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Dr. M. Evan Hersh, Department of Developmental Therapeutics, The University of Texas and Tumor Institute, Houston, Texas 77025/USA

Problems of Radiation Dosimetry in Endolymphatic Therapy with Radioactive Isotopes

P. Pfannenstiel, H. Weißleder, G. Hoffmann

Nuclear Medicine Unit and X-ray Department of the University Hospital for Internal Medicine Freiburg i. Br., West-Germany

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To date we have applied endolymphatic therapy using ^{131}I labelled oily contrast medium to 35 patients and using ^{32}P- ^{131}I labelled Lipiodol to 8 patients suffering from Hodgkin's disease and metastases involving the retroperitoneal lymphnodes (11). In 30 of these patients we investigated the course of the radioactive material in order to calculate the radiation doses absorbed by the lymphnodes and other tissues. Some of these results have been recently published (4, 5).

For daily external measurements of the ^{131}I-distribution following the administration of ^{131}I to the lymph channels of the dorsum of both feet the following method was applied:

The patient lies on a couch over which a 2 inch sodium-iodide scintillation – counter is moved horizontally at a distance of about 35 cm. The counter is shielded by a slit collimator so that it responds to the ^{131}I in the whole width of the body, but lengthwise to only the short section opposite the counter. A strip chart recorder draws a „profile" curve, indicating the ^{131}I distribution along the length of the body.

The topographic positions corresponding with the peaks on the profile curves were identified by rectilinear area scanning methods (Picker Magna Scanner III with photorecording system) as well as by radiological studies of the distribution of the contrast medium.

Fig. 1 shows the variations of ^{131}I in the region of the abdomen and thorax. These variations can be determined by planimetry of the individual sections of the curves, shown here by hatched areas. Similar methods for studying the body distribution of ^{131}I labelled oily contrast medium have also been described by *zum Winkel* et al. (12) and by *Heinzel* et al. (3).

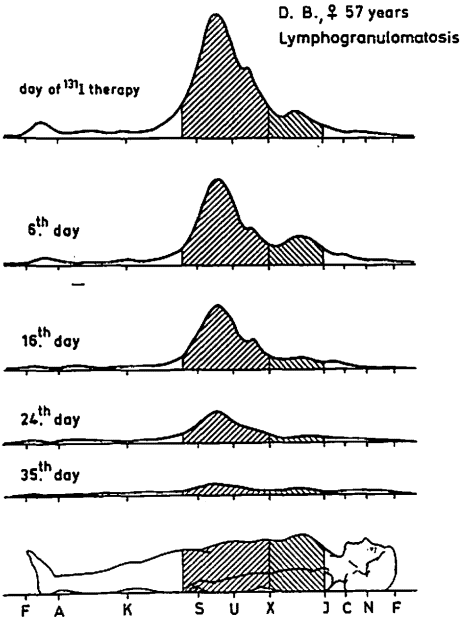

Fig. 1 ^{131}I-distribution as measured by a profile scanner on successive days demonstrating the different rates at which ^{131}I is discharged from the abdominal and the thoracic region in a case of Hodgkin's disease.

The radioactivity in the whole body and lungs, as well as in the pelvic and paraortal lymphnodes is measured at definite time intervals following ^{131}I administration. By plotting radioactivity against time a curve showing the ^{131}I retention in different parts of the body is obtained.

Fig. 2 shows an example of this, with high uptake of radioactivity in the retroperitoneal lymphnodes and only small amounts of radioactivity over the thoracic region due to overflow tf the ^{131}I labelled contrast medium from the thoracic duct to the lungs. Usually about 75% of the applied radioactivity is retained by the inguinal, iliac and retroperitoneal lymphnodes, and about 25% is found in the lungs.

As yet we have not observed ^{131}I reaching other organs, particularly the liver and spleen, in any significant quantity. The average peak of radioactivity in the peripheral

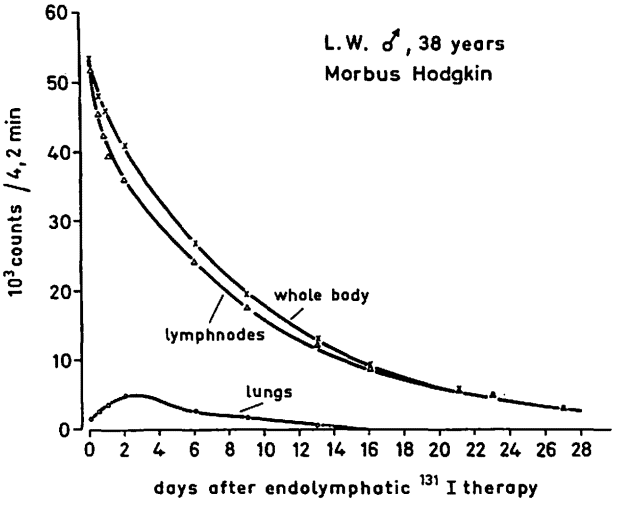

Fig. 2 ^{131}I-retention in the whole body, lungs, pelvic and paraortal lymphnodes in a patient with Hodgkin's disease measured over a period of 28 days by serial whole body profile scans.

