THE ANALYSIS OF 6- AND 24-HOUR IODINE-131 THYROID UPTAKE IN PATIENTS WITH GRAVES' DISEASE AT UNIVERSITAS HOSPITAL

by

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DECLARATION

I declare that the work hereby submitted, is the result of my own independent investigation. Where help was sought, it is acknowledged. I further declare that this work is being submitted for the first time to the university/faculty towards a Master's degree in nuclear medicine and it has never been submitted to any other university/faculty for the purpose of obtaining a degree.

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J. HORN **DATE**

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LIST OF ACRONYMS AND ABBREVIATIONS

ACE	angiotensin-converting ensyme
act.	activity
ACTH	adrenocorticotrophic hormone
ALARA	as low as reasonably achievable
ANOVA	analysis of variance
CAA	calculated administration activity
CI	Confidence Interval
cm	centimetre
CNS	central nervous system
CPM	counts per minute
CSF	cerebrospinal fluid
CUT	Central University of Technology
dif.	difference
DIT	diiodotyrosine
DNA	deoxyribosenucleic acid
EANM	European Association of Nuclear Medicine
f	frequency
FT_4I	free thyroxine index
g	gram
GIT	gastrointestinal tract
Gy	gray
Gy/MBq	gray per megabequerel
hr	hour
^{131}I	iodine-131

^{131}I	jodium-131
^{123}I	iodine-123
^{124}I	iodine-124
IAA	intrathyroid absorbed activity
IAEA	International Atomic Energy Association
keV	kilo electronvolt
kg	kilogram
MBq	megabequerel
MBq/g	megabequerel per gram
MeV	mega electronvolt
mg	milligram
Max	maximum
Min	minimum
MIT	monoiodotyrosine
ml	millilitre
mIU/l	millilitre units per litre
mm	millimeter
MRI	Magnetic Resonance Imaging
mU/l	milliunits per litre
NaI[Tl]	sodium iodide-thallium
ng/dl	nanogram per decilitre
NMD	Nuclear Medicine Departments
Q	Quartile
rad	unit of absorbed dosage has been replaced by gray
RAJO	radioaktiewe jodiumopname

RAI	radioactive iodine
RAIU	radioactive iodine uptake
RCC	Radiation Control Committee
RT_3	reverse triiodothyrononine
SAG	South African Government
SAGD	Suid-Afrikaanse Gesondheidsdienste
SAHS	South African Health Services
SD	Standard Deviations
T_3	triiodothyronine
T_4	thyroxine
T_{eff}	effective half-life
^{99m}Tc-pertechnetate	Technetium-99-metastable-pertechnetate
TRH	thyroid-releasing hormone
TSH	thyroid-stimulating hormone
TSH/ml	thyroid-stimulating hormone per millilitre
TSI	thyroid-stimulating immunoglobulin
UFS	University of the Free State
UKGD	Universitas Kerngeneeskundige Departement
UNMD	Universitas Nuclear Medicine Department
UV	Universiteit van die Vrystaat
VI	Vertrouensinterval
µCi/g	microcurie per gram
µg	microgram
µg/dl	microgram per decilitre
µU	microunits

µU/ml	microunits per millilitre
%	percentage

DEFINITION OF TERMINOLOGY

Terms referred to in this investigation are explained and extended on in the following paragraphs:

Antithyroid drug: A substance that inhibits the synthesis of thyroid hormones and can be used in the treatment of Graves' disease (Anderson 1998:109). There is a variety of antithyroid drugs including thioamides, such as propylthiouracil and methimazole. Antithyroid drugs are also used to control hyperthyroidism during awaiting remission and before a thyroidectomy.

Beta rays: Atoms of disintegrating radioactive elements emits a stream of beta particles. This stream of beta particles is known as beta rays (Anderson 1998:186).

Euthyroid: A normal functioning thyroid gland (Anderson 1998:595).

Gamma rays: During a nuclear disintegration emitted from the nucleus of an atom is electromagnetic radiation of a short wavelength (Anderson 1998:672). Gamma rays travel at the speed of light and lack mass and electric charge.

Goitre: Swelling of the neck area associated with an enlarged thyroid gland (Anderson 1998:702). The cause of this enlarged thyroid gland can be linked to hyperthyroidism, hypothyroidism and even normal levels of thyroid function. The appearance of the goitre may be cystic or fibrous, containing a number of follicles or nodules.

Graves' disease: It is an autoimmune disease of unknown origin and there is evidence that it is familial (Anderson 1998:712). In more that 60% of patients

with Graves' disease antibodies to thyroglobulin or thyroid microsomes are found.

Hyperthyroidism: It is mainly associated with hyperactivity of the thyroid gland (Anderson 1998:795). The metabolic processes of the body are accelerated with hyperthyroidism and the thyroid gland is enlarged with the secretion of greater than normal amounts of thyroid hormones.

Hypothyroidism: This is a thyroid state resembling thyroid deficiency, with decreased activity in the thyroid gland (Anderson 1998:803).

Iodide: The substance is an anion of iodine (Anderson 1998:871). The salts most commonly used in medications are potassium iodide and sodium iodide.

Iodine: Iodine has an atomic mass of 126.90 and an atomic number of 53 (Anderson 1998:871). This non-metallic element falls within the halogen group. Iodine is present in the thyroid gland in the human body, mostly in the form of thyroglobulin. In the human body where it is deficient, it can result in goitre or cretinism.

Myxoedema: The most rigorous form of hypothyroidism (Anderson 1998:1075).

Organification: It is a process that occurs within the thyroid gland in which iodide is oxidised and integrated into tyrosyl residues of thyroglobulin (Anderson 1998:1156). Through the enzyme thyroid peroxidase the process of organification is catalysed.

Radioactive iodine: A radionuclide of iodine, used as a tracer in medicine and biology (Anderson 1998:1378).

Radioactive iodine uptake test: It is the administration of a tracer dosage of RAI orally in a test of thyroid function where the thyroid absorbs and incorporates the RAI (Anderson 1998:1378). This uptake of iodine by the thyroid is then measured by a probe to indicate the uptake percentage by the thyroid gland.

Thyroidectomy: A surgical procedure in which the thyroid gland is removed (Anderson 1998:1616).

Thyroid gland: An organ of high vascular origin that can be found in the region of the front neck area (Anderson 1998:1616). The thyroid gland weighs about 30g and consists of two lobes connected in the middle by the isthmus.

Thyroid hormone: The thyroid gland secretes an iodine containing compound mostly known as T_4 and in smaller amounts T_3 (Anderson 1998:1617). T_4 and T_3 have various abilities and functions in the human body, for example increasing the rate of metabolism; affecting body temperature; regulating protein, fat and carbohydrate catabolism in all the cells; skeletal maturation; sustaining growth hormone secretion, cardiac rate, force and output; supporting the central nervous system (CNS) development; and stimulating the synthesis of many enzymes. They are, in addition, needed for muscle tone and vigour.

Thyroid-stimulating hormone (TSH): A secreted substance from the anterior lobe of the pituitary gland directs the release of thyroid hormones (Anderson 1998:1617). TSH is essential for the growth and function of the thyroid gland. TSH secretion in turn is regulated by the thyrotropin-releasing factor present in the region of the median eminence of the hypothalamus. The normal levels present in the blood are two to 10 milliunits per litre (mU/l).

Thyroid storm: Medical emergency of uncontrollable hyperthyroidism caused by a release of increased amounts of thyroid hormones into the bloodstream (Anderson 1998:1617). The cause of this thyroid condition may be spontaneous, stress, infection or by a thyroidectomy performed on a patient who is inadequately prepared with antithyroid drugs.

Thyroxine (T_4): It is derived from tyrosine and is a hormone of the thyroid gland that influences the metabolic rate (Anderson 1998:1618).

Triiodothyronine (T_3): It is a hormone of the pituitary gland. T_3 has various functions in the human body, for example helping to regulate growth and development; helping to control metabolism and body temperature; and by a negative-feedback mechanism, acting to inhibit the secretion of thyrotropin by the pituitary gland (Anderson 1998:1654). T_3 is produced in the peripheral tissues, but is also synthesised and stored in the thyroid gland as amino acid residue of the protein thyroglobulin. The normal value present in the blood of an adult is 110 to 230 nanogram per decilitre (ng/dl).

SUMMARY

Key terms: radioactive iodine uptake; 24-hour iodine-131 uptake; Graves' disease; 6-hour iodine-131 uptake; thyroid; therapeutic dosage

In the South African Health Services (SAHS) it is each health worker's responsibility to find ways to reduce health care cost and improve health service to the public. The measurement of radioactive iodine uptake (RAIU) by the thyroid gland for diagnostic purposes has been used as early as the 1940s. The 24-hour (hr) iodine-131 (^{131}I) uptake measurement is traditionally used for the calculation of the ^{131}I administered activity for therapy dosage. This entails that the patient's hospitalisation is prolonged, which increases the costs. The literature also indicates that the 24-hr ^{131}I uptake value can be discarded and only the 6-hr ^{131}I uptake measurement is needed to calculate administered activity for therapeutic dosages for Graves' patients. Therefore, if it can be confirmed that the 6-hr ^{131}I uptake measurement alone is needed, the SAHS could decrease hospitalisation costs.

The overall goal of the investigation was to analyse the 6-hr and 24-hr ^{131}I uptake measurements of patients with Graves' disease at the Universitas Hospital. The aim was to determine the relationship between the 6-hr and 24-hr RAIU values to establish the therapeutic dosage for Graves' disease.

To achieve the aim, three objectives were set. First, to serve as a background to the investigation, a literature survey relating to the RAIU measurements of patients with Graves' disease was made. Second, a retrospective analysis was performed by collecting the 6-hr and 24-hr ^{131}I uptake measurements of patients with proven Graves' disease at the Universitas Nuclear Medicine Department (UNMD). Finally, the data obtained from the retrospective

analysis was analysed, summarised and compared to answer the investigation questions.

The investigation group included patients with confirmed Graves' disease who had undergone both the 6- and 24-hr ^{131}I RAIU at the Universitas Hospital from the beginning of 2004 to the end of 2005. Graves' disease is confirmed by the following factors at the UNMD, namely: Suppressed TSH, elevated T_4 and T_3 values, an increased uptake on the ^{99m}Tc-pertechnetate scan and increased 6- and 24-hr ^{131}I RAIU values. The UNMD statistics show that 178 patients were diagnosed with Graves' disease during this period. The patients of the investigation group included both male and female patients from different races, ranging from 15-75 years. In order to increase the validity of the investigation, all factors that could influence the accuracy of the ^{131}I thyroid uptake test were excluded. After the exclusion and inclusion criteria had been applied, the final investigation group was made up of 124 Graves' disease patients.

The data obtained from the patient files was noted on the different data sheets (see Appendix A) for further analysis. The information from these data sheets was then used to obtain the investigation results. The Department of Biostatistics of the University of the Free State (UFS) was consulted for recommendations regarding the management of data and the processing of results. All values were summarised by means and Standard Deviations (SD) or percentiles. Mean or median differences were calculated with a 95% Confidence Interval (CI). A regression analysis was made between the 6-hr and 24-hr ^{131}I RAIU values.

