DOSIMETRIC STUDY OF RESIDUAL BRAIN CONTAMINATION AFTER THE INJECTION OF A SOLUTION OF YTTERBIUM-169-DTPA IN THE CEREBROSPINAL FLUID

ZERBIB J.C. - Mme IMBERT L. - BONLEU M. - JOFFRE H.
Centre d'Etudes Nucléaires de Saclay - France
Service de Protection contre les Rayonnements

Dr DE TOVAR G. - Dr BEAUFILS F. - Mme COLLONGE M.
Service des Radioisotopes - Professeur TRIAL R.
Centre Médico-Chirurgical Foch - SURESNES - France

Abstract

Using radionuclides for medical purposes raises the question of the dosimetry of the radiation emitted by the radioactive products which are taken up in the system, whether preferentially or not.

The authors deal with a concrete case, namely ; the retention of ytterbium-169-DTPA after sub-occipital injection of the product. This kind of injection is made for an examination with a view to diagnosis.

A spectrometric analysis enabled the activity of the ytterbium taken up in the patient's brain mass to be known. A simulation carried out on a phantom was made using as guide :

- the space distribution of the radionuclides observed by scintiscanning
- the quantitative results of gamma spectrometry.

The measurements made on the patient as well as on the phantom enabled the observed dose due to the photons to be determined.

Along a horizontal plane passing through the eyes of the patient, the average absorbed dose is of several tens of rads in the central area of the brain.

In two other patients, the scintiscanning results showed a 20 to 30 % retention of the ytterbium-169 injected, after a rapid initial elimination phase.

The authors also made autoradiography of a frontal section of the brain of a patient on whom an isotopic study was made five weeks before death. This autoradiography showed that the radioactive product had spread throughout the brain and was taken up preferentially near the ventricular walls.

Introduction

In the case of a sub-occipital injection of ytterbium-169-DTPA a retention greater than expected wa observed by hasard on one patient (a retention also found later on other patients for lumbar injections).

The residual ytterbium-169 activity was determined a few weeks after sub-occipital injection of a know quantity of this radionuclide into the cerebrospinal fluid.

Knowing the activity, the absorbed dose is estimated for several points on the brain-pan.

I - Measurement methods

To determine the activity fixed by the brain the internal contamination is simulated using a "RANDO" type phantom head.

This phantom (human skeleton covered with a "tissue - equivalent" material) is designed for external irradiation measurements.

1.1. Simulation of internal contamination

Seven sealed cylindrical sources of ytterbium-169 roughly simulate the actual contamination.

Figure 1 shows the radiography of the phantom superimposed on the scintigraphy of the patient.

Figure 2 defines the location of the sources in an element of the phantom.

Figure 3 shows the radiography of the phantom superimposed on the scintigraphy obtained with the seven cylindrical sources in place.

Assuming that this simulation is a good enough approximation of the contamination, the activities measured by a spectrometrie device, for two identical measurement geometries (patient and phantom), are in the ratio of the total absorption peak surfaces associated with the photon fluences emitted by ytterbium-169.

Figure 4 shows the four geometries for which measurements were made on the patient (once) and on the phantom (twice).

1.2. Activity estimation

For each measurement geometry the total absorption peak surfaces taken into consideration relate to photons of 110 keV (18 %), 131 keV (11 %), 177 keV (22 %), 198 keV (35 %), 261 keV (1,7 %) and 308 keV (10 %). The emission percentages are those given by C.M. LEDERER [1].

Two experiments have been made which gived the account following :

Experiment No 1 : mean activity = 98 $\pm$ 15 µCi

Experiment No 2 : mean activity = 105 $\pm$ 19 µCi

The two sets of measurements give the activity values calculated on the date of the measurement carried out on the patient (40 days after injection of 900 μCi ytterbium-169). These values are obtained from one set of measurements on the patient and two sets of measurements on the phantom. The reproducibility obtained is satisfactory.