blood was found to be 3–4 days after the endolymphatic administration of ^{131}I. This is due to a decomposition of ^{131}I labelled oily contrast medium, thus releasing free iodine into the circulation. If the thyroid gland is blocked with Lugol's solution (4 x 40 drops three days before until three days after ^{131}I therapy) any free iodine is quickly cleared by the kidneys. Radioactivity in the urine accounted for 3–5% of the administered dose over a period of one week.

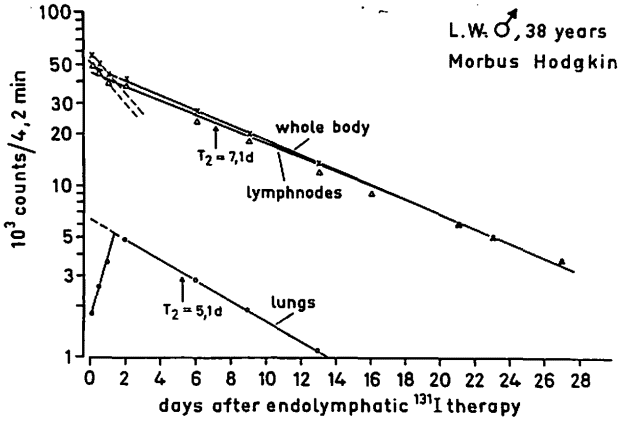

Fig. 3 Semilogarithmic plot of the data from Fig. 2. The effective half-life (T_2) of the ^{131}I can be seen on the time scale, to be 7.1 days for the lymphnodes and 5.1 days for the lungs (see text).

In Fig. 3 the measured radioactivity data are plotted in a semilogarithmic system against the appropriate dates. This gives a straight line, which, when extrapolated to zero time, gives the value of the initial average ^{131}I concentration in different parts of the body (2).

From this curve we derive the rate at which ^{131}I is discharged from certain parts of the body. The effective half life (T_2) of ^{131}I accumulated in the lymphnodes varies from 5.3 to 8 days with an average of 7.0 days as apposed to 0 to 6.4 (average 4.2) days in the lungs.

For dosimetry an average absorbed energy of 0.203 MeV for ^{131}I was assumed ($\overline{E}_{abs} = \overline{E}\beta + \overline{E}\gamma_{abs} = 0.187 + 0.016$). When ^{32}P was used together with ^{131}I an average absorbed energy of 0.685 MeV was assumed. The absorbed radiation is calculated by the formula:

$$D\beta + \gamma \text{ (rad)} = 73.8 \times \overline{E}_{abs} \times \frac{\mu Ci}{gm} \times T_2.$$

For dosage calculations we have attempted to assess the weights of the lymphnodes, as is demonstrated in Fig. 4. Given an ellipsoidal shaped lymphnode the depth can be considered to be the same as the breadth, and the length and the breadth are measured on the anterior-posterior x-ray. Using a focus-film distance of 110 cm and an average object film distance of 17 cm the volume of the lymphnode was given by this formula:

$$V = \frac{4}{3} \pi \times \frac{\text{length}}{2} \times \left(\frac{\text{breadth}}{2}\right)^2 \times \left(\frac{110-17}{110}\right)^3$$

$$V = 0.312 \times \text{length} \times (\text{breadth})^2$$

This method was proved by estimating the weight of the lymphnodes from their projections on the x-rays of lymphnodes of known weights. Thus the above formula

was shown to be reliable. The total weight of the retroperitoneal lymphnodes averages 20 gm. However, in patients suffering from chronic lymphatic leucaemia the weight is significantly higher, up to 300 gm.