The highest RAIU value is the best to calculate the therapeutic dosage, as this gives a true reflection of the thyroid function of a Graves' disease patient. In the investigation group the median of the 24-hr ^{131}I RAIU values was higher

than the 6-hr ^{131}I RAIU values. The findings showed that the 24-hr ^{131}I RAIU in most of the investigation group was the highest value and most effective to calculate the ^{131}I therapeutic dosage.

At a time when research-based practice is taking on an increasingly important role, it is essential for nuclear medicine departments to make evidence-based recommendations. This investigation found that the correlation between the 6-hr and 24-hr RAIU clearly justified the cost spent on Graves' disease patients who must stay overnight for the 24-hr ^{131}I RAIU procedure.

SAMEVATTING

Sleutelterme: Radioaktiewe jodiumopname; 24-uur-jodium-131-opname; Graves se siekte; 6-uur-jodium-131-opname; skildklier; terapeutiese dosis

In die Suid-Afrikaanse Gesondheidsdienste (SAGD) is dit elke gesondheidswerker se verantwoordelikheid om wyses te vind om gesondheidsdienste se uitgawes te verlaag en om gesondheidsdienste aan die publiek te verbeter. Die meting van die radioaktiewe jodiumopname (RAJO) van die skildklier vir diagnostiese doeleindes is al sedert die 1940's in gebruik. Die opnamewaarde van die 24-uur-jodium-131 (^{131}I) is tradisioneel gebruik vir die berekening van die toedieningsaktiwiteit van die ^{131}I vir die terapeutiese dosis. Dit behels dat die pasiënte se hospitalisasie verleng moet word en die uitgawe daaraan verbonde, verhoog word. Die literatuurstudie het ook aangedui dat die 24-uur-^{131}I-opnamewaarde geïgnoreer kan word en dat slegs die 6-uur-^{131}I-opnamewaarde nodig is vir die berekening van die toedieningsaktiwiteit vir die terapeutiese dosis vir 'n pasiënt met Graves se siekte. As dit gevolglik bevestig kan word dat die 6-uur-^{131}I-opnamewaarde alleen nodig is, dan kan die SAGD se uitgawes van hospitalisasie verlaag word.

Die algehele doel van die ondersoek was die analise van die 6- en 24-uur-^{131}I-opnamewaardes van pasiënte met Graves se siekte by die Universitas Hospitaal. Die doel was om te bepaal wat die verhouding tussen die 6- en 24-uur-RAJO-waardes is om te beslis wat die terapeutiese dosis vir Graves se siekte is.

Om die doel te bepaal, is drie doelstellings gevolg. Eerstens, om te dien as agtergrond tot die ondersoek, is 'n literatuurstudie met betrekking tot die RAJO-waardes van pasiënte met Graves se siekte gedoen. Tweedens is 'n

retrospektiewe analise gedoen deur die versameling van die 6-uur- en 24-uur-^{131}I-opnamewaardes van pasiënte met bevestigde Graves se siekte by die Universitas Kerngeneeskundige Departement (UKGD). Laastens is die data wat versamel is vir die retrospektiewe analise geanaliseer, opgesom en vergelyk vir antwoorde tot die ondersoekvrae.

Die ondersoekgroep sluit pasiënte in met bevestigde Graves se siekte wat gegaan het vir beide ‘n 6- en 24-uur-^{131}I-RAJO by die Universitas Hospitaal vanaf die begin van 2004 tot die einde van 2005. Graves se siekte is bevestig deur die volgende faktore by die UKGD, naamlik: onderdrukte TSH; verhoogde T_4- en T_3-waardes, ‘n verhoogde opname op die ^{99m}Tc-pertechnetaatondersoek en ‘n verhoogde 6- en 24-uur-^{131}I-RAJO-waardes. Die UKGD-statistiek wys dat 178 pasiënte gediagnoseer is met Graves se siekte gedurende hierdie periode. Die pasiënte vir die ondersoekgroep het beide manlike en vroulike pasiënte van verskillende rasse tussen 15-75 jaar ingesluit. Met die doel om die geldigheid van die ondersoek te verhoog, is alle faktore wat die akkuraatheid van die ^{131}I-skildklieropnametoets beïnvloed, uitgesluit. Na die uitsluitings- en insluitskriteria toegepas is, het die finale ondersoekgroep uit 124 pasiënte met Graves se siekte bestaan.

Die data versamel uit die pasiëntlêers is aangedui op verskillende datablaaie vir verdere analise (kyk Bylae A). Die inligting vir hierdie datablaaie is daarna gebruik vir die ondersoekresultate. Die Departement van Biostatistiek van die Universiteit van die Vrystaat (UV) is genader vir aanbevelings in verband met die bestuur van data en die prosessering van resultate. Alle waardes is opgesom deur gemiddelde en Standaard deviasie of presentiele. Die gemene of mediaanlyn van verskille is bereken met ‘n 95% Vertrouensinterval (VI). ‘n Regressie-analise is gemaak tussen die 6-uur- en 24-uur-^{131}I-RAJO-waardes.

Die hoogste RAJO-waarde is die beste vir die berekening van die terapeutiese dosis, omdat dit ‘n ware refleksie gee van die skildklierfunksie van ‘n pasiënt met Graves se siekte. Die ondersoekgroep se gemiddelde 24-uur-^{131}I-RAJO-waarde was hoër as die gemiddelde 6-uur-^{131}I-RAJO-waardes. Die bevinding dui daarop dat die 24-uur-^{131}I-RAJO in die meeste van die ondersoekgroep die hoogste was en mees effektief is vir die berekening van die ^{131}I terapeutiese dosis.

In ‘n tyd wanneer navorsingsgebaseerde praktyk ‘n toenemende belangrike rol speel, is dit noodsaaklik vir kerngeneeskundige departemente om getuienis-gebaseerde aanbevelings te maak. Die ondersoek het gevind dat die verband tussen die 6-uur en 24-uur duidelik die uitgawes regverdig wat spandeer word om pasiënte met Graves se siekte te laat oornag vir die 24-uur-^{131}I-RAJO-prosedure.

CHAPTER 1

ORIENTATION TO THE INVESTIGATION

1.1 INTRODUCTION

The measurement of radioactive iodine uptake (RAIU) by the thyroid gland for diagnostic purposes has been used as early as the 1940s (Hayes, Akre & Gorman 1990:519). This technique has been used worldwide in the assessment of thyroid function and in thyroid diagnostic testing (Braunwald, Isselbacher, Petersdorf, Wilson, Martin & Fauci 1987:1736). RAIU of the thyroid not only reflects the early phase of thyroid hormonegenesis, but also reveals information about the overall function of the thyroid gland (Early & Sodee 1995:627). RAIU could provide additional information with regard to hyperthyroidism, euthyroidism and hypothyroidism (Hayes *et al.* 1990:519). In addition, RAIU value is used to accurately calculate the iodine-131 (^{131}I) treatment dosages for patients with hyperthyroidism.

The correct calculation of the radioactive iodine (RAI) treatment dosage is important to prevent undertreatment and possible recurrence of disease. The 24-hour (hr) ^{131}I uptake values are traditionally used to calculate the therapeutic dosage (Braunwald *et al*. 1987:1736). This entails that the patient's hospitalisation may be prolonged resulting in an increase in health care costs. Hayes *et al.* (1990:519) suggested that the 24-hr ^{131}I uptake value can be discarded and that the 6-hr ^{131}I uptake value alone could be used to calculate the therapeutic dosage. In the South African Health Services (SAHS) it is each health worker's responsibility to find ways to reduce health

care cost and improve health service to the public. Yet, if it could be confirmed that the 6-hr ^{131}I uptake value of a Graves' disease patient alone can be used, the SAHS could decrease the cost. With these considerations in mind a brief overview of relevant physiological and clinical factors associated with Graves' disease is indicated.

1.1.1 Formation and secretion of thyroid hormones

Ganong (1995:291) states that the main hormones secreted by the thyroid are triiodothyronine (T_3) and thyroxine (T_4) (Kasper, Fauci, Longo, Braunwald, Hauser & Jameson 2005:2104). These hormones are iodine-containing amino acids. T_3 and T_4 are synthesised by iodination and condensation of tyrosine molecules in the colloid, bound by peptide linkage with thyroglobulin. T_3 is especially formed in the peripheral tissues by deiodination of T_4. Other compounds like mono-iodotyrosine and reverse triiodothyronine (RT_3) are also found in the thyroid venous blood. RT_3 is inactive, whereas T_3 is more active than T_4. The thyroid cells thus have three main functions, namely first to transport and collect iodine from the circulation, second, to synthesise T_3 and T_4 and store them in the colloid and, last, to remove the thyroid hormones from thyroglobulin and secrete the thyroid hormones into the circulation, the latter regulated by pituitary secreted thyroid-stimulating hormone (TSH) through a negative feedback mechanism.

1.1.2 Clinical correlation

Ganong (1995:300) further indicates that the signs, symptoms and complications of both hypothyroidism and hyperthyroidism in humans are a predictable consequence of the physiological effects of thyroid hormones or the lack thereof. Graves' disease is an autoimmune disease of the thyroid gland in which T-lymphocytes (T-cells) activated by antigens stimulate the B-lymphocytes (B-cells) to produce circulating antibodies against these antigens (Ganong 1995:301).

A patient with Graves' disease may have a diffuse goitre, pretibial myxoedema and ophthalmopathy, but over 50% of these patients do not present with all these signs (Freitas 1999:297). Therefore, Graves' disease is confirmed biochemically by a suppressed serum TSH [<0.05 millilitre units per litre (mIU/l)] and elevated free T_4 or T_3 levels (Freitas 1999:297-298). The difference in biochemistry between hyperthyroidism and hypothyroidism as different clinical states is provided in Table 1.1.

Table 1.1: The difference in biochemistry between hyperthyroidism and hypothyroidism

Clinical state	Concentrations of Binding Proteins	Total Plasma T_4, T_3, RT_3	Free Plasma T_4, T_3, RT_3	Plasma TSH
Hyperthyroidism	Normal	High	High	Low
Hypothyroidism	Normal	Low	Low	High

Source: Ganong (1995:295)

Graves' disease is best differentiated from other thyrotoxic entities by a thorough clinical history and examination. These examinations include a Technetium-99-metastable-pertechnetate (^{99m}Tc-pertechnetate) thyroid scan to confirm a diffuse enlarged gland with homogeneous increased uptake and an increased 24-hr ^{131}I RAIU value provide diagnostic information about the thyroid gland of a Graves' disease patient (Kasper *et al.* 2005:2115) (Freitas 1999:298).

1.1.3 Hormone measurement

Different diagnostic tests are necessary in order to distinguish Graves' disease from single toxic nodule and toxic multinodular goitre, as well as iodine induced hyperthyroidism (McDougall 1991:81). These tests include clinical evaluation, biochemical measurements, RAIU and scintigraphy of the thyroid. Laboratory methods (*in vitro* tests) of the thyroid hormones give an

indication of thyroid function (Early & Sodee 1995:623). Graves' disease has increased levels of thyroid hormones because of the increased synthesis and secretion of these hormones (Harbert & Da Rocha 1984:30; Kasper *et al.* 2005:2115). Graves' disease can thus be confirmed, among others, by biochemical tests that include the *in vitro* measurement of the thyroid hormones T_4, T_3 and TSH (McDougall 1991:92).