The arithmetical mean activity value (all energies and all incidences = 24 values) for the two experiments, for a 95 % probability (student's criterion) is :

$$A_{av} = 101 \pm 12 \ \mu Ci$$

1.3. Elimination of ytterbium-DTPA by the organism

Several studies have been carried out with ytterbium-169-DTPA[2,3,4,5,6]. Recent measurements by KIRCHNER, KUSICH and WAGNER[7] showed a two-component exponentiel elimination of the product. The fast component involves 95 to 97 % of the injected product, which is eliminated with a half-life between 6 and 36 hours. The slow component covers the remaining 5 to 3 % which disappears with a half-life of 30 days, close to the half-life of ytterbium (32 days), and is thus due to radioactive decay alone.

In the case under investigation, if the activity value measured 40 days after the injection is extrapolated to time t = 0, we obtain :

$$A_0 = 254 \pm 30 \ \mu Ci$$

This means that slowly eliminated fraction represents about 30 % of the initial activity, which can lead to high absorbed doses.

II - Measurement of absorbed dose

From the absorbed dose due to photons, measured by setting lithium fluoride dosimeters into the phantom in the presence of contamination-simulating sources, the absorbed dose to which the patient is exposed after injection of ytterbium-169-DTPA can be calculated.

The absorbed dose D delivered between times t_1 and t_2 is equal to :

$$D_{rad} = \int_{t_1}^{t_2} d(t)dt$$

The mean absorbed dose rate, per unit activity, at a point i on the phantom is :

$$d_i = \frac{D}{(t_2 - t_1).A_{mean}} \quad rad. \mu Ci^{-1} . d^{-1}$$

A_{av} = mean activity of sources in the phantom, between times t_2 and t_1 expressed in μCi

$t_2 - t_1$ = irradiation time in days.

The mean absorbed dose rate, per unit activity, delivered to the patients is the same as that measured in the phantom if for both geometries :

1) the contamination is identically distributed
2) the absorbing media are comparable in every way.

If these conditions are respected, the absorbed dose rate measured, at a point i, can be used to calculate the absorbed dose received at this point after a time t :

$$D_i = d_i \int_0^t A(t)dt = d_i \int_0^t A_0 . \exp(-0.693 \frac{t}{T})dt$$

$$D_i = \frac{A_0 . D.T}{(t_2 - t_1).A_{mean} . 0.693} \left[1 - \exp(-0.693 \frac{t}{T})\right]$$

A_0 is the extrapolated activity calculated above (254 µCi).

Two distinct exposures were carried out and gave very similar results. For exemple, the conditions of the first experiment (A_{av} = 381 µCi, $t_2 - t_1$ = 3.71 d) lead to :

$$D_i = 8.29 \, D \left| 1 - \exp(-0.693 \frac{t}{T}) \right|$$

Figure 5 shows the isodoses for a horizontal plane passing through the patient's eyes. The values are calculated for zero exponential and hence represent the absorbed doses after complate elimination of the radionuclide.

The small circles represent the lithium fluoride detectors.

It must be stressed that the dosimetric measurements only refer to the photons emitted by ytterbium-169. The doses due to electron emission are much higher in the immediate vicinity (about a tenth of a millimeter) of the contaminated areas.

III - Clinical studies

3.1. Decays observed during gamma-camera measurements

Figure 6 shows the variation with time of the number of impulses measured on the skull by gamma-camera for three cases.

Case number one is that studied by dosimetry above. These results are expressed in percentages on figure 7 and the curves obtained lie close together, but do not comply with the decay scheme described by KIRCHNER, KUSICH and WAGNER[7].

3.2. Autoradiography of a brain section

This observation concerns a patient for whom the diagnosis of hydrocephalus at normal pressure was debated. The isotopic examination was carried out five weeks before death. A frontal brain section passing through the third ventricle was autoradiographed two months after autopsy (figure 8) revealing the preferential fixation of ytterbium-169, free or bound, by the ependyma tissue, combined with an appreciable diffusion through out the brain.

IV - Conclusions

Gamma-camera measurements show that in the three cases investigated only 70 to 80 % of the activity injected is elimineted during the first few days, whereas according to other work[7] this decrease involves 93 to 97 % of the initial activity.

