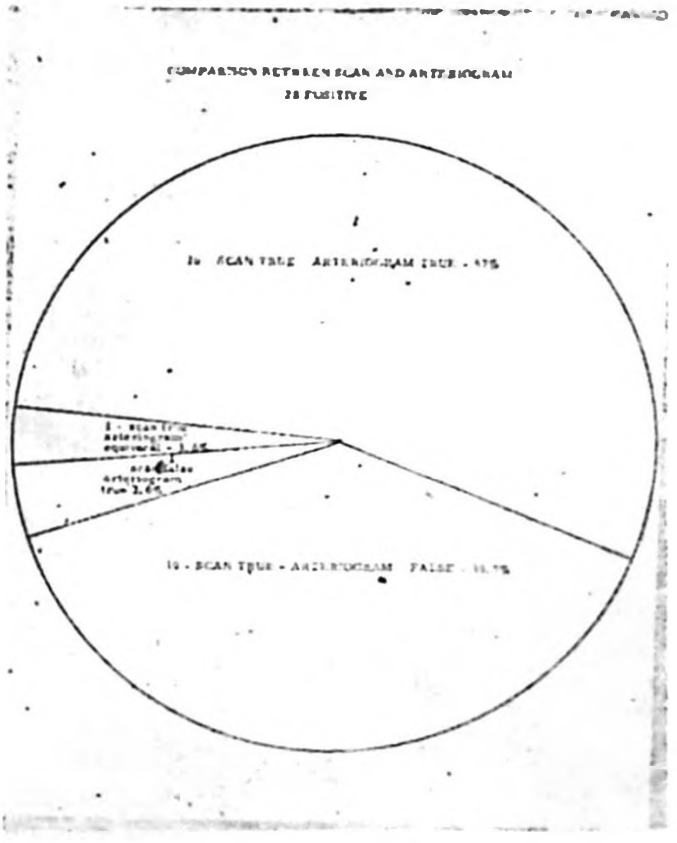


Figure 6. Comparison between scan and arteriogram in 28 cases in which both arteriogram and scan were available to us.