The normal range for T_4 is 4.7-11 microgram per decilitre (µg/dl) and for TSH 5-25 microunits (µU) after injection of 400 to 500 microgram (µg) of thyroid-releasing hormone (TRH) (Kaplan 1985:871; Kasper *et al.* 2005:2108). Graves' patients' laboratory tests usually show an increased serum T_4 or serum T_3, reduced TSH and increased RAIU values (Braunwald *et al.* 1987:1744). Therefore, both T_4 and RAIU have abnormally increased levels in a Graves' disease patient. As T_4 and RAIU values confirm the diagnosis for Graves' disease it would be interesting to see if there is a correlation between the values of the thyroid hormones and RAIU (see Appendix A:1).

Laboratory tests of thyroid hormones such as TSH give an indication of thyroid function (Early & Sodee 1995:623). Harbert and Da Rocha (1984:35) confirm that a good indicator of thyroid hormone production will always be TSH. In Graves' patients TSH concentrations are below 0.05 microunits per millilitre (µU/ml) (Early & Sodee 1995:625). Laboratory tests demonstrate the physiological function of the thyroid hormones, but the ^{131}I thyroid uptake technique demonstrates the organification and uptake of ^{131}I in the thyroid gland. The next section will concentrate on the ^{131}I thyroid uptake technique.

1.1.4 ^{131}I thyroid uptake technique

The ^{131}I thyroid uptake technique described by the International Atomic Energy Association (IAEA) was developed to standardise RAIU worldwide. The prerequisites includes the following (IAEA 1961:536-538):

- The probe to be used should have a sodium iodide-thallium [NaI(Tl)] crystal size of not less than 2.5 x 2.5 centimetre (cm).
- The thyroid-to-crystal distance should be between 20 and 30 cm (it should always be kept at a fixed distance).
- The perspex neck phantom should be cylindrical in shape.
- The phantom diameter calculation is 15 cm and 15 cm in height and the distance from the edge of the phantom to the surface of the hole should be 0.5 cm.
- The patient dosage capsules as well as the standard for the quality control are placed in the neck phantom that corrects for attenuation by simulating the thickness of neck structures.
- The capsules used for the ^{131}I RAIU standard are dissolved in 30 millilitre (ml) of hot water and then inserted into the neck phantom. Both the patient's dosage capsules and the standard for the quality control are counted at a similar distance from the probe as to be used when the patient will be counted.
- The ^{131}I capsules given to the patient are orally administered.
- At the UNMD the decay factor is provided for in the computer programme used to automatically calculate the RAIU value. The counts per minute (CPM) are obtained and thyroid uptake value as pointed out by Datz (1993:6) is calculated as follows (also see Appendix B:4):

$$\text{Percentage (\%) Uptake} = \frac{\text{CPM Thyroid x 100}}{\text{CPM dosage administered x decay factor}}$$

1.1.5 Normal values for RAIU

No single figure (range) can be accepted for a normal 24-hr RAIU value, because there is a wide regional disparity in dietary iodine (Bernier, Christian & Langan 1994:233). It is thus advisable that nuclear medicine departments

should establish their own physiologic range for RAIU values. Bernier *et al.* (1994:233) indicate that RAIU values below 12% are considered low and above 35% increased. At the Universitas Hospital Nuclear Medicine Department (UNMD) a ^{131}I RAIU value range between 10-35% is considered to be normal (the normal range UNMD was considered due to the Free State dietary iodine intake).

1.1.6 Factors influencing RAIU

The ^{131}I RAIU uptake value is influenced by a variety of medications and substances that can lower the uptake of iodine (Becker, Charkes, Hurley, McDougall, Price, Royal, Sarkar & Dworkin 2003:35) (see Appendix C:5). Therefore, the medication history of the patient is of great importance and efforts should be made to ensure that the patient is not ingesting iodine containing materials, thyroid hormone or antithyroid drugs, all of which can influence the RAIU value. Other causes of iodine contamination should also be excluded, for example iodine containing X-ray contrast media.

1.1.7 The ideal radionuclide for uptake and measurement

There are various radionuclides that can be used for uptake and measurement in the thyroid gland. These radionuclides include iodine-123 (^{123}I), iodine-124 (^{124}I), ^{99m}Tc-pertechnetate and ^{131}I. ^{123}I is not preferred for RAIU measurements, because of the short half-life (13 hours), presence of long-lived impurities, especially high-energy ^{124}I, associated with down-scatter problems (Datz 1993:5). ^{123}I is also very expensive and not always available (Bernier *et al.* 1994:231). ^{99m}Tc-pertechnetate can be used for thyroid imaging and is advantageous because of its low cost, ready availability, low radiation exposure and high-quality imaging (Wagner, Szabo & Buchanan 1995:599). ^{99m}Tc-pertechnetate is not organified in the thyroid gland and does not provide adequate thyroid functional uptake information. ^{99m}Tc-pertechnetate also has other characteristics that make it unsuitable for thyroid uptake

testing, including the low absolute uptake of pertechnetate; high neck background; and the activity in the neck area which constantly changes because of the biodistribution of pertechnetate. ^{131}I is used mostly for thyroid uptake measurement values, even though it has a high radiation dosage (Wagner *et al.* 1995:598). Since it is organified in the thyroid, it is made ideal for thyroid functional testing.

The administered activity recommended by the IAEA (1961:535) for ^{131}I uptake measurement should not exceed 0.37 megabequerel (MBq) ^{131}I. The radiation exposure for ^{131}I to the thyroid is very high, namely 0.27-0.54 gray per megabequerel (Gy/MBq). At the UNMD the dosage used for the ^{131}I uptake measurements is between 0.30 and 0.37 MBq, which still falls within the IAEA recommendations.

1.1.8 ^{131}I therapeutic treatment of Graves' disease

The first RAI therapy for Graves' disease was administered by Hertz and Roberts in the early 1940s (Freitas 1999:297). Nordyke and Gilbert (1991:411) also indicated that in the early years of dosage calculation measurement, mathematical formulas involving thyroid uptake, estimated gland size and tracer retention, were used. This approach met with several major failures, since it is difficult to estimate the thyroid weight (size) by palpation, even when done consistently by the same person (Nordyke & Gilbert 1991:414). There are various therapeutic options to treat Graves' disease, including thionamide drug therapy (Kasper *et al.* 2005:2115), subtotal thyroidectomy and RAI (De Bruin, Croon, De Klerk & Van Isselt 1994:507). According to De Bruin *et al.* (1994:507-508), RAI became the best treatment option for Graves' disease, since it is easy to use and safe. RAI is also used to treat Graves' disease at the UNMD. The calculation of the correct therapeutic administration activity for Graves' disease is important, since the destruction of thyroid follicular cells by RAI to a large extent

depends on the amount of ^{131}I activity absorbed. ^{131}I RAIU should thus be performed to (i) confirm the diagnosis of Graves' disease; and (ii) to calculate the administration activity for therapeutic dosage.

A ^{131}I administration activity of sufficient quantity to induce relief of hyperthyroidism by beta particle irradiation of follicular cells must be calculated for a Graves' disease patient (Freitas 1999:302). The result will be cellular necrosis or affective deoxyribosenucleic acid (DNA) damage to surviving cells to reduce the overproduction of thyroid hormones (prevent replication of cells causing Graves' disease).

Dworkin, Meier and Kaplan (1995:212) state that most of the patients receiving ^{131}I for Graves' disease eventually become hypothyroid (due to the basic pathophysiology of Graves' disease). Patients treated with moderate administered therapeutic dosage activity of ^{131}I have an incidence of 50% for developing hypothyroidism within 10 years (Maisey, Britton & Gilday 1991:209; Kasper *et al.* 2005:2116). Treatment success of Graves' disease is reduced with smaller ^{131}I administration activity, as well as the risk of developing hypothyroidism. Therefore, a small ^{131}I administration activity will delay the development of hypothyroidism, but - on the other hand - may cause more relapses of Graves' disease (Riccabona 1994:12). Since Graves' disease patients in many cases end up with hypothyroidism, those patients receiving ^{131}I therapy should be monitored for further treatment. The development of hypothyroidism induced by ^{131}I administration activity after Graves' disease requires lifelong thyroxine therapy.

1.1.9 Adequate absorbed activity for the intrathyroid tissue

The calculation of the correct therapeutic dosage for Graves' disease is important, since the destruction of thyroid follicular cells by RAI to a large extent depends on the dosage of ^{131}I absorbed (De Bruin *et al.* 1994:508).

Maisey *et al*. (1991:209) state that a large single ^{131}I administration dosage, for example 555 MBq ^{131}I, has a high cure rate for hyperthyroidism and prevents return of Graves' disease. On the other hand, according to Alexander and Larsen (2002:1073), an absorbed activity of 296 MBq ^{131}I in the thyroid is an effective treatment for most patients with Graves' disease. The UNMD uses the RAIU for the calculation of the ^{131}I therapeutic dosage for Graves' patients so that the intrathyroid absorbed activity (IAA) received is 296 MBq ^{131}I. The ranges of ^{131}I absorbed activity per gram (g) of thyroid tissue for the effective treatment of Graves' disease as given by the European Association of Nuclear Medicine (EANM) (2003:30) is from 2.2-3.0 MBq/g up to 6.0-7.0 MBq/g. Hence, for a thyroid weighing 50g, the ^{131}I therapeutic dosage should be between 110 MBq and 350 MBq for the effective treatment of Graves' disease. A Graves' disease patient who receives an IAA of more than 350 MBq, consequently has received unnecessary ^{131}I therapeutic activity to the thyroid gland. A Graves' disease patient who receives an IAA of more than 350 MBq is considered by the UNMD to have received a less accurate therapeutic dosage. Therefore, when calculating the different therapeutic dosages with the 6-hr ^{131}I RAIU value or the 24-hr ^{131}I RAIU value, the IAA should not be more than 350 MBq of ^{131}I, otherwise the patient will receive unnecessary ^{131}I activity to the thyroid gland.

In a normal person who received ^{131}I orally to determine RAIU value, the measured uptake increases gradually and then reaches a plateau between 18- and 24-hr after intake (Harbert & Da Rocha 1984:9). Van Isselt, De Klerk, Koppeschaar and Van Rijk (2000:609) indicated that the 24-hr ^{131}I RAIU value is traditionally used for the calculation of the ^{131}I administration activity for therapeutic dosage. According to these authors, the 24-hr ^{131}I RAIU value is most effective for the calculation of the administration activity (CAA) for patients with Graves' disease (Van Isselt *et al.* 2000:609). Wagner *et al.* (1995:598) also suggest that the 24-hr ^{131}I uptake value is highly

recommended for treatment of Graves' disease. The 24-hr ^{131}I RAIU value is therefore the favourite choice for therapeutic dosage calculations. The reason why 24-hr ^{131}I RAIU value is preferred is that rapid turnover of ^{131}I in the first two hours and a lower 24-hr RAIU value in Graves' disease are supposed to be rare (Harbert & Da Rocha 1984:12). Yet, Graves' disease (hyperthyroidism) can show different characteristic curves and turnover points of thyroid uptake after ^{131}I oral administration (see Figure 1.1).

