COMPARISON OF RADIOIODINE DOSES AND CLINICAL RESULT IN GRAVES' HYPERTHYROIDISM: A PRELIMINARY STUDY

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COMPARISON OF RADIOIODINE DOSES AND CLINICAL RESULT IN GRAVES' HYPERTHYROIDISM: A PRELIMINARY STUDY

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ABSTRACT

Radioactive iodine (^{131}I) is an effective treatment for Graves' hyperthyroidism. However, there has been no general agreement as to the appropriate dose regimen for ^{131}I. This study was performed at the Nuclear Medicine Division of Sappasittiprasong Hospital, Ubonratchathanee Province from 2004 to 2005 with the aim to determine the effects of ^{131}I dose regimens on the treatment outcomes of Graves' hyperthyroidism. Seventy-four patients were enrolled and investigated by clinical and biological assessment (serum FT_3, FT_4 and TSH) and thyroid ultrasound. Patients were categorized into two treatment groups by thyroid weight (TW), one with TW<40g receiving non-ablative therapy by sliding-scale method, and the other with TW≥40g receiving ablative therapy by dose calculation. Each group was then randomized into two-subgroups receiving low and high ^{131}I doses. At 3-month follow up, in the non-ablative group of TW <40g, among 28 patients who received conventional (low) and advanced (high) doses, a euthyroid was achieved in 12 patients (42.8%), 1 patient (3.6%) were hypothyroid and 15 patients (53.6%) remained hyperthyroid (hyperthyroid was eliminated in 46.4% and 53.6% remained uncured). In the ablative group (TW≥40g), 46 patients who received 100 μCi/g and 150 μCi/g, 19 patients (41.3%) were euthyroid, 2 patients (4.4%) were hypothyroid and 25 patients (54.3%) remained hyperthyroid (hyperthyroid was eliminated in 45.6% and 54.3% remained uncured). No significant difference was found between non-ablative and ablative doses in 3-month follow up.

By comparison between low and high dose regimens, 38 patients who received a low dose, euthyroid was achieved in 13 patients (34.2%), none were hypothyroid and 25 patients (65.8%) remained hyperthyroid. Of the 36 patients who received a high dose, 18 patients (50%) were euthyroid, 3 patients (8.3%) were hypothyroid and 15 patients (41.7%) remained hyperthyroid. A significant difference in the treatment outcomes was found (p=0.044). When responders and non responders to treatment in the low and the high dose groups were compared, no-significant advantage in response rate was gained by using a high dose (p=0.065).

In conclusion, when low ^{131}I dose is used, no hypothyroid case was observed while few cases of early hypothyroidism were induced by the high doses. However, we could not demonstrate any advantage to using an adjusted high dose in the 3-month follow up. For more rapid therapeutic effect at the expense of an increased rate of hypothyroidism (as a success outcome), high doses of ^{131}I may be required in patients with larger thyroid glands.

KEY WORDS : GRAVES' HYPERTHYROIDISM / RADIOIODINE THERAPY

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การศึกษาเบื้องต้นเพื่อเปรียบเทียบปริมาณไอโอดีนรังสีและผลการรักษาในผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ (COMPARISON OF RADIOIODINE DOSES AND CLINICAL RESULT IN GRAVES' HYPERTHYROIDISM: A PRELIMINARY STUDY)

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บทคัดย่อ

ไอโอดีนรังสี (^{131}I) มีประสิทธิภาพในการรักษาโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ อย่างไรก็ตาม ยังไม่มีข้อตกลงร่วมกันในการใช้ปริมาณไอโอดีนรังสีที่เหมาะสม การศึกษาครั้งนี้ทำที่งานเวชศาสตร์นิวเคลียร์ โรงพยาบาลสรรพสิทธิประสงค์ จังหวัดอุบลราชธานี ระหว่าง ปี พ.ศ.2547-2548 มีจุดประสงค์เพื่อเปรียบเทียบปริมาณไอโอดีนและผลการรักษาในผู้ป่วยไทรอยด์เป็นพิษชนิดเกรฟส์ มีผู้ป่วยเข้าร่วมโครงการ 74 รายและได้ถูกประเมินทางคลินิก ผลปฏิบัติการ (FT_3, FT_4 และ TSH) และอัตราซาวด์ไทรอยด์ แบ่งกลุ่มผู้ป่วยตามน้ำหนักต่อมไทรอยด์ เป็น 2 กลุ่ม คือ 1) รักษาแบบ non-ablative ด้วยวิธี sliding-scale (<40g) และ 2) รักษาแบบ ablative ด้วยวิธีคำนวณปริมาณไอโอดีนรังสี (≥40g) จากนั้นทำการสุ่มเข้าสู่กลุ่มย่อยของปริมาณไอโอดีนรังสีต่ำ (low) และสูง (high) ติดตามผลหลังการรักษาที่ 3 เดือน พบว่า ในกลุ่ม non-ablative ผู้ป่วย 28 ราย เข้าสู่ภาวะ euthyroid 12 ราย (42.8%), 1 ราย (3.6%) เป็น hypothyroid และ 15 ราย (53.6%) ยังคงเป็น hyperthyroid รวมผู้ป่วยหายจากภาวะไทรอยด์เป็นพิษ 13 ราย (46.4%) สำหรับกลุ่ม ablative ผู้ป่วยจำนวน 46 ราย เข้าสู่ภาวะ euthyroid 19 ราย (41.3%), 2 ราย (4.4%) เป็น hypothyroid และ 25 ราย (54.3%) ยังคงเป็น hyperthyroid รวมผู้ป่วยหายจากภาวะไทรอยด์เป็นพิษ 21 ราย (45.7%) พบว่า ไม่มีความแตกต่างอย่างเป็นนัยสำคัญ ระหว่างการรักษาแบบ non-ablative และ ablative

ในการเปรียบเทียบผลระหว่างปริมาณรังสีต่ำและสูง โดยในกลุ่มรังสีปริมาณต่ำ ผู้ป่วย 38 ราย เข้าสู่ภาวะ euthyroid 13 ราย (34.2%), ไม่พบ hypothyroid และ 25 ราย (65.8%) ยังคงเป็น hyperthyroid สำหรับกลุ่มปริมาณรังสีสูง ผู้ป่วย 36 ราย เข้าสู่ภาวะ euthyroid 18 ราย (50.0%), 3 ราย (8.3%) เป็น hypothyroid และ 15 ราย (41.7%) ยังคงเป็น hyperthyroid พบว่า มีความแตกต่างอย่างเป็นนัยสำคัญ ($p=0.044$) ระหว่างผลที่ได้รับหลังการรักษา (outcomes) ในขณะที่ผลตอบสนองการรักษา (หาย/ไม่หาย) ระหว่างปริมาณรังสีต่ำและสูง พบว่า ไม่มีนัยสำคัญ ($p=0.065$) ที่แสดงข้อได้เปรียบในการใช้รังสีปริมาณสูงว่าเหนือกว่ารังสีปริมาณต่ำ

สรุปได้ว่า ไม่พบภาวะขาดไทรอยด์ฮอร์โมนในคนไข้ที่รักษาด้วยไอโอดีนรังสีปริมาณรังสีต่ำ พบเพียงไม่กี่รายในคนไข้ที่รักษาด้วยไอโอดีนรังสีปริมาณสูง อย่างไรก็ตาม การศึกษาและติดตามผลภายใน 3 เดือน ยังไม่สามารถแสดงข้อได้เปรียบของการใช้ไอโอดีนรังสีปริมาณสูงในการรักษาไทรอยด์เป็นพิษ เพื่อให้ผู้ป่วยหายจากภาวะไทรอยด์เป็นพิษโดยเร็ว โดยถือว่าภาวะขาดไทรอยด์ฮอร์โมนเป็นผลประสบความสำเร็จในการรักษา สำหรับผู้ป่วยที่ต่อมไทรอยด์มีขนาดใหญ่ ควรได้รับการรักษาด้วยไอโอดีนรังสีปริมาณสูง

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LIST OF ABBREVIATIONS

Abbreviation	Term
ATD	antithyroid hormone drug
DIT	diiodotyrosine
EU	early uptake
est. LU	estimation of late uptake
FT_4	free- thyroxine
FT_3	free-triiodothyronine
GD	Graves' disease
Gy	gray
hr	hour
IRMA	immunoradiometric assay
KeV	kilo electron volt
LU	late uptake
MBq	mega becquerel
MeV	mega electron volt
MHz	mega hertz
MMI	methimazole
µCi	microcurie
µCi/g	microcurie per gram
µg	microgram
mCi	millicurie
mg	milligram
mm	millimater
MIT	monoiodotyrosine
ng/dl	nanogram per decilitre
PTU	propythiouracil

LIST OF ABBREVIATIONS (Continued)

Abbreviation	Term
RaI	radioactive iodine (^{131}I)
RIA	radioimmunoassay
RAIU	radioiodine uptake
^{99m}Tc	technetium-99 metastable
Tg	thyroglobulin
TPO	thyroid peroxidase
TSH	thyroid-stimulating hormone
TSHR-Abs	thyroid-stimulating hormone receptor-stimulating antibodies
T_4	thyroxine
T_3	triiodothyronine

CHAPTER I
INTRODUCTION

Graves' disease (GD) is an autoimmune disorder in which thyroid-stimulating hormone (TSH) receptor antibodies stimulate the thyroid gland to synthesize and release large amounts of thyroid hormones to the circulation. It was found that there have elevated thyroid hormones, decreased TSH and an elevated radioiodine uptake (RAIU) in GD patients.

The treatments for GD are antithyroid hormone drug (ATD), surgery and radioactive iodine (RaI) therapy. The factors to be considered in treating GD included age, thyroid size, symptoms and severity, disease duration, other diseases and willingness of patients. The treatment of ATD is suitable for young patients and symptom of disease not severe. However, it found that highly likely for relapse. The treatment of surgery is costly and a chance of complications. Therefore, the RaI therapy is active only at thyroid gland, highly effective with a low side effect, convenient and not costly. Then, the RaI therapy under a supervision of radiologist is more popular, appropriate for middle-aged patient with moderate to severe disease.

The method of RaI therapy for GD can be fixed equal dose for all patients, calculated dose of RaI considers by thyroid weight and percentage of ^{131}I thyroid uptake for each individual patient or sliding scale dose of RaI determine from symptoms and thyroid weight.

In Thailand, the RaI therapy had been used for 50 years, but the study about RaI therapy was less and controversial. In Sappasittiprasong Hospital, Ubonratchathanee, calculated dose of 100 μCi/g of thyroid was used. The outcome after treatment by a single dose has shown that higher rate of patients still being in hyperthyroidism.

In this study, controlling factors affecting treatment effectiveness such as ATD, size and weight of the thyroid gland and RaI administered dose were included in the investigation. The randomization double-blind controlled trial was used to divide the patients into groups.

Objectives of the thesis

1. To study the doses of RaI therapy for GD in Nuclear Medicine Division of Sappasittiprasong Hospital, Ubonratchathanee.
2. To compare the clinical result of RaI therapy for GD in Nuclear Medicine Division of Sappasittiprasong Hospital, Ubonratchathanee.

Expected outcomes

Expected benefits were to increase effectiveness in treatment of thyrotoxicosis caused by GD, less costly and took less time. Besides, it could be save the medical cost in patients and hospital.

CHAPTER II
LITERATURE REVIEW

2.1 Thyroid gland

The thyroid gland is a part of endocrine (hormone) system. It was located anterior of lower neck, extending from the level of the fifth cervical vertebra down to the first thoracic vertebra. The thyroid gland has 2 lobes (Fig. 1), which joins at the base by thyroid tissue called isthmus. The gland varies from an H to a U shape. Normal adult thyroid weighs average 15-25 grams. The thyroid gland consists of follicular cells that appear as circles of cells surrounding lumens on microscopic sections. The apical membrane is the inner surface contacts with the lumen of follicle, and the basal membrane is the outer surface contacts with blood supply. The follicular cells synthesize and store thyroid hormone in the form of colloid in the lumen. The thyroid gland has two main endocrine functions: secretion of thyroid hormones by follicular cells into the blood circulation and secretion of calcitonin by the C cells which are important in calcium homeostasis (1, 2).

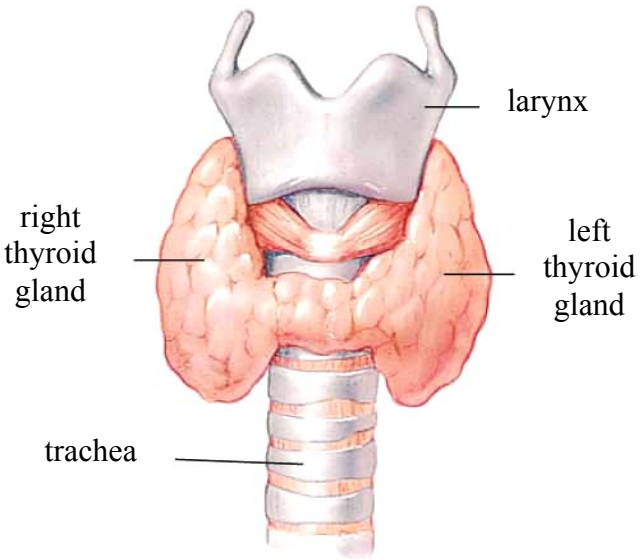


Figure 1. Thyroid gland

2.2 Regulation of thyroid function

The thyroid gland is an organ composed primarily of endoderm-derived follicular cells; it is responsible for thyroid hormone production in all vertebrates. The main regulator of thyroid function is thyrotropin or thyroid-stimulating hormone (TSH), which is synthesized and secreted from the pituitary gland and is under the control of thyrotropin-releasing hormone (TRH), secreted by the hypothalamus. Thyroid secretion and serum concentrations of thyroxine (T_4) and 3,5,3′-triiodothyronine (T_3) are maintained by a negative feedback loop involving inhibition of TSH and TRH secretion by T_4 and T_3, and by tissue specific and hormone-regulated expression of the three iodothyronine deiodinase enzymes that metabolize thyroid hormones. Thus, the regulation of thyroid function depends on the normal development of the hypothalamic-pituitary-thyroid axis (Fig. 2), which occurs independently but coordinately during embryonic and neonatal life.

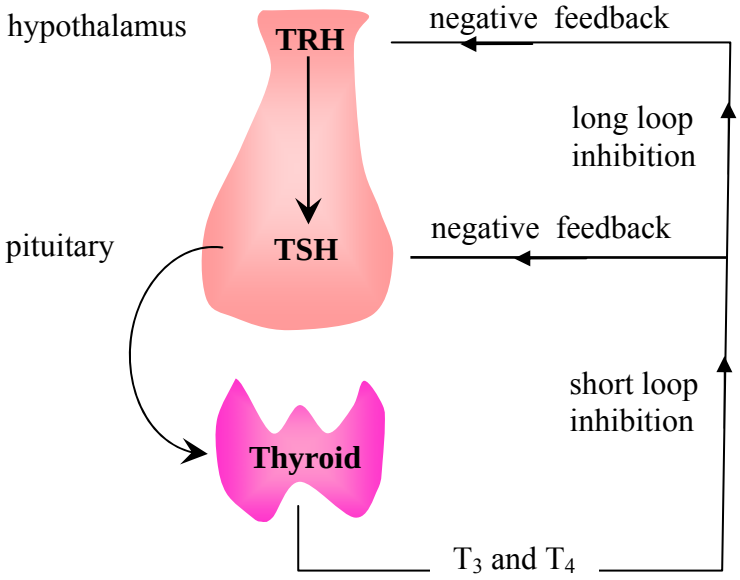


Figure 2. The hypothalamic-pituitary-thyroid axis

2.3 The synthesis and secretion of thyroid hormone

The synthesis and secretion of thyroid hormone starts when TSH binds to the TSH receptor on the basal membrane (Fig. 3).

(1) Iodine concentration by Na^+ and I^- symporter (NIS), plasma iodine in the form of iodide across the basal membrane in the apical membrane (thyroid cells) by thyroid peroxidase (TPO), an energy requiring active transport mechanism.

(2) Thyroglobulin (Tg) is synthesized within follicular cells and transported into the follicular lumen where it is the major component of colloid.

(3) Tg iodination in apical membrane by H_2O_2 and TPO, activated iodide binds to tyrosyl residues on Tg, forming monoiodotyrosine (MIT) and diiodotyrosine (DIT), these are subsequently coupled under the influence of TPO, forming the iodothyronine thyroid hormones. The coupling of two DITs yields T_4, whereas coupling of one MIT and one DIT yields T_3.

(4) In the process of thyroid hormone secretion and Tg proteolysis, the Tg enters follicular cells by pinocytosis and form colloid droplets. It fuses with lysosome, forming phagolysosomes in which Tg broken down by proteolysis, releasing T_4 and T_3 to diffuse into the circulation.

