Dosimetry Study in Patients with Autonomous Thyroid Nodule Who Are Candidates for Radioiodine Therapy

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A dosimetry study was performed on 26 patients with an autonomous thyroid nodule and suppressed serum thyroid-stimulating hormone, to determine the dose to extranodular tissue when the nodule receives 300 Gy for ^{131}I therapy. **Methods:** Parameters of radioiodine turnover to be used in the dosimetry formula were separately obtained for the nodule and the contralateral lobe, as a measurable example of the extranodular tissue, using 55 MBq ^{123}I and a computer-assisted gamma camera. The biologic half-life of ^{123}I was then converted into the effective half-life of ^{131}I, and the volumes of the nodule and the lobe were obtained by scintigraphy or sonography. **Results:** The mean dose to the contralateral lobe from uptake and irradiation by the nodule was calculated to be 32 Gy, and that to the ipsilateral lobe was estimated to be 34 Gy. **Conclusion:** During radioiodine therapy for autonomous thyroid nodules, the extranodular tissue receives a higher dose than is generally assumed, which explains the relatively high rate of post-treatment hypothyroidism reported in the literature.

Key Words: autonomous thyroid nodule; radioiodine treatment; dosimetry study

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Radioiodine treatment of autonomous thyroid nodules (ATNs) has been used for more than 50 y. The results in eliminating nodule hyperfunctioning have been generally good (*1–20*). Post-treatment hypothyroidism was initially considered negligible because of the suppression of iodine uptake by extranodular tissue as a consequence of thyroid-stimulating hormone (TSH) inhibition by elevated circulating thyroid hormones. The publication in 1983 of an article by Goldstein and Hart (*4*) reporting a 40% prevalence of hypothyroidism after radioiodine treatment of ATN was therefore a surprise. After this report, many groups reviewed their data and reported consistently lower rates of hypothyroidism (*5–8,21*). However, the data of Goldstein and Hart did not remain isolated, and many articles since have reported an elevated prevalence of hypothyroidism (*10–15,20*). Very few studies have investigated extranodular tissue dosimetry during radioiodine treatment of ATN (*2,17,22*). Reported here is such a study performed on 26 patients with ATN. The results explain the different hypothyroidism rates described in the literature after radioiodine treatment of ATN.

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MATERIALS AND METHODS

Twenty-six patients with ATN were studied. Seventeen had elevated concentrations of free thyroxine (FT4) or free triiodothyronine (FT3) in serum (toxic patients), and 9 had free-circulating thyroid hormone levels within the normal range (nontoxic patients); serum TSH concentrations were below the normal range in all patients (Table 1). After the initial finding of a palpable thyroid nodule associated with clinical signs of hyperthyroidism of varying severity as well as variously elevated circulating thyroid hormone and subnormal TSH levels, the patients underwent a pertechnetate scintigraphy and uptake study showing radionuclide concentration to be almost completely limited (more than 90% of thyroid uptake) to the nodule; only on overexposed images was faint uptake by the extranodular tissue visible. The patients were then examined with ^{123}I to confirm that the nodules were really hyperfunctioning and not of the trapping-only type (*23*) and to collect data for dosimetry calculations if the patients and the referring endocrinologists eventually chose radioiodine as the method of definitive ablation. ^{123}I (55 MBq) was injected intravenously; the activity of the syringe was measured before and after injection in a Perspex (Imperial Chemical Industries PLC, London, UK) neck phantom under a gamma camera equipped with a low-energy, general-purpose, parallel-hole collimator. The neck of each patient was imaged for 5 min at 1, 24, 48 and 72 h after injection. Regions of interest for uptake measurements were drawn separately on the nodule and the contralateral lobe. For lobe visualization the images were overexposed, and in most patients, a faint image of the lobe was seen, especially at 24 h, when the counting rate was still high and the background was already greatly reduced (Fig. 1). In the few patients in whom the lobe was not clearly visible, the region of interest was drawn over its presumed anatomic region. The calculation of the dose to extranodular tissue was primarily made on the contralateral lobe because the normal tissue adjacent to the nodule could not be easily separated from it, and measurements of uptake and volume could not be made. A region of interest for background subtraction was drawn on the path of the subclavian

TABLE 1
Demographic and Hormone Data and Final Treatment of 26 Patients with Autonomous Thyroid Nodule

