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A Study of Extra-Thyroidal Neck Radioactivity Using a Radioisotope Scanner[1]

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The activity of radioiodide in the neck viewed by a standard uptake counter is distributed in thyroidal and extra-thyroidal regions. In investigations of thyroid gland uptake soon after radioiodide administration, correction has to be made for the extra-thyroidal activity. This factor is of little importance if the gland uptake is high. If, however, the gland uptake is low, an accurate correction may be essential. Various workers have made different assumptions with regard to this extra-thyroidal activity. Myant, Corbett, Honour and Pochin (1) and Goolden and Mallard (2) have corrected for extra-thyroidal activity by monitoring the uptake over the thigh. Berson *et al* (3) have assumed that at 2 min after the injection of ^{131}I, all the activity in the neck is extrathyroidal and at subsequent times the extrathyroidal activity is a constant fraction of total body radioiodide not in the thyroid or excreted by the kidneys. Koutras and Sfontouris (4) considered that the activity in the neck at 2 min was entirely extra-thyroidal but that this activity decreased in a similar manner to blood activity.

A radioisotope scanner produces a map related to the isotope distribution within the scanned region. The number of counts recorded by the scanner, which is related to the number of dots on the map, due to thyroid gland uptake, may be separated from those due to extra-thyroidal activity distributed in the volume of the neck viewed by a standard uptake counter. The number of dots from each of these components can be expressed as a fraction of the number in a similar scan of an aliquot of the isotope dose placed in a thyroid phantom. The aim of the present study was to measure the contribution from this extra-thyroidal activity to the counts recorded by the scanner and to compare the value for neck activity as measured by the scanner with that as measured by a standard uptake counter. The results have been analyzed, taking into consideration the calculated errors in the method.

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METHODS

Fifty μCi of ^{131}I was injected intravenously into each of 15 patients. An area 16 cms × 16 cms, from below the sternal notch to the chin, was scanned starting one minute later. The scanner used was a Picker Magnascanner V with a 5″ NaI (Th) crystal. A 5″ broad focus collimator was used and by scanning at 100 cm/sec and using a wide line spacing (0.85 cm), the scan was completed in about four minutes. With nine of the patients, an I.A.E.A. collimated scintillation counter with crystal size 1¾″ dia × 2″ (5) was placed at 8.5 cm from the neck and a 40 sec count taken after each scan. Scanning was continued until 40 min after the injection of ^{131}I, producing 4 to 6 scans for each patient. After scanning the patient, a thyroid phantom (similar to the standard I.A.E.A. phantom (6) but filled with water) containing an aliquot of the injection solution was scanned under the same conditions as for the patient. This phantom was also counted with the I.A.E.A. collimated scintillation counter. Blood samples were taken from the patient during the scanning procedure. These samples were separated and the plasma ^{131}I measured in a NaI (Th) well scintillation counter. Both the pulse height analyzers of the scanner and the uptake counter were set to detect pulses equivalent to the energy range 310-410 keV.

In order to study the background activity in the thyroid region, one patient who had a total thyroidectomy and had received an ablation dose of ^{131}I, was investigated. It was assumed that all the dots in the scanned area were due to extrathyroidal activity. To reduce counting errors, 500 μCi of ^{131}I was administered.

CALCULATION

As the I.A.E.A. collimator was placed at 8.5 cm from the neck, the average sensitive volume viewed by the I.A.E.A. collimator was approximately equal to the volume represented by a 15.8 cm circle drawn on the scans. (At 15.0 cm from the end of our collimator, the cross sectional diameter of the volume of maximum optical sensitivity is 15.8 cm.) A circle of this diameter was drawn on each scan, with the centre of the circle corresponding to the centre of the volume viewed by the I.A.E.A. collimator. The dots in this circle were counted and after subtracting the dots due to the room background, were compared with the number of dots from the thyroid phantom. In this way, the dots in the 15.8 cm circle were expressed as a percentage of the dose given (Us%). A circle, usually 4 cm radius and with centre midway between the lines of dots on the scan, was drawn covering an area including the thyroid gland (usually easily distinguished by the increased uptake). A semi-circle of equal radius was drawn below the thyroid circle with centre near the sternal notch and mid way between the lines, the circumference touching that of the circle round the thyroid gland. Twice the number of dots in this semi-circle was taken as the background dots in the circle containing the thyroid gland. The background calculated in this way was subtracted from the dots in the circle and the remainder expressed as a percentage of the dose given (T%). The counts from the neck detected by the counter with the I.A.E.A. collimator were also expressed as a percentage of the dose given, (Uc%). T% was taken as representing the absolute uptake of ^{131}I in the thyroid gland. Us and Uc are the apparent uptakes of ^{131}I in the neck measured by the scanner and the uptake counter, respectively. Therefore, the contribution from the extra-thyroidal neck activity (E.T.A.) in the sensitive volume viewed by the I.A.E.A. collimator measured by the scanner was (Us − T)%. This contribution from extra-thyroidal neck activity was expressed as a percentage of total body extra-thyroidal activity neglecting urinary excretion, that is,