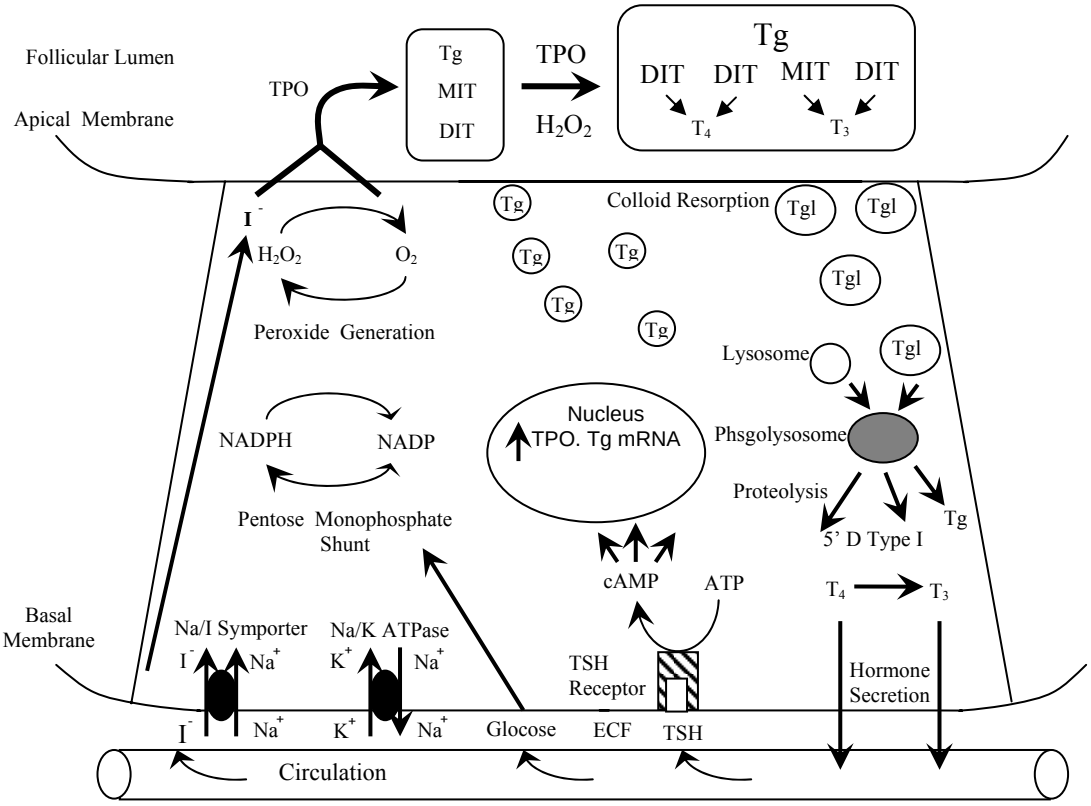
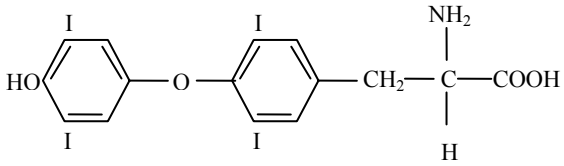


Figure 3. The diagram of thyroid hormones synthesis by follicular cell

2.4 Thyroid hormones and their related hormones

The thyroid hormones regulate a wide range of cellular and physiologic activities such as growth, development and metabolism (3-5). There are iodothyronines, the result of two coupled iodotyrosines, and are the only iodine-containing hormones in vertebrates (Fig. 4). Without iodine there is no biosynthesis of thyroid hormones. Therefore, thyroid function ultimately depends on an adequate supply of iodine.

3,5,3′,5′-Tetraiodothyronine (L-thyroxine, T_4)



3,5,3′-Triiodothyronine (T_3)

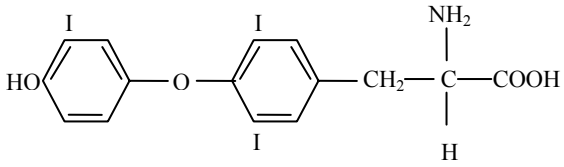


Figure 4. Structures of thyroid hormones

2.4.1 Tetraiodothyronine (L-thyroxin, T_4) is the major thyroid hormone in blood, which has a mean serum concentration of 8.6 μg/dl or 110 nmol/L. All circulating T_4 derives from thyroidal secretion, in normal adults is about 90 μg/day. The circulating of T_4, 99.97% is protein bound, whereas only 0.03% is free. The half-time of disappearance of T_4 from the circulation is 7 days.

2.4.2 Triiodothyronine (T_3) is the minor thyroid hormone in blood**,** the mean serum concentration of T_3 is 135 ng/dl or 2.1 nmol/L, only 1.5% that of T_4. The production rate of T_3 is about 26 μg/day. The major source of circulating T_3 is conversion of T_4 to T_3 in peripheral tissues, only about 6.5 μg/day is secreted by the thyroid. The circulating of T_3, 99.7% is protein bound, and the half-time of disappearance of T_3 is 1 to 1.5 days (6, 7).

More than 99% of circulating T_4 and T_3 are bound to specific binding sites on serum proteins, and only a small fraction is free. The bound and free hormones are in equilibrium, so that as free hormone leaves the circulation it is replaced by the dissociation of bound hormone. This system serves both to store thyroid hormone in a readily accessible form and as a buffer to maintain a constant level of free hormones. The result is a stable supply of thyroid hormone to the cells despite changes in the rate of secretion or metabolism (8-10).

2.5 Factors that control thyroid function

In additional, thyroid hormone synthesis is dependent on the predominantly regulated by TSH and the actions of iodide.

2.5.1 Thyroid-Stimulating Hormone

TSH is synthesized by thyrotroph cells in the anterior pituitary. Secretion of TSH is stimulated by TRH that secreted from hypothalamus and passes via the portal system to anterior pituitary, where TSH synthesis and release are stimulated. Thyroid hormones diminish TSH production through a negative feedback mechanism. The glycoprotein TSH then stimulates receptors on the thyroid gland that promote both, the thyroid gland proliferation and the release of thyroid hormones, which then feed back to the pituitary.

2.5.2 Iodide

An ionized form of iodine (I^-) has several actions on synthesis and secretion of thyroid hormone. Under physiological conditions, the thyroid iodide concentration is 20 to 40 times higher than the serum iodide concentration, and iodide uptake occurs against a cell-to-plasma electrochemical gradient of about -40mV (11). Administration of small amounts of iodide results in increased synthesis without increased secretion. Acute administration of large amounts of iodide causes a progressive decrease in iodination of Tg. This phenomenon is called the *Wolff-Chaikoff effect* for the investigator who first described it. It is dependent on the concentration of iodide in thyroid cells. Chronic administration of large amounts of iodide results in an increase in iodide uptake and binding to Tg while secretion of T_4 remains normal. This is accompanied by release of nonhormonal iodide from the gland, termed the iodide leak

(12). The effect is transient and it overcome by an adjustment of the iodide transport system, which lowers intracellular iodide concentration.

The normal distribution of iodine in thyroid, salivary glands, gastric mucosa, small and large bowel, urinary bladder, liver, and breast (during lactation). The excretion of iodine goes to both renal (up to 75% in 24 hours) and GI tract. The normal daily dietary intake of iodine is about 500 μg.

2.6 Thyrotoxicosis

Thyrotoxicosis is the condition that results from an elevation of circulating thyroid hormone, resulting in increased thyroid hormone action in peripheral tissues. A decrease in serum TSH concentration is the earlist measure of thyroid overactivity (subclinical thyrotoxicosis), followed by an increase in serum of thyroid hormones concentrations (overt thyrotoxicosis). Usually, the results from increased production of thyroid hormone, in which case the term hyperthyroidism is used, can also result from excess intake of thyroxine, or from release into the circulation of stored thyroid hormone, as occurs in thyroiditis. The causes and types of thyrotoxicosis are given as follows (13).

Type	**Cause**
Autoimmune	Graves' disease
	Hashimoto's thyroiditis
Autonomous	Toxic multinodular goiter
	Solitary toxic adenoma
Transient	Postpatum thyroiditis
	Subacute thyroiditis
	Painless thyroiditis
Drug-induced	Iodine- induced (Jod-Basedow)
	Thyroxine or T_3 (factitious)
Secondary	TSH secreting tumour
	Syndromes of inappropriate TSH secretion
	Trophoblastic tumours
Ectopic	Struma ovarii
	Metastatic follicular carcinoma

2.6.1 Clinical features of thyrotoxicosis

The clinical features resulting from excess thyroid hormone in the circulation are common to the various types of thyrotoxicosis, regardless of the cause. The clinical manifestations are in symptoms and signs. The symptoms are nervousness, fatigue, weakness, increased perspiration, heat intolerance, tremor, hyperactivity, palpitation, increased appetite, weight loss, menstrual disturbances. The signs are tachycardial or atrial arrthythmia, systolic hypertension, warm skin, moist and smooth skin, stare and eyelid retraction, tremor, hyperreflexia, muscle weakness. Additional clinical features are associated with specific types of thyrotoxicosis.

Metabolism effects. The increase in metabolic rate resulting from excess thyroid hormone reaching the peripheral tissue leads to weight loss, typically associated with an increased appetite.

(1.) Cardiovascular features. Palpitations are common and may be associated with sinus tachycardia, supraventricular tachycardia, or atrial fibrillation. The pulse rate is increased during sleeping as well as in walking hours. The pulse pressure tends to be wide and the character of the pulse may be collapsing.

(2.) Catecholamine-like effects. The features of thyrotoxicosis are suggestive of increased catecholamine activity, and it has long been considered that thyroxine patients have increased sensitivity to catecholamine (14). The features that respond to β-adrenergic blocking agents include a fine tremor of the outstretched hands, excess sweating, tachycardia, nervousness and a starting appearance of the eyes due to retraction of eye lids.

(3.) Neuropsychiatric features. Nervousness and irritability are very common symptoms. Insomnia and inability to relax despite fatigue are also encountered frequently. Patients are hyperkinetic and this is more readily apparent by their inability to sit still during a conversation (15).

(4.) Miscellaneous features. In the muscle function, proximal myopathy is common (16). It is characterized by atrophy and weakness. However, the symptoms, clinical signs and biochemical abnormalities depend upon such factors as severity of the disease, the length of the history, the age of the patient and perhaps the presence of additional pre-existing disease.

The clinical features (symptoms and clinical signs) and laboratory tests were used with specific diseases in thyrotoxicosis. The most common cause of thyrotoxicosis is GD, followed by toxic multinodular goiter.

2.7 Graves' disease

More than 200 years ago, Caleb Parry described cardiological manifestations of hyperthyroidism (17). Robert Graves first identified the association of goiter, palpitations, and exophthalmos in 1835 (18). GD is an autoimmune disease characterized by thyrotoxicosis, caused by hypersecretion of the thyroid gland, thyroid hyperplasia, infiltrative ophthalmopathy and localized myxedema. The hypersecretion and hyperplasia of thyroid are caused by TSH receptor-stimulating antibodies (TSHR-Abs), which are antibodies against the TSH receptor on the cell membrane of thyroid follicular cells that mimic the effects of TSH.

2.7.1 Clinical features of Graves' disease

The clinical features of hyperthyroidism are common to any condition in which increases in thyroid hormone biosynthesis and secretion by the thyroid gland. The patients may present with any of the clinical features noted, the most common include weight loss, palpitations, heat intolerance, flushing and sweating, goiter, muscle wealness and menstrual change.

(1.) Thyroid enlargement or goiter is almost always present in GD. It is typically symmetrical, diffuse enlargement, without nodularity. The thyroid gland may be easily visible and will be seen to move on swallowing. When palpated, this is found to be a soft smooth enlargement of both lobes. The vascularity is apparent from increased pulsation in the neck and a bruit is very often audible over the thyroid.

(2.) Ophthalmopathy or orbitopathy. The most obvious pathological change within the orbit is the enlargement of extraocular muscles. In most cases, microscopy reveals that the muscle fibers are preserved and the increase in muscle bulk probably reflects changes in the connection tissue: fibroblasts are numerous and there is excessive deposition of collagen and of glycosaminoglycans, which lead to interstitial oedema. There is also some lymphocytic infiltration. The ophthalmopathy is found in mild approximately 60% of patients with GD, moderate severe in about 10%, and severe in about 3% of patients.

(3.) Dermopathy. The rare accompaniment of this feature occurs in about 3% of patients. It is closely associated with ophthalmopathy, with a high titre of TSH-R Ab and often with recurrent hyperthyroidism.

(4.) Additional features. When thyrotoxicosis is due to GD, additional features may include thyroid acropachy, lymphadenopathy and splenomegaly. There may be additional evidence of autoimmunity, such as vitiligo or association with myasthenia gravis or with other autoimmune endocrine disorders.

2.7.2 Diagnosis of Graves' disease

The diagnosis of GD is based on the clinical and biochemical manifestations of hyperthyroidism. Laboratory findings to confirm the diagnosis of thyroid overactivity, to establish the cause and guide therapeutic decision making are as follows:

(1.) Measurement of serum TSH. It is a useful screening test for the presence of hyperthyroidism because very small increases in thyroid secretion reduce the secretion of TSH. All patients with thyrotoxicosis have low or undetectable serum TSH concentration. Therefore, a normal serum TSH concentration is strong evidence that the patient is euthyroid. In Thailand, with higher incidence of T_3 toxicosis, is has been shown that the efficacy of FT_3 and TSH to diagnosis of thyrotoxicosis is very high with a sensitivity of 97.57% and a specificity of 100% (19).

(2.) Measurement of thyroid uptake of RaI. In thyrotoxicosis cause by GD, the percentage of fractional uptake in 24 hours is 35-95%.

(3.) Thyroid imaging. The thyroid is usually enlarged (goiter). The distribution of radionuclide in thyroid gland and the echo pattern of ultrasonography are homogeneous, but it may be nodular in patients with long-standing disease.

2.7.3 Examination of Graves' disease

(1.) In vitro function test. ^{125}I is used for RIA and other in vitro procedures. The agent decays by electron capture with a physical half-life of 60.2 days. It emits a gamma photon of 35 keV. The in vitro technique, allows clinical diagnosis without the patient being exposed to radiation. A blood sample taken from the patient is sent to the laboratory and examined through nuclear techniques such as radioimmunoassay (RIA) or immunoradiometric assay. (IRMA). The tests are available for evaluation of thyroid function. Most thyroid function tests are performed on serum. In general,

measurements of serum TSH and the thyroid hormones (T_3 and T_4) should be performed to determine thyroid status.

a. Radioimmunoassay (RIA)

The RIA was first described in 1960 by Yalow and Berson (20). It is the radiotracer technique using a radioisotope with remarkable sensitivity and a high degree of specificity that is widely used for the estimation of a variety of molecules present in complex matrices. The application of this technique spans over a wide spectra of substances such as hormones, steroids, vitamins, drugs, tumor markers and viral antigens.

The fundamental concept of RIA is based on the competition between unlabelled antigen and a finite amount of the corresponding radiolabeled antigen for a limited number of antibody binding sites in a fixed amount of antiserum. After equilibrium system is occurred, complete separation of labeled antibody-bound and unbound antigen by solid phase antibodies method. The radioactivity in the bound fraction is measured and a standard is plotted, the concentration of analyte in unknown specimen can be determined from the standard curve.

The RIA technique has seen several refinements over the years to make it simpler to user. One of the improvements is the introduction of solid phase separation technique. In solid phase assays, the reagent antibody is immobilized on solid phase such as polystyrene tubes, and the separation is carried out by simply decanting the contents of the reaction tube.

b. Immunoradiometric Assay (IRMA)

The IRMA was first described in 1968 by Miles and Hales (21). It is a more sensitive and specific technique which is an improvement of the RIA principle. The standard curve of IRMA is linear over the wide range of the concentration.

In IRMA, the analyte is incubated with an excess of radiolabeled antibody. Two-site IRMA technique, a further modification of the IRMA technique, uses two antibodies for sandwiching the analyte of which one of the antibodies is labeled with ^{125}I.

(2.) In vivo radionuclide tests and imaging

a. Thyroid radioiodine uptake (RAIU)

The thyroid RAIU is used to evaluate the functional status of the thyroid gland, primarily to differentiate among the various causes of hyperthyroidism and to help determine the amount of RaI to be given for treatment of hyperthyroidism. To perform the test a known quantity of RaI is administered orally, it is rapidly and completely absorbed and distributed in body. A portion is taken up by the thyroid gland, and the remainder is excreted in the urine. Because stable iodine and RaI are chemically identical, the thyroid collects the same proportion of RaI as of stable iodine in the diet. At a specified time interval the amount of RaI present in the thyroid gland is determined using a collimated scintillation detector and expressed as a percentage of administered RaI. Either ^{131}I or ^{123}I can be used to determine thyroid uptake. ^{123}I is generally preferred since the radiation dose to the thyroid is significantly less, but it is more expensive. In Thailand, ^{131}I is used to determine thyroid uptake, the dose of ^{131}I is 4 to 10 μCi (0.15 to 0.37 MBq).

The most common time interval for determination of thyroidal RAIU is 24 hours, but 4-hour uptakes are also common. Hayes et al (22) had used an early of thyroid RAIU at 4 hours to estimate the late uptake (24 hours) by the formula:

$$\text{Est. LU} = -55.7 + 73.2 \log \text{EU}$$

When Est. LU is estimation of late uptake (24 hours) and the EU is early uptake (4 hours).

A few patients with severe hyperthyroidism and low thyroidal content of stable iodine will have rapid release of RaI from the gland in the form of radiolabeled T_4 and T_3. They may have high thyroidal uptakes when determined at 2 to 6 hours but normal uptakes at 24 hours (23, 24). Therefore, interpretation of RaI uptake is usually done in conjunction with thyroid function tests in serum, measurements of TSH and the thyroid hormones (T_3 and T_4).

Patient preparation for RAIU. The RaI should never be given to a pregnant woman. If there is any doubt, the procedure should be scheduled for the week after start of the next menstrual period or a pregnancy test should be performed. Patients should be asked to omit vitamins and food supplements containing iodine and to avoid foods high in iodine for 5 to 7 days before the test. If water-soluble radiographic contrast has been given the test should be delayed for 3 to 4 weeks. Skin antiseptics containing iodine should be discontinued 1 week.

b. Thyroid scan is imaged in patients with documented hyperthyroidism and palpable thyroid abnormalities to differentiate among solitary hyperfunctioning nodules, toxic nodular goiter, and GD arising in a preexisting nodular goiter. It is also useful in locating ectopic thyroid tissue in infants with congenital hypothyroidism. Imaging in adults can be performed following oral administration of 200 to 400 μCi (7.5 to 15 MBq) ^{123}I, or intravenous administration of 2 to 10 mCi (75 to 370 MBq) ^{99m}Tc pertechnetate. ^{131}I is no longer used for imaging, because its high-energy gamma radiation is not suited to current imaging equipment, delivers significantly more radiation to the thyroid. In GD all of the thyroid follicular cells are equally stimulated and the distribution of radiotracer is uniform.

c. Ultrasonography of thyroid is based on the emission of high-frequency sound waves and their subsequent reflection as they pass through the tissue. The ultrasonographic examination of the neck is performed using high-frequency transducers (7 to 13 MHz) with the patient in the supine position and the neck hyperextended. The transducer is coupled to the skin with gel because the sound waves do not pass through air. Ultrasonography can detect thyroid lobes or lesions as small as 2 mm. It allows accurate estimation of thyroid size gives a rough estimate of tissue density (echogenicity), shows vascular flow and velocity (color-flow doppler), aids in the accurate placing of needles for diagnostic or therapeutic purposes (25, 26). Images are obtained in the transverse (axial) and longitudinal (sagittal) planes, for measurement of thyroid size to estimate of thyroid weight.

