# Clinical experience with outpatient radioiodine therapy in hyperthyroidism

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## Abstract

BACKGROUND: Since 1993, outpatient radioiodine therapy has been available in Hungary. The reported study evaluated the efficacy of outpatient radioiodine treatment in subjects with hyperthyroidism.

METHODS: The data on 238 patients with Graves' disease and 123 patients with thyroid autonomy were analyzed retrospectively. All patients were treated within the period 1994–1999. The activities of radioiodine were calculated individually. The dose applied in Graves' disease was 150 Gy, and that in thyroid autonomy was 300 Gy. The efficacy of the treatment was evaluated 3, 6 and 12 months after radioiodine therapy. In patients with persistent hyperthyroidism, repeated therapy was performed.

RESULTS: Overall, the radioiodine therapy was successful in 84% of the Graves' disease patients. In thyroid autonomy, treatment with 300 Gy was successful in 79% of the patients. The efficacy of radioiodine treatment was similar to the results of one-dose application.

CONCLUSIONS: It was concluded that radioidine therapy with an absorbed dose of 150 Gy in Graves' disease and with an absorbed dose of 300 Gy in thyroid autonomy proved successful by the method applied.

**Key words: radioiodine therapy, Graves' disease, thyroid autonomy, outpatient therapy**

## Introduction

Radioiodine therapy is very effective in the treatment of hyperthyroidism. With exact indications, it can replace surgical intervention. Contraindications include pregnancy or a suspicion of malignant thyroid disease. Radioiodine therapy can be used in the management of Graves' disease with recurrent hyperthyroidism or thyroid autonomy. We prefer surgical intervention to radioiodine therapy in cases involving a young patient or a large goiter producing serious compression symptoms. The advantages of $^{131}$I therapy are certain in toxic multinodular goiters, in the treatment of smaller goiters, and in patients suffering from other serious diseases, e.g. cardiac disease (1, 2). Radioiodine therapy can replace anti-thyroid drug treatment in the event of resistance, allergy or hematological complications. The treatment is cheap, effective and devoid of complications (2–4). Outpatient radioiodine therapy has been available in Hungary since 1993. The Methodological Letter of the Institute of Hungarian Radiology and Radiation Physics and the departmental order of the Ministry of Public Welfare deal with the conditions of the treatment (5, 6).

In this study, we report on the efficacy of outpatient radioiodine treatment provided in the Department of Nuclear Medicine, Albert Szent-Györgyi Medical University, during the period 1994–1999.

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## Patients and methods

$^{131}$I treatment was provided to 363 patients in our department during the period from 1994 to 1999. In 238 (204 women, 34 men; average age: 52±13 years) Graves' disease, and in 123 (104 women, 19 men; average age: 62±12 years) thyroid autonomy was verified via the blood chemistry and different imaging modalities (Table 1).

**Table 1. Patient data**

| | Graves' disease | | Thyroid autonomy | |
|---|---|---|---|---|
| Thyrostatic drugs as premedication | 57% | (135/238) | 33% | (40/123) |
| Exophthalmus | 40% | (96/238) | 2% | (3/123) |
| Ultrasonography: hypodense thyroid tissue | 36% | (63/173) | 12% | (14/115) |
| Ultrasonography: nodule | 17% | (29/173) | 97% | (114/117) |
| Scintigraphy: struma diffusa | 74% | (175/238) | 0% | (0/123) |
| Scintigraphy: hot nodule | 0% | (0/238) | 93% | (114/123) |
| TSH < normal | 91% | (205/226) | 99% | (122/123) |
| T3 > normal | 62% | (141/226) | 59% | (73/123) |
| T4 > normal | 50% | (114/226) | 39% | (48/123) |
| TRAK positive | 69% | (104/150) | 8% | (8/97) |
| TRAK negative | 31% | (46/150) | 92% | (89/97) |
| Iodine uptake: | | | | |
| High iodine uptake | 61% | (146/238) | 37% | (45/123) |
| Accelerated iodine turnover | 11% | (25/238) | 1% | (1/123) |
| Normal | 19% | (46/238) | 53% | (65/123) |

In every patient, the treatment was performed by a nuclear medicine specialist after referral by an endocrine specialist. Before treatment an interview and clinical examination were carried out which extended to the complaints, the history and present illness, physical examination, thyroid scintigraphy, ultrasonography, and iodine uptake measure with a test dose of 37 kBq. We measured the serum T3 (LIA mat T3, Byk-Sangtec, Dietzenbach, Germany), T4 (LIA mat T4, Byk-Sangtec, Dietzenbach, Germany), and TSH (LIA mat TSH, Byk-Sangtec, Dietzenbach, Germany) levels. In 247 patients, TRAK was also determined.