Patient no.	Age (y)	Sex	Serum FT4* (pmol/L)	Serum FT3* (pmol/L)	Serum TSH* (mU/L)	Hormone status	Final treatment
1	45	F	19.3	6.9	0.01	NT	Ethanol
2	61	F	32.7	12.3	0.02	T	Surgery
3	52	F	43.7	18.6	0.02	T	Ethanol
4	40	F	31.7	8.0	0.10	T	Ethanol
5	53	F	33.5	16.8	0.01	T	Unknown
6	45	M	25.7	17.0	0.10	T	Surgery
7	67	F	19.0	10.7	0.04	T	Ethanol
8	62	F	16.5	7.0	0.01	NT	Ethanol
9	22	F	16.3	6.2	0.10	NT	Ethanol
10	57	F	22.9	12.2	0.01	T	Radioiodine
11	65	M	31.7	10.9	0.10	T	Ethanol
12	69	F	17.9	6.9	0.10	NT	None
13	48	M	50.0	15.6	0.07	T	Ethanol
14	80	F	34.2	16.4	0.01	T	Methimazole
15	53	F	50.0	17.5	0.07	T	Ethanol
16	66	F	21.1	7.6	0.03	T	Methimazole
17	63	M	22.0	9.2	0.07	T	Radioiodine
18	67	M	15.0	5.2	0.22	NT	Radioiodine
19	43	M	11.6	6.5	0.10	NT	Radioiodine
20	57	F	15.1	4.5	0.06	NT	Radioiodine
21	39	M	14.9	10.6	0.01	T	Radioiodine
22	66	F	16.2	4.5	0.07	NT	Radioiodine
23	67	F	25.9	6.0	0.07	T	Radioiodine
24	55	F	19.4	8.4	0.01	T	Radioiodine
25	60	M	14.4	7.4	0.03	NT	Radioiodine
26	55	M	28.3	13.9	0.01	T	Radioiodine
Mean	56		25.0	10.3	0.06		
SD	12		10.8	4.5	0.05		

*Normal ranges: 7.7–19.3 pmol/L for FT4; 4.0–8.6 pmol/L for FT3; 0.4–4.5 mU/L for TSH.
FT4 = free thyroxine; FT3 = free tri-iodothyronine; TSH = thyroid-stimulating hormone; NT = nontoxic; T = toxic.

vessels. Nodule and lobe volumes were calculated with the formula for the ellipsoids ($\pi/6 \times a \times b^2$, where a is the longest axis and b is the shortest axis), measuring the axes on scintigraphic images (*5,13,16*). When the lobe was not clearly visible on overexposed images, the measurements were made using sonography. A single gamma camera image was acquired at each time interval; the data were processed three times to obtain mean values for the uptake and axes of the nodule and contralateral lobe. The mean coefficients of variation were 0.5% and 3% for uptake and axis values, respectively, for the nodule. The same values were higher (7% and 5%) for the contralateral lobe because of the less favorable counting statistics.

The biologic half-life of radioiodine was separately calculated for the nodule and the contralateral lobe on the basis of uptake values at 24, 48 and 72 h. The biologic half-life was then converted into the effective half-life of ^{131}I. These parameters were subsequently introduced into the dosimetry formula to calculate the activity of ^{131}I to be administered to deliver a predetermined dose to the nodule and to calculate the dose to the contralateral lobe. The calculated doses to the lobe are those received when 300 Gy are delivered to the nodule, which is the most frequently used value to ablate autonomous nodules (*11,12,18,19,22*).

The following formula was used for dose calculations:

$$A = \frac{25.2 \times D \times m}{U_{max} \times T_{1/2}eff},$$

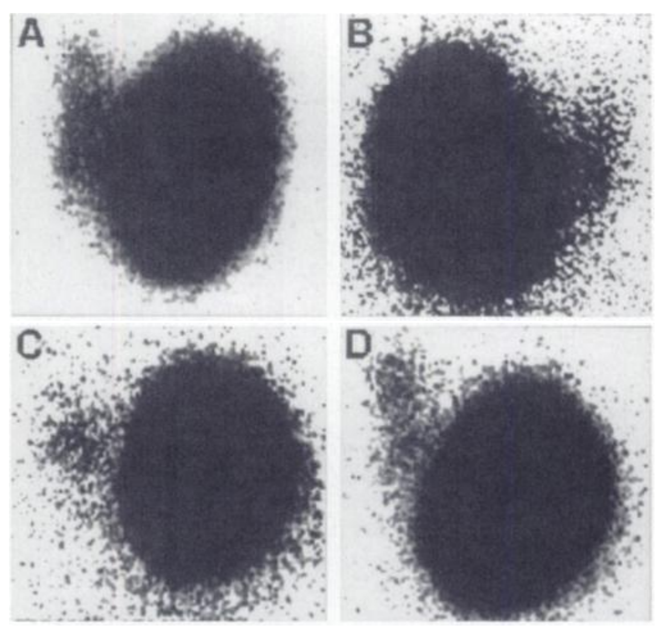

FIGURE 1. Examples of overexposed ^{123}I scintigraphic images at 24 h show "burned" nodule and varying degrees of contralateral lobe visualization in patients 2 (A), 6 (B), 8 (C) and 10 (D). At normal exposure only nodule was visible.

where A is the activity in megabecquerels, D is the dose to be given in grays, m is the tissue mass in grams, U_{max} is the maximum radioiodine uptake as a percentage of administered activity, $T_{1/2}eff$ is the effective half-life of ^{131}I in days and 25.2 is a constant value taking into account the energy and the type of radiation emitted by ^{131}I and assuming a thyroid mass of 20 g.

Once the activity to be given had been determined, the same formula was used to calculate the dose received by the contralateral lobe using D as the unknown value and the lobe parameters. The formula gives the absorbed dose resulting from the uptake of radioiodine (about 90% from beta rays and 10% from gamma rays). The portion of the total dose received by the contralateral lobe because of irradiation from the photons leaving the nodule was calculated separately using the electron gamma shower, version 4, transport code (*24*) and measuring the distance between nodule and lobe in each patient. We also estimated the dose received by the ipsilateral lobe assuming that the radioiodine concentration was the same as that measured on the contralateral lobe and calculating the dose from irradiation assuming that a lobe of the same shape and dimensions as the contralateral one was in contact with the nodule.

In most patients subsequently treated with radioiodine, we calculated the dose really absorbed by tissues using the same protocol. Uptake measurements were prolonged to 96 h, and dose calculation was limited to the nodule because uptake by the contralateral lobe was difficult to measure as a result of high penetration of the collimator septa by the high-energy photons of ^{131}I.

Serum FT4 and FT3 were measured by a radioimmunoassay method (*25*). Serum TSH was measured using a sensitive immunoradiometric assay, and the results were given in units of the 80/558 reference preparation of the World Health Organization. Normal values were 7.7–19.3 pmol/L for FT4, 4.0–8.6 pmol/L for FT3 and 0.4–4.5 mU/L for TSH.

RESULTS

Table 2 shows the parameters obtained from ^{123}I scintigraphic studies and used for calculation of the dose received by the nodule and the contralateral lobe. As expected, there was great variability in the handling of radioiodine by nodules, both in uptake and in dismission, as reflected by the biologic half-life. Taking 20 d as the lower limit of the normal range (*26*), 14 of the 26 patients had a value shorter than normal, and 3 patients had an extremely short value. Radioiodine uptake by the contralateral lobe was generally very low, but variability was great and maximum uptake ranged from 0.23% to 2.29% of the administered activity. The uptake curve of the lobe was different from that of the nodule, and the biologic half-life was generally slightly

TABLE 2
Thyroid Mass and Parameters of Radioiodine Turnover in 26 Patients with Autonomous Nodule