The sonographic methods for quantitating thyroid size are available. It is based on the volume of an ellipsoid, the Brunn's formula (27) is:

$$\text{Volume } (cm^3) = 0.52 \text{ (length} \times \text{width} \times \text{thickness)}$$

This method is 80% to 85% accurate, the accuracy decreasing with increasing size and degree of irregularity of the thyroid. The volume in cubic centimeters determined by ultrasound was equated to the weight in grams by a 1:1 ratio (28, 29). Thus,

Thyroid volume (cm^3) = Thyroid weight (g)

The normal thyroid gland by ultrasonography

Normal thyroid lobes have a characteristic homogeneous medium-level echogenicity, whereas that of the muscles anterior and anterolateral to the thyroid is lower (30). Posterolaterally, the thyroid is bordered by the sonolucent common carotic artery and internal jugular vein, and medially by the trachea. The esophagus with its echogenic mucosa can usually be seen behind and to the left of the trachea (Fig. 5).

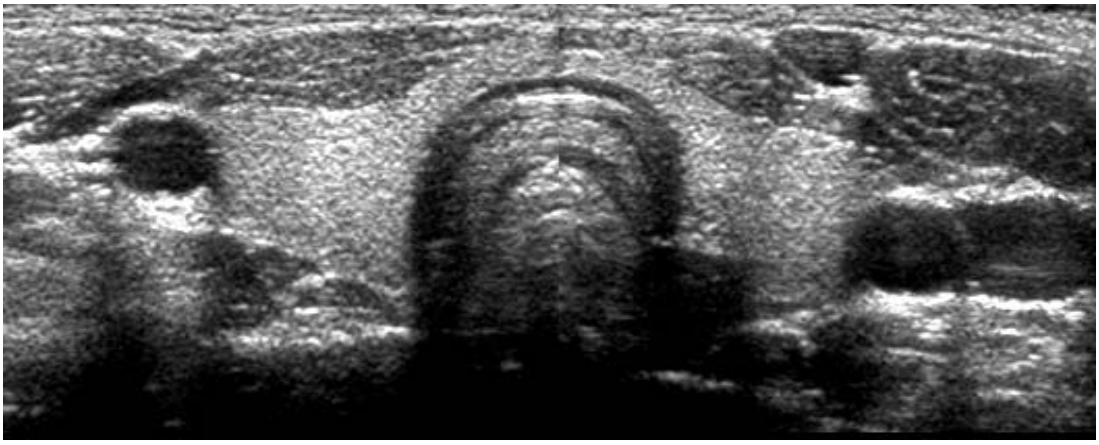


Figure 5. Normal thyroid gland by ultrasound

2.8 Management of Graves' disease

The objectives of treatment of GD at the present time are to render the patient euthyroid as soon as possible and without the need for long-term drug treatment, to avoiding the complications of treatment, and in particular to prevent the development or deterioration of opthalmopathy. Current treatment is directed to reverse the hypersecretion of thyroid hormones by the thyroid follicular cells.

The alternatives available for treatment of the hyperthyroidism are medication therapy, surgery and RaI therapy, but there are no the best treatment, the choice depends on several factors. Among the most important are the physician's experience and the patient's preference. In some situations (e.g., in pregnant women and elderly patients), the therapeutic choices are more limited.

2.8.1. Medication therapy

The medication therapy is the first choice for thyrotoxicosis caused by GD. The length of time for which the ATD is given varies from 6 months to 2 years or more; the remission rate can be improved to a small degree by prolonging the course of treatment (31). Thus, in patients with mild disease where the expectation of remission is high, 6 months course of treatment is probable adequate, whereas 2 years course is probably to be recommended in those with more severe disease

(1.) Anti-thyroid drugs

The ATD acts by decreasing thyroid hormone production. The agents in use are thionamide group of drugs (carbimazole, methimazole and propythiouracil), their major action is to block thyroid hormone biosynthesis which they do by inhibition of iodine oxidation and organification by blocking the coupling of iodotyrosines to form T_3 and T_4. In the group of GD, the definitive treatment of indications for ATD are young adults, juvenniles, neonates, pregnancy, mild hyperthyroidism and with severe opthalmophathy.

a. Methimazole (MMI)

MMI is almost completely absorbed from the gastrointestinal tract. Peak serum concentrations occur 1 to 2 hours after ingestion and are in the range of 300 ng/mL (2.6 mmol/L) after a 15 mg oral dose. The serum half-life of MMI is 6 to 8 hours, but a little is bound to serum proteins and similar in patients with thyrotoxicosis (32, 33). Drugs clearance is unchanged in patients with renal disease (34), but is

slowed in those with hepatic disease (33). The intrathyroidal turnover of MMI is slow, the concentrations 17 to 20 hours after ingestion being similar to those 3 to 6 hours after ingestion (35). Given MMI relatively long serum (and intrathyroidal) half-life and its long duration of action, it is effective when given as a single daily dose (36, 37).

b. Propylthiouracil (PTU)

Orally administered PTU is almost completely absorbed. Peak serum concentrations occur about 1 hour after ingestion, with peak concentrations of about 3 mg/mL (18 mmol/L) after a 150 mg oral dose (38). Serum PTU concentrations correlate with the drug's effects on iodine oxidation and organification, and with inhibition of T_4-deiodinase activity (36). The serum half-life of PTU is in the range of 1 to 2 hours, and it is not altered in patients with thyrotoxicosis (37) or hepatic (39) or renal failure (40). The duration of action of PTU is about 12 to 24 hours (41, 42).

PTU and MMI are available in Thailand (43, 44), they are thioamides that concentrated in thyroid tissue and inhibit hormone biosynthesis. PTU is more popular than MMI because it is effective and less expensive. In patients with severe hyperthyroidism or excessively large goiters, more doses may be advisable.

The retrospective studies (45-48) that indicated an effect of PTU to significantly lower the efficacy of subsequent RaI therapy. Two prospective of randomize-controlled trials (49, 50) compare the effective of RaI therapy after MMI pretreatment with none medication treatment. None involving MMI demonstrated an alteration in the effective of RaI therapy, withdrawal of MMI and CMZ is 4 days, there are no an effect for RaI therapy for GD and can be restart ATD in 7 days after RaI administration (51). In contrast, the treatment of PTU before RaI therapy, the dose of RaI could be increased by 25% to overcome the radio-resistant effects of PTU (52), withdrawal of PTU is 5 days, it have a effect for RaI therapy for GD and recommended time of PTU withdrawal is 10 days (53). The other shows a group of discontinued ATD for 2 days before RaI administration, more effective (is increase to 50%) than the group of ATD which was stopped 1-5 days after RaI administration (54).

The effects of ATD (PTU and MMI) have an effect on outcomes of RaI therapy. The ATD must be discontinued for a sufficient time prior to RaI administration. Recommended time of withdrawal is 3 days (55) or 3-7 days (56) for ATD. Therefore, MMI would be preferable one choice of medication treatment before RaI therapy.

Side effects of antithyroid drugs

ATD have multiple potential side effects. Most are considered to be allergic reactions. Fever, urticaria or other rashes, and arthralgia occur in 1% to 5% of patients, usually within the first several weeks or months after initiation of therapy, and are more common in patients treated with higher doses (57). The more serious and rarer toxic reations (major side effects) are agranulocytosis, aplastic anemia, hepatitis (with PTU) (58) and cholestasis (with MMI) (58), polyarthritis and a lupus-like syndrome or vasculitis. All of which, the possible exception of agranulocytosis, are more common in patients treated with PTU. Agranulocytosis, the most feared problem, probably occurs with equal frequency with both drugs (about 0.2% to 0.5%). The other severe reactions are less common.

(2.) Other drugs

a. β-adrenoceptor blocking drugs

β-blocking (propranolol) is the most commonly used for symptomatic treatment in thyrotoxicosis, and it has some advantages over more selective agents. It acts at the level of the β-adrenoceptors on peripheral tissue cells and also blocks the conversion of T_3 and T_4, as well as having a direct effect on myocardium. It is particularly useful in patients with supraventricular arrhythmias due to thyrotoxicosis, but it should not be use in patients with asthma or in pregnant patients.

The dose of propranolol necessary to induce β-blockade is in excess of that required in euthyroid patients. The initial dose will usually be 160-240 mg/day, given either in divided doses or as a depot preparation, adequacy of β-blockade should be checked by measurement of exercise pulse rate and the dose increased as necessary (59).

b. Iodine

Iodine is used only rarely now in the management of hyperthyroidism. Its therapeutic action is probably achieved by inhibition of thyriod hormone release rapidly within hours. Thus, its major use is for patients in whom a very prompt response is necessary, treatment of thyrotoxic crisis or emergency surgery in a previously undiagnosed thyrotoxic patient. It can also be used in preparation for thyroid surgery in patients who have developed adverse reactions to thionamide drugs. However, if iodide is given for more than a few weeks there is the danger of an escape phenomenon occurring in which thyroid hormone release is no longer suppressed, but rather there is increase in hormone synthesis and secretion. Iodine is given in the form of potassium iodide 15 mg three times daily, or iodine-containing contrast material sodium ipodate can be used (60).

c. Lithium carbonate

Lithium carbonate is well known to have antithyroid actions, but its mechanism (s) of action is still not understood. Primary action is to inhibit T_3 and T_4 release, a process that is stimulated by TSH and mediated by cyclic adenosine monophosphate (61). It also may inhibit T_3 and T_4 synthesis (62). In practice, it should not be given as primary treatment for thyrotoxicosis, but it is an option for patients with severe thyrotoxicosis who are allergic to iodide, and it may have an adjunctive role in patients treated with radioiodine and in that amiodarone-induced thyrotoxicosis (63). The dose of lithium is 300 or 450 mg orally every 8 hours, the goal being to maintain serum lithium concentrations in the range of 1 mEq/L.

2.8.2. Surgery

Subtotal thyroidectomy is one of the most effective methods of treatment for GD. A small remnant of thyroid tissue is left (approximately 8 gram tissue), postoperatively the majority of patients go into permanent remission, and within the course of a few months the thyroid remnant becomes normal both functionally and histologically. Careful preparation of the thyrotoxic patient for surgery is mandatory, such that the patient is euthyroid and stable at the time of operation by antithyroid drugs. If this is not done and the patient is hyperthyroid at operation there is then a risk of developing thyrotoxic crisis, which may be fatal. Alternatives are the use of propanolol, in dosage adequate to produce demonstrable β-blockade (short-term

treatment only), or iodine. Neither of these agents given alone is satisfactory for routine preoperative treatment. The results of surgery for GD are excellent, between 70 and 80% of patients can be expected to become euthyroid and remain in permanent remission.

Postoperative complications are hypoparathyroidism, haemorrhage, laryngeal nerve damage, thyroid crisis, hypothyroidism and recurrent hyperthyroidism. The incidence of recurrent hyperthyroidism is small; being about 1% per year, the incidence of postoperative hypothyroidism is between 20 and 30% in most series.

The surgery should probably be recommended when patients not go into remission after a course of ATD, especially with large goiter and severe hyperthyroidism.

2.8.3. Radioiodine therapy

RaI therapy continues to play a major role in the definitive treatment of hyperthyroidism; it is convenient, effective and safety. It affects on thyroid epithelial cells through the production of an intense radiation thyroditis. Followed by progressive interstitial fibrosis and glandular atrophy resulting in destruction of the synthetic capacity of the thyroid, such that over a period of weeks or months patients become first euthyroid and ultimately, over months or years, many will become hypothyroid. The two most important undesirable effects of RaI are late development of hypothyroidism, or continued inadequately controlled hyperthyroidism. These results are from the problems of dosimetry.

(1.) Radioactive iodine (^{131}I)

^{131}I has a physical half-life of 8.1 days with a principal gamma ray of 364 keV and a principal beta particle with a maximum energy of 0.61 MeV, an average energy of 0.192 MeV. The range in tissue is 0.8 mm (55).

The RaI can be administered in liquid or capsule form, but the prescribed amount must be verified in a dose calibrator prior to administration. If a liquid form is used, strategies for minimizing volatilization during dosage preparation and administration should be employed such as venting the dose into a filtering system, such as a fume hood and administering the dose to the patient shortly thereafter (55).

(2.) Indications for RaI therapy

The patients to be excluded are: (a) pregnant or lactating, (b) have thyroid associated opthalmopathy and (c) very young. Although children and adolescents are being treated with RaI with increasing frequency (64), an ATD is usually preferred in this age group (65). Others believe that all patients with thyrotoxicosis caused by GD should be given a trial of ATD therapy, in the hope that a remission will occur. However, remissions are uncommon in patients with moderate or severe thyrotoxicosis.

RaI therapy is the most appropriate and perhaps cost-effective therapy because it permanently ameliorates thyrotoxicosis quickly and safely. Its use can be considered for the majority of patients with proven hyperthyroidism cause by GD, patients with large goiter or severe hyperthyroidism, patients with recurrent hyperthyroidism after ATD therapy or who had complicated with ATD therapy.

(3.) Methods of RaI administration

a. Fixed dose; fixed dose of ^{131}I was administered to the patients, low fixed dose is 3-5 mCi and high fixed dose is 8-10 mCi**.**

b. Sliding scale dose; the dose of I-131 was administered to the patients relating to thyroid gland size and clinical signs and symptoms, 3-5 mCi with hyperthyroidism, 7-15 mCi with large goiter or severe hyperthyroidism and 20-25 mCi with a very large goiter or very severe hyperthyroidism.

c. Calculated doses are wanted to achieve a high cure rate with a single dose of RaI, two techniques of RaI depend on dose of ^{131}I, thyroid weight and iodine uptake:

(i) Radioactivity concentration method (in milliculies): According to the Society of Nuclear Medicine procedure guidelines for RaI therapy for GD (55) is between 80-200 μCi/g (2.96-7.4 MBq/g) and divides the dose of ^{131}I into 3 groups, low dose (50-75 μCi/g), middle dose (100 μCi/g) and high dose (150-200 μCi/g). The administered dose of ^{131}I to obtain 80 to 200 μCi/g of ^{131}I/g of thyroid (66) was calculated as follow:

$$\text{RaI activity } (\mu\text{Ci}) = \frac{\mu\text{Ci } ^{131}\text{I/g} \times \text{thyroid weight (g)} \times 100}{\text{24-hour of RAIU}}$$

(ii) Absorbed dose method: The administered dose of ^{131}I to deliver an absorbed dose (rad) to the thyroid, some study (67) was satisfied with 50 Gy. Other study shows a strong correlation between the success of therapy and the radiation dose actually absorbed by the thyroid, the success rate was 11% for a target dose of 50 Gy, 50% for 100 Gy, 67% for 150 Gy, 80% for 200 Gy, 84% for 250 Gy, 88% for 300 Gy, 90% for 350 Gy and 93% for 400 Gy (68). The administered dose of ^{131}I was calculated according to the following equation (69).

$$\text{RaI activity (mCi)} = \frac{\text{Absorbed dose (rad)} \times \text{thyroid weight (g)} \times 6.67}{T_{1/2(eff)}\,\text{(day)} \times \text{24-hour of RAIU}}$$

Where $T_{1/2(eff)}$ is the effective (i.e., radioactive decay–uncorrected) half-life of RAI in the thyroid, which is given by the following equation:

$$\frac{1}{T_{1/2(eff)}} = \frac{1}{T_{1/2(phys)}} + \frac{1}{T_{1/2(bio)}}$$

Where $T_{1/2(bio)}$ is the biological (i.e., radioactive decay–corrected) half-life of RaI in the thyroid, assuming a monotonically decreasing monoexponential timeactivity curve and taking the 24-hour percentage uptake as the zero-time percentage uptake; $T_{1/2(phys)}$ is the physical half-life of ^{131}I (8.04 days).

(4.) The dose of RaI therapy

a. Conventional dose of RaI therapy

The patients were referred specifically for RaI therapy, mostly following relapse after stopping medical treatment by ATD. The ATD was always stopped mostly about 7 days prior to oral ^{131}I before the test of RAIU and RaI therapy, the RAIU was measured at 4 or 24 hours. The thyroid weight in grams was estimated by radiologist's palpation. After RaI therapy, beta-blockers were often given according to the physician's preferences and a few of patients restarted ATD. Prior to being reassessed at the third month, a repeat dose might be prescribed, if indicated clinically and/or as dictated by thyroid function test.

In 2003, according to the protocol was used in Nuclear Medicine Division, Sappasittiprasong Hospital, Ubonratchathanee. The conventional dose of RaI therapy was 100 μCi/g of thyroid weight. However, the outcomes are more likely to fail to response to a single dose of RaI. Of all patients, 75% still hyperthyroid and needed a repeat dose especially patients with large-volume thyroid glands. Despite, 28 patients (25% of them) were cured by a single dose of RaI therapy.

The estimated dose of RaI (101.4 ± 11.4 μCi/g ; range between 80 to 125 μCi/g) in thyroid gland (thyroid weight between 20 to 120 gram) by Hayes's formula (22), the estimated of late uptake (24 hours) from early uptake (4hours). It was analyzed and plotted a linear correlation ($R^2 = 0.95$) as shown in Figure 6.