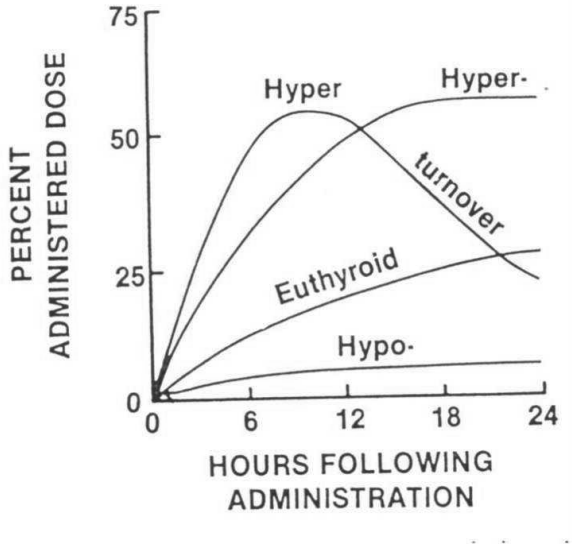


Figure 1.1: The different characteristic curves of thyroid uptake of ^{131}I after oral administration (courtesy of Harbert & Da Rocha 1984:12.)

The highest thyroid uptake value is the optimal value to calculate the effective and accurate therapeutic dosage calculation (Harbert & Da Rocha 1984:12). The 24-hr RAIU value is usually higher than the 6-hr RAIU value in Graves' disease, therefore the 24-hr RAIU value is regarded as the better choice for therapeutic dosage calculation. The transit patterns of the 6-hr and 24-hr ^{131}I RAIU values need to be investigated to see if the 24-hr RAIU in Graves'

disease patients at the UNMD is the higher RAIU value and most effective to calculate ^{131}I therapeutic dosage.

The IAA activity received by a Graves' disease patient should therefore fall within the recommended range of 110 MBq to 350 MBq. A 5% value difference between the 6-hr and 24-hr RAIU values would make a less than 1 MBq difference to the CAA for the Graves' disease patient as long as the aimed IAA stays the same. At the UNMD a 5% value difference between the 6-hr and 24-hr RAIU values would be acceptable, as the patient radiation dosage received would not be significantly higher. Hence, if it could be proven that there is in most of the Graves' disease patients a 5% or less value difference between the 6-hr and 24-hr RAIU values, only the 6-hr RAIU can be used to determine the CAA.

1.2 STATEMENT OF THE PROBLEM

The 24-hr ^{131}I RAIU measurement following the 6-hr ^{131}I RAIU measurement for patients with Graves' disease requires a costly prolonged stay in hospital or the return to the clinic on an outpatient basis. McDougall (1991:86) indicates that there is a possibility for same day diagnosis, dosage calculation and treatment of the patient, as there are some reports of a predictable correlation between the early (6-hr) RAIU and the late (24-hr) RAIU values. If the 6-hr ^{131}I RAIU value alone confirms to be sufficient to calculate the therapeutic administration activity for Graves' disease patient cost and hospital stay could be significantly reduced.

1.2.1 Investigation questions

To address the problem statement, the investigation sought to answer the following questions:

- Is the 6-hr ^{131}I RAIU value alone sufficient to calculate the optimal therapeutic administration activity for ^{131}I for patients with Graves' disease?
- How do the 6-hr and 24-hr ^{131}I RAIU values correlate with the T_4 values of patients with Graves' disease?
- How do the 6-hr ^{131}I RAIU values correlate with the 24-hr RAIU values when the transit patterns in patients with Graves' disease are analysed?

1.3 GOAL, AIM AND OBJECTIVES OF THE INVESTIGATION

In the next section a closer look will be taken at the goal, aim and the objectives of the investigation.

1.3.1 Aim

The overall aim of the investigation is to analyse the 6-hr and 24-hr ^{131}I RAIU values of patients with Graves' disease at Universitas Hospital. As to determine if there is a correlation between the 6-hr and 24-hr RAIU values to establish if only the 6-hr RAIU value can be used to calculate the therapeutic dosage for Graves' disease.

1.3.2 Objectives

To achieve the aim, the following steps were taken:

- To serve as a background to the investigation, a literature survey relating to the RAIU values of patients with Graves' disease was undertaken.
- A retrospective analysis was performed by comparing the 6-hr and 24-hr ^{131}I RAIU values of patients with proven Graves' disease at the UNMD.

- To answer the investigation questions, the data obtained from the literature and the retrospective analysis was then analysed, summarised and compared.

1.4 SIGNIFICANCE OF THE INVESTIGATION

A 6-hr ^{131}I RAIU value which does not differ significantly from the 24-hr value may lead to a decrease in hospitalisation time, as the patient will not have to stay overnight or return the next day for the 24-hr ^{131}I uptake value (Hayes *et al.* 1990:519). If the 6-hr ^{131}I uptake value does not correlate with the 24-hr value, the latter will be essential to calculate the correct ^{131}I therapeutic administration activity. The disparity between the 6-hr and 24-hr ^{131}I uptake values may justify the extra cost with regard to prolonged hospitalisation or additional outpatient visits.

1.5 SCOPE OF THE INVESTIGATION

The investigation was conducted in the field of nuclear medicine health care. This field provides a diagnosis of functional thyroid disease through the ^{131}I uptake measurement. The topic that was addressed was the comparison between the 6-hr and 24-hr ^{131}I RAIU values of patients with Graves' disease at the UNMD.

1.6 METHODS OF INVESTIGATION

1.6.1 Investigation design

The investigation design was two-fold. Firstly, a literature review was carried out to determine the significance of the 6-hr and 24-hr RAIU values in patients with Graves' disease. Secondly, a retrospective analytical investigation was conducted to analyse and compare the 6-hr and 24-hr RAIU values of patients with proven Graves' disease in the Free State referred to the UNMD (see Figure 1.2 for the investigation design).

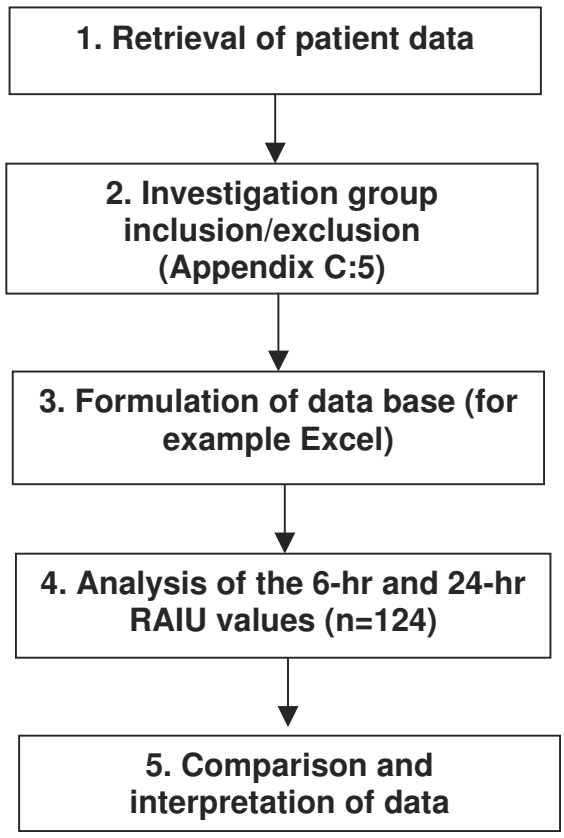


Figure 1.2: Investigation design

1.6.2 Patient inclusion and exclusion criteria

The investigation included patients with confirmed Graves' disease who had undergone both 6- and 24-hr ^{131}I RAIU studies at the Universitas Hospital from the beginning of 2004 to the end of 2005. Graves' disease was confirmed by the following factors at the UNMD namely: Suppressed TSH; elevated T_4 or T_3; a diffuse increased uptake of ^{99m}Tc-pertechnetate; and an increased 6-hr and 24-hr ^{131}I RAIU value. The UNMD statistics showed that 178 patients were diagnosed with Graves' disease during this period.

Male and female patients, varying in age, were included. Patients with serious systemic disease, iodine contamination, thyroid nodules or other causes of hyperthyroidism were excluded from the study. These factors were excluded due to their effect on the physiology of the thyroid and therefore the uptake of RAI (see paragraph 1.1.6).

1.7 FORMULATION OF DATABASE

The data obtained from the patient files was noted on the different data sheets (see Appendix A) for further analysis. There was a need for a data sheet containing information about patient ^{131}I RAIU values and biochemistry information (see Appendix A:1). The second data sheet contained information about the patient age and sex (see Appendix A:2). A data sheet to note the patient 6- and 24-hour therapeutic dosage information (see Appendix A:3) was used.

1.8 DATA ANALYSIS

The department of Biostatistics at the University of the Free State (UFS) was consulted for recommendations regarding the management of data and the processing of results (see Appendix D:7). Chapter 3 outlines the method used for the data analysis of this research project.

1.9 ETHICAL ASPECTS

The protocol was approved by the Ethics Committee of the UFS (ETOVS Nr. 40/06) with all the necessary application forms to evaluate the ethical aspects (see Appendix F:8). There was no need to obtain consent from the Radiation Control Committee (RCC), as the ^{131}I uptake measurement done at the Universitas Hospital falls within the RCC rules and regulations. Letters requesting permission (see Appendix F:9) to perform this research project at the UNMD were written to the chief specialist and the director of the UNMD. Informed consent was obtained from the director of the Universitas Hospital (see Appendix F:10) and the chief specialist (see Appendix F:11) for patient data to be used for this retrospective investigation.

1.10 ARRANGEMENT OF THE INVESTIGATION

The course of the investigation report, the methods used to find answers to the investigation questions, and the outcome of the study will be reported on as follows:

In this chapter, Chapter 1, a brief introduction and background to the investigation was given.

Chapter 2, **The ^{131}I thyroid uptake procedure: Background and related factors**, as well as the uptake technique, the calculation of the ^{131}I RAIU and the calculation of the ^{131}I therapeutic dosage will be discussed and explained in detail.

Chapter 3, **Investigation design and methods**, will provide a description of the methodology applied in the investigation. Theoretical aspects of the study design and the methods of investigation will be discussed. Measurement and analysis factors of the retrospective investigation will be reported in this chapter.

Chapter 4, **Results and findings**, will be presented in the form of appropriate tables and figures.

Chapter 5, **Discussion and recommendations**, the final chapter in the research report, will in particular deal with the outcome of the study. Recommendations regarding the diagnosis and RAI treatment of patients with Graves' disease at the UNMD and possibilities for future research will be provided.

1.11 CONCLUSION

In the SAHS it is each health worker's responsibility to find ways to reduce health care cost and improve health service to the public. The investigation determined if the 6-hr ^{131}I RAIU value alone can be used to calculate the therapeutic dosage for Graves' disease and if hospital and patient expenses

can be reduced significantly. Therefore, to explore the possibility of using a 6-hr ^{131}I RAIU value alone, analysing and comparing the 6-hr and 24-hr ^{131}I RAIU values seemed meaningful.

CHAPTER 2

THE ^{131}I THYROID UPTAKE PROCEDURES: BACKGROUND AND RELATED FACTORS

2.1 INTRODUCTION

During the 1940s the RAIU test was introduced and is now used worldwide in the evaluation of thyroid function (Hayes *et al*. 1990:519). Since the thyroid gland has the ability to accumulate iodine, RAI is used as the basis for the RAIU test (Grayson 1960:397). The thyroid gland is the ideal organ for the use of ^{131}I for the RAIU test, as it is the only tissue to retain iodine for a prolonged interval (Volpé 1977:2). The RAIU test may give the perception of being simple, but the dynamics of normal iodine metabolism is complicated and there are various factors that can influence the diagnostic results (Grayson 1960:397). Quantitatively the avidity of the thyroid gland for iodide is established by the RAIU test or qualitatively by using a thyroid scan (Meier, Brill, Becker, Clarke, Silberstein, Royal & Balon 2002:857).