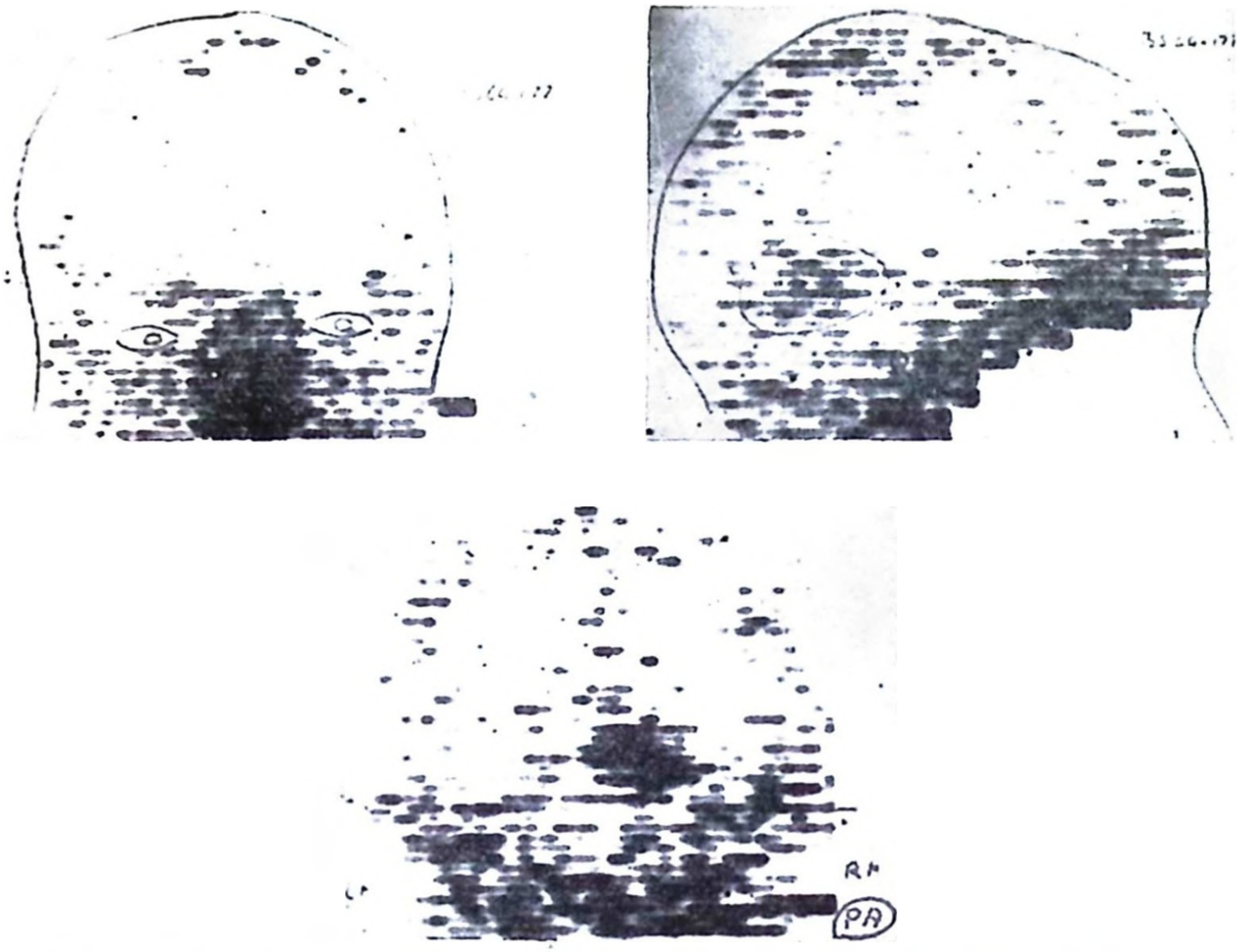


Figure 7, 8, 9, The AP scan is completely negative. The lateral scan reveals an occipital area of localized activity which is again seen in the PA projection in parasagittal position.
Final diagnosis: glioblastoma multiformis.

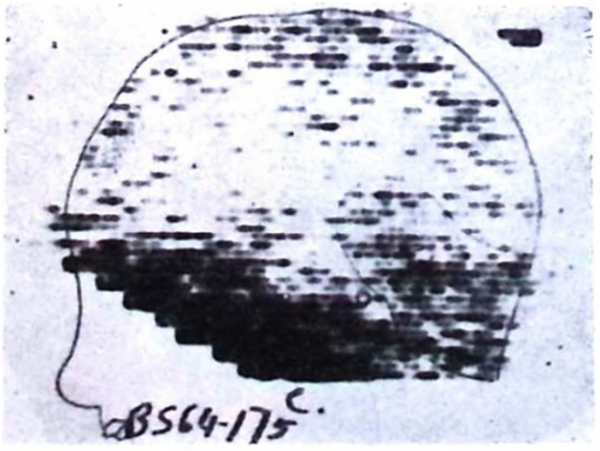


Figure 10. Notice the area of localized activity in the posterior temporal and occipital region. The uptake is uneven and the margins of the area of activity are ill defined,
Final diagnosis: brain infarct.

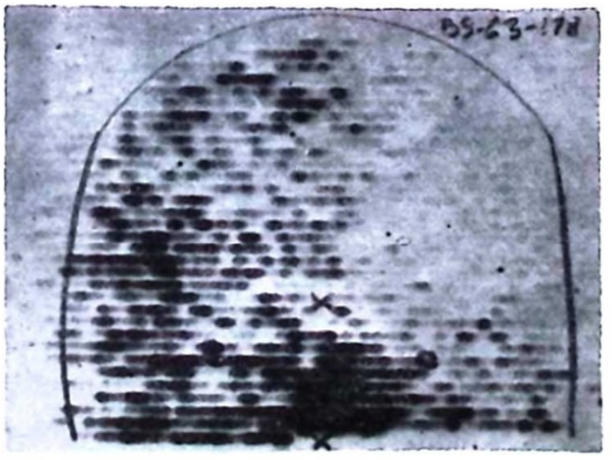


Figure 11. The right hemisphere reveals diffuse activity whereas the left hemisphere is completely negative. A lateral projection in this case which is not shown reveals only slight and diffuse "salt and pepper" effect.

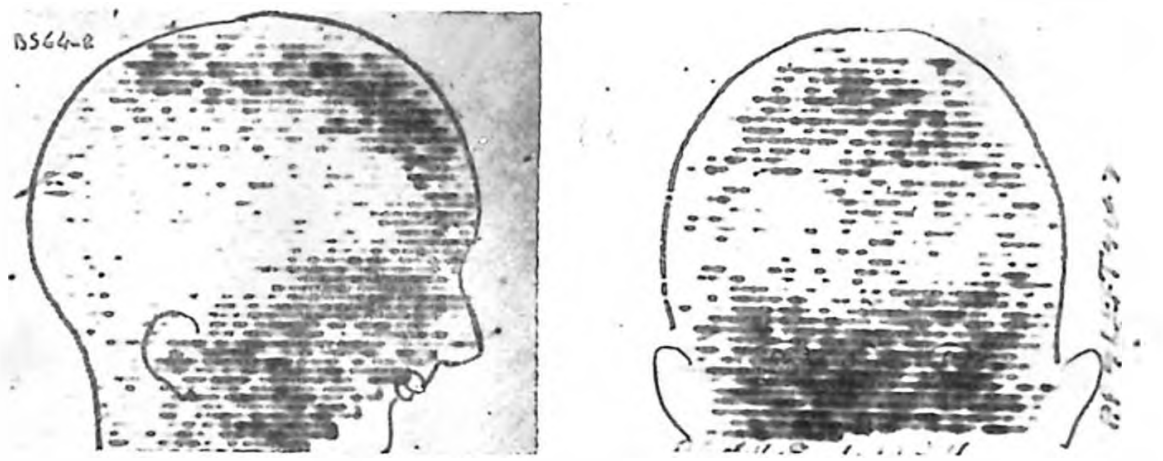


Figure 12, 13. Diffuse activity along the frontal bone. In AP projection the activity may be mistaken as affecting the frontal lobes.
Final diagnosis: metastatic carcinoma to frontal bone (primary breast carcinoma).