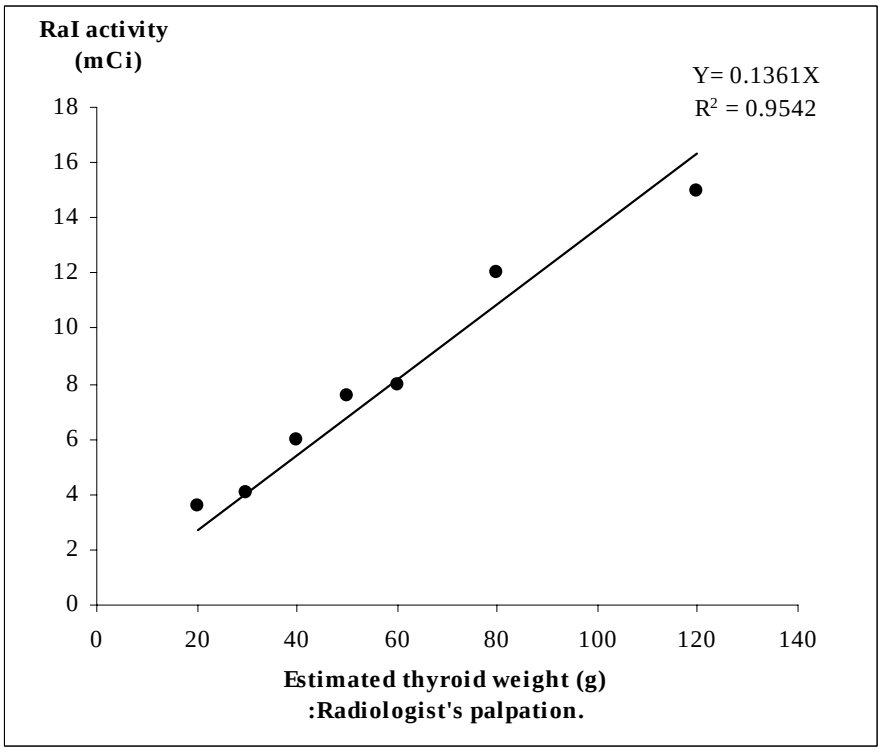


Figure 6. Correlation of cured 28 patients with a single dose of RaI therapy

Where X axis is estimated thyroid weight (g) and Y axis is mean of RaI activity (mCi). The formula of RaI therapy for conventional dose (by sliding scale) is:

$$Y = 0.136 \times (X)$$

In Thailand, the calculated dose of 100 μCi/g of thyroid weight was used for RaI therapy at Siriraj Hospital. After a single dose of RaI therapy shows 43.5% of patients still hyperthyroidism (thyroid weight is 49.35 ± 12.17 g), the 2 groups of euthyroid and hypothyroidism are smaller goiter (36.39 ± 14.66 and 35.31 ± 16.13 g). Also investigate the calculated dose of 120 μCi/g of thyroid weight for RaI therapy with large thyroid gland (70). Similarly at Songklanakarind Hospital, 48% of patients were cured with a single dose of RaI therapy. Follow up found permanent hypothyroid at rates of 40 to 50%, 70 and 80% at 1-3 and greater than 3 years (71). Other country follows the patients up one year later, 47.7% of patients were persistently hyperthyroidism significant to patients with larger thyroid gland (72).

In addition, the report of Doi et al (73) suggested of fixed dose of RaI therapy (Table 1) between 5-10 mCi (185–310 MBq) for optimized non-ablative with expected cure rates of 85% and less than 10% of hypothyroid at 1 year (74-76), only palpation was used to decide dosing.

Table 1. Suggested the fix-dose regimen for optimized non-ablative dosing by Doi et al (73).

Thyroid grade	**Palpation**	**Standard activity**
0	Not easily visible even with neck extension, just palpable (est 10 g).	185 Mbq (5 mCi)
1	Visible only with neck extension but easily palpable (est 20 g).	259 MBq (8 mCi)
2	Visible without neck extension (est 40 g).	370 MBq (10 mCi)
3	Visible easily from afar (est 80 g).	444 MBq (12 mCi)

The variability in the effectiveness of RaI therapy in GD seems related to factors that determine the actual radiation effect of RaI. The weight of thyroid gland is important to determinants of thyroid function and size after therapy and should be considered in dose calculation (77). The outcomes of RaI therapy have been reported to depend on the weight of thyroid gland below or above 40 gram (78), the cure rate of patients with large goiter is lower than patients with small goiter. Patients with larger goiter might need higher dose (79), many of studies (80-82) suggested the RaI therapy for large goiters there is an additional dose adjustment to obtain a faster therapeutic response, increase is needed over the usual linear or size driven calculation.

b. Advanced dose of RaI therapy

In advanced dose method was increased following by Leslie et al (83), the low and high dose showed 50% of difference. Comparing the outcomes of the four doses, low-fixed (235 MBq), high-fixed (350 MBq), low-adjusted of 80 μCi/g of thyroid (2.96 MBq) and high-adjusted of 120 μCi/g of thyroid (4.44 MBq). The analysis did not demonstrate any difference in the term of outcome between the fixed and adjusted dose methods, but it is clinically significant at $p = 0.02$ when compared the euthyroid rate between low dose and high dose.

(i) Non-ablative of advanced (high) dose: The advanced dose of RaI therapy for patients with thyroid weight lower than 40 gram by sliding scale method depended on thyroid weight. The formula of advanced dose was adjusted by an increase in 50% of conventional dose (from 350 MBq/235 MBq and 120 μCi/80 μCi = 1.5), when Y axis is RaI activity (mCi) and X axis is thyroid weight (g):

$$Y = (0.136 \times 1.5)\,(X)$$
$$= 0.204\,(X)$$

The comparison of doses is between conventional sliding-scale, advanced sliding-scale demonstrated by Doi et al (73) as shown in Figure 7.

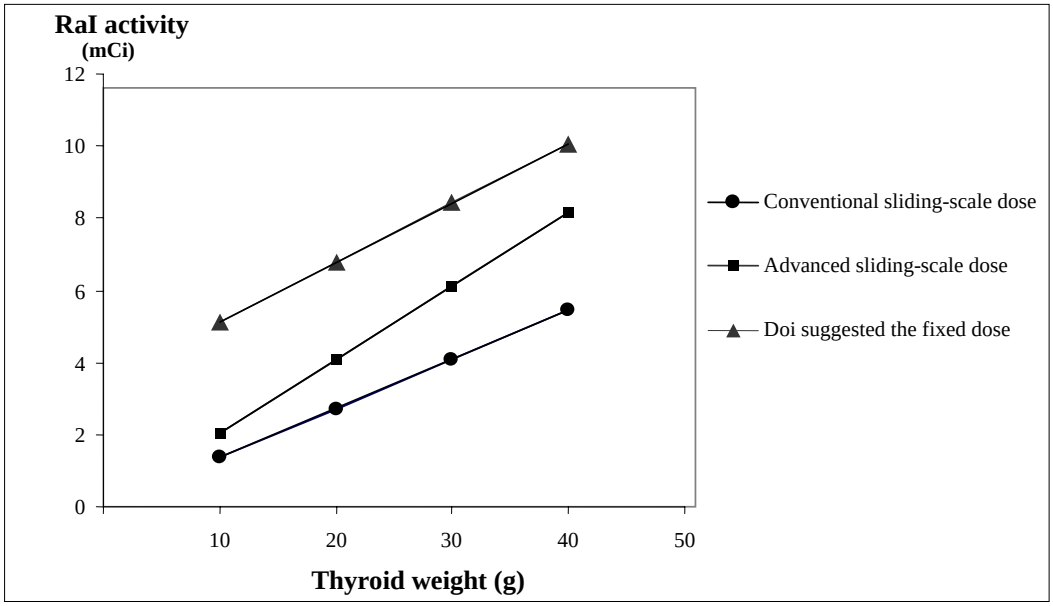


Figure 7. Comparison of doses of RaI therapy between RaI activity (mCi) and thyroid weight (g).

(ii) Ablative of advanced (high) dose: The advanced dose of RaI therapy in patients with large thyroid gland (40 gram and more). The RaI calculated dose depends on thyroid weight and thyroid uptake. It was adjusted the dose of RaI by an increase in 50% (100 μCi/g × 1.5 = 150 μCi/g) of conventional (low) calculated dose. The report of Erik and Larsen (84) shown the high calculated dose of RaI as follows 8 mCi × 100 and divide by percentage of thyroid uptake at 24 hours, the success of treatment was directly related to the dose of RaI retained per estimated weight of thyroid tissue, but this relationship is not linear (Fig 8). None of patients became hypothyroidism if the estimated 24 hours dose of RaI was less than 80 μCi (3.0 MBq/g) of thyroid. The failure rate decreased progressively to reach approximately 10% at 128–155 μCi (4.7–5.7 MBq/g) of thyroid and did not decrease appreciably below that despite doses up to 400 μCi (14.8 MBq/g) of thyroid. Assuming an average goiter weight of approximately 50 gram and a dose of approximately 8 mCi (296 MBq), the treatment protocol was to deliver 150–175 μCi (5.5–6.5 MBq) ^{131}I per gram of thyroid tissue at 24 hours. It should be to induce hypothyroidism within 1 year.

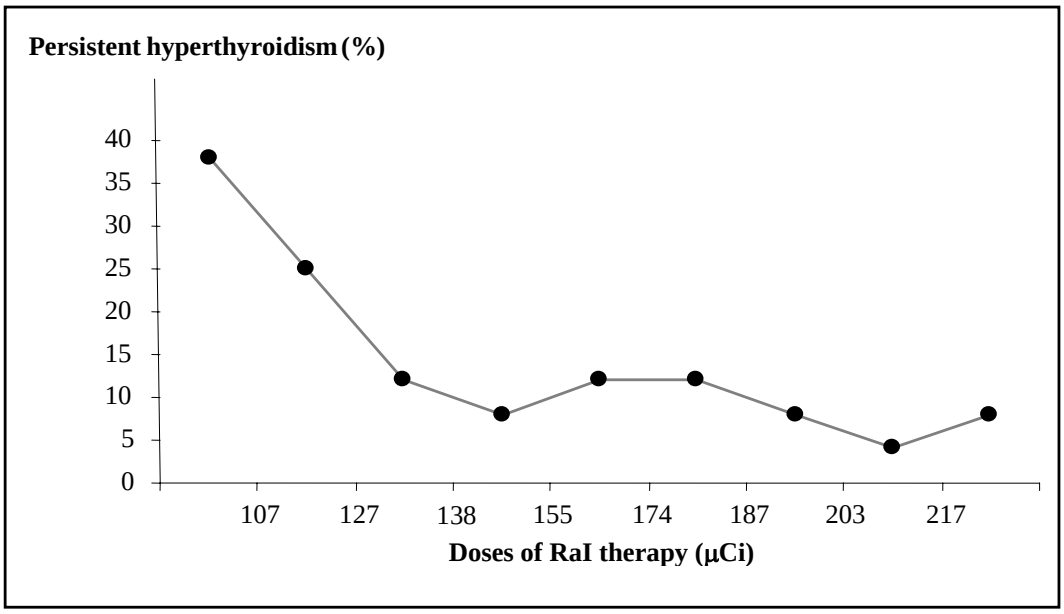


Figure 8. The correlation of persistent hyperthyroidism (%) and the dose of RaI therapy (μCi/g) of thyroid.

(5.) Complications and potential risks of Radioiodine therapy

Complications of RaI for Graves' disease are very rare, the most complication is early hypothyroidism. Side effects are generally dose related. In the first 5 to 7 days after treatment, the early radiation thyroiditis in a one percent incidence or lower, may lead to a transient exacerbation of hyperthyroid symptoms. While this is rarely a problem, it should not be forgotten when treating patients with either very severe hyperthyroidism or very large goiters causing tracheal compression. Giving a large dose of RaI therapy may lead to earlier and more profound destructive effects and developing early hypothyroidism, whereas a smaller dose may result in adequately controlled hyperthyroidism. Rarely, there can be transient neck soreness and/or exacerbation of hyperthyroid symptoms secondary to radiation thyroiditis. Long term analysis of patients treated with RaI for Graves' disease revealed no greater risk of developing malignances than patients who have been treated with drugs or surgery.

Hypothyroidism is the most common clinical disorder of thyroid function. The most often caused by some disorder of the thyroid gland leads to a decrease in thyroidal production and secretion of T_3 and T_4. The hypothyroidism is an inevitable consequence of radioiodine therapy (85), in the past several decades its frequency has increases, and it has appeared sooner after radioiodine administration (86-88),

probable because of the use of higher dose as well as the increased case of detection of hypothyroidism using serum TSH determinations. The hypothyroidism develops within the first year is depends on the dose of RaI, with a continuing rate of 3% per year thereafter (89). In addition to permanent hypothyroidism, some patients have transient hypothyroidism (90-93).

The clinical manifestations of hypothyroidism are symptoms and signs. The symptoms are fatigue, lethargy, sleepiness, mental impairment, depression, cold intolerance, hoarseness, dry skin, decreased perspiration, weight gain, and decreased appetite, constipation, menstrual disturbances, arthralgia and parasthesia. The signs are slow movements, slow speech, hoarseness, bradycardia, hyporeflexia, nonpitting edema (myxedema) and delayed relaxation of reflexes. However, hypothyroidism is usually considered a goal of treatment rather than complication. Hypothyroidism is easy to treat, safe, simple and avoids the need for continuous long-term follow-up for later hypothyroidism in patients treated with lower doses.

CHAPTER III
MATERIALS AND METHODS

Materials

Patients

The patients in this study were hyperthyroid patients attending for thyroid treatment at Nuclear Medicine Division of Sappasittiprasong Hospital, Ubonratcha-thanee. They were asked to participate in the the study, if they agreed, information about the program was provided verbally and from brochures (appendix A)**.** Each patient was asked to sign-in consent form.

Graves' disease was defined as the presence of biochemical hyperthyroidism, raised serum FT_4 concentration and undetectable TSH, together with a palpable diffuse goiter. The inclusion and exclusion criteria are as follows:

Inclusion criteria

1. Graves' disease.
2. Age more than 18 years old.
3. Medication failure or want to be treated by RaI therapy.
4. Estimated 24 hours of ^{131}I thyroid uptake more than 50%.

Exclusion criteria

1. Toxic multinodular goiter or solitary toxic adenoma.
2. Unable to reliably establish the final diagnosis was excluded.
3. Had received thyroidectomy.
4. Had been previously treated by RaI therapy before.
5. Pregnant or breastfeeding.

Seventy-four patients were enrolled, consisting of 56 females and 18 males, age from 18 to 60 years. Each patient was investigated by clinical and biochemical assessment, thyroid ultrasound and 4 or 24 hours thyroid RaI uptake.

Categorization of patients

Patients were divided by thyroid weight into two groups of non-ablative and ablative method, the non-ablative method by sliding-scale dose for thyroid weight lower than 40 grams, and ablative method by calculated dose for thyroid weight 40 grams and more. After that, patients were randomized into two sub-groups by the dose of RaI therapy. The follow-up time is 3 months after treatment of RaI.

Group 1, low dose (conventional) of RaI therapy. Thirty-eight patients consisting of 27 females and 11 males aged 18–57 yrs (36.0 ± 10.0 yrs).

Group 2, high dose (advanced) of RaI therapy. Thirty-six patients consisting of 29 females and 7 males aged 19–61 yrs (39.9 ± 10.4 yrs).

Sample size

The medical records (2003) of patients, who received a single dose of RaI therapy for Graves' disease at Nuclear Medicine Division of Sappasittiprasong Hospital, Ubonratchathanee were examined. The calculated ^{131}I dose was 100 μCi/g of thyroid weight as estimated by physical examination. Analysis of 138 patients showed that 70% remained hyperthyroid, 30% were euthyroid and none were hypothyroid. In this study, to avoid persistent hyperthyroidism, especially when the thyroid is large, 50% increase of the RaI dose should provide the best outcome. The decrease rate of hyperthyroid to 30% of the patients is expected.

To determine how many patients that would be needed to monitor a difference of 30% with α = 0.05 and power = 0.80 (β = 0.20), Z-values are 1.96 and 0.84 respectively. The calculation is as follow:

When Hyperthyroid rate in control group (P_0) = 0.70

Hyperthyroid rate in case group (P_1) = 0.40

$\bar{p} = (p_1 + p_0) / 2 = (0.4 + 0.7)/2 = 0.55$

$\bar{q} = 1 - \bar{p} = 1 - 0.55 = 0.45$

Formulation by one-sided test is:

$$n = \frac{\left[Z_\alpha \sqrt{2\bar{p}\bar{q}} + Z_\beta \sqrt{p_1 q_1 + p_0 q_0}\right]^2}{(p_1 - p_0)^2}$$

$$n = \frac{\left[1.645\sqrt{2(0.55)(0.45)} + 0.840\sqrt{(0.4)(0.6)+(0.7)(0.3)}\right]^2}{(0.4-0.7)^2}$$

$$n = \frac{[1.15736 + 0.5635]^2}{(-0.3)^2}$$

$$n = \frac{2.9484}{0.09}$$

$$n = 32.76$$

Equipment

1. Diagnostic ultrasound system 3535 with linear probe type 8560 (8 MHz)
2. The set of thyroid uptake with program of Captus2000
3. Dose calibrator (CAPINTEC CRC-15R)
4. Gamma counters (LKB Wallac 1277 Gammamaster)

Radioimmunoassay and immunoradiometric assay kits

RIA techniques of FT_3 and FT_4 were tested by CIS bio international.

IRMA technique of TSH was tested by CIS bio international.

Methods

1. The patients were categorized according to the gland mass into small (<40 g) and large size (≥40g).

2. The weight of the gland is estimated by thyroid ultrasound by measuring length and depth of each lobe of the thyroid gland, the volume of the gland was estimated using Brunn's formula (27).

$$\text{Volume } (cm^3) = 0.52 \times \text{wide} \times \text{length} \times \text{deep (cm)}$$

The total weight of the thyroid gland was estimated from the thyroid volume by ratio 1:1.

3. Patients' data were collected form chart review for clinical and laboratory data. Baseline characteristics obtained include age at diagnosis, gender, thyroid weight and body weight before RaI therapy.

4. Each patient received 4 or 24 hours of RAIU with approximately 20 μCi of ^{131}I in capsule form (Thailand Institute of Nuclear Technology).

5. The study was designed as a double-blinded randomized prospective outcome trial. After patients were randomized into two groups of RaI dose, the treatment regimens were assigned as follows in Figure 9.

6. At 3-month after RaI therapy, Clinical details of patients were collected again. These included thyroid weight by ultrasound, body weight and laboratory characteristics (FT_3, FT_4 and TSH).

7. Thyroid status was assessed at 3-month follow-up period. Patients were judged to be euthyroid if serum FT_3 concentrations within the normal range and off the ATD therapy. Patients were classified as persistently hyperthyroid if serum FT_3 concentrations above normal range and need the ATD therapy or repeat dose of RaI therapy. Finally, hypothyroid status if serum FT_4 of patients was below the normal range and serum TSH above normal range. The successful treatment of hyperthyroidism after RaI therapy, the patients is considered euthyroid or hypothyroid, and failure when the patients remained hyperthyroid at 3-month after initial dose of RaI therapy.