	Thyroid mass (g)		^{123}I Thyroid uptake (%)						Biologic half-life (d)		Effective ^{131}I half-life (d)	
			Nodule			Contralateral lobe						
Patient no.	Nodule	Contralateral lobe	24 h	48 h	72 h	24 h	48 h	72 h	Nodule	Contralateral lobe	Nodule	Contralateral lobe
1	14.4	8.1	15.7	16.3	15.9	0.80	0.93	0.85	∞	∞	8.0	8.0
2	23.4	9.2	29.5	29.1	—	1.25	1.37	—	48.9	∞	6.9	8.0
3	24.2	8.4	29.2	27.7	27.2	0.22	0.24	0.21	19.3	32.1	5.7	6.4
4	19.1	6.4	19.0	14.9	13.0	0.23	0.20	0.23	3.6	∞	2.5	8.0
5	31.3	11.0	30.8	30.6	—	0.80	0.91	—	106.5	∞	7.4	8.0
6	30.0	10.1	36.6	34.7	32.1	0.50	0.54	0.52	10.7	∞	4.6	8.0
7	30.8	8.4	40.2	38.4	35.7	0.66	0.66	0.64	11.7	45.5	4.8	6.8
8	17.1	8.9	19.3	18.5	17.1	0.51	0.46	0.49	11.7	32.8	4.8	6.4
9	11.8	8.3	17.7	16.0	14.0	2.09	2.29	2.17	6.0	∞	3.4	8.0
10	17.9	7.6	30.4	30.4	29.0	0.63	0.74	0.77	29.5	∞	6.3	8.0
11	18.9	10.4	29.8	28.8	28.3	0.43	0.44	0.47	27.4	∞	6.2	8.0
12	13.0	6.0	18.2	18.6	16.9	0.44	0.52	0.52	21.1	∞	5.8	8.0
13	11.4	6.0	29.2	22.6	18.7	0.34	0.38	0.36	3.0	∞	2.2	8.0
14	12.6	7.6	23.6	23.7	22.4	1.56	1.61	1.55	27.8	220.6	6.2	7.7
15	24.7	8.0	22.1	13.6	10.2	0.26	0.25	0.25	1.7	34.9	1.4	6.5
16	22.5	8.0	49.1	46.3	44.5	1.72	1.85	1.84	14.4	∞	5.2	8.0
17	7.4	8.1	27.3	27.9	26.7	0.29	0.35	0.43	67.1	∞	7.1	8.0
18	18.1	9.8	33.3	32.5	32.1	1.27	1.34	1.38	36.7	∞	6.6	8.0
19	18.8	10.9	34.6	33.6	31.6	0.95	1.05	0.89	15.2	∞	5.3	8.0
20	9.6	3.3	16.8	17.2	16.2	0.46	0.48	0.47	36.1	∞	6.6	8.0
21	16.3	10.1	26.1	23.8	23.4	0.27	0.28	0.30	12.0	∞	4.8	8.0
22	15.0	5.7	37.8	37.4	33.1	0.63	0.67	0.64	10.8	∞	4.6	8.0
23	10.0	5.1	31.8	30.0	28.4	0.27	0.26	0.27	12.6	177.1	4.9	7.7
24	25.4	8.1	25.8	28.4	27.1	0.94	1.00	1.00	∞	∞	8.0	8.0
25	18.8	9.7	32.5	32.7	31.8	2.09	1.97	2.02	72.4	32.9	7.2	6.4
26	19.4	7.7	34.2	32.3	28.9	0.83	0.82	0.86	8.3	∞	4.1	8.0
Mean	18.5	8.1	28.5	27.2	25.2	0.79	0.83	0.80			5.4	7.7
SD	6.6	1.9	8.1	8.2	8.4	0.56	0.58	0.58			1.7	0.6

prolonged, as expected for normal thyroid tissue scarcely stimulated by TSH. The calculated dose to the extranodular tissue was relatively high but varied from one patient to another (Table 3). The mean value was more than one tenth of the dose received by the nodule (about 32 Gy to the contralateral lobe and 34 Gy to the ipsilateral lobe for 300 Gy to the nodule). The component that was caused by irradiation by the nodule was relatively constant, whereas the proportion received through uptake was much higher and more variable, depending on the different combinations, in nodule and lobe, of the parameters that influence the dose calculation (maximum uptake, biologic half-life and tissue weight).

In 9 patients, the nodule was ablated by intranodular ethanol injection (*27*). Two patients underwent surgical resection of the nodule, 2 patients refused definitive treatment and were managed with antithyroid drugs, 1 patient was simply followed up and 1 patient was lost to follow-up (Table 1). Eleven patients (patients 10 and 17–26) were treated with radioiodine. Patient 18 was treated under further TSH suppression by exogenous levothyroxine. Results are already evaluative for 8 of the patients, who have a mean follow-up period of 9 mo (range 3–26 mo). The patients are euthyroid after receiving a mean intended dose of 158 Gy (range 110–230 Gy), and the mean serum TSH level after treatment was 1.9 mU/L (range 0.9–3.4 mU/L). The comparison between the intended dose, calculated with pretreatment dosimetry, and the delivered dose, calculated with the therapeutic ^{131}I activities, gave results in close agreement (mean intended dose 144 Gy; mean delivered dose 133 Gy) in 9 evaluated patients.