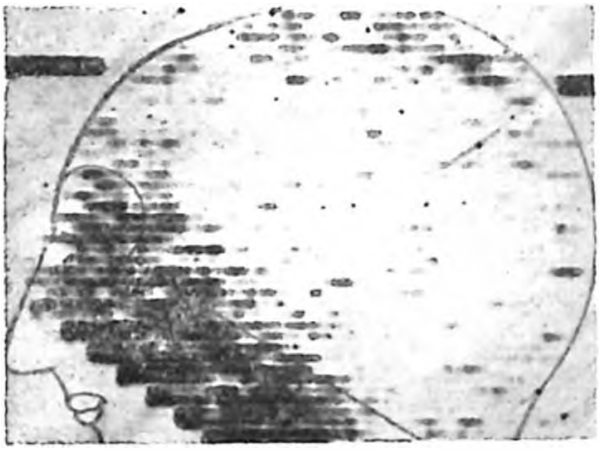


Figure 14. High level of localized uptake localized to the left orbit.
Final diagnosis: glioma of the retina.

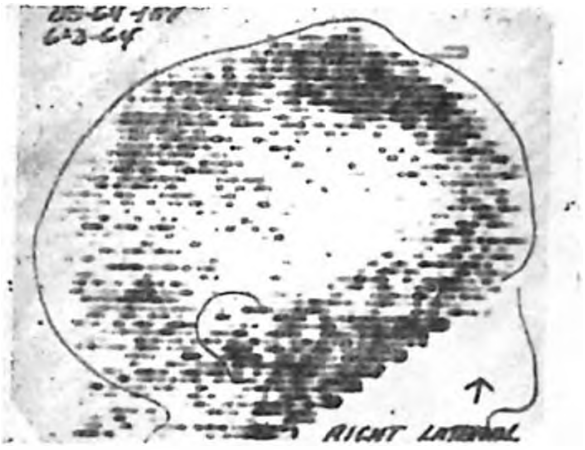


Figure 15. Paget's disease of bone. Notice diffuse activity along the cranial vault.

Figure 16. Minimal activity in posterior frontal area seen in five passes of the probe. Similar activity was detected in AP projection.
Final diagnosis: grade I glioma of frontal lobe.

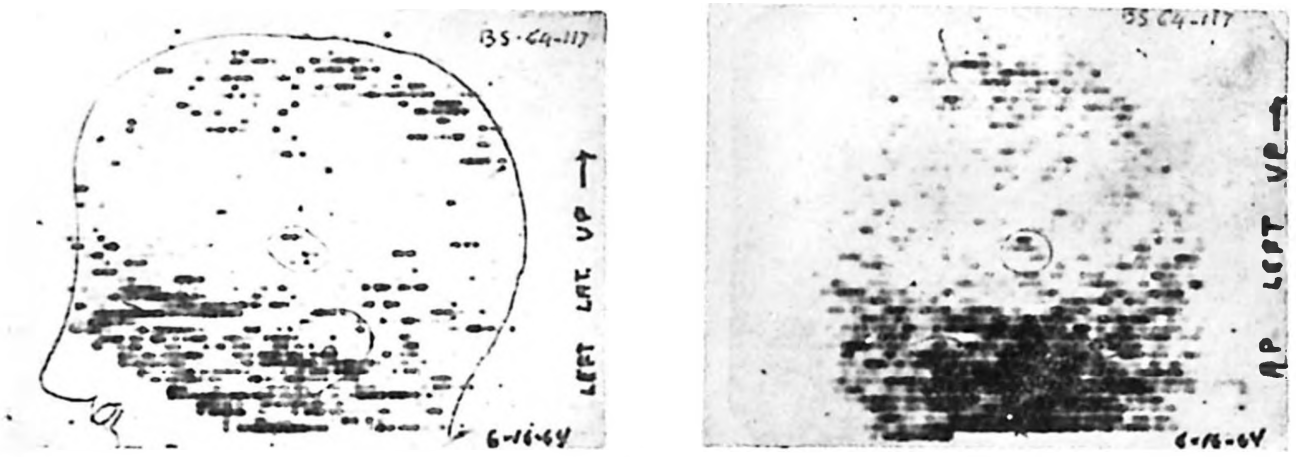


Figure 17, 18, Low target/non – target ratio activity localized in the area of the sella turcica. Notice that the activity is above an ideal line connecting the bridge of the nose to the auricular canal.
Final diagnosis: chromophobe adenoma of the pituitary gland.

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