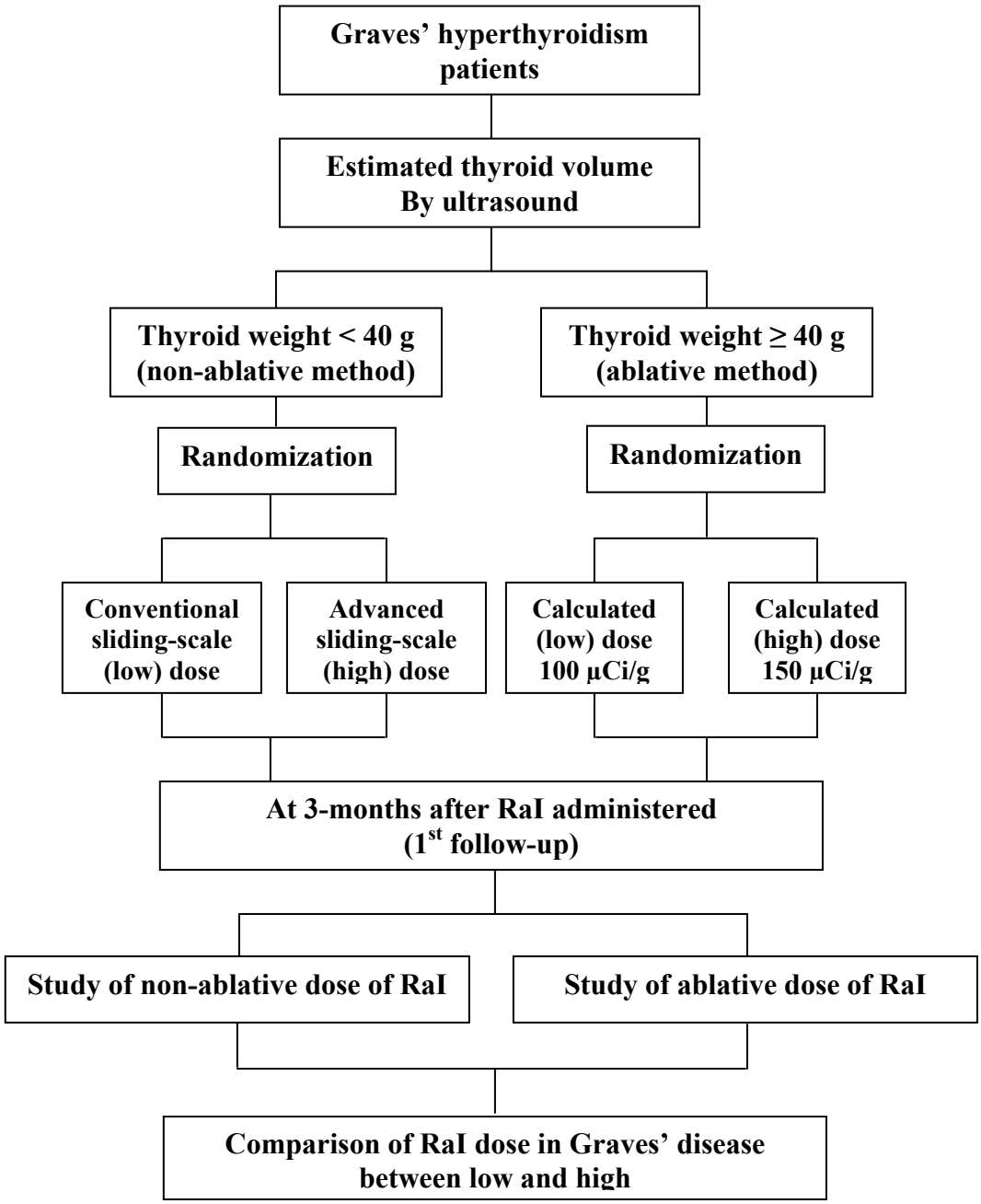


Figure 9. The flow chart of RaI treatment regimens

Statistical of Data analysis

All statistical analysis was performed with SPSS (version 10.0). P values less than 0.05 were considered statistically significant. Data are present as the mean ± SD. Cure or failure rate are presented as percentage of the total within category examined. The *t*-test and unpaired *t*-test were used to compare continuous variables, and χ^2 tests were to compare discrete variables between groups.

Expected outcome

The RaI treatment of hyperthyroid GD with large initial dose in high (advanced) dose regimen may be more effective than low (conventional) dose regimen and with this dosage a more rapid and predictable control of GD is obtained.

Ethical issue

This study was approved by the Committee on Human Rights, Faculty of Medicine Siriraj Hospital, Mahidol University on May 24, 2004.

CHAPTER IV
RESULTS

The results of radioiodine (RaI) therapy with single-dose were presented in 3 parts as follow: 4.1) results of non-ablative dose in patients with thyroid weight lower than 40 gram, 4.2) results of ablative dose in patients with thyroid weight equal and more 40 gram, 4.3) comparison of the outcome and clinical result between the non-ablative and ablative doses of RaI therapy, and 4.4) comparison between the low and high doses of RaI therapy.

Part 4.1: Non-ablative dose (thyroid weight <40 gram)

The results of RaI therapy by sliding–scale method in 28 patients with Graves' hyperthyroidism were examined for thyroid function and clinical sign, 16 patients were treated with conventional (low) dose and 12 patients with advanced (high) dose. The thyroid weight of patients was measured by ultrasound, only patients with thyroid weight lower than 40 gram were included in this group. Categorizations by gender are presented in Table 2, the male to female ratio is 1:6.

Table 2: The gender of patients.

Gender	Conventional dose (n=16)		Advanced dose (n=12)		Total (n=28)		
	n	%	n	%	n	%	Ratio
Male	3	18.8	1	8.4	4	14.3	1:6
Female	13	81.2	11	91.6	24	85.7	

The baseline characteristics include age, body and thyroid weight of pre-RaI therapy and the percentage of 24 hours thyroid uptake are presented in Table 3. To reduce time and for patient convenience, the 24 hrs uptake in this study was estimated from early (4 hrs) of RaI uptake.

Table 3: Baseline characteristics of patients.

Characteristics	Conventional dose (n=16)	Advanced dose (n=12)	Total (n=28)
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.
Age (year)	38.7 ± 8.0	39.58 ± 9.7	39.07 ± 8.6
Body weight (kg)			
Pre-RaI therapy	53.8 ± 8.2	51.63 ± 6.2	52.86 ± 7.4
Thyroid weight (g)			
Pre-RaI therapy	28.8 ± 9.0	25.63 ± 7.7	27.44 ± 8.5
Thyroid uptake (%)			
Early uptake (4hrs)	65.2 ± 16.7	52.29 ± 17.4	59.26 ± 17.9
Est. late uptake (24hrs)	75.0 ± 10.3	69.12 ± 11.0	72.44 ± 10.8

The average age was 39 and 40 years, thyroid weight averaged approximately 29 and 26 gram (below 40 gram) and the average 24 hrs ^{131}I uptake was 75% and 70% for groups receiving conventional and advanced sliding-scale doses respectively. These pretreatment variables were similar for the 2 dose groups.

Table 4: The dose of RaI administered.

The dose of RaI	Conventional dose (n=16)		Advanced dose (n=12)	
	Mean ± S.D.	Range	Mean ± S.D.	Range
RaI activity (mCi)	3.9 ± 1.2	2.0-5.3	5.0 ± 1.5	2.5-7.2
Dose of RaI (μCi/g)	101.2 ± 13.8	74.1-120.9	135.2 ± 24.6	102.8-174.3

The administered dose of RaI (mCi) and dose delivered to the thyroid (μCi/g) are presented in Table 4, the mean of calculated dose were 3.9 ± 1.2 mCi (range 2.0-5.3 mCi) and 101.22 ± 13.8 μCi/g (range 74.1-120.9 μCi/g) of thyroid tissue for conventional (low) sliding-scale dose protocol. The means of calculated dose were 5.0 ± 1.5 mCi (range 2.5-7.2 mCi) and 135.2 ± 24.6 μCi/g (range 102.8-174.3 μCi/g) of thyroid tissue for advanced (high) sliding-scale dose protocol respectively.

At the end of 3 months after RaI therapy, biochemical and clinical response to treatment were evaluated. Diagnosis of hyperthyroidism was based on clinical signs and evaluated FT_3 and FT_4 (normal range: 2.0-4.25 pg/ml and 0.7-1.8 ng/dl respectively) and suppressed serum TSH concentration (normal range: 0.5-3.7 mU/L). Laboratory results were shown in Table 5.

Table 5: Thyroid function after 3-month therapy according to the treatment assignment.

In vitro test	Conventional dose (n=16)		Advanced dose (n=12)		Total (n=28)	
Thyroid hormone	Mean ± S.D.		Mean ± S.D.		Mean ± S.D.	
FT_3 (pg/ml)	6.9 ± 4.5		4.2 ± 3.0		5.7 ± 4.2	
FT_4 (ng/dl)	3.4 ± 2.5		4.4 ± 10.5		3.8 ± 6.8	
TSH level	n	%	n	%	n	%
<0.5 mU/L	12	75.0	6	50.0	18	64.2
0.5-3.7 mU/L	3	18.7	2	16.7	5	17.9
>3.7 mU/L	1	6.3	4	33.3	5	17.9

The outcomes of patients as shown in Table 6 were diagnosed by thyroid function test and TSH level. Among 16 patients who received conventional (low) dose, 5 patients (31.3%) were euthyroid, none was hypothyroid, and 11 patients (68.7%) remained hyperthyroid. Among the other group of 12 patients who received advanced (high) dose, 7 patients (58.3%) were euthyroid, 4 patients (33.3%) remained hyperthyroid, and only 1 (8.4%) was hypothyroid. There were no significant differences between the groups of conventional (low) and advanced (high) sliding-scale doses at $p > 0.05$.

Overall at 3 months, of 28 patients who received a non-ablative single dose of RaI therapy, 15 patients (53.6%) remained hyperthyroid, a euthyroid was achieved in 12 patients (42.8%) and 1 patient (3.6%) was hypothyroid.

Table 6: Clinical outcomes of RaI treatment as related to dose.

Outcomes	Conventional dose (n=16)	Advanced dose (n=12)	Total (n=28)	χ^2	P value
Euthyroid	5 (31.3%)	7 (58.3%)	12 (42.8%)		
Hypothyroid	0 (0%)	1 (8.4%)	1 (3.6%)	4.113	0.128
Hyperthyroid	11 (68.7%)	4 (33.3%)	15 (53.6%)		

Table 7: The results of RaI therapy by a single-dose.

Results	Conventional dose (n=16)	Advanced dose (n=12)	Total (n=28)	χ^2	P value
Cure	5 (31.3%)	8 (66.7%)	13 (46.4%)	2.181	0.140
Uncured	11 (68.7%)	4 (33.3%)	15 (53.6%)		

The cure and uncured of RaI therapy by an ablative single-dose were shown in Table 7. In the group received conventional (low) dose, 5 patients (31.3%) were cured and 14 patients (68.7%) were uncured. Despites, in the group received advanced (high) dose, 8 patients (66.7%) were cured and 4 patients (33.3%) were uncured.

In study of non-ablative dose, 13 patients (46.4%) were cured and 15 patients (53.6%) were uncured. There were no significant differences between the groups of conventional (low) and advanced (high) sliding-scale doses at $p > 0.05$.

Part 4.2: Ablative dose (thyroid weight ≥40 g)

The results of RaI therapy by calculated method in 46 patients with Graves' hyperthyroidism were examined for thyroid function and clinical sign, 22 patients were treated with low dose of 100 μCi/g (conventional) and 24 patients with high dose of 150 μCi/g (advanced). The thyroid weight of patients was measured by ultrasound, only patients with thyroid weight equal and more than 40 g were included in this group. Distributions by gender of these patients are shown in Table 8, the male to female ratio is 1:2.3.

Table 8: Gender of patients.

Gender	100 μCi/g (n=22)		150 μCi/g (n=24)		Total (n=46)		
	n	%	n	%	n	%	Ratio
Male	8	36.4	6	25.0	14	30.4	1:2.3
Female	14	63.6	18	75.0	32	69.6	

Their baseline characteristics included age, body and thyroid weight of pre-RaI therapy and the percentage of thyroid uptake are presented in Table 9. To reduce time and for patient convenience, the 24 hrs uptake in this study was estimated from early (4 hrs) of RaI uptake.

Table 9: Baseline characteristics of patients.

Characteristics	100 μCi/g (n=22)	150 μCi/g (n=24)	Total (n=46)
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.
Age (year)	34.0 ± 10.9	40.0 ± 11.0	37.11 ± 11.2
Body weight (kg)			
Pre-RaI therapy	56.1 ± 6.9	51.9 ± 9.8	53.9 ± 8.7
Thyroid weight (g)			
Pre-RaI therapy	83.7 ± 37.0	76.13 ± 26.6	79.7 ± 31.8
Thyroid uptake (%)			
Early uptake (4hrs)	67.4 ± 14.3	68.8 ± 15.8	68.1 ± 14.9
Est. late uptake (24hrs)	78.0 ± 7.8	79.5 ± 9.5	78.8 ± 8.7

The pretreatment variable for the 2 treatment groups as shown in Table 9 were in the same magnitude. The average gland mass was equal or above 40 g, 83.7 ± 37.0 and 76.13 ± 26.6 g in the low (100 μCi/g) and high (150 μCi/g) dose groups respectively. The mean estimated 24 hrs uptake was almost the same for both groups.

The average dose in the low (100 μCi/g) dose group was 10.6 ± 4.3 mCi (range 5.0-23.5 mCi), and the calculated dose to thyroid tissue was 99.8 ± 1.1 μCi/g. In the high (150 μCi/g) dose group, the average dose was 14.4 ± 4.8 mCi (range 8.0-24.7 mCi) and the calculated dose of 150.0 ± 3.9 μCi/g to the thyroid tissue as shown in Table 10.

Table 10: The dose of RaI administered.

The dose of RaI	100 μCi/g (n=22)		150 μCi/g (n=24)	
	Mean ± S.D.	Range	Mean ± S.D.	Range
RaI activity (mCi)	10.6 ± 4.3	5.0-23.5	14.4 ± 4.8	8.0-24.7
Dose of RaI (μCi/g)	99.8 ± 1.1	97.3-101.9	150.0 ± 3.9	139.9-164.2

After RaI administration, the patients were followed at the end of 3 months. As shown in Table 11, the FT_3 normal range is 2.0-4.25 pg/ml, the FT_4 normal range is 0.7-1.8 ng/dl. Despite, the TSH normal range is 0.5–3.7 mU/L, the TSH results were divided into 3 groups, below normal, normal and above normal.

Table 11: Thyroid function after 3-month therapy according to the treatment assignment.

In vitro test	100 μCi/g (n=22)		150 μCi/g (n=24)		Total (n=46)	
Thyroid hormone	Mean ± S.D.		Mean ± S.D.		Mean ± S.D.	
FT_3 (pg/ml)	10.4 ± 8.0		7.6 ± 7.2		8.9 ± 7.7	
FT_4 (ng/dl)	5.8 ± 6.5		3.2 ± 3.3		4.5 ± 5.2	
TSH level	n	%	n	%	n	%
<0.5 mU/L	18	81.8	17	70.8	35	76.1
0.5-3.7 mU/L	1	4.6	4	16.7	5	10.9
>3.7 mU/L	3	13.6	3	12.5	6	13.0

Table 12: Clinical outcomes of RaI treatment as related to dose.

Outcomes	100 μCi/g (n=22)	150 μCi/g (n=24)	Total (n=46)	χ^2	P value
Euthyroid	8 (36.4%)	11 (45.8%)	19 (41.3%)		
Hypothyroid	0 (0%)	2 (8.4%)	2 (4.4%)	2.752	0.253
Hyperthyroid	11 (63.6%)	11 (45.8%)	25 (54.3%)		

The outcomes of patients as shown in Table 12 were diagnosed by thyroid function test and TSH level. Base on the dose of RaI administered, 22 patients receive doses between 97.3% to 101.9 μCi/g, 14 patients (63.6%) remained hyperthyroid, none was hypothyroid, and 8 patients (36.4%) were euthyroid. Twenty-four patients receive doses between 139.9% to 164.2 μCi/g, 11 patients (45.8%) remained hyperthyroid, 11 patients (45.8%) were euthyroid and 2 patients (8.4%) were hypothyroid. There were no significant differences between the groups of 100 μCi/g (conventional) and 150 μCi/g (advanced) calculate doses at $p > 0.05$.

Overall at 3 months, of 46 patients who received an ablative single dose of RaI therapy, 25 patients (54.3%) remained hyperthyroid, a euthyroid was achieved in 19 patients (41.3%) and 2 patient (4.4%) was hypothyroid.

Table 13: The results of RaI therapy by single-dose.

Results	100 μCi/g (n=22)	150 μCi/g (n=24)	Total (n=46)	χ^2	P value
Cure	8 (36.4%)	13 (54.2%)	21 (45.6%)	0.837	0.360
Uncured	14 (63.6%)	11 (45.8%)	25 (54.4%)		

The cured and uncured of RaI therapy by an ablative single-dose were shown in Table 13. In the group received 100 μCi/g, 8 patients (36.4%) were cured and 14 patients (63.6%) were uncured. Despites, in the group received 150 μCi/g, 13 patients (54.2%) were cured and 11 patients (45.8%) were uncured.

In study of ablative dose, 21 patients (45.6%) were cured and 25 patients (54.4%) were uncured. There were no significant differences between the groups of 100 μCi/g (conventional) and 150 μCi/g (advanced) calculate doses at $p > 0.05$.

Part 4.3: Comparison of the outcome and clinical result between non-ablative and ablative dose

This study was presented to compare the outcome and clinical result between non-ablative and ablative doses of RaI therapy in hyperthyroidism caused by GD. Among 74 patients, 28 patients were treated with non-ablative dose and 46 patients with ablative dose.

Table 14: The dose of RaI administered.

The dose of RaI	Non-ablative dose (n=28)		Ablative dose (n=46)	
	Mean ± S.D.	Range	Mean ± S.D.	Range
RaI activity (mCi)	4.4 ± 1.4	2.0-7.2	12.6 ± 4.9	5.8-24.7
Dose of RaI (μCi/g)	115.8 ± 25.4	74.1-174.3	126.0 ± 25.5	97.3-164.2

Table 14 summarized dose administered to the patient, the mean of the non-ablative dose was 4.4 ± 1.4 mCi (range between 2.0-7.2 mCi), and the mean dose to thyroid tissue was 115.8 ± 25.4 μCi/g (range between 74.1-174.3 μCi/g). The mean of the ablative dose was 12.6 ± 4.9 mCi (range between 5.8-24.7 mCi), and the mean dose to thyroid tissue was 126.0 ± 25.5 μCi/g (range between 97.3-164.2 μCi/g).