The fixed ytterbium-169 activity, estimated by simulating the contamination in a phantom, corroborates the results obtained by gamma-camera counting. This absolute measurement of the activity shows beyond doubt the high retention level of the radioactive product.

The mean absorbed dose due to photons is several tens of rads in the central region of the brain throughout the contamination period and for an injection of 900 μCi ytterbium-169-DTPA.

The ytterbium migrates than is fixed in the brain mass in an undetermined chemical form. Two hypotheses are possible :

a) the complex is destroyed in vivo or in vitro and the radionuclide is fixed on the tissues,
b) after destruction of the complex, new laballed molecules are formed in the tissues with the freed ytterbium.

Il the complex is in fact destroyed as it migrates the fixation of ytterbium-169 is increased. Until these fixation phenomen are better understood it is preferable to reduce the amount of product injected.

It is also important to use a product containing very little non-complexed ytterbium (<1 %). In the event of long-term storage (3 to 4 weeks) it is wise to check the substance by chromatography before injection.

ooo

We wish to thank Madame PARMENTIER (CEA, Health Physics Department, Fontenay-aux-Roses, Nuclear Research Center) and Monsieur BOURDOISEAU (CEA, Radioelements Department, Saclay Nuclear Research Center) for their suggestions, criticisms and material help.

ooo