Radioiodine doses were estimated individually (Figure 1) (7, 8). For determination of the maximal thyroid uptake and effective half-life, a radioiodine test with measurements 6, 24, 48 and 168 hours after the oral administration of $^{131}$I was performed. Thyroid weight was determined via the thyroid scintigram. The desired intrathyroidal absorbed dose was 150 Gy in Graves disease and 300 Gy in thyroid autonomy. In cases of serious hyperthyroidism, for preparation we gave the patients anti-thyroid drugs. The anti-thyroid treatment was interrupted 2 days before radioiodine therapy until a few days after therapy. Before the treatment, the patient was informed by a specialist about the therapy, the regime and hygienic regulations. We used $^{131}$I NaI capsules during the radioiodine therapy (Mallinckrodt, Petten, The Netherlands). In cases with a calculated activity above 550 MBq, we provided fractional radioiodine treatment.

Post-treatment follow-up examinations were made routinely at 3 and 6 months and 1 year, with hormone level determinations (serum T3, T4 and TSH), physical examination, thyroid scintigraphy and ultrasonography. In Graves' disease, the goal was to terminate hyperthyroidism. The treatment was successful if the patient became euthyroid or hypothyroid. In thyroid autonomy, the treatment was effective if the patient became euthyroid and the thyroid scintigram normalized. In patients with persistent hyperthyroidism, repeated therapy was performed.

## Results

Overall the therapy was successful in 84% of the Graves' disease after 6 months and in 79% after 1 year (Table 2). The $^{131}$I treatment was repeated in 49 cases.

$$\text{activity} = \frac{\text{dose (Gy) x thyroid mass (g) x 22.5}}{\text{max. iodine uptake (\%) x effective half-life time (day)}}$$

$$\text{thyroid mass} = 0.214 \times \text{projection (cm}^2\text{)}^{3/2}$$

$$1/T_{1/2eff} = 1/T_{1/2fiz} + 1/T_{1/2biol}$$

**Figure 1.** Formula for calculation of the required activity for $^{131}$I treatment.

**Table 2. Overall efficacy of radioiodine therapy in Graves' disease after 3, 6 and 12 months**

| Control | 3 months (n=154) | 6 months (n=147) | 12 months (n=112) |
|---|---|---|---|
| Euthyroidism | 21%(33/154) | 24%(35/147) | 23%(26/112) |
| Hypothyroidism | 59%(90/154) | 60%(88/147) | 56%(63/112) |
| Hyperthyroidism | 20%(31/154) | 16%(24/147) | 20%(23/112) |

In thyroid autonomy, the treatment with 300 Gy was successful in 79% of the patients.

Repeated treatment was performed in 15 cases (Table 3).

We also analyzed the results on those patients who underwent fractional treatment. The efficacy of fractional treatment was similar to that of one-dose application (Table 4).

## Discussion

Hyperthyroidism is a common disease. In Hungary, several thousand people are treated with a thyroid hyperfunction (9). Since 1993, outpatient radioiodine therapy has been available in Hungary. The treatment is cheap, and with correct indications, effective. In thyroid autonomy, radioiodine therapy is generally the firstchoice of treatment. In Graves' disease, the firstchoice of treatment is anti-thyroid drugs; radioiodine therapy is used if anti-thyroid drug treatment is ineffective, in the event of drug side-effects and in recurrent hyperthyroidism. Absolute contraindications are malignant thyroid disease and pregnancy; relative contraindications are a large goiter or nodule (with or without compression symptoms) and a young age (1).

There are two methods to determine the required activity for the radioiodine therapy. The first method uses fixed activities depending on the thyroid disease. This method is used in those countries where the prevalence of goiter is low (10, 11). In iodine-deficient areas such as Hungary, a calculated dose method is used because of the patient's individual iodine turnover (11, 12). We calculate the required activity via the data of the thyroid or nodule mass, the maximal thyroid uptake and the effective half-life. The thyroid or nodule mass is determined by thyroid ultrasonography or scintigraphy. With ultrasonography, it is possible to measure the thyroid diameters exactly, and with the application of the ellipsoid model, the thyroid mass can be estimated. The scintigram shows the active thyroid tissue, which correlates more closely with the functioning thyroid mass. For determination of the maximal thyroid uptake and effective half-life, a radioiodine test was used with measurements 6, 24, 48 and 168 hours after the oral administration of $^{131}$I (11–15). Several groups report that late measurements are unnecessary, because the radioiodine elimination is