At the end of 3 months after RaI therapy, biochemical and clinical response to treatment were evaluated. Diagnosis of hyperthyroidism was based on clinical signs and evaluated FT_3 and FT_4 (normal range: 2.0-4.25 pg/ml and 0.7-1.8 ng/dl respectively) and suppressed serum TSH concentration (normal range: 0.5-3.7 mU/L).

The outcomes of patients as shown in Table 15 were diagnosed by thyroid function test and TSH level. Twenty-eight patients of non-ablative received the mean dose to thyroid tissue was 115.8 ± 25.4 μCi/g, one of patient was hypothyroid (3.6%), 12 patients (42.8%) were euthyroid, and 15 patients (53.6%) remained hyperthyroid. Forty-six patients received the mean dose to thyroid tissue was 126.0 ± 25.5 μCi/g, 2 patients (4.3%) were hypothyroid, 19 patients (41.4%) were euthyroid, and 25 patients (54.3%) remained hyperthyroid. There were no significant differences between the groups of non-ablative and ablative doses at $p > 0.05$.

Table 15: Clinical outcomes of RaI treatment as related to dose.

Outcomes	Non-ablative dose (n=28)		Ablative dose (n=46)		χ^2	P value
	n	%	n	%		
Euthyroid	12	42.8	19	41.4	0.038	0.981
Hypothyroid	1	3.6	2	4.3		
Hyperthyroid	15	53.6	25	54.3		

Table 16: The results of RaI therapy by single-dose.

Results	Non-ablative dose (n=28)		Ablative dose (n=46)		χ^2	P value
	n	%	n	%		
Cure	13	46.4	21	45.7	0.000	1.000
Uncured	15	53.6	25	54.3		

The cure and uncured of RaI therapy were presented in Table 16. The non-ablative dose, 13 patients (46.4%) were cured and 15 patients (53.6%) were uncured. Despites, the ablative dose, 21 patients (45.7%) were cured and 25 patients (54.3%) were uncured. There were no-significant differences between the non-ablative and ablative doses at $p > 0.05$.

Part 4.4: Comparison between low and high doses of RaI therapy.

This study was presented to compare the low with high dose of RaI therapy by single dose in hyperthyroidism caused by GD. Among 74 patients as shown in Table 17, 38 patients were treated with low dose and 36 patients with high dose. The male to female ratio was 1:3.

Table 17: Gender of patients.

Gender	Low dose (n=38)		High dose (n=36)		Total (n=74)		
	n	%	n	%	n	%	Ratio
Male	11	28.9	7	19.4	18	24.3	1:3
Female	27	71.1	29	80.6	56	75.7	

Statistical analysis in Table 18 shows the mean ± S.D. of patient's characteristics. There were no significant differences of the age, pre and post treatment variables between groups of low and high dose of RaI therapy by *t*-test or unpaired *t*-test at $p > 0.05$ level.

Table 18: Baseline characteristics of patients.

Characteristics	Low dose (n=38)	High dose (n=36)	P value
	Mean ± S.D.	Mean ± S.D.	
Age (year)	36.0 ± 10.0	39.9 ± 10.4	0.103
Body weight (kg)			
Pre-RaI therapy	55.1 ± 7.5	51.8 ± 8.6	0.085
Post-RaI therapy	55.1 ± 7.8	53.9 ± 9.3	0.618
Diff-BW	-0.06 ± 3.7	1.8 ± 4.6	0.069
Thyroid weight (g)			
Pre-RaI therapy	60.6 ± 39.5	59.3 ± 32.7	0.901
Post-RaI therapy	31.7 ± 15.9	29.7 ± 17.8	0.550
Diff-TW	-25.3 ± 24.6	-29.6 ± 24.1	0.312

Table 19: The percentage of thyroid uptake.

Percentage of thyroid uptake	Low dose (n=38)	High dose (n=36)	P value
	Mean ± S.D.	Mean ± S.D.	
Early uptake (%)	66.5 ± 15.1	63.2 ± 18.0	0.476
Est. late uptake (%)	76.7 ± 8.9	76.1 ± 11.1	0.974

In Table 19 shows the mean ± S.D. of thyroid uptake (%). There were no significant differences of the thyroid uptake between groups of low and high dose of RaI therapy at $p > 0.05$ level.

Table 20: The dose of RaI administered.

The dose of RaI	Low dose (n=38)		High dose (n=36)	
	Mean ± S.D.	Range	Mean ± S.D.	Range
RaI activity (mCi)	7.8 ± 4.7	2.0-23.5	11.3 ± 6.0	2.5-24.7
Dose of RaI (μCi/g)	100.4 ± 8.9	74.1-120.9	145.0 ± 15.8	102.8-174.3

Table 20 summarized dose administered to the patient, the mean of the low dose was 7.8 ± 4.7 mCi (range between 2.0-23.5 mCi), and the mean dose to thyroid tissue was 100.4 ± 8.9 μCi/g (range between 74.1-120.9 μCi/g). The mean of the high dose was 11.3 ± 6.0 mCi (range between 2.5-24.7 mCi), and the mean dose to thyroid tissue was 145.0 ± 15.8 μCi/g (range between 102.8-174.3 μCi/g).

At the end of 3 months after RaI therapy, biochemical and clinical response to treatment were evaluated. Diagnosis of hyperthyroidism was based on clinical signs and evaluated FT_3 and FT_4 (normal range: 2.0-4.25 pg/ml and 0.7-1.8 ng/dl respectively) and suppressed serum TSH concentration (normal range: 0.5-3.7 mU/L).

In Table 21 showed the FT_3 and FT_4 levels, in FT_3 level was no significant differences between the groups of low and high dose at $p > 0.05$. In contrast, the FT_4 level was significant differences ($p = 0.007$) between the groups of low and high dose at $p < 0.05$. And in Table 22 showed TSH level, it was no significant differences between the groups of low and high dose at $p > 0.05$.

Table 21: FT_3 and FT_4 levels.

Thyroid hormone	Low dose (n=38)	High dose (n=36)	P value
	Mean ± S.D.	Mean ± S.D.	
FT_3 (pg/ml)	9.0 ± 6.9	6.4 ± 6.3	0.080
FT_4 (ng/dl)	4.8 ± 5.3	3.4 ± 6.3	0.007

Table 22: TSH level.

TSH level	Low dose (n=38)		High dose (n=36)		χ^2	P value
	n	%	n	%		
<0.5 mU/L	30	79.0	23	63.9	2.09	0.352
0.5-3.7 mU/L	4	10.5	6	16.7		
>3.7 mU/L	4	10.5	7	19.4		

The outcomes of patients as shown in Table 23 were diagnosed by thyroid function test and TSH level. Thirty-eight patients received the mean dose to thyroid tissue was 100.4 ± 8.9 μCi/g (range between 74.1-120.9 μCi/g), 25 patients (65.8%) remained hyperthyroid, none was hypothyroid, and 13 patients (34.2%) were euthyroid. Thirty-six patients received the mean dose to thyroid tissue was 145.0 ± 15.8 μCi/g (range between 102.8-174.3 μCi/g), 15 patients (41.7%) remained hyperthyroid, 18 patients (50.0%) were euthyroid and 3 patients (8.3%) were hypothyroid. There was significant differences ($p = 0.044$) between the groups of low and high dose at $p < 0.05$.

Table 23: Clinical outcomes of RaI treatment as related to dose.

Outcomes	Low dose (n=38)		High dose (n=36)		χ^2	P value
	n	%	n	%		
Euthyroid	13	34.2	18	50.0	6.257	0.044
Hypothyroid	0	0.0	3	8.3		
Hyperthyroid	25	65.8	15	41.7		

Table 24: The results of RaI therapy by single-dose.

Results	Low dose (n=38)		High dose (n=36)		χ^2	P value
	n	%	n	%		
Cure	13	34.2	21	58.3	3.415	0.065
Uncured	25	65.8	15	41.7		

The cure and uncured of RaI therapy were presented in Table 24. In the group of low dose, 13 patients (34.2%) were cured and 25 patients (65.8%) were uncured. Despites, in the group of high dose, 21 patients (58.3%) were cured and 15 patients (41.7%) were uncured. There was analyzed by χ^2 test (2×2 tables) and no significant differences ($p = 0.065$) between the groups of low and high dose at $p > 0.05$.

CHAPTER V
DISCUSSION

Radioactive iodine (RaI) has become the most widely used therapy for patients with hyperthyroidism due to Graves' disease (GD) for more than 50 years (94), remains a lack of consensus regarding the optimal dose of RaI therapy and general agreement as to the best approaches to RaI dose selection. However, there are 2 common approaches for determining the administered dose, 1) a fixed dose is commonly in the range of 185-555 MBq (5-15 mCi) for all patients, some may make certain adjustments to the dose according to the degree of estimated thyroid gland size or the severity of disease, and 2) calculate a dose based on the weight of the thyroid and its percentage uptake (95).

Non-ablative of RaI dose by sliding-scale method

The non-ablative dose of RaI therapy need the prolonged of euthyroid without the ultimate risk of hypothyroidism, the efficacy of sliding scale was evaluated in patients with thyroid weight <40 gram. After a single dose of RaI therapy, the outcome of conventional (low; 101.2 ± 13.8 μCi/g) sliding scale dose was shown none of hypothyroidism, but the euthyroid rate was lower (31%) than advanced (high; 135.2 ± 24.6 μCi/g) sliding-scale dose (58%). Despite, the advanced (high) sliding-scale dose was shown 9% of patients to be hypothyroidism, but the hyperthyroid rate was lower (33%) than conventional (low) sliding-scale dose (69%).

Finally, the cure rate of advanced sliding-scale dose was shown higher (67%) than conventional sliding-scale dose (31%). The non-ablative of RaI dose by advanced (high) sliding-scale is more effective than conventional (low) sliding-scale, but the more rapid therapeutic effect at the expanse of an increased rate of hypothyroid.

Members of University of Chicago Thyroid Group were early proponents of a low-dose ^{131}I protocol designed to take into account the higher doses needed by larger thyroid gland (96). A sliding scale based on gland size resulted in retained doses at 24-hour ranging form 40 μCi/g for gland weighing 10 to 20 gram to 100 μCi/g for gland weighing more than 100 gram. After 1 year, 10% of patients were hypothyroid, 60% euthyroid and 30% still hyperthyroid. Thus, approximately 30% of patients required second or third doses. Then, after 10 years, 60% were hypothyroid and 40% euthyroid (96). However, the sliding-scale method of non-ablative of RaI therapy is save and convenient, appropriate for patients with small goiter, not severe hyperthyroidism.

Ablative of RaI dose by calculate method

The ablative of RaI therapy aims to control hyperthyroidism, the efficacy of calculate dose method was evaluated in patients with thyroid weight ≥40 g. After a single dose of RaI therapy, the outcome of advanced (150 μCi/g) calculated dose was shown 46% of patients still hyperthyroid, it was lower than the conventional (100 μCi/g) calculated dose (64%). Despite, the euthyroid (46%) and hypothyroid (8%) rate of the advanced (150 μCi/g) calculated dose was higher than conventional (100 μCi/g) calculated dose.

Finally, the cure rate of advanced (150 μCi/g) calculated dose was higher (54%) than conventional (100 μCi/g) calculated dose (36%). The ablative dose of RaI therapy by advanced (150 μCi/g) calculated dose is more effective than conventional (100 μCi/g) calculated dose.

The calculated dose of RaI therapy of 150 μCi/g (300 μCi/g was used when thyroid weight more than 70 g) shows 20% of hyperthyroidism and 13% to be hypothyroidism (97). The calculate dose of 200 μCi/g shows 16% of hyperthyroidism and 56% to be hypothyroidism (49). The threshold dose of RaI therapy of 170 μCi/g (6.3 MBq/g) is separating the non-hyperthyroid group from the hyperthyroid group (98). In additional, Doi et al (73) suggested the best outcome in terms of cure and early hypothyroidism (predicts a 90% hypothyroidism rate at 1 year) by calculated dose of 300 μCi/g (11 MBq/g).

However, the calculate method of ablative of RaI therapy is safe, simple and avoid the need for continuous long-term follow-up for later hypothyroidism in patients treated with lower doses, appropriate for patients with large goiter and severe hyperthyroidism.

The method of RaI doses in Graves' hyperthyroidism treatment

No significant difference in the success rate was found between non-ablative and ablative methods in 3-month follow up. The results of non-ablative dose were seem as ablative dose of RaI therapy, 46% of patients were cured (42% of euthyroid and 4% of hypothyroid) and 54% of them were uncured (still hyperthyroid). However, there has been 5 approaches to dose selection in patients with GD have been employed: 1) small doses repeated as necessary, 2) a large ablative dose, 3) a "sliding scale" based on thyroid size or weight, 4) a standard formula for the administered dose based on estimated thyroid size, and 5) precise dosimetry for the administered dose (99).

The goal of RaI therapy is to cure the thyrotoxic condition. However, there use to be considerable debate about whether the goal of treatment was to render the patient euthyroid without the need for thyroid hormone or to reduce the function to below normal and replace L-thyroxine. It is now generally accepted that titrating the administered dose to sender all patients euthyroid is not possible or wise (100). The dose of RaI should be sufficient to cure hyperthyroidism in reasonable time (<6 months), and both patients and physicians should recognize and accept that thyroid hormone replacement will be required (100).

The comparison of RaI doses between low and high Graves' hyperthyroidism.

All characteristics (gender, age, percentage of thyroid uptake, body weight and thyroid weight before RaI therapy) of patient were compared between 2 groups of low and high doses; there was no significant difference ($p > 0.05$). Three months after a single dose of RaI therapy, the patients were followed-up. The thyroid hormones (FT_3 and FT_4) and TSH were tested, only FT_4 was significant difference ($p = 0.007$), other tests were no significant.

The outcomes (euthyroid, hypothyroid and hyperthyroid) of RaI therapy between low and high doses were compared by χ^2, it was significant difference ($p = 0.044$). On the other hand, the results of cure (euthyroid and hypothyroidism) and uncured (still hyperthyroidism) were compared by χ^2 (2×2 tables). There were no significant difference ($p = 0.065$) between low and high doses.

Selection of dose of RaI therapy in Graves' hyperthyroidism

Recommendation for the desired dose per gram of tissue is very widely (101). Including, a one-dose cure with ^{131}I to minimize the duration of the hypothyroidism and frustration, morbidity, and expanse associated with repeat doses (101). The recommended ^{131}I dosages (101) for hyperthyroidism were reviewed by Kaplan et al (1998), using desired dose per gram values in the previous formula that based on thyroid size as given in Table 25. Using these guidelines, approximately 95% of patients are cured of hyperthyroidism with one RaI dose, and less than 1% required more than two doses.

Table 2: Recommended ^{131}I dosage schedules for hyperthyroidism.

Source	Desired 131I dose/g
Cooper (102)	80-120 µCi
Becker and Hurley (103)	
Usual patients	55-80 µCi
Severely hyperthyroid	160-200 µCi
Kaplan et al (101)	
Thyroid size	
50 g or less	100-120 µCi
50 to 80 g	150-175 µCi
More than 80 g	200 µCi

For thyroid glands of average size and uptake, fixed doses of ^{131}I are effective, provided that sufficient ^{131}I is administered. Each therapist needs to select the preferred dose but should analyze the outcome; 370-555 MBq (10-15 mCi) is an appropriate range. Similar, those who use a formula for calculating the administered dose should not have to retreat a significant proportion of patients when doses of 5.55-7.4 MBq (150-200 µCi) are used. The same applies to those who calculate the specific absorb dose (100). Cooper (102) suggests doses 80 to 120 µCi/g which generally results in the doses of 5 to 15 mCi and absorbed doses of 50 to 100 Gy. Backer and Hurley suggest the doses of 55 to 80 µCi/g for the usual patient, resulting in absorbed doses of 50 to 70 Gy. To minimize the duration of symptoms, they propose larger doses per gram of thyroid weight (160 to 200 µCi/g) in severely hyperthyroid patients or in patients with underlying cardiac disease.

The small risk of hypothyroidism after RaI therapy and critically discussing the three common methods (fixed dose, calculated activity administered dose and absorbed dose) of RaI dosing. At 3-month after RaI therapy, among the group of euthyroid was over half (54%) will be hypothyroid about a year or so later. The last dose remained so, the rest became definite or probable hypothyroid with add up finally to 70% hypothyroid at 1-3 years and 80% after 3 years (71). That clear for euthyroid rates initially rises as the dose increases and then falls off as hypothyroidism ensures (73). The hypothyroidism develops within the first year is depends on the dose of RaI, with a continuing rate of 3% per year thereafter (89).

The several weaknesses of this study, almost all patients we were used the formula to estimate thyroid uptake at 24 hours by early uptake (4 hrs). Few of them were lost some details about body or thyroid weight (pre or post RaI therapy). The most important is period time and outcomes indication of this study, all of patients were follow-up post 3 months after a single dose of RaI therapy and post-tested only to indicative the outcomes by thyroid hormones and level of TSH.

CHAPTER VI
CONCLUSION

The optimization of RaI therapy regimens aims at selection of the administered radioactivity that gives the highest cure and lowest euthyroid rate (ablative) or the former with a maximum euthyroid (non-ablative). The patients with small goiter and not severe hyperthyroidism need the prolonged of euthyroid without the ultimate risk of hypothyroidism, and it is appropriate for non-ablative dose of RaI therapy. Besides, the patients with large goiter and severe hyperthyroidism, it is appropriate for ablative dose of RaI therapy.

In this study, in the success rate in 3-month follow up, 46.4% of non-ablative dose and 45.6% of ablative dose were eliminated hyperthyroid. The results of RaI therapy of non-ablative dose by sliding-scale method (thyroid gland <40 gram) were seem as ablative dose by calculate method (thyroid gland ≥40 gram), no significant difference between them. Despite, the outcomes of RaI therapy between low (100.4 ± 8.9 μCi/g) and high (145.0 ± 15.5 μCi/g) doses are significant difference. The patients of hyperthyroidism in low dose are decrease and move to be patients of hypothyroidism in high dose, the hypothyroid rate of high dose was 8.3% of patients but none of low dose. However, in term of cure and uncured rate, there is no significant difference between the low and high doses.

When the low dose of ^{131}I is used, no hypothyroid case was observed while few cases of early hypothyroidism were induced by the high dose. However we could not demonstrate any advantage to using an adjusted high dose in 3-month follow up. For more rapid therapeutic effect at the expanse of an increased rate of hypothyroidism (as a success outcome), high dose of ^{131}I may be required in patients with larger thyroid glands and severity of disease.