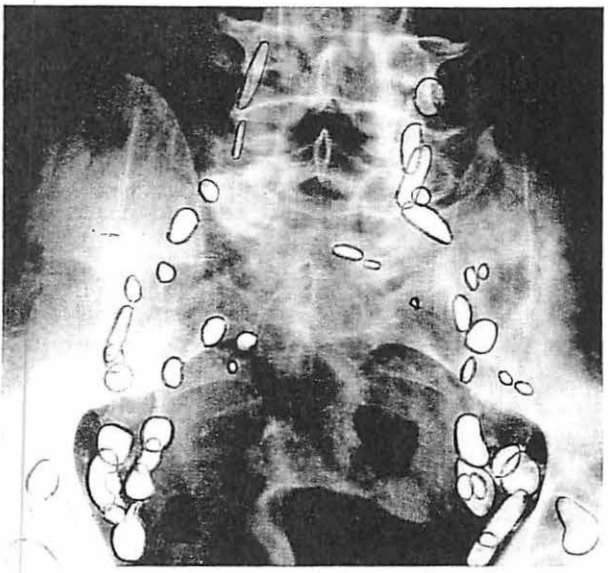

Fig. 4 In order to calculate the weight of the lymphnodes the length and breadth of each lymphnode as projected on the anterior-posterior x-ray is measured (formula see text).

Table 1 Endolymphatic ^{131}I-therapy.

Diagnosis	Case No.	adm. mCi ^{131}I	pelv. & paraortal lymph-nodes			lungs	(~ 1000 gm)
			weight (gm)	T_2 (days)	rad	T_2 (days)	rad
Morbus Hodgkin	1	45	5	5.3	288.000	5.1	3180
	2	46	16	8.0	273.000	5.2	1760
	3	48	16	7.2	183.000	3.3	1240
	4	13	6	6.0	57.000	3.5	510
	5	32	18	7.1	161.000	5.1	290
	6	40	19	7.5	183.000	3.4	160
	7	35	28	5.8	124.000	–	0
	8	40	19	8.0	202.000	4.8	360
Lymphnode metastases	9	34	17	6.3	155.000	5.2	1210
	10	40	70	6.3	49.000	4.2	690
	11	40	32	7.6	109.000	3.8	560
	12	39	13	6.8	209.000	5.0	800
	13	36	23	6.4	98.000	3.8	700
	14	34	16	7.0	192.000	5.9	500
	15	33	15	6.9	191.000	5.4	430
	16	39	19	7.3	166.000	3.8	310
	17	21	9	8.0	228.000	3.6	210
	18	14	14	8.0	771.000	5.2	200
	19	37	30	6.9	113.000	6.4	190
	20	17	3	6.3	353.000	5.4	100
	21	9	6	6.5	57.000	3.5	100
	22	37	7	8.0	496.000	–	0
	mean	33	18	7.0	180.000	4.2	600

In table 1 the measurement data and calculated radiation doses are summarized. The average ^{131}I dose administered amounted to 33 mCi. The absorbed radiation doses in the region of the pelvic and paraortal lymphnodes vary according to the ^{131}I distribution in the body, the effective half-life (T_2), and the calculated volume (gm) of the lymphnodes. They were found to range from 4900 to 771 000 rads. These doses are only approximate, as the calculations presume a homogenous distribution of the contrast medium in all the lymphnodes, and this is seldom the case, particularly when dealing with diseases of the lymphatic system.

However, a gross discrepancy between tissue assay techniques and external assessment of the ^{131}I-concentration in lymphnodes was observed. This may be partly due to different geometries, but more important to the assumption of a homogenous activity from external probes. Since the assumption of homogenous ^{131}I deposition is not valid, only gross assessments of the absorbed radiation doses can be made.

A minimal dose of 20 000 rads will reach the lymphnodes, even if half the amount of ^{131}I is administered. Such doses are more than sufficient to destroy lymphnode tissue and are greater than those given to lymphnode malignancies by percutaneous radiation therapy, even though a difference in dose-rate has to be considered when external and internal radiations are compared. One has to assume that a continuous ^{131}I-radiation with small dose rates is only half as effective as a fractionated external irradiation with a high dose rate.

The radiation doses after endolymphatic ^{131}I therapy as reported in the literature, range from 5000 to 70 000 rads (8, 6, 1, 12). However, we would like to point out, that we administered ^{131}I doses which were twice as high, and that our calculated lymphnode weights were on average 3 times below those stated in the literature. Also, to the best of our knowledge, no exact in vivo lymphnode weights are reported, except in a contribution by *Tilak* et al. (9).

The main complications encountered with endolymphatic ^{131}I therapy are pulmonary micro emboli. The radiation doses received by the lungs are listed in the last column of table 1. Here a standard lung weight of 1000 gm is assumed, as is an even distribution of ^{131}I within the lungs. The radiation hazards are significant in cases which exceed 1.500 rads.