1 LEDERER C.M., HOLLANDER J.M., PERLMAN I.
Table of isotopes - Sixt Edition (1967) - Edit. John Wiley and Sons, inc.

2 DELAND F.H., JAMES A.E., WAGNER H.N., HOSAIN F.
Journal of Nuclear Medicine, vol 12, n° 10, pp. 683-688 (1971).

3 HOSAIN F., REBA R.C., WAGNER H.N.
Radiology, vol 91, pp. 1199-1203 (december 1968).

4 HOSAIN F., REBA R.C., WAGNER H.N.
Radiology, vol 93, pp. 1135-1138 (november 1969).

5 DELISLE M.J., BOUVY F. et VALEYRE J.
AED-Conf- 118-009 (1971).

6 WAGNER H.N., HOSAIN F., DELAND F.H. and SOM P.
Radiology, vol 95, pp. 121-125 (april 1970).

7 KIRCHNER P.T., KUSICK K.M. and WAGNER H.N.
Journal of Nuclear Medicine, vol 13, n° 6, p. 442 (1972).

Fig.1_Scintigraphy of the patient

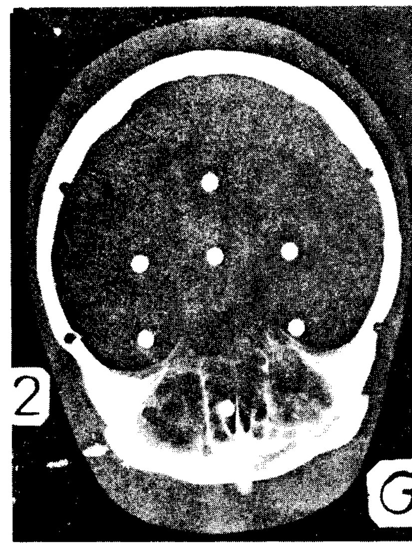


Fig. 2_Location of Ytterbium_169 sources

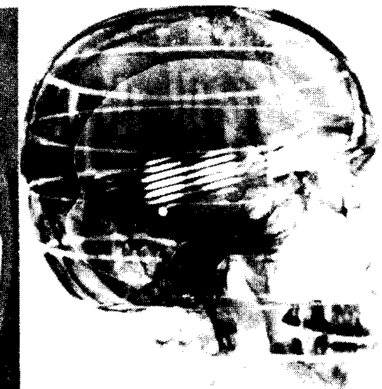


Fig.3_Scintigraphy of the phantom

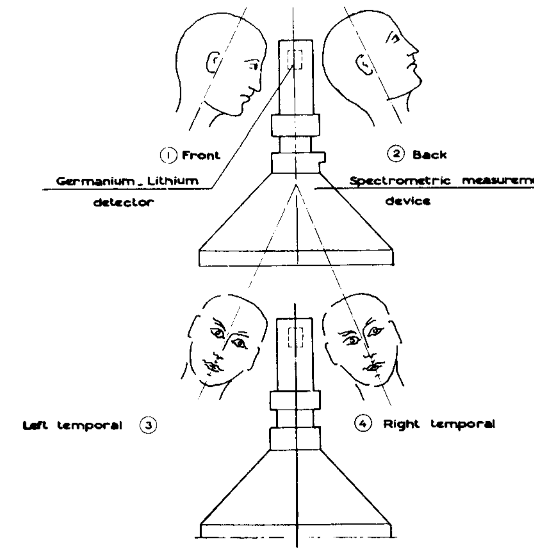


Fig. 4_Measurements geometries

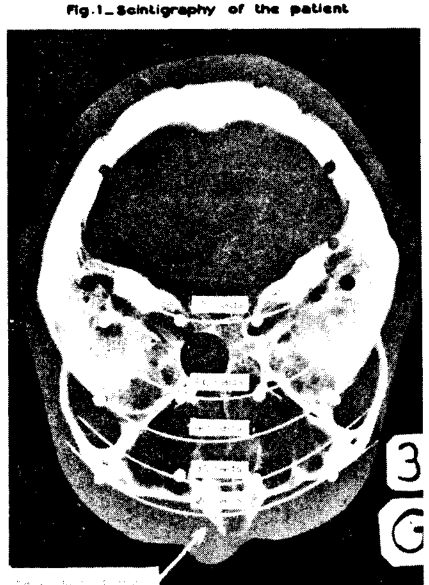
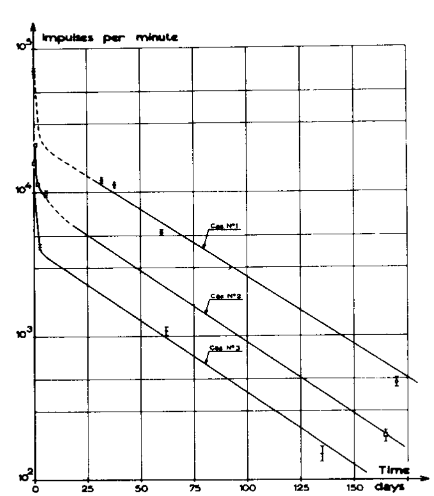


Fig. 5_Isodoses for a horizontal plane passing through the eyes of the patient



NOTE: The activity injected is identical in all three cases: 900 μCi

Fig. 6 _ Variation with time in the number of impulses measured in the skull

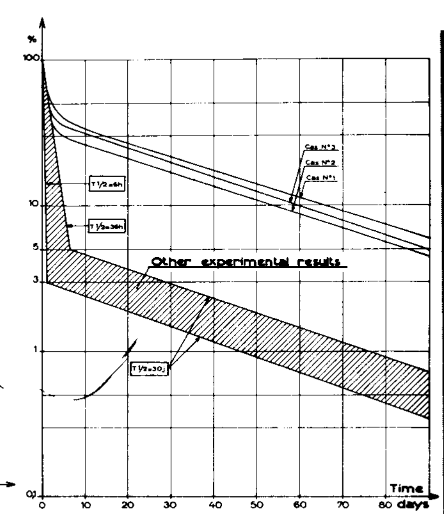
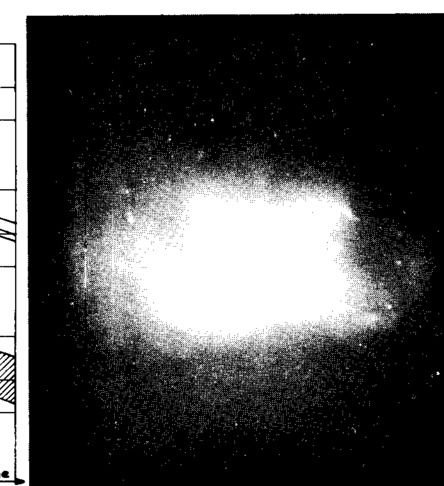


Fig. 7_ Change with time in the count rate of impulses measured on the skull by gamma camera



Autoradiograph of a frontal section of the brain

Fig. 8