Suggestion for further study

Larger sample size and long term to follow up the patients are needed, and more patient's information of relapse or complication should be studies. Some informations of RaI therapy by a single dose could be the choice to select the dose of RaI therapy in Graves' hyperthyroidism.

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APPENDIX

APPENDIX A

Consent form

หนังสือแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยทางการแพทย์
(ฉบับปรับเปลี่ยนครั้งที่ 1/ วันที่ 2 กรกฎาคม พ.ศ. 2547)

วันที่……..เดือน……พ.ศ. ……..

ข้าพเจ้า……อายุ……ปี อาศัยอยู่บ้านเลขที่ ……..
ถนน……ตำบล……..……อำเภอ……..…….
จังหวัด……โทรศัพท์ (บ้าน/มือถือ)…..……โทรสาร……
ขอแสดงเจตนายินยอมเข้าร่วมโครงการวิจัยเรื่องการศึกษาเบื้องต้นในการเปรียบเทียบปริมาณไอโอดีนรังสีในโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ โดยข้าพเจ้าได้รับทราบเกี่ยวกับรายละเอียดของโครงการ ดังต่อไปนี้

วัตถุประสงค์

1. เปรียบเทียบผลของการรักษาโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ด้วยไอโอดีนรังสี ด้วยวิธีปรับเลื่อนตามขนาดของต่อมธัยรอยด์ ระหว่างแบบดั้งเดิม (Conventional sliding-dose) และแบบก้าวหน้า (Advance sliding-dose) ในต่อมไทรอยด์ที่มีน้ำหนักน้อยกว่า 40 กรัม

2. เปรียบเทียบผลของการรักษาโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ด้วยไอโอดีรังสี ด้วยวิธีคำนวณปริมาณไอโอดีนรังสี ระหว่าง 100 μCi/g และ150 μCi/g ในต่อมไทรอยด์ที่มีน้ำหนักมากกว่า 40 กรัม

ประโยชน์ที่คาดว่าจะได้รับ

- เพิ่มประสิทธิภาพในการรักษามากยิ่งขึ้น ลดจำนวนครั้งในการรักษา
- ช่วยประหยัดเวลาและลดค่าใช้จ่ายแก่ผู้ป่วย
- ช่วยลดต้นทุนในการให้บริการรักษาผู้ป่วยแก่โรงพยาบาล
- เป็นแนวทางในการปรับเพิ่มปริมาณไอโอดีนรังสี ในการรักษาผู้ป่วยโรคเกรฟส์

ความเสี่ยงหรือผลข้างเคียงที่อาจเกิดขึ้น

- อาจมีอาการไทรอยด์เป็นพิษมากขึ้น ในช่วงหยุดยาต้านไทรอยด์ฮอร์โมน
- อาจเกิดภาวะต่อมไทรอยด์ทำงานน้อยกว่าปกติ

แนวทางป้องกัน/แก้ไข ความเสี่ยงหรือการแก้ไขผลข้างเคียงที่อาจเกิดขึ้น

- แพทย์ให้ยาต้านไทรอยด์ฮอร์โมน เพื่อช่วยลดอาการไทรอยด์เป็นพิษ
- แพทย์ให้ไทรอยด์ฮอร์โมนทดแทน เพื่อรักษาภาวะต่อมไทรอยด์ทำงานน้อยกว่าปกติ

รายละเอียดและขั้นตอนที่ผู้ร่วมโครงการวิจัยได้รับการปฏิบัติ

1. ผู้วิจัยวัดขนาดต่อมไทรอยด์ด้วยเครื่องอัลตราซาวด์ ในผู้ป่วยโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ ในงานเวชศาสตร์นิวเคลียร์ โรงพยาบาลสรรพสิทธิประสงค์ อุบลราชธานี เพื่อหาปริมาตรและน้ำหนักของต่อมไทรอยด์
2. ผู้วิจัยได้อธิบายและมอบคู่มือระหว่างการเข้าร่วมโครงการแก่ผู้ป่วย เพื่อรับทราบและเชิญผู้ป่วยเข้าร่วมโครงการวิจัย โดยให้เซ็นยินยอมเข้าร่วมโครงการวิจัย
    - บันทึกข้อมูลทั่วไปของผู้ป่วย ได้แก่ Hospital Number (HN), เพศ, อายุ, น้ำหนักตัว และน้ำหนักของต่อมไทรอยด์ก่อนรักษาด้วยไอโอดีนรังสี
    - นัดวันตรวจ thyroid uptake ด้วยไอโอดีนรังสี โดยเตรียมผู้ป่วยให้พร้อม เช่น หยุดยาเกี่ยวกับไทรอยด์ 7 วัน, หลีกเลี่ยงยาและอาหารที่มีไอโอดีนสูง
3. ผู้ป่วยได้รับการตรวจ ^{131}I thyroid uptake ตามวันและเวลาที่นัด ซึ่งผู้ป่วยจะได้กินไอโอดีนรังสีขนาด 20 μCi จากนั้นวัดค่า ^{131}I thyroid uptake ที่ 4 หรือ 24 ชั่วโมง
4. ผู้ป่วยเข้าพบรังสีแพทย์ เพื่อทำการสุ่มแบ่งกลุ่มควบคุมและกลุ่มทดลอง
5. รังสีแพทย์กำหนดวิธีและคำนวณปริมาณไอโอดีนรังสีแก่ผู้ป่วย
    - ผู้ป่วยที่ต่อมไทรอยด์มีน้ำหนักน้อยกว่า 40 กรัม ใช้วิธีปรับเลื่อนปริมาณไอโอดีนรังสี ตามน้ำหนักของต่อมไทรอยด์
    - ผู้ป่วยที่ต่อมไทรอยด์มีน้ำหนักมากกว่า 40 กรัม ใช้วิธีคำนวณปริมาณไอโอดีนรังสี จากน้ำหนักของต่อมไทรอยด์และค่าร้อยละของ ^{131}I thyroid uptake
6. ผู้วิจัยอธิบายการปฏิบัติตน ระหว่างการรักษาด้วยไอโอดีนรังสีแก่ผู้ป่วย และการได้รับไอโอดีนรังสีโดยวิธีการกิน
7. ติดตามผลการรักษาครั้งที่ 1 ในอีก 3 เดือนถัดไป โดยใบนัดตรวจ ระบุวันและเวลา, สถานที่ พร้อมเบอร์โทรศัพท์ เพื่อติดต่อผู้วิจัย ในกรณีที่ผู้ป่วยไม่สะดวกมาตามนัดได้ หรือต้องการเลื่อนวัน, เวลานัดตรวจ

8. ในวันนัดติดตามผลหลังการรักษาครั้งที่ 1 ผู้ป่วยได้รับการเจาะเลือดวัดระดับไทรอยด์ฮอร์โมน FT_3 FT_4 และ TSH พร้อมทั้งวัดขนาดของต่อมไทรอยด์ด้วยอัลตราซาวด์อีกครั้งหลังการรักษาครั้งที่ 1 โดยผู้วิจัย
9. ผู้ป่วยเข้าพบรังสีแพทย์ พร้อมผลระดับไทรอยด์ฮอร์โมนและขนาดของต่อมไทรอยด์ โดยแพทย์สังเกตอาการผู้ป่วย และประเมินผลหลังการรักษาครั้งที่ 1 ซึ่งแบ่งออกเป็น 3 สภาวะ
    - Euthyroid
    - Hyperthyroidism
    - Hypothyroidism
10. การติดตามผลการรักษา
    - Euthyroid ครั้งที่ 2 ในอีก 3 เดือนถัดไป
      ครั้งที่ 3 ในอีก 6 เดือนถัดไป (ครบ 1 ปี)
    - Hypothyroidism ครั้งที่ 2 ในอีก 3 เดือนถัดไป
      ครั้งที่ 3 ในอีก 6 เดือนถัดไป (ครบ 1 ปี)
    - Hyperthyroidism นัดตรวจและรักษาครั้งต่อไป ทุกๆ 3 เดือน จนครบ 1 ปี
      หรือจนกว่าเข้าสู่ภาวะ euthyroid หรือ hypothyroidism

การติดต่อกับผู้ป่วยในกรณีที่มีปัญหา (ตลอด 24 ชั่วโมง) ตามหมายเลขโทรศัพท์ทั้งที่บ้านหรือโทรศัพท์เคลื่อนที่ ทั้งของผู้ป่วยและญาติที่ใกล้ชิด

หากข้าพเจ้าได้รับผลข้างเคียงหรือฤทธิ์ไม่พึงประสงค์หรือภยันตรายจากการวิจัย ข้าพเจ้าจะได้รับการปฏิบัติ/การชดเชยดังนี้

- แจ้งแก่ผู้วิจัยทางโทรศัพท์ ตลอด 24 ชั่วโมง เพื่อขอนัดวันและเวลาเข้าพบรังสีแพทย์
- ผู้วิจัยช่วยอำนวยความสะดวกภายในโรงพยาบาลทุกขั้นตอน เพื่อเข้าพบรังสีแพทย์

หากผู้วิจัยมีข้อมูลเพิ่มเติมทั้งด้านประโยชน์และโทษที่เกี่ยวข้องกับการวิจัยนี้ ผู้วิจัยแจ้งให้ข้าพเจ้าทราบอย่างรวดเร็วโดยไม่ปิดบัง และข้าพเจ้ามีสิทธิ์ที่งดการเข้าร่วมโครงการวิจัยโดยไม่ต้องแจ้งให้ทราบล่วงหน้า โดยการงดการเข้าร่วมการวิจัยนี้ ไม่มีผลกระทบต่อการได้รับบริการหรือการรักษาที่ข้าพเจ้าได้รับแต่ประการใด

ข้าพเจ้าได้รับทราบข้อมูลของโครงการข้างต้น ตลอดจนข้อดีและข้อด้อย ที่ได้รับจากการเข้าร่วมโครงการในครั้งนี้ และข้าพเจ้ายินยอมที่เข้าร่วมในโครงการดังกล่าว โดยขอให้ผู้วิจัยงดการเปิดเผยชื่อ-ประวัติ ตลอดจนข้อมูลที่เกี่ยวข้องกับข้าพเจ้า แก่ผู้อื่นได้รับทราบ

ลงชื่อ ..... ผู้ให้ความยินยอม/ผู้แทน

( )โดยชอบธรรม (ระบุความเกี่ยวข้อง)

วันที่ .....

ลงชื่อ ..... พยาน

( )

ลงชื่อ ..... พยาน

( )

เอกสารแนะนำสำหรับอาสาสมัคร

โครงการศึกษาเบื้องต้นในการเปรียบเทียบปริมาณไอโอดีนรังสี ในโรคต่อมธัยรอยด์เป็นพิษชนิดเกรฟส์

ความสำคัญและที่มาของปัญหา

โรคต่อมไทรอยด์เป็นพิษ (Hyperthyroidism) เป็นภาวะที่ต่อมไทรอยด์ทำงานมากเกินไป และสร้างฮอร์โมนไทรอยด์เข้าสู่กระแสโลหิตมากขึ้น เกิดอาการที่เรียกว่า “ไทรอยด์เป็นพิษ” โดยกลุ่มโรคเกรฟส์ (Graves’ disease) ซึ่งต่อมไทรอยด์จะมีขนาดโตขึ้นทั่วทั้งต่อม เป็นสาเหตุพบบ่อย ปัจจุบันนี้ งานเวชศาสตร์นิวเคลียร์ โรงพยาบาลสรรพสิทธิประสงค์ จังหวัดอุบลราชธานี ได้กำหนดปริมาณไอโอดีนรังสีขนาด 100 μCi/g ของต่อมไทรอยด์ ในการรักษาโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ พบว่า หลังการรักษาครั้งที่ 1 ผู้ป่วยยังคงอยู่ในภาวะไทรอยด์เป็นพิษสูงถึงร้อยละ 75 และต้องการไอโอดีนรังสีเพิ่มเติมในครั้งที่ 2 โดยกลุ่มผู้ป่วยที่ต่อมไทรอยด์มีขนาดเล็ก มีโอกาสหายจากโรคมากกว่าผู้ป่วยที่ต่อมไทรอยด์มีขนาดโต

แนวทางการรักษาโรคต่อมไทรอยด์เป็นพิษ

- ยาต้านไทรอยด์ฮอร์โมน
- การผ่าตัด
- ไอโอดีนรังสี

การรักษาโรคต่อมไทรอยด์เป็นพิษ ด้วยยาต้านไทรอยด์ฮอร์โมน เหมาะสำหรับผู้ป่วยอายุน้อย อาการไม่มาก แต่มีข้อด้อย คือ โอกาสกลับมาเป็นโรคซ้ำสูง สำหรับการรักษาด้วยวิธีการผ่าตัดมีขั้นตอนซับซ้อน ราคาแพง และมีโอกาสเกิดผลแทรกซ้อนในการผ่าตัด ดังนั้น การรักษาโรคต่อมไทรอยด์เป็นพิษชนิดเกรฟส์ด้วยไอโอดีนรังสี ภายใต้ความดูแลของรังสีแพทย์ มีประสิทธิภาพสูง, ปลอดภัย, ออกฤทธิ์เฉพาะที่, มีผลต่ออวัยวะข้างเคียงต่ำ, ราคาไม่แพง, สะดวกในการรับไอโอดีนรังสีโดยวิธีการกิน จึงได้รับความนิยมอย่างมากทั้งในและต่างประเทศ

จากภาคนิพนธ์ของนักศึกษาวิทยาศาสตร์บัณฑิต (รังสีเทคนิค) มหาวิทยาลัยมหิดล เรื่อง ปัจจัยที่มีผลต่อการรักษาผู้ป่วยโรคต่อมไทรอยด์เป็นพิษ พบว่า ผลหลังการรักษาครั้งที่ 1 ผู้ป่วยยังคงอยู่ในภาวะต่อมไทรอยด์เป็นพิษสูงถึง 43.5% รวมทั้ง รายงานผลการรักษาโรคต่อมไทรอยด์เป็นพิษของโรงพยาบาลสงขลา พบว่า ผู้ป่วยจะยังคงอยู่ในภาวะต่อมไทรอยด์เป็นพิษหลังการรักษาครั้งที่ 1 สูงถึง 62% ผู้วิจัยจึงมีแนวคิดที่ว่า หากปรับเพิ่มปริมาณไอโอดีนรังสีมากขึ้นจากเดิม ช่วยเพิ่มประสิทธิภาพการรักษา อันเป็นแนวทางที่เหมาะสมในการรักษาผู้ป่วยมากยิ่งขึ้น

ขั้นตอนในการตรวจและรักษา

ผู้ป่วยมารับบริการรักษาโรคต่อมธัยรอยด์เป็นพิษ ในงานเวชศาสตร์นิวเคลียร์ โรงพยาบาลสรรพสิทธิประสงค์ จังหวัดอุบลราชธานี

- ❑ พบรังสีแพทย์ เพื่อการตรวจ โดยการซักประวัติและสังเกตอาการ
- ❑ วัดขนาดต่อมไทรอยด์ด้วยเครื่องอัลตราซาวด์
- ❑ นัดตรวจการทำงานของต่อมไทรอยด์ (thyroid uptake)
  วันที่ …….. เวลา 8.30 น.
- ❑ การเตรียมตัวก่อนตรวจการทำงานของต่อมไทรอยด์
  - งดยาต้านไทรอยด์ฮอร์โมน เริ่มวันที่ ……
  - งดยาที่มีไอโอดีนเป็นส่วนประกอบ เช่น ยาทาแผล ยาแก้ไอ
  - งดอาหารที่มีไอโอดีนสูง
  - งดอาหารก่อนตรวจ 4 ชั่วโมง
- ❑ พบรังสีแพทย์ เพื่อรับการรักษาโรคต่อมธัยรอยด์เป็นพิษด้วยไอโอดีนรังสี
- ❑ ผู้วิจัยอธิบาย การปฏิบัติตนระหว่างการรักษาแก่ผู้ป่วย
- ❑ ได้รับไอโอดีนรังสีโดยการกิน จากผู้วิจัย
- ❑ การให้ยาควบคู่ หลังกินไอโอดีนรังสี ได้แก่ ……
- ❑ นัดติดตามผลการรักษาในอีก 3 เดือน วันที่ …… เวลา 8.30 น.
  (แต่ถ้ามีอาการผิดปกติ สามารถมาพบแพทย์ก่อนนัดได้)
- ❑ เจาะเลือดและวัดขนาดของต่อมไทรอยด์ด้วยอัลตราซาวด์ หลังการรักษาครั้งที่ 1
- ❑ พบแพทย์หลังการรักษาครั้งที่ 1 ฟังผลหลังการรักษาครั้งที่ 1
- ❑ นัดติดตามผลการรักษาครั้งที่ 2 วันที่ …… เวลา 8.30 น.
- ❑ นัดติดตามผลการรักษาครั้งที่ 3 วันที่ …… เวลา 8.30 น.
- ❑ นัดติดตามผลการรักษาครั้งที่ 4 วันที่ …… เวลา 8.30 น.

ผลข้างเคียงที่อาจเกิดขึ้น

- อาการไทรอยด์เป็นพิษมากขึ้นในช่วงการตรวจและรักษา ได้แก่ เนื่องจากการหยุดยาต้านไทรอยด์ฮอร์โมน การให้ยาที่มีฤทธิ์ยับยั้งผลของไทรอยด์ฮอร์โมน (β-blocker) ร่วมด้วย ช่วยลดอาการดังกล่าว
- อาจเกิดภาวะต่อมไทรอยด์ทำงานน้อยกว่าปกติ มีอุบัติการณ์การเกิดสูง เป็นผลต่อผู้ป่วยแบบถาวร สามารถแก้ไขด้วยการให้ยาไทรอยด์ฮอร์โมน (Eltroxin) กินทดแทน

ประโยชน์ที่คาดว่าจะได้รับ

- ศึกษาและเปรียบเทียบปริมาณไอโอดีนรังสีในการรักษาผู้ป่วยโรคเกรฟส์
- เพิ่มประสิทธิภาพในการรักษามากขึ้น
- ช่วยประหยัดเวลาการรักษาและลดค่าใช้จ่ายแก่ผู้ป่วย
- ช่วยลดต้นทุนในการให้บริการรักษาผู้ป่วยแก่โรงพยาบาล

หากต้องการข้อมูลเพิ่มเติม

ติดต่อผู้วิจัย

นายจิรชัย เริงศิริ เจ้าหน้าที่รังสีการแพทย์
งานเวชศาสตร์นิวเคลียร์ กลุ่มงานรังสีวิทยา
โรงพยาบาลสรรพสิทธิประสงค์ อุบลราชธานี
หมายเลขโทรศัพท์

- 045-244973 ต่อ 327
- 045-250285 (สายตรง)
- 01-8536574 (มือถือ)

APPENDIX B

Table 26. Patients' data of conventional (low) sliding-scale dose.