A variety of diagnostic procedures that provide information about the thyroid function exists. Some examples are thyroid iodine clearance, the thyroid iodine accumulation rate, the thyroid accumulation gradient, the ^{131}I conversion ratio, the ^{131}I urinary excretion and a number of thyroid scanning procedures (Grayson 1960:397). Some of the above-mentioned procedures have specific value in the study of thyroid function (Kasper *et al.* 2005:2115), but the 24-hr RAIU test has been the standard test in most centres worldwide. The RAIU test is also preferred as the diagnostic test of choice at the UNMD

to provide information about the thyroid function and iodine status. A variety of time intervals from one to 48 hours has been used for the measurement of uptake in the thyroid for the RAIU test (Grayson 1960:397; Wagner *et al.* 1995:598). The time intervals used at the UNMD for the RAIU test with Graves' disease patients are six hours and 24 hours after ^{131}I administration.

The radionuclide needed for the RAIU must have characteristics such as ^{131}I to be taken up and organified in the thyroid gland (Wagner *et al.* 1995:598). ^{131}I is a radionuclide which has been used over the years to diagnose thyroid disease in different ways, including the RAIU test (Grayson 1960:397). At the UNMD ^{131}I is the radionuclide of choice for the RAIU test.

In 1835 Robert Graves' described the clinical signs of three women, namely goitre, palpitations, forceful heartbeat and tachycardia and from this the eponym Graves' disease was derived (McDougall 1991:79). The signs that are usually present with Graves' disease are hyperthyroidism, diffusely enlarged thyroid gland and in some patients ophthalmopathy, dermopathy, finger clubbing and nail changes (Kasper *et al*. 2005:2114). McDougall (1991:92) stated that Graves' disease is an autoimmune disorder related to a specific organ, namely the thyroid gland. Graves' disease causes high levels of thyroid hormones in the blood (McDougall 1991:79) and is the most common cause of hyperthyroidism (Lind 2002:453). In order to confirm Graves' disease and differentiate it from other causes of hyperthyroidism, a complete clinical evaluation, biochemical measurements, RAIU and - if indicated - scintigraphy must take place (McDougall 1991:79).

Various scientists have contributed to the discovery of the use of iodine in making a diagnosis and the treatment of Graves' disease. A short historical review of these scientists' discoveries will be provided to give an overview of

the use of iodine in Nuclear Medicine Departments (NMD) as we currently know it.

2.2 HISTORICAL REVIEW OF THE USE OF RAI

Various scientists and clinicians, namely Baumann, Marine, Plummer, Fermi, Compton, Chapman and Evans as cited in Chapman and Maloof (1955:263-267) made the following contributions to the diagnosis and treatment of thyroid disease: During the 1890s Baumann discovered iodine in the thyroid gland and recognised the avidity that the thyroid holds for iodine (Chapman & Maloof 1955:263). Marine made another important contribution by demonstrating the value of iodine in the prevention of iodine-deficient endemic goitres. In 1923 Plummer disclosed a report in which he indicated the use of iodine in the smoothing of the post-operative course of patients with hyperthyroidism (Chapman 1983:2043). Because of this concept of Plummer's report, various thyroid clinics then proceeded to give iodine before and after surgery in the place of thyroidectomy. At the Massachusetts General Hospital, Means and his associates described the iodine response, the effective dosage, the cause of failure, as well as the several clinical results of iodine treatment (Chapman 1983:2043).

Chapman and Maloof (1955:264) further report that Fermi, an Italian scientist, succeeded in producing radioactive iodine. Compton (as quoted in Chapman & Maloof 1955:264) based the use of RAI in treating patients with hyperthyroidism on the following three concepts:

- The thyroid has a natural avidity for collecting either stable or radioactive iodine.

- RAI decays in the thyroid by emitting high-energy beta rays, which only penetrate a few millimetres of thyroid tissue.
- Beta-rays can destroy thyroid tissue in a similar fashion as the secondary electrons produced by x-rays.

In 1946 Chapman and Evans concluded that RAI on its own is effective in controlling hyperthyroidism (Chapman & Maloof 1955:264). In 1951 the IAEA reported that more than 130 hospitals and clinics were using ^{131}I in the treatment of hyperthyroidism. RAI has become an accepted form of therapy due to the research that has been performed in past years (Chapman & Maloof 1955:266). The UNMD also uses ^{131}I mainly as therapy choice for the treatment of Graves' disease.

2.3 GRAVES' DISEASE

A background and an understanding of the pathogenesis, etiology, morphology, clinical correlation and prevalence of Graves' disease are needed to understand the role of the ^{131}I RAIU test in the diagnosis and treatment of Graves' disease.

2.3.1 Pathogenesis

The pathogenesis of Graves' disease was suggested by Robbins and Kumar (1987:681) to be an autoimmune disease. The characteristics that indicate Graves' to be an autoimmune disease are the presence of thyroid microsomal autoantibodies in 85% of patients with Graves' disease and thyroglobulin antibodies in about 30% of these patients. The pathologic characteristics of Graves' disease are a diffusely enlarged, soft and vascular thyroid gland (Braunwald *et al*. 1987:1743). Another essential pathological

characteristic present in Graves' disease is the presence of parenchymatous hypertrophy and hyperplasia.

2.3.2 Aetiology

The specific cause of Graves' disease is not yet fully known (Braunwald *et al.* 1987:1743). There is a variation of manifestations and no single factor is responsible for this condition. Hyperthyroidism, the main disorder in Graves' disease, is caused by a haemostatic disruption resulting from the presence of an abnormal thyroid stimulator.

2.3.3 Morphology

The thyroid gland of a patient with Graves' disease is in most cases diffusely and symmetrically enlarged (Robbins & Kumar 1987:681). When dissected, the thyroid gland in a patient with Graves' disease has a red-brown muscle like appearance. In the untreated Graves' disease patient the most important histological features have a "too many follicular cells and too little colloid" appearance.

2.3.4 Clinical correlation

A patient with Graves' disease may present with a diffuse goitre, pretibial myxoedema and ophthalmopathy, but over 50% of these patients do not present with all these signs (Freitas 1999:297). Therefore Graves' disease should be confirmed biochemically by suppressed serum TSH (<0.05 mIU/L) and elevated free T_4 or T_3 levels (Freitas 1999:297-298). Graves' disease is best distinguished from other thyrotoxic entities by a thorough clinical history and examination, which is then combined with a ^{99m}Tc-pertechnetate thyroid scan (to confirm a diffuse enlarged gland with homogeneous increased uptake) and an increased 24-hr ^{131}I RAIU value (Freitas 1999:298).

2.3.5 Prevalence

Graves' disease is especially common in the thirty- to forty-year age group but can occur at any age (Braunwald *et al.* 1987:1743). It manifests more in women than in men. For investigation purposes it is always interesting and of value to look at the prevalence of the disease; to determine if it stays constant as time goes by; and whether the prevalence is the same for different parts of the world. For future investigation purposes it would be interesting to compare UNMD prevalence investigation data with data stated by Braunwald *et al.* (1987:1743).

2.4 THYROID HORMONES

The thyroid hormones influence the uptake of iodine by the thyroid gland and therefore the RAIU value. For better understanding of the physiologic interaction between the thyroid hormones and iodine uptake a short summary of applicable physiological factors is given.

2.4.1 Formation and secretion of thyroid hormones

The hormones mainly secreted by the thyroid gland are T_3 and T_4 (Ganong 1995:291; Kasper *et al.* 2005:2105-2106). These hormones are from the iodine-containing amino acids monoiodotyrosine (MIT) and diiodotyrosine (DIT). Thus T_3 and T_4 are synthesised by iodination and condensation of thyrosine molecules in the colloid that binds in peptide linkage with thyroglobulin. Through the process of deionisation of T_4 in the peripheral tissues T_3 is formed. Other compounds like MIT and RT_3 are also present in the thyroid venous blood. RT_3 is inactive, whereas the hormones T_3 and T_4 are active. T_3 is more active than T_4. The thyroid cells therefore have three vital functions, namely: Firstly, to transport and collect iodine; secondly, to synthesise thyroglobulin and store it in the colloid; and, lastly, to remove the

thyroid hormones from thyroglobulin and secrete the thyroid hormones into the circulation.

2.4.2 The metabolic pathways of iodine and the thyroid hormones

The gastrointestinal tract (GIT) provides a medium through which iodide, iodine and iodate taken by mouth are rapidly absorbed and then transferred into the bloodstream (Chapman & Maloof 1955:266). Iodine and iodate are reduced to iodide before being absorbed. Through the process of diffusion iodide is transferred from the bloodstream into the iodide space of the body. A fraction of iodide is concentrated by the thyroid gland to form thyroid hormones while the kidneys excrete the rest. The two thyroid hormones T_4 and T_3 are bound in the bile as glucuronides. There is an excretion of iodine in the faeces of humans of about 5-12%.

The thyroid iodine metabolism can be categorised in the following three processes (Grayson 1960:397-398):

- Iodide trapping: In this process iodide is selectively concentrated within the thyroid cell to provide the substrate for subsequent steps.
- Hormonal synthesis: This process includes the activation of iodide by oxidation, with sequential iodination of tyrosine residues of thyroglobulin to form monoiodotyrosines and diiodotyrosines. The binding of iodotyrosines gives rise to T_4, T_3 and traces of other iodo-thyronines.
- Hormonal release: Through thyroglobulin the amino acids are liberated by proteolytic enzyme(s) secreted by the thyroid cell. Inside the thyroid follicular cell the iodotyrosines are selectively deiodinated, but this does not include T_4 and T_3 that are spared and permitted to enter the bloodstream.

2.4.3 Thyroid hormone measurement

Various diagnostic tests are available to distinguish between single toxic nodule, toxic multinodular goitre and induced iodine hyperthyroidism (McDougall 1991:81). These tests, as previously mentioned, include clinical evaluation, biochemical measurements, RAIU and scintigraphy of the thyroid. Laboratory methods (*in vitro* tests) of the thyroid hormones give an indication of thyroid function (Early & Sodee 1995:623). Increased levels of thyroid hormones are present in Graves' disease because of the increased synthesis and secretion of thyroid hormones (Harbert & Da Rocha 1984:30). Therefore, Graves' disease can be confirmed by biochemical tests that included the *in vitro* measurement of thyroid hormones (T_4 and T_3) and TSH (McDougall 1991:92).

The normal biochemical value for T_4 is between 4.7-11 µg/dl and for TSH after 400 to 500 µg of TRH is 5-25 µU TSH/ml (Kaplan 1985:871; Kasper *et al.* 2005:2108). Graves' disease patients' laboratory test indicate an increased serum T_4 or serum T_3 reduced TSH and increased RAIU (Braunwald *et al.* 1987:1744). Therefore, in Graves' disease, there is an abnormally increased T_4 and ^{131}I RAIU values and both of these diagnostic tests provide information about thyroid function. As T_4 and RAIU tests confirm the diagnosis for Graves' disease, it would be valuable to see if there is any correlation between the values of the thyroid hormones and RAIU (see Appendix A:1).