Recently we have succeeded in improving the technique for the application of the radioactive oily contrast medium. The volume of the Lipiodol was reduced to about 3.5 ml, since we had found that satisfactory concentration of contrast medium can be produced even with this small amount in all retroperitoneal lymphnodes. As is shown in table 2, the radiation doses to the lungs are then reduced significantly.

The assumption of a homogenous ^{131}I-distribution in the chest may lead to grossly erroneous dosimetry calculations since the alveolar spaces do not contain as much radioactivity as the pericapillary cells in the lungs, and the degree of inhomogeneity depends only upon how microscopic or macroscopic one assesses the deposition of energy. Using ^{131}I there is no question that tissue absorption occurs on a microscopic level and, therefore, it may be erroneous to assess a whole region of the body, particularly an air containing structure such as the lung, as homogenous in isotopic content or meaningful energy deposition.

In all patients the radiation load to the peripheral blood was also determined from the ^{131}I-concentration in the blood, according to the method of *Seidlin* et al. (7). During an observation period of 6 weeks the blood radiation dose was always less than 1.5 rad. Apart from the lungs, no significant radiation doses are received by other tissues as a result of ^{131}I circulating in the blood. Due to the fact that the β-particles of ^{131}I will travel only 2.2 mm no significant radiation effects are to be observed outside the lymphnodes.

Table 2 Endolymphatic ^{32}P-^{131}I-therapy for lymphnode metastases (Standard dose: 4 mCi ^{32}P + 2 mCi ^{131}I).

Case No.	pelvic & paraortal lymphnodes		lungs (~ 1000 g)
	weight (gm)	rad	rad
1	53	45.350	—
2	17	495.000	—
3	9	284.600	—
4	5	147.500	120
5	14	144.300	420
6	37	74.500	—
7	28	110.200	720
8	13	433.200	790
Mean	~22	~216.800	~250

Because of the short penetration of the ^{131}I β-particles tri-n-octyl-ester of phosphoric acid labelled with ^{32}P was recently introduced as a radioactive substance for endolymphatic therapy (10). ^{32}P has an energy and range greater than ^{131}I. Thus it is possible, even with unequal distribution of the contrast medium, to produce high radiation doses concentrated in the lymphnodes of about 50.000 rads/mCi. We have been recently using ^{32}P labelled contrast medium in 15 patients. For doses of 4 mCi ^{32}P mixed with 2 mCi ^{131}I (for external distribution measurements) an average radiation dose of 200.000 rads was calculated (table 2).

Summary

Radiation dosimetry after endolymphatic therapy with ^{131}I and ^{32}P labelled oily contrast medium was performed in 30 patients. The total dose applied averaged 33 mCi ^{131}I and 4 mCi ^{32}P respectively. By measuring the changes in concentration of the radioactivity in different parts of the body with a specially equipped profile scanner during the first two or three weeks, the radiation doses were calculated approximately from the rate of decomposition of the radionuclide in the different parts of the body and from the volume of the tissue. Assuming homogenous distribution in the pelvic and paraortal lymphnodes, the dosage is massive, up to 700 000 rads. A rather high percentage of radioactive labelled contrast medium is received by the lungs and consequently high radiation doses may occur here. However, serious limitations have to be considered in the reported measurements due to the marked inhomogenity of dose distribution in lymphnodes and lungs.

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Dr. P. Pfannenstiel, Med. Univ. Klinik, 78 Freiburg im Breisgau, Hugstetter Str. 55

Instruments for Lymphography*

B. Damascelli, R. Musumeci, C. Uslenghi

Istituto di Radiologia della Universitá di Milano/Italy

Lymphology 2 (1969) 166–169

Lymphography is a well known and widely used radiologic investigation, devised by *Kinmonth* (3) in 1952. Several investigators have suggested modifications of the original method, to render the execution easier (1, 2, 4, 5, 6, 7, 8, 9, 10).

Our experience covers 1500 lymphographies, since September 1961. We have considered many of the technical innovations proposed by other workers but finally we found that we had to design new instruments in order to greatly reduce the difficulties of exposing and cannulating lymph vessels.

Fig. 1 shows the special clamp, forceps and needles that we currently use for lymphography. Clamp (a) is used for holding the isolated lymph vessel, separated from its tunica adventitia with the aid of the special forceps (b). Details (c, d, e and f) illustrate how the tips of the forceps and clamp are made. The clamp has a groove running along the two jaws; the inside of the upper jaw has small teeth that grip the lymph vessel. The cone-shaped tip of the forceps (b) also has a groove to admit the vessel and at the end of the groove there is a cylindrical chamber to collect the adventitial

* The instruments are made by Messrs Mayo-Milano, Italy.