$$ETA' = \frac{(Us - T)}{100 - T} \times 100\%$$

ERRORS

(1) *Random errors*

Random errors are likely to cause the measured values of a given parameter at a given time, after injection on the same patient, to be normally distributed about a mean value. The main sources of such errors in our study are (a) statistical variation in the source count rate, (b) counting of dots, (c) repositioning of patients and (d) injection calibration.

(a) Statistical variation in the source count rate

If we observe N dots on a scan, the standard deviation of the number of dots is $\sqrt{N/F}$ where F is the dot factor, i.e. the number of counts per dot.

(b) Counting of dots

The dot factor was minimized to give the best visual picture in order to easily distinguish the thyroid gland. A dot was counted if its mid-point appeared to be within the circle. In our estimation the error in counting a large number of dots using this procedure is unlikely to result in a standard deviation of greater than 1% of the dots counted.

(c) Repositioning of Patients

Great care was taken to reposition the counters accurately and to minimize movement of the patient during scanning. It is to be noted that the scanner is a good deal less sensitive to variations in distance than the I.A.E.A. collimated scintillation counter. Allowing a reproducibility in distance of better than ± 0.75 cm, this would result in measurements made by the I.A.E.A. collimator having a standard deviation of about 2% and those made by the scanner having a standard deviation of about 1%.

(d) Injection Calibration

Inaccuracies in estimating the injected volumes resulted in the standards being in error by about 2% (S.D.).

(2) Systematic errors

Systematic errors cause the observed values of a parameter at a given time on the same patient to be in constant error to the true value. Sources of such errors in our study are (a) estimation of background, (b) duration of scan, (c) depth of thyroid and (d) estimation of the sensitive volume viewed by I.A.E.A. uptake collimator.

(a) Estimation of background

(1) The number of dots corresponding to room background were subtracted from the number of dots in the 15.8 cm diameter circle. Activity outside the scanned volume was found to give a negligible contribution to the number of dots.

(2) To estimate the number of dots in the circle round the thyroid gland which are not due to gland uptake, the number of dots in the semi-circle below the thyroid gland were doubled. It is possible that the activity in the background region differs and varies differently from the background in the thyroid region. For two patients (11 and 12) with no thyroid uptake the mean difference between the true background in the thyroid circle and the estimated background in the semi-circle was nearly zero. The standard deviation of this mean was about 10% of the number of dots derived from the semi-circle below the thyroid which are not due to room background.

e.g. Estimated background = 3.5% dose (=2xbgd in semi-circle)

Room background contribution = 1%

∴ standard deviation = 0.25% dose

∴ true background over thyroid has 95% chance of being in range $3.5\% \pm 2 \times 0.25\%$

(b) Duration of scan

The mid point of the thyroid was made, if possible, the mid point of the scan. We assumed that the observed values of Us, ETA and ETA′, which are the average values over the period of measurement, are the values at the mid point of the scans. This is true if these parameters vary linearly with time throughout the experiment, which may not always be the case. By inspection of some rapidly varying plasma and neck activity curves, we estimate that due to this assumption, the measured values of ETA′ are likely to have errors, which vary with time after injection, in the range ± 2%.