Number	H.N.	Gender	Age (yr)	Body weight (kg)			Thyroid weight (g)		
				bef_RaI	Aft_RaI	Diff_BW	bef_RaI	Aft_RaI	Diff_TW
1	1070512	F	39	58.0	55.0	-3.0	37.9	22.9	-15.0
2	1069832	F	46	55.0	56.0	1.0	14.2	9.1	-5.1
3	1076404	F	19	46.0	48.0	2.0	19.2	20.6	1.4
4	1079468	F	41	70.0	66.5	-3.5	39.2	46.7	7.5
5	1053264	M	29	60.0	70.0	10.0	26.6	21.0	-5.6
6	1089851	F	38	53.0	53.0	0.0	31.5	28.2	-3.3
7	416545	F	33	48.0	46.0	-2.0	38.4	25.6	-12.8
8	1086246	F	38	50.0	51.0	1.0	39.3	17.1	-22.2
9	1096244	F	47	65.0	66.0	1.0	20.6	19.2	-1.4
10	890136	F	35	44.0	50.0	6.0	36.1	33.8	-2.3
11	1126766	M	43	54.0	52.0	-2.0	19.1	19.6	0.5
12	1124092	F	34	55.0	-	-	38.6	17.3	-21.3
13	507281	M	44	54.5	50.0	-4.5	26.0	23.1	-2.9
14	180803	F	47	46.0	46.0	0.0	15.6	15.9	0.3
15	1139619	F	51	63.0	55.0	-8.0	26.6	28.0	1.4
16	1147780	F	35	39.0	40.0	1.0	31.8	26.5	-5.3

Table 26. Patients' data of conventional (low) sliding-scale dose (continued).

Number	H.N.	Thyroid Uptake (%)		RaI activity (mCi)	Dose of RaI (μCi/g of thyroid)
		4-hour	Est. 24-hour		
1	1070512	71.5	80.7	5.2	110.7
2	1069832	-	52.6*	2.0	74.1
3	1076404	74.4	82.0	2.6	111.0
4	1079468	57.8	74.0	5.3	100.1
5	1053264	69.3	79.7	3.5	104.9
6	1089851	91.5	88.6	4.3	120.9
7	416545	72.4	81.0	5.2	109.7
8	1086246	72.7	81.3	5.3	109.6
9	1096244	70.2	80.0	2.8	108.7
10	890136	72.3	81.1	4.9	110.1
11	1126766	-	72.2*	2.6	98.3
12	1124092	86.5	86.8	5.2	116.9
13	507281	41.0	63.0	3.5	84.8
14	180803	56.7	73.4	2.0	94.1
15	1139619	38.3	61.3	3.6	83.0
16	1147780	38.6	61.1	4.3	82.6

* The dose of RaI therapy was calculated by 24-hour thyroid uptake.

Table 26. Patients' data of conventional (low) sliding-scale dose (continued).

Number	H.N.	Thyroid hormones level		TSH levels	Outcomes (patients status)
		FT3	FT4		
1	1070512	13.04	7.26	<0.03	Hyperthyroid
2	1069832	8.42	6.11	<0.03	Hyperthyroid
3	1076404	2.43	2.67	<0.03	Euthyroid
4	1079468	4.67	1.66	<0.03	Hyperthyroid
5	1053264	2.05	0.18	19.45	Euthyroid
6	1089851	8.79	5.80	<0.03	Hyperthyroid
7	416545	10.19	5.37	<0.03	Hyperthyroid
8	1086246	2.15	0.81	1.58	Euthyroid
9	1096244	8.11	3.39	<0.03	Hyperthyroid
10	890136	2.03	0.74	0.45	Euthyroid
11	1126766	13.35	5.40	<0.03	Hyperthyroid
12	1124092	6.10	2.99	<0.03	Hyperthyroid
13	507281	6.90	2.14	<0.03	Hyperthyroid
14	180803	1.95	0.90	1.41	Euthyroid
15	1139619	16.20	7.50	<0.03	Hyperthyroid
16	1147780	4.50	1.30	<0.03	Hyperthyroid

Table 27. Patients' data of advanced (high) sliding-scale dose.

Number	H.N.	Gender	Age (yr)	Body weight (kg)			Thyroid weight (g)		
				bef_RaI	Aft_Rai	Diff_BW	bef_RaI	Aft_Rai	Diff_TW
1	1069757	F	43	55.0	63.0	8.0	30.3	16.4	-14.0
2	1077466	F	30	56.0	54.0	-2.0	30.4	27.7	-2.7
3	628838	F	24	48.0	51.0	3.0	26.0	12.0	-14.0
4	1082560	F	42	51.0	54.0	3.0	15.5	5.8	-9.7
5	1085164	F	48	47.0	50.0	3.0	21.2	13.1	-8.1
6	1089849	M	38	48.0	50.0	2.0	12.5	7.5	-5.0
7	1094751	F	40	58.5	65.0	6.5	35.0	28.9	-6.1
8	1096827	F	28	55.0	55.0	0.0	15.4	10.3	-5.1
9	1064557	F	53	42.0	41.0	-1.0	35.2	12.8	-22.4
10	1102635	F	44	63.0	65.0	2.0	28.0	21.8	-6.2
11	1124850	F	31	44.0	44.0	0.0	29.7	21.3	-8.4
12	1112665	F	54	52.0	52.0	0.0	28.3	17.1	-11.2

Table 27. Patients' data of advanced (high) sliding-scale dose (continued).

Number	H.N.	Thyroid Uptake (%)		RaI activity (mCi)	Dose of RaI (μCi/g of thyroid)
		4-hour	Est. 24-hour		
1	1069757	42.3	64.0	6.0	126.7
2	1077466	27.5	50.4	6.2	102.8
3	628838	52.4	70.9	5.0	136.3
4	1082560	75.3	82.4	3.2	170.1
5	1085164	59.5	74.9	4.3	151.9
6	1089849	35.2	58.2	2.5	116.4
7	1094751	61.9	76.2	5.6	121.9
8	1096827	37.5	60.2	3.0	117.3
9	1064557	82.3	85.2	7.2	174.3
10	1102635	34.5	57.6	5.0	102.9
11	1124850	52.6	71.0	6.0	143.4
12	1112665	66.5	78.4	5.7	157.9

Table 27. Patients' data of advanced (high) sliding-scale dose (continued).

Number	H.N.	Thyroid hormones level		TSH levels	Outcomes (patients status)
		FT3	FT4		
1	1069757	1.67	0.74	9.07	Eutyroid
2	1077466	11.10	36.03	<0.03	Hyperthyroid
3	628838	1.42	0.70	15.14	Hypothyroid
4	1082560	2.75	0.67	0.06	Eutyroid
5	1085164	7.45	1.84	<0.03	Hyperthyroid
6	1089849	3.16	0.07	29.78	Eutyroid
7	1094751	1.42	0.42	76.52	Eutyroid
8	1096827	3.11	0.92	0.67	Eutyroid
9	1064557	2.58	0.87	0.65	Eutyroid
10	1102635	6.13	3.01	<0.03	Hyperthyroid
11	1124850	2.26	0.98	<0.03	Eutyroid
12	1112665	6.86	3.23	0.04	Hyperthyroid

Table 28. Patients' data of conventional (100 μCi/g) calculated dose.

Number	H.N.	Gender	Age (yr)	Body weight (kg)			Thyroid weight (g)		
				bef_RaI	Aft_Rai	Diff_BW	bef_RaI	Aft_Rai	Diff_TW
1	975675	F	32	49.0	45.0	-4.0	114.2	63.0	-51.2
2	1019609	F	31	47.0	47.0	0.0	64.3	23.7	-40.6
3	1062985	M	50	55.5	53.0	-2.5	40.9	15.4	-25.5
4	1061640	M	18	48.0	45.0	-3.0	67.0	32.5	-34.5
5	1065378	F	32	47.0	49.0	2.0	86.1	39.8	-46.3
6	1091486	F	37	70.0	66.0	-4.0	58.3	36.7	-21.6
7	721796	M	30	57.5	58.0	0.5	104.2	58.9	-45.3
8	831932	F	18	62.0	-	-	56.9	-	-
9	1097655	M	35	60.0	64.0	4.0	125.6	23.6	-102.0
10	1104303	M	57	70.0	67.0	-3.0	98.7	46.8	-51.9
11	1097917	M	35	55.0	59.0	4.0	102.7	34.9	-67.8
12	1115156	F	32	62.0	55.0	-7.0	192.4	-	-
13	1073753	F	31	49.0	52.0	3.0	53.6	23.8	-29.8
14	1092140	M	38	55.0	55.0	0.0	64.4	-	-
15	873232	F	22	51.0	51.0	0.0	123.6	62.3	-61.3
16	1138398	F	19	55.0	54.0	-1.0	130.0	81.2	-48.8
17	1143344	F	45	63.0	65.0	2.0	52.0	27.0	-25.0
18	553241	F	27	50.0	-	-	46.5	29.1	-17.4
19	1119948	F	36	62.0	65.0	3.0	79.0	41.8	-37.2
20	857264	F	26	54.0	-	-	61.7	23.2	-38.5
21	128704	M	56	57.0	62.0	5.0	48.2	-	-
22	1154863	F	40	-	-	-	70.6	40.4	-30.2

Table 28. Patients' data of conventional (100 μCi/g) calculated dose (continued).

Number	H.N.	Thyroid Uptake (%)		RaI activity (mCi)	Dose of RaI (μCi/g of thyroid)
		4-hour	Est. 24-hour		
1	975675	87.9	87.3	13.0	99.4
2	1019609	34.1	57.2	11.2	99.6
3	1062985	70.9	80.5	5.0	98.4
4	1061640	42.6	64.0	10.5	100.3
5	1065378	78.4	83.7	10.3	100.1
6	1091486	62.6	76.5	7.6	99.7
7	721796	59.0	74.6	14.0	100.2
8	831932	71.5	80.7	7.0	99.3
9	1097655	78.6	84.0	15.0	100.3
10	1104303	71.7	80.8	12.2	99.9
11	1097917	80.5	84.5	12.0	98.7
12	1115156	73.9	81.8	23.5	99.9
13	1073753	59.8	75.0	7.2	100.7
14	1092140	57.4	73.8	8.5	97.3
15	873232	84.3	86.0	14.0	97.4
16	1138398	77.4	83.3	15.5	99.3
17	1143344	51.6	70.4	7.5	101.5
18	553241	67.9	79.0	6.0	101.9
19	1119948	45.7	66.5	12.0	101.0
20	857264	67.8	79.0	7.8	99.9
21	128704	77.1	83.1	5.8	100.0
22	1154863	81.6	85.0	8.3	99.9

Table 28. Patients' data of conventional (100 μCi/g) calculated dose (continued).

Number	H.N.	Thyroid hormones level		TSH levels	Outcomes (patients status)
		FT3	FT4		
1	975675	20.17	14.66	<0.03	Hyperthyroid
2	1019609	1.77	1.03	<0.03	Euthyroid
3	1062985	2.65	2.13	45.96	Euthyroid
4	1061640	2.58	29.99	<0.03	Euthyroid
5	1065378	18.39	3.09	<0.03	Hyperthyroid
6	1091486	18.35	7.40	<0.03	Hyperthyroid
7	721796	11.51	7.64	<0.03	Hyperthyroid
8	831932	26.46	8.69	<0.03	Hyperthyroid
9	1097655	2.57	1.15	6.78	Euthyroid
10	1104303	14.75	7.47	<0.03	Hyperthyroid
11	1097917	1.45	0.38	7.53	Euthyroid
12	1115156	12.86	6.82	<0.03	Hyperthyroid
13	1073753	7.63	2.63	<0.03	Hyperthyroid
14	1092140	4.51	3.38	<0.03	Hyperthyroid
15	873232	21.11	6.91	<0.03	Hyperthyroid
16	1138398	18.50	6.22	<0.05	Hyperthyroid
17	1143344	2.82	1.34	<0.03	Euthyroid
18	553241	6.30	2.26	<0.03	Hyperthyroid
19	1119948	10.00	2.86	0.05	Hyperthyroid
20	857264	19.53	9.15	<0.03	Hyperthyroid
21	128704	3.22	2.05	<0.03	Euthyroid
22	1154863	2.41	0.85	0.35	Euthyroid

Table 29. Patients' data of advanced (150 μCi/g) calculated dose.

Number	H.N.	Gender	Age (yr)	Body weight (kg)			Thyroid weight (g)		
				bef_RaI	Aft_Rai	Diff_BW	bef_RaI	Aft_Rai	Diff_TW
1	484693	M	38	50.0	45.0	-5.0	105.6	62.2	-43.4
2	1061644	F	37	54.0	55.0	1.0	75.0	19.3	-55.7
3	1061932	F	53	49.0	55.0	6.0	62.9	13.3	-49.6
4	1065168	F	52	56.0	62.0	6.0	49.5	17.3	-32.2
5	1066866	F	35	46.0	43.0	-3.0	128.4	34.5	-93.4
6	160536	F	44	44.0	54.0	10.0	111.0	28.0	-83.0
7	1080944	F	44	40.0	41.0	1.0	119.4	51.6	-67.8
8	1078859	M	61	67.0	68.0	1.0	74.7	51.6	-23.1
9	1095986	F	48	47.5	56.0	8.5	47.6	24.8	-22.8
10	721209	F	22	45.0	49.0	4.0	56.2	25.8	-30.6
11	1106369	F	43	57.0	50.0	-7.0	67.3	36.8	-30.5
12	1082998	F	35	51.0	54.0	3.0	55.2	37.4	-17.8
13	1131665	F	29	50.0	63.0	13.0	58.4	28.3	-30.1
14	1099976	F	33	53.0	51.0	-2.0	121.1	32.1	-89.0
15	1120232	F	56	53.0	48.0	-5.0	47.7	39.0	-8.7
16	1076713	M	40	66.0	74.0	8.0	63.3	35.7	-27.6
17	1137557	F	46	49.0	50.0	1.0	44.8	22.5	-22.3
18	1087023	M	19	43.0	46.0	3.0	99.8	52.3	-47.5
19	1124029	F	20	41.0	45.0	4.0	50.5	21.6	-28.9
20	1146432	M	35	45.0	47.0	2.0	97.4	89.7	-7.7
21	1125151	F	37	48.0	42.0	-6.0	78.3	40.5	-37.8
22	1119684	F	37	55.0	54.0	-1.0	49.1	12.6	-36.5
23	1145089	M	43	.	63.0	.	91.7	49.7	-42.0
24	957420	F	53	84.0	81.0	-3.0	72.3	49.0	-23.3

Table 29. Patients' data of advanced (150 μCi/g) calculated dose (continued).

Number	H.N.	Thyroid Uptake (%)		RaI activity (mCi)	Dose of RaI (μCi/g of thyroid)
		4-hour	Est. 24-hour		
1	484693	76.2	82.8	19.0	149.0
2	1061644	42.6	64.0	16.4	139.9
3	1061932	86.4	86.8	10.8	149.0
4	1065168	65.5	77.9	9.5	149.5
5	1066866	65.7	78.0	24.7	150.0
6	160536	.	95.2*	18.0	154.4
7	1080944	72.2	81.0	22.0	149.2
8	1078859	45.6	66.4	16.9	150.2
9	1095986	73.3	81.5	8.7	149.0
10	721209	64.2	77.3	10.9	149.9
11	1106369	59.8	75.0	13.5	150.4
12	1082998	27.1	50.0	16.5	149.5
13	1131665	71.6	88.8	10.8	164.2
14	1099976	90.1	88.0	20.6	149.7
15	1120232	66.8	78.5	9.0	148.1
16	1076713	63.9	77.2	12.0	146.4
17	1137557	79.7	84.2	8.0	150.4
18	1087023	87.6	87.2	17.0	148.5
19	1124029	81.4	84.9	9.0	151.3
20	1146432	49.4	70.0	20.8	149.5
21	1125151	86.5	86.8	13.5	149.7
22	1119684	75.5	82.5	9.0	151.2
23	1145089	80.7	84.6	16.3	150.4
24	957420	70.8	80.4	13.5	150.1

* The dose of RaI therapy was calculated by 24-hour thyroid uptake.

Table 29. Patients' data of advanced (150 μCi/g) calculated dose (continued).

Number	H.N.	Thyroid hormones level		TSH levels	Outcomes (patients status)
		FT3	FT4		
1	484693	8.89	4.70	<0.03	Hyperthyroid
2	1061644	1.84	2.81	<0.03	Euthyroid
3	1061932	1.18	0.87	<0.03	Euthyroid
4	1065168	1.26	0.59	34.93	Euthyroid
5	1066866	6.38	11.90	<0.03	Hyperthyroid
6	160536	5.07	1.49	<0.03	Hyperthyroid
7	1080944	14.50	6.46	0.31	Hyperthyroid
8	1078859	2.97	1.06	<0.03	Euthyroid
9	1095986	4.00	1.18	<0.03	Euthyroid
10	721209	3.10	0.82	2.08	Euthyroid
11	1106369	3.15	0.84	<0.03	Euthyroid
12	1082998	3.17	0.97	2.16	Euthyroid
13	1131665	2.82	1.22	<0.03	Euthyroid
14	1099976	12.30	2.03	<0.03	Hyperthyroid
15	1120232	26.45	8.74	<0.03	Hyperthyroid
16	1076713	0.71	0.05	5.59	Hypothyroid
17	1137557	1.95	0.40	24.48	Hypothyroid
18	1087023	9.90	2.49	<0.03	Hyperthyroid
19	1124029	3.09	0.76	0.25	Euthyroid
20	1146432	23.85	5.00	<0.03	Hyperthyroid
21	1125151	16.49	6.70	<0.03	Hyperthyroid
22	1119684	2.56	0.79	<0.03	Euthyroid
23	1145089	11.51	2.06	<0.03	Hyperthyroid
24	957420	14.23	9.59	<0.03	Hyperthyroid

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