**Table 3. Overall efficacy of radioiodine therapy in thyroid autonomy after 3, 6 and 12 months**

| Control | 3 months | 6 months | 12 months |
|---|---|---|---|
| $^{131}$I dose 300 Gy | (n=60) | (n=49) | (n=28) |
| Euthyroidism | 60%(36/60) | 65%(32/49) | 79%(22/28) |
| Hypothyroidism | 7%(4/60) | 6%(3/49) | 0%(0/28) |
| Hyperthyroidism | 33%(20/60) | 28%(14/49) | 21%(6/28) |

**Table 4. Efficacy of first fractional radioiodine therapy after 12 months**

| | Graves' disease | Thyroid autonomy |
|---|---|---|
| Hypothyroidism | 28%(3) | 0% |
| Euthyroidism | 36%(4) | 75%(3) |
| Hyperthyroidism | 36%(4) | 25%(1) |

constant in the different thyroid diseases in a determined geographical area; only the maximal thyroid uptake is determined with the help of a 24-hour (sort) protocol (16, 17). Our findings indicate that the biological half-life of radioiodine is individually different, so that late measurements are required.

The applied radioiodine dose depends on the nature of the thyroid disease and the therapeutic conception. In Graves' disease, the application of 150–200 Gy is most frequent (11, 18). In some clinics, an ablative dose of 250–300 Gy is used in recurrent hyperthyroidism (8, 11, 19). The desired intrathyroidal absorbed dose in thyroid autonomy is 300–400 Gy (11, 14, 20). In our department, the dose applied in Graves' disease was 150 Gy, and in thyroid autonomy 300 Gy.

Radioiodine therapy can be applied in fractional ablation form, where small activities are given at intervals of a few months. The disadvantage of this therapy form is that the hyperthyroidism lasts longer, and there is a higher risk of late hypothyroidism (1, 11, 21). In Hungary the maximum permitted activity is 550 MBq; if more is needed outpatient fractional therapy can be given. The efficacy of fractional treatment is similar to that of one-dose application. More data in this relation are currently under evaluation.

Thyroid drugs may influence the efficacy of the therapy. In thyroid autonomy, the therapy must be carried out under endogenous or exogenous TSH suppression. If needed, L-thyroxine must be given according to the blood TSH level for exogenous suppression before radioiodine therapy in order to avoid damage to the normal thyroid tissue (2, 11). In Graves' disease, there is no uniform attitude in this question. Some authors consider that anti-thyroid drugs do not influence the efficacy of radioiodine therapy (11, 22). Others state that anti-thyroid drugs increase the risk of recurrent hyperthyroidism (23), while some report that it is necessary to produce euthyroidism with anti-thyroid drugs before radioiodine treatment (3, 24, 25). When anti-thyroid drugs are used as premedication, the rate of late hyperthyroidism can be decreased (2, 23, 24). We have found that interruption of anti-thyroid treatment before radioiodine therapy causes an accelerated iodine turnover, which decreases the efficacy of the therapy. We presume that in Graves' disease with an accelerated iodine turnover, low dose anti-thyroid drug treatment (propylthiouracil, thiamazol, lithium carbonate) might be useful. In patients with extreme hyperthyroidism, anti-thyroid drug treatment is highly recommended. In these cases, the anti-thyroid drug dose can be decreased 1–2 months after radioiodine treatment.

The goal of the treatment is to eliminate hyperthyroidism. The efficacy of the treatment and the rate of late hypothyroidism in Graves' disease depend on the dose of radioiodine. The use of lower doses (60–80 Gy) produces recurrent hyperthyroidism, but the rate of late hypothyroidism is low (1, 20). An ablative dose (250–300 Gy) eliminates hyperthyroidism, but late hypothyroidism is quite frequent (8, 19). When 150 Gy was applied, more than 70% of the hyperthyroidism could be eliminated; rate of late hypothyroidism is over 40%. Repeated therapy caused hypothyroidism in 60% of the patients and eliminated 83% of the hyperthyroidism. Post-treatment hypothyroidism is rare in thyroid autonomy because of the TSH suppression. Euthyroidism is the goal in the treatment of thyroid autonomy. When 300 Gy was applied, the efficacy was 79%. These data are similar to those in the literature (1, 8, 11).

Our findings indicate that a dose of 150 Gy should be used in Graves' disease and 300 Gy in thyroid autonomy in order to terminate hyperthyroidism. During our outpatient radioiodine therapy since 1994, no complications were found. We consider that outpatient radioiodine therapy is a very effective method in the management of hyperthyroidism.

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