(c) Depth of Thyroid

The thyroid gland may vary from very close to the neck surface to 7 cm in depth below the neck surface with a mean depth of about 3 cm (7). The depth of the centre of our thyroid phantom from the surface was 2 cm. For a given patient the correction factors which would have to be applied to allow for thyroid depth for the scanner and I.A.E.A. collimated counter are likely to be different. The magnitude of the correction factor for the scanner affects the significance of the statement that T% is a good estimate of the absolute thyroid uptake of ^{131}I. Variations in the thyroid depth and distribution of extra-thyroidal activity affect the correlation of Us and Uc.

(d) Estimation of the sensitive volume viewed by the I.A.E.A. Collimator

In our study we have taken a circle of 15.8 cm diameter on the scan to represent the average sensitive volume viewed by the collimated counter. The difference between Us and Uc depends on the diameter of the circle drawn on the scan to represent the volume viewed by the I.A.E.A. collimated counter. We show here the values of Us obtained by taking 15.8 cm and 15 cm diameter circles on the scans from one of the patients with no uptake.

For a 15.8 cm diam. circle, Us (=ETA) = 6.55% dose
For a 15.0 cm diam. circle, Us (=ETA) = 5.75% dose.

15.8 cm is approximately the cross sectional diameter, at mid neck depth, of the sensitive volume of our collimator 8.5 cm distant from the surface of a uniform cylindrical neck of diameter 13.0 cm 15.0 cm is the cross section of the comparable volume at the mid depth of a uniform cylindrical neck of 8 cm diameter.

TABLE I

APPARENT NECK ACTIVITY (% DOSE) AS MEASURED BY THE SCANNER (US) AND THE I.A.E.A. COLLIMATED SCINTILLATION COUNTER (UC) AT 7 MIN AND 24 MIN AFTER INJECTION

Patient	*Time 7 mins*			*Time 24 mins*		
	Us	*Uc*	*Diff. ± S.D. as % dose*	*Us*	*Uc*	*Diff. ± S.D. as % dose*
1	7.2	7.3	0.1 ± 0.55	6.5	7.3	0.8 ± 0.55
2	13.0	13.0	0 ± 0.7	17.6	17.6	0 ± 0.8
3	13.4	14.2	0.8 ± 0.7	23.6	22.8	0.8 ± 0.9
4	22.3	22.3	0 ± 0.9	40.4	38.8	1.6 ± 1.5
5	13.2	16.0	2.8 ± 0.75	23.7	25.0	1.3 ± 0.95
6	8.0	8.5	0.5 ± 0.55	11.2	11.5	0.3 ± 0.65
7	11.8	11.8	0 ± 0.65	22.4	21.3	1.1 ± 0.9
8	5.1	5.1	0 ± 0.55	5.1	5.1	0 ± 0.55
9	6.3	6.4	0.1 ± 0.55	7.0	7.4	0.4 ± 0.55