Harbert and Da Rocha (1984:35) mention that a good indicator of thyroid hormone production will always be TSH. Other laboratory tests of thyroid hormones such as TSH also give an indication of thyroid function (Early & Sodee 1995:623). The value of TSH concentrations in Graves' disease is typically below 0.05 µU/ml (Early & Sodee 1995:625). It would be interesting

to see if there is any correlation between values of TSH and ^{131}I RAIU, as both provide information about thyroid function in Graves' disease.

2.5 NORMAL DAILY INTAKE OF IODINE

Iodine intake can consequently influence the uptake ^{131}I by the thyroid gland for the RAIU test. The recommended daily intake of iodine for adults to satisfy the physiologic requirement is two to four µg per kilogram (kg) of body weight (Grayson 1960:399). The average daily urinary iodine excretion is about 150 µg and the mean of the daily normal thyroid accumulation of iodine is about 75 µg. The optimal daily iodine intake, without affecting the uptake of the thyroid gland, is 200 µg for an adult weighing 70 kg. The amount of iodine to depress RAIU in the case of Graves' disease is one milligram (mg) of iodide (Grayson 1960:400).

2.6 SOURCES OF EXCESS IODINE INTAKE

There are various external sources of iodine, for example drugs, iodised salt, foods and X-ray contrast media (Grayson 1960:400). The iodine metabolism can be affected by various drugs and toxic substances that contain iodine (Grayson 1960:397). These drugs and toxic substances act as discrete sites in the steps involved in the formation and release of thyroid hormones in the thyroid metabolism process. As these drugs and toxic substances influence the thyroid metabolism, they will also affect the RAIU test. As various substances and conditions influence the ^{131}I RAIU, a short summary of these factors is provided as part of the exclusion criteria for the investigation report (Grayson 1960:397).

2.6.1 Medication

Potassium iodide and other iodides are present in various medication used. Lugol's solution, for example, contains five to eight mg of iodine per drop. Lower RAIU values will be the result of the administration of these preparations.

2.6.2 Vitamins and minerals

Grayson (1960:401) suggests that even some vitamin tablets containing iodide are sufficient to lower the 24-hr ^{131}I RAIU values significantly.

2.6.3 Iodine in food

The ^{131}I RAIU values can be lowered by increased dietary iodine provided by an excessive seafood diet (Grayson 1960:402). Other foods that are not from the sea may have a variation in their iodine content. This factor of iodine content is mainly dependent on the iodine concentration of the soil in which they were produced.

2.6.4 Iodine in X-ray contrast media

During X-ray procedures various types of contrast media (for example Urograffin) are used which contain large amounts of iodine (Grayson 1960:402). X-ray contrast media can lower the ^{131}I RAIU values, because in some of these contrast media, iodine is released from its organic binding as iodide and increases the total body pool. The excess iodide that is produced decreases the values of the ^{131}I RAIU test. The RAIU test may be interfered with as long as one month from iodinated compounds used during intravenous pyelography (Grayson 1960:403).

2.6.5 Hormones

Hormones can have an effect on the uptake of iodine by the thyroid gland and various have been studied in this regard, including adrenocorticotropic

hormone (ACTH), cortisone, epinephrine, desiccated thyroid, T_4, T_3, oestrogen, progesterone, desoxycorticosterone, testosterone and the TSH. A decrease in value of the ^{131}I RAIU can be caused for example by cortisone (Grayson 1960:407). The 24-hr ^{131}I RAIU value is increased by epinephrine.

^{131}I RAIU uptake value is decreased by the administration of desiccated thyroid, T_4 and T_3, because this causes the inhibition of the release of TSH by the anterior pituitary (Grayson 1960:408). The hormones progesterone and testosterone also decreased ^{131}I RAIU test values, whereas estrogens showed no consistent changes.

2.6.6 Antibiotics

Antibiotics affect the ^{131}I uptake by the thyroid gland (Grayson 1960:409). Therefore, antibiotics can influence the values of the ^{131}I RAIU test. As antibiotics can influence the values of the ^{131}I RAIU test, patients in the investigation group that used antibiotics were excluded from the investigation.

2.7 INDICES OF THYROID FUNCTION

Various accurate indices of thyroid function have contributed to the process of thyroid diagnostic testing, for example value measurements of TSH, T_4, T_3 and the detecting of thyroid stimulating immunoglobulins (TSI) (Hayes *et al.* 1990:519). According to Chapman and Maloof (1955:267), the thyroid function may be determined by several procedures, namely:

- RAIU test and the retention of RAI by the thyroid.
- The protein-bound iodine of the serum procedure in which the concentration of thyroid hormone is estimated in blood.
- The basal metabolic rate.

The ^{131}I RAIU test is the thyroid function procedure that will mainly be concentrated on to perform the investigation.

2.8 UPTAKE OF RAI IN THE THYROID GLAND

The uptake value obtained by the RAIU test is determined by the function of a thyroid gland. Consequently, the RAI value could be influenced by whether the thyroid gland is in a euthyroid, hypothyroid or hyperthyroid functional state. The 5th *MIRD Dosage Estimate Report* (1975:858) states that the maximum uptake of RAI in a euthyroid patient is approximately two days after administration. The maximum uptake of iodine in a Graves' patient and a euthyroid subject will be different as the RAIU of a Graves' patient is increased. The time of maximum uptake of iodine in the thyroid is also dependent on the physical half-life of the radionuclide of iodine administered. The oral administration of RAI will delay the appearance of RAI in the blood by 10 to 15 minutes compared to an intravenous injection, but has minimal effect on the actual levels of activity in the blood and no relative effect on the final thyroid uptake (*MIRD Dosage Estimate Report* 1975:858). Therefore, whether the RAI is orally or intravenously administered, will not affect the value obtained from the RAIU test. At the UNMD the ^{131}I for the RAIU test is orally administered.

2.9 ^{131}I CHARACTERISTICS FOR UPTAKE, MEASUREMENT AND TREATMENT

^{131}I has characteristics that make it suitable for the uptake and measurement of RAI in the thyroid gland. ^{131}I has the radionuclide nature to be organified

and taken up by the thyroid gland and this characteristic makes it ideal for RAIU test use. The radionuclide ^{131}I is also a beta particle emitter with a physical half-life of 8.1 days, a gamma ray of 364 kilo electronvolt (keV) and a beta particle with a maximum energy of 610 keV (Meier *et al.* 2002:856). ^{131}I has an electron energy of 192 keV and its range in tissue is 0.8 millimeter (mm). ^{131}I in the thyroid gland usually has an effective half-life of 5.4-6.4 days (Early & Sodee 1995:629).

Wagner *et al.* (1995:598) indicate that the 24-hr ^{131}I uptake measurement value is highly recommended for the treatment of Graves' disease and toxic nodular goitre. ^{131}I is used predominantly for thyroid uptake measurement even though it has a high radiation dosage. The administration activity suggested by the IAEA (1961:535) for ^{131}I uptake measurement is to be not more than 0.37 MBq ^{131}I. The radiation exposure for ^{131}I to the thyroid is very high, namely 0.27-0.54 Gy/MBq. At the UNMD the single dosage used to calculate the 6-hr and 24-hr ^{131}I RAIU values is between 0.30 and 0.37 MBq and still falls within the IAEA recommendations.

In order to prevent volatilisation of iodine, sodium iodide is supplied in a basic solution containing a reducing agent to minimise the conversion to iodate (*MIRD Dosage Estimate Report* 1975:857). Sodium iodide is available in liquid and capsule forms for administration. Sterile solutions of sodium iodide are also available for intravenous use, even though iodide is mostly administered orally. Very small quantities of stable iodine might be present in ^{131}I, but it does not affect the biological distribution, therefore the radionuclide and radiochemical purity can be assumed to be 100%.

2.10 CLINICAL RESPONSE TO ^{131}I

Chapman and Maloof (1955:282) state that RAI has a good response as treatment option for Graves' disease, for example the relief of symptoms, an increase in weight, a decrease in the size of the goitre and a fall in the indices of thyroid function. The reason why the UNMD uses ^{131}I to treat Graves' disease patients is because of favourable experience in this regard.

2.11 ^{131}I THERAPY DOSAGE CALCULATION

Consensus has not been reached worldwide about treating Graves' disease patients with a fixed dosage or a calculated ^{131}I dosage (therapeutic administration activity) (Lind 2002:454). There is a variety of procedures and approaches that are followed in the management and treatment of Graves' disease (Hayes *et al.* 1990:520). It is for this reason that the method of therapy dosage calculation in Graves' disease patients for different instituitions may vary.

Various formulas are used to calculate the treatment dosage for Graves' disease patients (Nordyke & Gilbert 1991:414). Formulas that use µCi/g of thyroid tissue to calculate the treatment dosage are not very accurate, since it is so difficult to estimate thyroid weight by palpation. The formula that uses thyroid weight to calculate the treatment dosage is not used at the UNMD. Thyroid weight estimation by palpation is even difficult when done consistently by one person or aided by scinitigraphy. Compared to the thyroid weight estimation treatment formula, the fixed dosage approach is a simpler alternative for deciding on the amount of ^{131}I to be administered.

2.12 CALCULATION OF THE RAIU VALUE

The definition provided by Becker *et al.* (2003:33) for the thyroid uptake test is the measurement of the fraction of an administered amount of RAI that accumulates in the thyroid at selected times following ingestion. The clearance of iodine by the thyroid is corresponding to the RAIU value (Hamburger 1971:287). According to Becker *et al.* (2003:33), the ^{131}I thyroid uptake test has some common indications, namely:

- It aids in calculating the amount of ^{131}I to be administered for the therapy of hyperthyroidism due to Graves' disease or toxic nodular goitre. The ideal is to perform the ^{131}I RAIU test close to the time of treatment.
- It provides information to distinguish subacute or painless thyroiditis and factitious hyperthyroidism from Graves' disease and other forms of hyperthyroidism.
- It also aids the diagnosis of hyperthyroidism and confirming the diagnosis, yet ^{131}I thyroid uptake measurement is of little value in the diagnosis of hypothyroidism.

A correctly designed protocol can eliminate technical errors. This is another reason why the RAIU test is preferred (Hamburger 1971:287). The RAIU value can provide unique information about thyroid function that can play an important role in the management of the patient. The information obtained by the RAIU value must be interpreted with due regard to the clinical picture in order to obtain an optimal diagnosis. The RAIU test can be used to distinguish between a patient with thyroiditis and those with Graves' disease (Hayes *et al.* 1990:519). The RAIU value for thyroiditis is very low, as for Graves' disease the RAIU value can be high to very high. The uptake of RAI in the thyroid is increased in the case of Graves' disease, toxic multinodular goitre or toxic adenoma (Kaplan 1985:878).