DISCUSSION

The opinion that hypothyroidism after radioiodine treatment of ATN is rare because of suppression of uptake in extranodular tissue has been prevalent for many years. The article by Goldstein and Hart (*4*) raised doubts about this idea, and in years since, several series with a high hypothyroidism rate have been reported (Table 4). The common opinion that the dose received by extranodular tissue is generally negligible is based on the fact that at simple inspection of normally exposed scintigraphic images,

TABLE 3
Calculated Dose to Extranodular Tissue from Uptake and from Irradiation When ^{131}I Activity that Delivers 300 Gy to Nodule Is Administered

Patient no.	Activity (MBq)	Dose to extranodular tissue from uptake* (A) (Gy)	Dose to contralateral lobe from irradiation (B) (Gy)	Dose to ipsilateral lobe from irradiation (C) (Gy)	Total dose to contralateral lobe (A + B) (Gy)	Total dose to ipsilateral lobe (A + C) (Gy)
1	835	30.44	0.86	2.75	31.30	33.19
2	869	41.08	1.13	3.74	42.21	44.82
3	1099	7.97	1.90	3.78	9.87	11.75
4	3040	34.68	1.27	3.81	35.95	38.49
5	1038	27.26	1.13	3.70	28.39	30.96
6	1347	22.86	1.24	3.92	24.10	26.78
7	1207	25.59	1.87	3.62	27.46	29.21
8	1395	20.30	1.22	2.80	21.52	23.10
9	1482	129.81	0.88	2.26	130.69	132.07
10	707	22.74	0.76	3.20	23.50	25.94
11	773	11.09	1.12	2.85	12.21	13.94
12	911	25.06	0.69	2.49	25.75	27.55
13	1342	26.98	1.17	2.64	28.15	29.62
14	648	41.94	0.98	2.36	42.92	44.30
15	6035	50.59	1.79	3.84	52.38	54.43
16	666	48.89	1.67	3.57	50.56	52.46
17	282	4.75	1.19	1.82	5.94	6.57
18	623	27.85	1.47	2.91	29.32	30.76
19	775	23.70	1.37	2.73	25.07	26.43
20	639	29.51	1.39	2.49	30.90	32.00
21	984	9.28	0.57	2.51	9.85	11.79
22	652	24.33	1.66	2.80	25.99	27.13
23	485	7.85	0.88	2.39	8.73	10.24
24	845	33.12	2.16	3.53	35.28	36.65
25	604	33.05	1.08	2.86	34.13	35.91
26	1046	37.09	1.67	3.12	38.76	40.21
Mean	1167	30.69	1.27	3.02	31.96	33.70
SD	1119	23.51	0.41	0.59	23.51	23.51

*Dose to extranodular tissue was calculated from uptake and volume values measured on contralateral lobe; same radioiodine concentration was assumed for calculating dose to ipsilateral lobe.

TABLE 4
Results of Radioiodine Treatment of Autonomous Thyroid Nodule According to Published Series, Including Thyroid-Stimulating Hormone Assay