TABLE II

CONTRIBUTIONS FROM EXTRA-THYROIDAL ACTIVITY (ETA AND ETA′) AT VARIOUS TIMES AFTER INJECTION

	Scan 1			*Scan 2*			*Scan 3*			*Scan 4*			*Scan 5*			*Scan 6*			*Max. diff. ± S.D. in ETA′ observed between any 2 scans*
Patient	*Time min*	*ETA*	*ETA′*	*Time min*	*ETA*	*ETA′*	*Time min*	*ETA*	*ETA′*	*Time min*	*ETA*	*ETA′*	*Time min*	*ETA*	*ETA′*	*Time min*	*ETA*	*ETA′*	
1	2.5	7.0	7.05	8.3	6.95	6.95	14.5	4.85	4.95	22	6.4	6.4	29.7	5.75	5.8	40	4.15	4.25	−2.8 ± 1.15
2	4	7.3	7.65	11.5	5.4	5.95	18.5	6.6	7.4	25.5	5.7	6.45	33.5	6.8	7.6				−1.7 ± 1.15
3	4	8.05	8.35	12	5.45	6.15	21	6.6	7.75	28	5.2	6.6							−2.2 ± 1.15
4	4	8.0	9.0	9	6.2	7.75	15	6.4	8.9	22	7.1	10.4							+2.65 ± 1.7
5	4	6.95	7.2	10	5.45	6.05	18	5.95	7.05	26	6.0	7.3							+1.25 ± 1.1
6	4	5.2	5.3	11	4.7	4.9	18	4.6	4.85	24	4.65	4.95	31.5	4.95	5.35				+0.5 ± 1.0
7	3.6	3.75	3.95	10.6	3.9	4.35	18.5	4.7	5.55	25.6	3.8	4.7	33.7	4.9	6.25				+2.3 ± 1.0
8	3	5.35	5.35	9	3.4	4	15	3.55	3.55	21	3.6	3.65	27	4.25	4.3	34	3.35	3.35	−2.0 ± 1.0
9	2.5	5.6	5.6	8	5.8	5.85	15	4.55	4.65	20	4.55	4.7	26	4.2	4.3	33	4.45	4.6	−1.55 ± 1.0
10	3.5	7.3	7.3	9.3	7.3	7.3	18	6.6	6.6	24.5	7.6	7.65	32.5	6.0	6.05				−1.6 ± 1.15
11	3.2	7.2	7.2	9	6	6	15.9	5.85	5.85	21.3	5.3	5.3	29.2	5.35	5.35	35.5	5.1	5.1	−2.1 ± 1.0
12	3.5	6.55	6.55	12.8	5.4	5.4	20.3	5.25	5.25	28	4.9	4.9	36	4.6	4.6	41.5	4.5	4.5	−2.05 ± 0.15
13	9.4	9.55	9.7	15	9.05	9.15	29	7.9	8.1	35	8.3	8.4	41	8.55	8.7	47.5	9.3	9.55	−1.6 ± 1.15
14	3	6.25	6.3	9	4.85	4.9	15	3.45	3.5	21	4.1	4.15	27	6.9	7.1	33	4.7	4.9	+3.6 ± 1.0
15	4	7.65	7.75	9	7.4	7.7	15	7.65	8.0	26	7.65	8.2	32	5.85	6.35				−1.85 ± 1.05
16	3	10.2	10.6	9	10.3	11.0	14	8.15	8.65	20.2	7.3	8.05	25	10.2	11.4	29	6.4	7.2	−4.2 ± 1.15

TABLE III

PERCENTAGE DIFFERENCES IN MEAN ETA, ETA′, PLASMA ACTIVITY AND CORRECTED PLASMA ACTIVITY (FIGS. 1, 2, 3 AND 4) BETWEEN 3, 10, 20 AND 30 MIN. AFTER INJECTION

ETA			*ETA′*			*PLASMA ACTIVITY*			*CORRECTED PLASMA ACTIVITY*		
Time min.	*Mean*	*% of value at 3 min.*	*Time min.*	*Mean*	*% of value at 3 min.*	*Time min.*	*Mean*	*% of value at 3 min.*	*Time min.*	*Mean*	*% of value at 3 min.*
3	7.05	100	3	6.95	100	3	.0127	100	3	.0128	100
10	6.36	90	10	6.50	94	10	.0088	69	10	.0094	74
20	5.71	81	20	6.0	86	20	.0064	50	20	.0068	53
30	5.42	77	30	5.62	81	30	.0063	50	30	.0064	50

The errors taken into account for Uc are those from the statistical variation of the source count rate and repositioning errors. The errors taken into account for Us are (a), (b) and (c) of 'Random Errors' and (b) of 'Systematic Errors.' The errors taken into account for ETA′ are (a), (b) and (c) of 'Random Errors' and (a2) and (b) of 'Systematic Errors'. They are combined thus:

$$\text{Total Error} = \sqrt{E_1^2 + E_2^2 + E_3^2 - - -}$$

These total errors were used only when comparisons of Us and Uc were made for each patient (Table I) and when the variation of ETA′ with time for each patient was examined (Table II).

RESULTS

In Table I the counts due to the neck activity of ^{131}I for each patient as recorded by the scanner (Us) and the I.A.E.A. collimated scintillation counter (Uc) at 7 and 24 min after the injection are tabulated. These values are derived from the best fit curves drawn through all the data from each patient. The difference between Us and Uc and one standard deviation of this difference is given. The results show that there was a significant difference between Us and Uc (that is a difference greater than three standard deviations) for only one patient. The standard deviations quoted are probably overestimated since they refer to single observations rather than values from a mean curve.