The 24-hr RAIU value has become very popular over the past 60 years with regard to thyroid function testing (Hamburger 1971:287). Hayes *et al.* (1990:519) state that the 24-hr RAIU value may only be used for the sake of tradition, as it demands a costly prolongation stay in hospital or the return of outpatient visits to the clinic. Hamburger (1971:287) points out that it is only necessary to obtain a single RAIU value and that any value between 15 and 30 hours after administration will be sufficient. According to Hamburger (1971:287), the need for short-interval RAIU values has also been overstressed. Hayes *et al.* (1990:519) had a theory that the early RAIU value could be used to calculate the ^{131}I therapeutic dosage (administration activity) for Graves' disease. The results obtained by the three- to six-hour RAIU value were supposed to be comparable to those of the 21- to 28-hour RAIU value for the calculation of the ^{131}I therapeutic dosage in the case of Graves' disease patients. McDougall (1991:86) indicates that there is a possibility for same day diagnosis, dosage calculation and treatment of the patient, as there are some reports of a predictable correlation between the early (6-hr) RAIU and the late (24-hr) RAIU values.

2.13 ^{131}I THYROID UPTAKE TECHNIQUE

The ^{131}I RAIU technique described by the IAEA is used worldwide as the basis for thyroid uptake techniques. The UNMD uses the ^{131}I RAIU technique described by the IAEA. The ^{131}I thyroid uptake technique described by the IAEA is outlined in Chapter 1.

2.14 NORMAL VALUES FOR THE ^{131}I RAIU TEST

In Columbia, Missouri, the normal values for the 24-hr RAIU test are considered to be as follows: Low 0-15%, normal 15-45% and high 45-100% (Grayson 1960:397). The normal values for ^{131}I RAIU test vary at different clinics, due to the variation in methods of instrumentation, time intervals and differences in mean iodine intake (Chapman & Maloof 1955:267). The determination of an exact standard statistical expression of normal values is not possible, due to the difference in measuring techniques, the difference of frequency distribution and a range of “normal” uptake in geographic areas. Therefore each nuclear medicine department should thus determine its own normal RAIU values. The normal RAIU values determined for the UNMD are between 15-35%.

2.15 INTERPRETATION CRITERIA

In order to make an interpretation of RAIU values obtained from a patient, reference values for thyroid uptake determinations of euthyroid individuals are needed (Becker *et al.* 2003:35). Each specific medical facility must determine its own RAIU reference values, as it is influenced by geographical changes. If the literature is consulted for the normal range of values for thyroid uptake measurement, it usually ranges between 6-18% for 4-hr RAIU and 10-35% for the 24-hr RAIU. Each facility must obtain its own specific normal thyroid uptake values according to its equipment, standard, uptake phantom and the individuals from its population with their iodine intakes.

In order to make a diagnosis of the patient the interpretation of the results requires some knowledge of the patient’s history, laboratory data, as well as the physical examination (Becker *et al.* 2003:35). As mentioned in paragraph

2.6, iodine containing materials, thyroid hormone or antithyroid drugs also have an influence on the RAIU. It is therefore of particular importance to check the patient's medical history. The information about the ingestion of the last iodine-containing medication is also of significance in the evaluation of the thyroid uptake results (Becker *et al.* 2003:35-36).

2.16 GRAVES' DISEASE TREATMENT OPTIONS

Different treatment options for Graves' disease are used in different parts of the world (Lind 2002:453). Even though over the years knowledge of the actiology and pathogenesis of Graves' disease has increased, there is still no straightforward therapeutic option (Peters, Fischer, Bogner, Reiners & Schleusener 1995:186). The overall goal of the different treatment options is the same, namely to eliminate the hyperthyroid state present in Graves' disease (Lind 2002:453). The therapeutic treatment choice by the physician for treating Graves' disease depends on cost, convenience, dietary and medical exposure to iodine; data concerning disadvantages and advantages of each treatment option; availability of surgical expertise; and personal bias (Solomon, Glinoer, Lagasse & Wartofsky 1990:1518). There are various factors that contribute to the choice of treatment, for example the geographical location, the size of the goitre, the age of the patient, the personal experience of the treating physician, and the degree of Graves' disease (Lind 2002:453). There are also other factors that play a role in the treatment of Graves' disease, for example patient economic aspects; cost associated with long-term antithyroid drugs; the need for ablative therapy; the possibility of recurrence; and the use of RAI treatment as first-line therapy (Lind 2002:453). There are mainly three treatment options for patients with Graves' disease, namely antithyroid drugs, thyroidectomy and RAI treatment (Hennemann, Krenning & Sankaranarayanan 1986:1369).

2.16.1 Antithyroid drugs

Antithyroid drugs are an alternative treatment option if radioiodine treatment is not favoured (Hennemann *et al.* 1986:1371). Antithyroid drugs may not be so effective in treating patients with Graves' disease and toxic multinodular goitre (Hennemann *et al.* 1986:1370). There is a relapse as high as 50% in patients with Graves' disease if they discontinue their antithyroid drug treatment (Peters *et al.* 1995:186). However, there is also an incidence of 5% of antithyroid drugs in causing allergic and toxic reactions in adult patients (Hennemann *et al.* 1986:1369). This low level of effectiveness of antithyroid drugs is a major disadvantage. Antithyroid drugs interfere with the organification process of iodine in the thyroid gland and this is the reason why the patient should stop all antithyroid medication before going for a ^{131}I RAIU test (McDougall 1991:87). The main role of beta blockers is to serve as an adjuvant while the patient is receiving antithyroid drugs or ^{131}I to relieve the symptoms of hyperthyroidism (McDougall 1991:89).

2.16.2 Thyroidectomy

There is a high incidence of operative complications related to thyroidectomy, therefore it would not be a good substitute of RAI (Hennemann *et al.* 1986:1371). Holm, Lundell, Israelsson and Dahlqvist (1982:106) also point out that the incidence of hypothyroidism after ^{131}I treatment is higher than after surgery. Graves' disease patients who underwent a thyroidectomy have a relapse rate of 1-12% (Hennemann *et al.* 1986:1370). The main disadvantages of thyroidectomy are the incidence of hypothyroidism afterwards and the risks associated with the operation (Hennemann *et al.* 1986:1370). There is an chance of 35-49% for developing hypothyroidism after thyroidectomy (Hennemann *et al.* 1986:1370). Thyroidectomy has the risk of damaging the recurrent laryngeal nerve and other surgical complications (Peters *et al.* 1995:186). Thyroidectomy is considered as a

treatment option at the UNMD in Graves' disease patients with very large goitres.

2.16.3 RAI treatment

^{131}I therapy in the case of Graves' disease has a very good safety record (Holm *et al.* 1982:106). In comparison with other therapeutic alternatives ^{131}I therapy is safe and there is also no increased risk of developing thyroid cancer (Holm *et al.* 1982:100). The disadvantages of RAI treatment with ^{131}I can be the potential hazard of developing hypothyroidism and genetic abnormalities (Hennemann *et al.* 1986:1370). The study results that are available show that the administration of RAI had no significant impact on the incidence of leukaemia. There is evidence that benign and malignant thyroid tumours can be caused by radiation. The radiation dosages received by the thyroid in the above-mentioned cases are much lower [from 9 (rad) to several 100 rad: 100 rad = 1 (Gy)] compared to those used therapeutically (5 000 to 25 000 rad). High ^{131}I dosages have the characteristic to terminate the cell's potential to divide and because of this characteristic eliminate the cell's potential for causing malignancy. Low radiation dosages on the other hand may stimulate both malignant and benign growth.

^{131}I as a treatment option has various advantages but also disadvantages, namely:

(i) Delay in controlling the hyperthyroidism, especially in cases of inadequate treatment dosage, as well as in some patients who are extraordinarily resistant to sodium iodide (^{131}I).

(ii) The incidence of hypothyroidism after ^{131}I treatment as the years goes on, but this is also a disadvantage of surgery (Safa & Skillern 1975:673).

Another disadvantage of ^{131}I treatment is that radiation thyroiditis can occur, although rare with release of stored thyroid hormone into the circulation after

^{131}I therapy (Meier *et al.* 2002:857). The release of stored thyroid hormone into the circulation can worsen the hyperthyroid state of Graves' disease causing thyroid storm.

^{131}I treatment for Graves' disease has several advantages, including that patients can be treated on an outpatient basis; recurrence rate is small; and the costs are low for patients as well as for the community (Holm *et al.* 1982:106). ^{131}I as treatment option for Graves' disease is used to treat most Graves' disease patients at the UNMD. ^{131}I treatment therapy has resulted in decreased mortality and morbidity of patients with Graves' disease (Safa & Skillern 1975:673). The research available indicates no harmful effects associated with ^{131}I therapy in children and adolescents, as well as on subsequent fertility, birth history of patients, health status and reproductive history (Holm *et al.* 1982:106).

Nordyke and Gilbert (1991:414) constructed a dosage-cure curve as a guide to individualised treatment. This dosage-cure curve demonstrated that a 185 MBq ^{131}I therapeutic dosage will have a cure rate of 70% and 370 MBq will have an 87% cure. From this dosage-cure curve the conclusion can be drawn that the higher 370 MBq therapeutic dosage has a higher cure and the better choice for a fixed dosage treatment. The aim of the treatment dosage is always to provide a cure for Graves' disease. This cure will be provided by the most accurately calculated treatment dosage. There are various factors that should be considered if the initial treatment dosage fails, for example the patient's direct cost in rands, time from work, and the patient morbidity are increased.

The maximum RAIU value is important for the calculation of the correct ^{131}I therapeutic dosage to treat Graves' disease. In the case of euthyroid patients, the maximum RAI uptake in the thyroid is between 24 and 48 hours

(Van Isselt *et al.* 2000:610). With Graves' disease the maximum RAI uptake in the thyroid may reach a peak earlier than 24 hours. Therefore it is suggested that an RAIU is taken before 24 hours, at a relatively early stage (4-6 hours), as well as at 24 hours. There is "rapid iodine turnover" in the case where the 5-hr/24-hr uptake ratio is >1. Van Isselt *et al.* (2000:610) defined the "rapid turnover" process of iodine as a short effective half-life (T_{eff}) of ^{131}I and a diminished therapeutic effect. In the cases where "rapid turnover" is present it is necessary to increase the ^{131}I therapeutic dosage as the 24-hr would give a low uptake value. As the 24-hr RAIU value is low and does not indicate the peak of the turnover it would lead to an undertreatment of this patient. The 6-hr RAIU value would therefore indicate the peak and maximum point of iodine turnover and could be used to adjust the treatment dosage. When using the 24-hr RAIU value to calculate the ^{131}I therapeutic dosage for a "rapid turnover" the Graves' disease patient may be undertreated if there is risk of recurrence of disease.

The investigation conducted by Van Isselt *et al.* (2000:614) showed that 9% of the Graves' disease patients used in their study had "rapid turnover". These patients could have received inappropriate ^{131}I therapy dosage if only the 24-hr RAIU value was used to calculate therapeutic dosage (administration activity). At the UNMD the 24-hr RAIU value was used for calculation dosage for Graves' disease. Yet in our study the percentage of the Graves' disease patients with "rapid turnover" was determined as well as the results of ^{131}I therapeutic treatment. This information gave an indication which of the 6-hr or the 24-hr RAIU value is best to calculate the ^{131}I therapeutic dosage.

Van Isselt *et al.* (2000:615) recommend that the ^{131}I therapeutic treatment should be given as soon as possible after the ^{131}I RAIU test is finished, because of the intra-individual changes in both the ^{131}I uptake and iodine

turnover in the thyroid gland. The ^{131}I therapeutic dosage for Graves' disease is administered the same day as the 24-hr ^{131}I RAIU test is done at the UNMD (not necessarily done for patient convenience and cost-effectiveness).