Source	Patient no.	Administered activity (MBq)		Dose to nodule (Gy)	Follow-up (y)		Hypothyroidism rate (%)	Relapse or retreatment rate (%)
		Mean	Range		Mean	Range		
Blum et al. (1)	14	792	370–1887			≤6	0 (0/14)	0 (0/14)
Ratcliffe et al. (8)	48	670	555–1665		3.1	2–10	0 (0/48)	16.6 (8/48)
Mariotti et al. (7)	138	466	204–1069		3.0	1–11	3.6 (5/138)	8.7 (12/138)
Hegedus et al. (6)	27	278	141–655			>1	3.7 (1/27)	7.4 (2/27)
Eyre-Brook and Talbot (3)	37		44–555	25–200	6.5		5.4 (2/37)	32.4 (12/37)
Bockisch et al. (16)	61		190–1100	150	1.0		6.5 (4/61)	26.2 (16/61)
Ross et al. (5)	45	381	137–814		4.9		6.7 (3/45)	13.3 (6/45)
Als et al. (19)	53			300	0.5	0.3–0.8	7.5 (4/53)	13.2 (7/53)
Guhlmann et al. (18)	230		290–900	310	1.0		8.2 (19/230)	6.9 (16/230)
Heinze and Bohn (9)	217			400	2.0	≤7	10.6 (23/217)	2.3 (5/217)
Moser et al. (10)	91	1125	445–2590	400	1.3	0.7–2.1	11.0 (10/91)	5.5 (5/91)
Clerc et al. (17)	88	305		80	6.4	0.25–15	13.6 (12/88)	13.6 (12/88)
Kinser et al. (11)	71		<370–>1887	300	9.0		14.1 (10/71)	9.8 (7/71)
Fontana et al. (2)	29			200–800		2–20	20.6 (6/29)	41.4 (12/29)
Huysmans et al. (13)	52	740			10.0	4–17	21.1 (11/52)	1.9 (1/52)
Moser et al. (10)	63	1125	445–2590	400	5.4	4.2–6.8	23.8 (15/63)	4.8 (3/63)
Berglund et al. (12)	25	555	426–1003	300	8.0	1–13	24.0 (6/25)	0 (0/25)
Steiner and Bauer (20)	11		500–1100	350	0.3		27.3 (3/11)	0 (0/11)
O'Brien et al. (15)	23	1077	729–3700		5.6	0.2–16	34.8 (8/23)	4.3 (1/23)
Goldstein and Hart (4)	22	851	555–2035		8.5	4–16	40.9 (9/22)	0 (0/22)
Ramos-Gabatin et al. (14)	12	984	370–1106			0.6–5.2	58.3 (7/12)	0 (0/12)
Total	1357						11.6 (158/1357)	9.2 (125/1357)

Series are listed in order of increasing hypothyroidism rates. Both clinical and subclinical hypothyroidism were considered.

the uptake seems almost completely confined to the nodular tissue. Our data, collected with modern instrumentation and relatively high-activity ^{123}I to provide sufficient statistics even with very low uptake, show that faint extranodular uptake occurs in most patients and can be measured and used in the dosimetry formula. In this series, the maximum contralateral lobe uptake ranged from 0.23% to 2.29% of the administered activity, with a mean value of 0.85%. This value was less than one thirtieth of the mean maximum nodule uptake (28.7%); however, considering that the biologic half-life was longer in the lobe and that the volume of the lobe was smaller than that of the nodule, the final mean dose to the lobe was more than one tenth of the dose to the nodule.

The long radioiodine half-life in extranodular tissue was first observed by Medeiros-Neto et al. (28) in 10 patients who were given double labeling (^{125}I 1 mo and ^{131}I 1 d before surgery). At day 1 nodule uptake per gram of tissue was 10 times higher than lobe uptake, whereas at day 30 lobe uptake was twice as high as nodule uptake. Despite this early evidence that extranodular tissue shows a small but long-lasting uptake of radioiodine, there are few data on the dosimetry of extranodular tissue. An article by Gorman and Robertson (22) has been frequently quoted to show that the dose to extranodular tissue is low; however, that work was a simple mathematical calculation, without experimental data, based on the assumption that no extranodular uptake occurs and that the dose to the lobe is entirely derived from photons leaving the nodule. Those authors calculated that when the nodule receives 300 Gy, the center of the contralateral lobe receives about 3 Gy. More realistic data have been reported by Fontana et al. (2) and by Clerc et al. (17). Although their work did not deal specifically with dosimetry, Fontana et al. calculated that the contralateral lobe receives 21.5 Gy when the nodule receives 200 Gy and that extranodular uptake is 16% of that of the nodule. This value is certainly an underestimation because the investigators attributed too large a fixed volume to the contralateral lobe (15 mL); in addition, it is not clear whether the effective half-lives of the nodule and lobe were measured separately. In 1995 Clerc et al. (17) published an article specifically focused on dosimetry at the same time the preliminary results of our study were published (29). Their work also showed several pitfalls because the doses to the nodule and contralateral lobe were separated retrospectively, using total uptake measures and dividing nodule and lobe uptake by digitizing the rectilinear scanner map taken 24 or 48 h after a tracer dose of ^{131}I. It was therefore impossible to calculate the nodule and lobe half-lives separately. The dose to the nodule was always lower than predicted, depending on the degree of extranodular uptake and lobe volume. Despite these technical limitations, the results are of great interest. In the series of Clerc et al. (17), in a group of patients without clearly visible extranodular activity, the mean total thyroid uptake was 46%, the mean uptake of the contralateral lobe was 1.3% and the corresponding doses for the calculated 80 Gy to the thyroid were 72 Gy to the nodule and 8.5 Gy to the lobe. In a group with clearly visible extranodular activity, the mean total uptake was 48%, the mean uptake of the contralateral lobe was 10.6% and the corresponding doses were 56.9 Gy to the nodule and 48.9 Gy to the lobe. In these patients, the sum exceeds the expected 80 Gy because the lobe volume was only about one third of the nodule volume, and therefore, lobe uptake was contained in a smaller volume.