In Table II the observed values of ETA and ETA′ at various times after injection are tabulated. The maximum difference in ETA′ between any two measurements, and one standard deviation of this difference are shown. If ETA′ is decreasing with time, then differences have a negative sign. The time variation of ETA and ETA′ for most of the patient was less than the possible error in our method. To investigate this time variation all the measurements of ETA and ETA′ were plotted against time after injection (Figs. 1 and 2).

The variations with time of plasma activity and plasma activity expressed as a percentage of total extra-thyroidal body activity of ^{131}I are shown in Figs. 3 and 4, respectively. The best fit line was drawn to these four figures by finding the second order polynomial with the least sum of squares to the points. This calculation was done using a Sirius computer. It was found that increasing the order of the polynomial did not change significantly the best fit line. The ETA and ETA′ decreased with time, but not as much as the comparable blood activities. (The accuracy of the best fit curves in Figs. 3 and 4 is less after 15 min due to the few estimations of plasma activity at those later times).

The values of ETA and plasma activity for the patient, who was given 500 μCi ^{131}I, are plotted against time in Fig. 5. As this patient had no thyroid uptake, ETA equals ETA′ and plasma activity equals corrected plasma activity. The value of ETA decreased with time but not as much as the plasma activity.

The results are summarized in Table III. The mean values and percentage decreases of ETA, ETA′, plasma activity and corrected plasma activity at various times are tabulated.

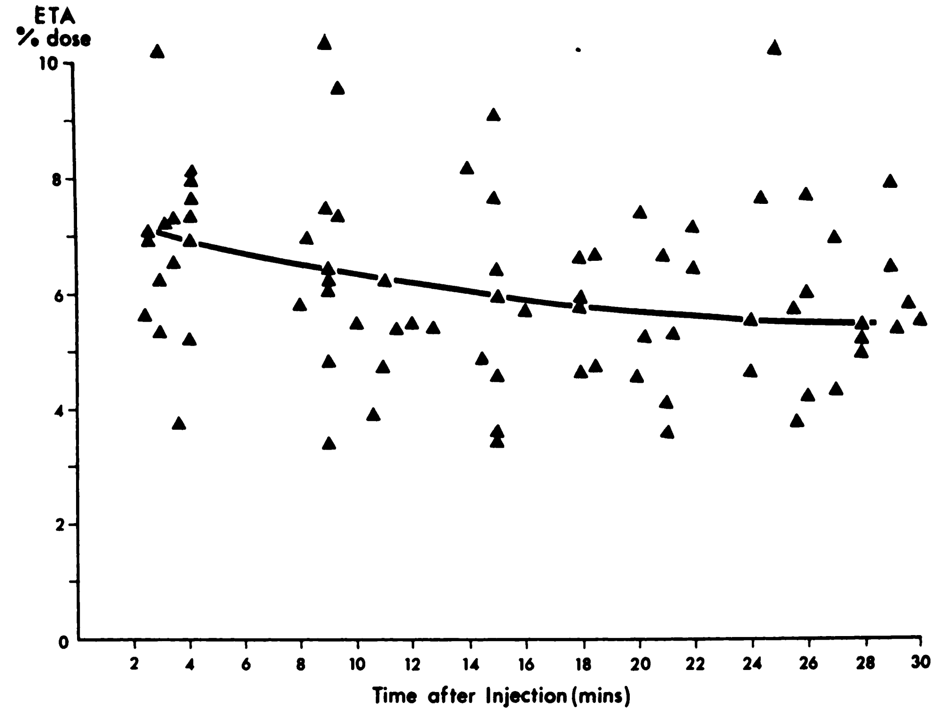

Fig. 1. Relation between the contribution from extra-thyroidal neck activity (ETA) and time after administration of the radioisotope in 16 patients.

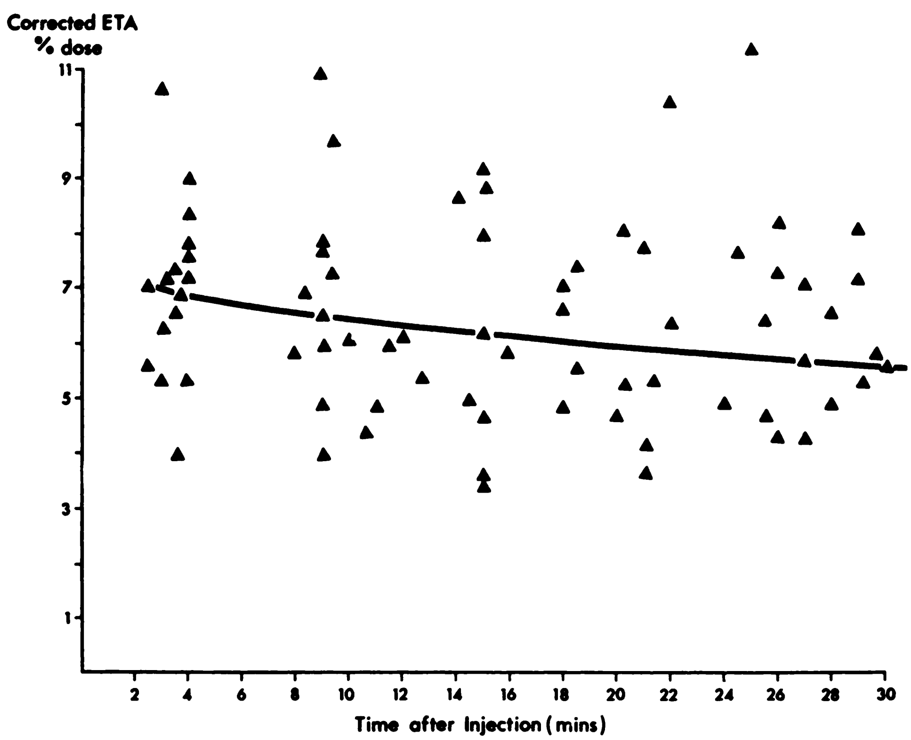

Fig. 2. Relation between the contribution from extra-thyroidal neck activity (as % dose not in thyroid) ETA′—and time after administration of the radioisotope in 16 patients.

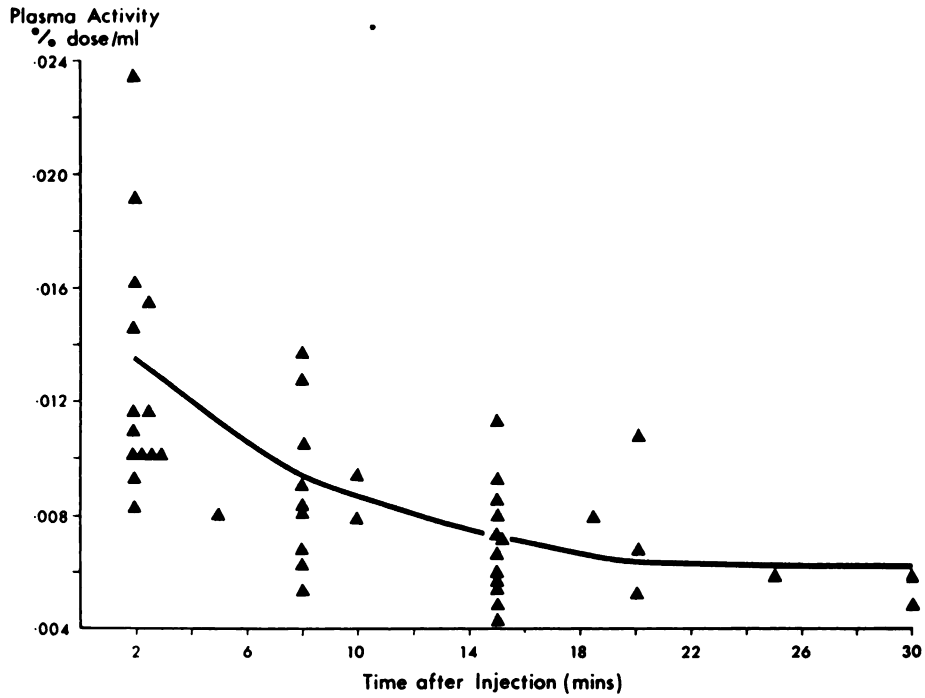

Fig. 3. Relation between plasma activity (% dose/ml) and time after administration of the radioisotope in 16 patients.