Our results, collected prospectively with modern equipment that allows measurement of nodule and contralateral lobe uptakes and half-lives separately, agreed with those of Clerc et al. (*17*) for their patients without clear extranodular activity. In our series, the mean maximum uptake of the nodule was 28.7% and that of the lobe was 0.85%; extranodular activity was visible only on overexposed images, and TSH levels were subnormal in all patients and 0.1 mU/L or lower in all but 1. The mean dose to the contralateral lobe calculated for 300 Gy to the nodule was 32 Gy, in close agreement with the data of Clerc et al. (8.5 Gy for 72 Gy, corresponding to 35 Gy for 300 Gy).

The dose to the ipsilateral lobe could not be measured directly and required assumptions, namely, that the radioiodine concentration was the same as that measured for the contralateral lobe and that a lobe of similar shape and dimensions was in contact with the nodule. In addition, the possibility that some β radiation can reach the surface of the lobe from the external portions of the nodule was not considered. Despite these limitations, the results are of interest and confirm that a dose from uptake is prevalent and that the ipsilateral lobe suffers essentially the same damage as the contralateral one. Therefore, both lobes contribute to the preservation of thyroid function, and this represents an advantage over surgery, which, with lobectomy, eliminates half of thyroid tissue.

Thyroid damage caused by the relatively high doses received by extranodular tissue is certainly the main cause of post-treatment hypothyroidism. Hegedus et al. (*6*) found, by sonography, a reduction in contralateral lobe volume after treatment instead of the expected increase as a result of the resumption of TSH secretion, and this phenomenon was observed even in a series treated with small activities and showing one of the lowest rates of hypothyroidism. High doses to the nodule, on the order of 300 Gy, were suggested when scintigraphy was the main criterion to judge the results of treatment, and transformation of the nodule into a scar was considered the best result (*30*). However, good clinical results have been obtained with lower doses or activities (Table 4). With reduced doses the prevalence of compensated results, namely, nodules incompletely inactivated on follow-up scintigraphy (*1,11,16,30–32*), increases, but with modern criteria, the aim of treatment is not complete nodule inactivation but a reduction of hormone production sufficient to allow resumption of TSH secretion. The only means to reduce hypothyroidism is to reduce the planned doses; 150 Gy are probably sufficient to inactivate most nodules, thus halving the dose to the extranodular tissue. It is also important to avoid therapeutic errors, such as treatment of patients with unsuppressed TSH or of patients pretreated with antithyroid drugs that increase TSH levels by reducing the circulating thyroid hormones (*31,33*). Individual dosimetry (*34*) allows excluding unsuitable patients from treatment, such as those with an excessively rapid radioiodine turnover in the nodule or those receiving excessively high doses to the extranodular tissue (for example, patients 9 and 15 of this series). The dose to the nodule can be individually adjusted by taking into account the dose that will be received by extranodular tissue.

This series was started as a pilot study for this individual, separate dosimetry, and many patients were treated with ethanol, mainly because this form of ablation is extensively used in our departments (*26,27,35*). We have now started using this dosimetry protocol in the patients we plan to treat with radioiodine. Our current policy is to deliver 150 Gy to the nodule; this value can be increased to 200 Gy when the dose to extranodular tissue is low and decreased to 100 or even 80 Gy (*17*) when high dose suggests risk of subsequent hypothyroidism. Soon we will collect data to judge the usefulness of this protocol in reducing the hypothyroidism rate relative to more primitive methods of dose calculation.

CONCLUSION

This study shows that during radioiodine therapy of ATN, extranodular tissue receives a dose greater than generally assumed, approximately 10% of the dose received by the nodule. This explains the relatively high prevalence of hypothyroidism reported in recent years, especially in patients treated with high radiation doses and followed up for long periods. The dose to the extranodular tissue can be decreased only by reducing the dose to the nodule. Individual, separate dosimetry is important to select a ^{131}I activity that is sufficient to inactivate the nodule without causing serious damage to the extranodular tissue.

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