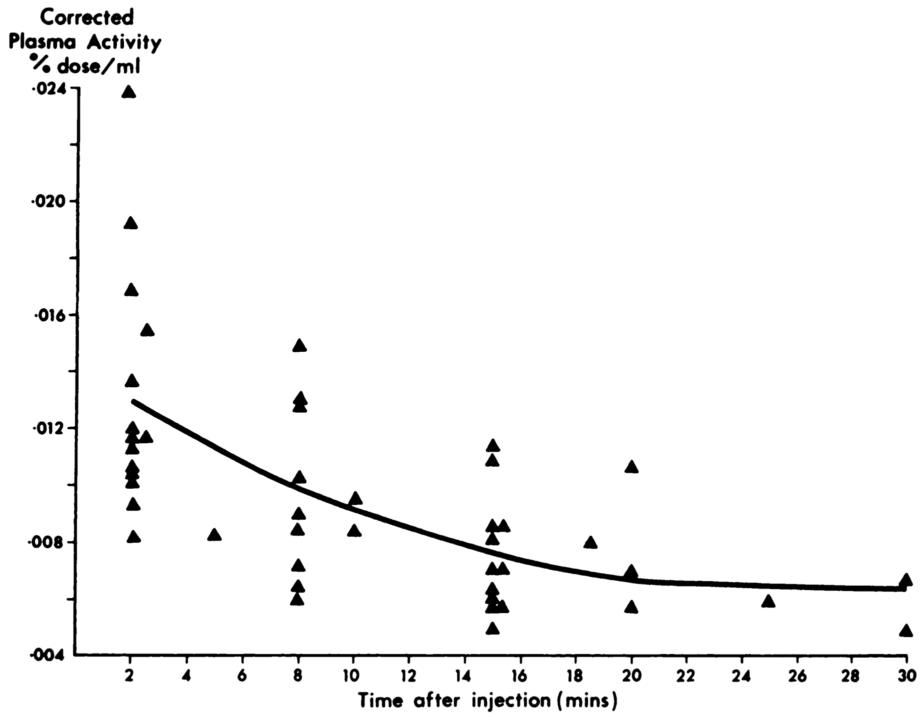

Fig. 4. Relation between plasma activity (% dose not in thyroid/ml) and time after administration of the radioisotope in 16 patients.

DISCUSSION

Comparison of the apparent neck uptakes of ^{131}I as measured by the scanner (Us) and collimated scintillation counter (Uc)

The collimator of the scanner has a different spatial response to a point source compared to the I.A.E.A. uptake collimator. Therefore, when we distribute a given amount of radioisotope in various ways throughout a given volume, the variations in counting efficiency for the scanner and I.A.E.A. collimated counter are different. One cannot state, therefore, that Us and Uc are the absolute percentage doses of ^{131}I in the sensitive volume viewed by the I.A.E.A. collimated counter and also that ETA is the absolute extra-thyroidal activity. We have shown, however, that there is no significant difference between the values obtained for Us and Uc throughout the period of measurement. Both, when the uptake is low (when most of the activity is extra-thyroidal) and when the uptake is high (when the ^{131}I is mainly concentrated in the thyroid gland) Us and Uc are not significantly different. The factor (Us − T)% is probably, therefore, a good estimate of the contribution of extra-thyroidal neck activity to the apparent neck activity measured by the I.A.E.A. collimated scintillation counter.

The variation of ETA and ETA′ with time

Figure 1 shows that ETA falls off with time. From the line of best fit, it can be calculated that by 30 min, the ETA has fallen to 77% of its value at 3 min (Table III). If ETA is expressed as a percentage of extra-thyroidal activity in the body (Fig. 2) this ETA′ falls after 30 min to 81% of its value at 3 min. In the same time interval, the ^{131}I activity in the plasma falls on average to 50% of its 3 min value (Table III, Fig. 3).

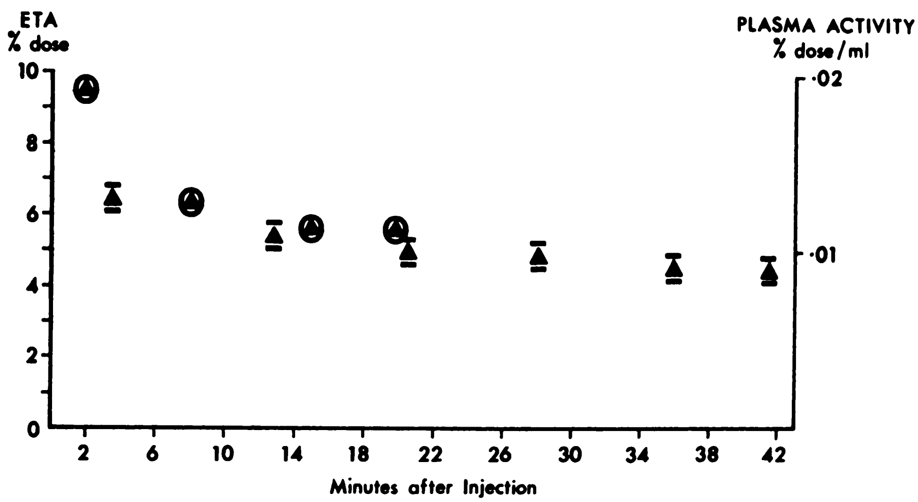

Fig. 5. Relation for one patient between ETA (% dose) and plasma activity (% dose/ml) and time after administration of 500 μCi ^{131}I.
ETA: triangles between parallel lines.
Plasma Activity: triangles in circles.

The body extra-thyroidal activity is calculated as the dose given less the thyroid uptake. More accurately, the body extra-thyroidal activity is the dose given less the thyroid uptake and renal excretion. The excretion of iodide by the kidneys rarely exceeds 10% of the dose given by 30 min, and is more commonly about 5% of the given dose. This will, therefore, not greatly affect our measurements of ETA′.

The ETA and ETA′, both fall with time, after administration of the radioisotope. The extra-thyroidal activity, however, does not decrease as rapidly as the plasma activity. Nor, does it appear to remain a constant fraction of the body extra-thyroidal activity. The decrease of ETA and ETA′ with time would appear to be somewhere between these two extremes. Although, the mean fall in ETA and ETA′ have been calculated, there is a scatter of values and to accurately measure gland uptake soon after injection in the individual case, it is necessary to use a scanner.

We have already shown (8) the clinical importance of correction for extra-thyroidal activity in the measurement of early thyroid clearance. In this investigation we found that the clearance calculated between 2 and 20 min could vary by 40%, depending on how the extra-thyroidal activity was calculated. We consider that the results of our study of extra-thyroidal activity (Table III) provide a basis for those using an I.A.E.A. collimated detector to measure the early uptake and clearance of radioiodide.

SUMMARY

The contribution of the extra-thyroidal ^{131}I neck activity to the counts recorded by a scanner has been measured, and the apparent neck activity measured by the scanner compared to that measured by an I.A.E.A. collimated uptake counter. The results have been analyzed taking into consideration the calculated errors in the method. No significant difference was found between the neck activity as measured by the scanner and as measured by the uptake counter. The contribution from extra-thyroidal activity falls with time after injection. The value at 30 min was 77% of the 3 min value. This decrease was less than the comparable fall in plasma activity. These results provide a basis for measurement of early uptake and clearance of ^{131}I using an I.A.E.A. collimated detector.

GLOSSARY

Uc. . . . . Neck uptake of ^{131}I as measured by the I.A.E.A. collimated scintillation counter expressed as a percentage of the dose given.

Us. . . . . .Number of dots within the 15.8 cm diam circle on the scan expressed as a percentage of the dose given.

T. . . . . Number of dots on the scan due to thyroid uptake expressed as a percentage of the dose given.

E.T.A. . . . . . (=Us−T) The dots on the scan within the 15.8 cm circle due to the extra-thyroidal activity.

E.T.A.′. . . . . $\left(= \frac{\text{ETA} \times 100}{100 - \text{T}}\right)$ The dots on the scan due to extra-thyroidal activity expressed as a percentage of the dose in the body but not in thyroid.

Corrected Plasma Activity. Plasma activity as % injected dose multiplied by $\left(\frac{100}{100 - \text{T}}\right)$

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