It is always important to consider the radiation burden to the patient, therefore the calculation of the ^{131}I treatment dosage should be done with great precision (Van Isselt *et al.* 2000:614). Therefore it is essential that the ^{131}I RAIU procedure be optimised for the calculation for a Graves' disease patient therapy dosage. According to Safa and Skillern (1975:675), ^{131}I therapy is currently considered as the best form of treatment for Graves' disease. The UNMD also considers ^{131}I therapy as the best treatment option for Graves' disease.

2.17 GUIDELINES FOR TREATMENT

RAI is the ideal treatment option in patients with relapsed Graves' disease (Hennemann *et al.* 1986:1371). In very large goitres the first optimal choice is subtotal thyroidectomy, as RAI is of limited value. Very large goitres are also treated with thyroidectomy at the UNMD. Holm *et al.* (1982:106) recommend that the optimal treatment choice for patients with large goitres and progressing eye symptoms is thyroidectomy. Surgery is also recommended in those few cases in which malignancy is suspected.

2.18 ^{131}I TREATMENT DOSAGE

Chapman and Maloof (1955:278) state that there are three main factors that influence the effects of RAI on the thyroid and thus the dosage received by the thyroid:

- The absorbed dosage received by the thyroid gland physically.
- The dispersion of RAI within the thyroid.
- The thyroid cell sensitivity to RAI.

The authors also point out that there is a variation in the dispersion of radioactivity in the thyroid (Chapman & Maloof 1955:281). This factor can explain the varied responses of patients to a similar dosage of the radionuclide.

2.19 ADEQUATE ABSORBED ACTIVITY FOR THE INTRATHYROID TISSUE

The calculation of the precise and accurate therapeutic dosage for Graves' disease is consequential, since the damage of thyroid follicular cells by RAI to a large extent depends on the absorbed dosage from ^{131}I administered (De Bruin *et al.* 1994:508). According to Alexander and Larsen (2002:1073), an absorbed activity of 296 MBq ^{131}I in the thyroid gland is an efficient treatment option for most patients with Graves' disease. The UNMD uses the RAIU test for the calculation of the ^{131}I therapeutic dosage for Graves' disease patients so that the intrathyroid absorbed activity received is 296 MBq ^{131}I. The scope of ^{131}I absorbed activity per g of thyroid tissue for the effective treatment of Graves' disease as given by the EANM (2003:30) is from 2.2-3.0 MBq/g up to 6.0-7.0 MBq/g. The conclusion that can be drawn is that a thyroid weighing 50g should receive a ^{131}I therapeutic dosage of between 110 MBq and 350 MBq for the effective treatment of Graves' disease. A Graves' disease patient who receives an intrathyroid absorbed activity of more than 350 MBq has received unnecessary ^{131}I therapeutic activity to the thyroid gland. The UNMD considers a Graves' disease patient who received an intrathyroid absorbed activity of more than 350 MBq to have received a less accurate therapeutic

dosage. In short, when calculating the different therapeutic dosages with the 6-hr or the 24-hr ^{131}I RAIU values the intrathyroid absorbed activity should not be more than 350 MBq of ^{131}I, otherwise the patient will receive unnecessary ^{131}I activity to the thyroid gland.

In a normal person who received ^{131}I orally for RAIU, the measured uptake increases progressively and then reaches a plateau between 18- and 24-hr after intake (Harbert & Da Rocha 1984:9). Van Isselt *et al.* (2000:609) point out that the 24-hr ^{131}I RAIU value is traditionally used for the calculation of the ^{131}I administration activity for therapeutic dosage. The 24-hr ^{131}I RAIU value is indicated by Van Isselt *et al.* (2000:609) to be the most efficient for the calculation of the ^{131}I administration activity for patients with Graves' disease. Wagner *et al.* (1995:598) also suggest that the value of the 24-hr ^{131}I RAIU is highly recommended for the calculation of the therapeutic dosage for Graves' disease.

The 24-hr ^{131}I RAIU value is considered the favourite choice for therapeutic dosage calculations, because "rapid turnover" of ^{131}I in the first two hours and a lower 24-hr RAIU is rare (Harbert & Da Rocha 1984:12). Graves' disease (hyperthyroidism) can show different characteristic curves and turnover points of thyroid uptake after ^{131}I oral administration (see Figure 1.1). The 24-hr RAIU value is usually higher than the 6-hr RAIU value, therefore the 24-hr RAIU value is regarded as the better choice, as the optimal thyroid uptake percentage needs to be determined for the effective administered therapeutic activity calculation. It would be interesting to see when the 24-hr ^{131}I RAIU value is used with the administration activity calculated by the 6-hr ^{131}I RAIU if the intrathyroid absorbed dosage received will still be 296 MBq. The following equation will be adjusted for this purpose in the data analysis (CAA = calculated administration activity; IAA = intrathyroid absorbed activity):

$$\text{CAA from } {}^{131}\text{I RAIU value} = \frac{\text{Aimed IAA}}{\%\text{ (value) of the 6- or 24-hr } {}^{131}\text{I RAIU}}$$

2.20 HYPOTHYROIDISM RELATED TO ^{131}I TREATMENT

According to Nordyke and Gilbert (1991:411), during the early years of the development of ^{131}I therapy there was a failure to recognise that most Graves' disease patients will eventually become hypothyroid regardless of the therapeutic dosage selected. Hypothyroidism has a cumulative incidence of as high as 70% after RAI treatment (Glennon, Gordon & Sawin 1972:721). Glennon *et al*. (1972:722) report that there is a variation in the incidence of hypothyroidism after ^{131}I treatment for hyperthyroidism. Treating hyperthyroid patients with low dosages of ^{131}I causes a decrease in first-year incidence of hypothyroidism, but overall the cumulative incidence may not be decreased (Glennon *et al.* 1972:723).

Gunasekera, Hesslewood, Notghi and Harding (2000:21) also state that the occurrence of hypothyroidism after ^{131}I treatment is believed to be proportional to the dosage. The conclusion was also made by Gunasekera *et al.* (2000:21) that hypothyroidism is initially lower in patients receiving activity less than 200 MBq, but this resulted in four-fold repeat therapy dosages compared to 400 MBq. The dosage of ^{131}I delivered to the thyroid gland when treating Graves' disease patients correlates with the incidence of hypothyroidism after treatment (Holm *et al.* 1982:106). The elimination of Graves' disease will only be prolonged with low-dosage ^{131}I therapy without any ultimate reduction in the incidence of hypothyroidism. Compared to the low-dosage ^{131}I therapy the higher ^{131}I treatment dosages result in higher cure rates and a decreased need for retreatment. Higher ^{131}I treatment

dosages are reported to increase the incidence of hypothyroidism after treatment for Graves' disease.

Currently the risk of developing thyrotoxic crisis after ^{131}I therapy is almost insignificant (Holm *et al*. 1982:106). Nowadays these patients can easily be identified and pretreated with antithyroid drugs and/or beta blockers. Corticosteroids in collaboration with antithyroid drugs and beta blockers can be used in cases where potential for thyrotoxic crisis was not detected before ^{131}I treatment.

Some researchers have suggested that Graves' disease patients are optimally treated by a single ^{131}I ablative dosage to the thyroid, arguing that the aim is eliminating hyperthyroidism; that larger therapy dosages accomplish it with more certainty; and that hypothyroidism will inevitably develop (Nordyke & Gilbert 1991:411). At the UNMD a large single ^{131}I ablative dosage is given to a Graves' disease patient with the aim to completely eliminate this hyperthyroid state.

Hypothyroidism after ^{131}I treatment in Graves' disease seems to continue to develop at a steady rate, even after 10 years (Hennemann *et al.* 1986:1370). These researchers also suggest that, when this inevitable hypothyroid state has developed, it is managed under the control of the physician (Nordyke & Gilbert 1991:411). Therefore if all Graves' disease patients eventually became hypothyroid after ^{131}I therapy, the goal of achieving a permanent state of normal thyroid function is unrealistic.

2.21 SUMMARY AND CONCLUSION

The ^{131}I RAIU test can be used to distinguish Graves' disease from other thyroid diseases (McDougall 1991:79). ^{131}I is predominantly used for the RAIU measurement and ^{131}I is also organified in the thyroid that makes it ideal for thyroid functional testing (Wagner *et al*. 1995:598). Hence, the ^{131}I RAIU test provides diagnostic information about the thyroid function (Grayson 1960:397). ^{131}I is not only used for the RAIU tests, but also for the treatment of Graves' disease. Consequently ^{131}I is a radionuclide that can be used for RAIU testing, as well as for the treatment of Graves' disease and it is used for these purposes at the UNMD.

There are various treatment options for Graves' disease, including antithyroid drugs, thyroidectomy and RAI (Lind 2002:453). According to Safa and Skillern (1975:675), ^{131}I therapy may not be the perfect form of treatment for Graves' disease, but it is still a much better option compared to surgical or antithyroid drug therapy. At the UNMD RAI is the primary treatment option for Graves' disease and the RAIU test is used for the calculation of the treatment dosage. The RAIU test procedure used at the UNMD is the RAIU test procedure prescribed by the IAEA (see paragraph 1.1.4).

The method of therapy dosage calculation for Graves' disease patients at different institutions may vary (Hayes *et al*. 1990:520). At the UNMD the ^{131}I RAIU test is used to determine the percentage uptake of iodine by the thyroid gland and then a treatment dosage is calculated for above normal uptake percentages. The result is that ^{131}I measurement aids in calculating the amount of ^{131}I to be administered for the therapy of hyperthyroidism due to Graves' disease.

At the UNMD a 6- as well as a 24-hr RAIU value is obtained to calculate the therapeutic dosage (administration activity) for Graves' disease. Hayes *et al*. (1990:519) have a theory that the early (6-hr) RAIU value alone can be used to calculate the ^{131}I therapeutic dosage for Graves' disease. The 3- to 6-hour RAIU value is supposed to be comparable with the 24-hr RAIU value for the ^{131}I therapeutic dosage calculation. McDougall (1991:86) indicates that there is a possibility for same day diagnosis, dosage calculation and treatment of a Graves' disease patient, as there are some reports of a correlation between the 6-hr and the 24-hr RAIU value. If this correlation is applicable at the UNMD and a 6-hr RAIU value only is needed to calculate the ^{131}I therapeutic dosage for Graves' disease patients, a same day diagnosis will also be possible. The same day diagnosis will lead to a decrease in hospital stay and patient expenses, as the patient will not have to return the following day to obtain a 24-hr value for the RAIU test.

The maximum RAIU value is important for the calculation of the correct ^{131}I therapeutic dosage to treat Graves' disease. When "rapid turnover" in the thyroid is present, the 6-hr RAIU value will be higher than the 24-hr RAIU value and will present the time of maximum thyroid uptake percentage (Van Isselt *et al*. 2000:610). The difference between the 6- and 24-hr values should be determined in all patients.

The next chapter, Chapter 3, entitled "Investigation design and methods" will explain the empirical approach and provide a description of the methodology that was used to achieve the aim of the investigation.

CHAPTER 3

INVESTIGATION DESIGN AND METHODS

3.1 INTRODUCTION

Chapter 3 provides information on the investigation design* and methods to seek answers to the questions stated in paragraph 1.2.1. This specific design enables the investigator to obtain sufficient information and answers. The investigation design and methods applied will be discussed next.

3.2 INVESTIGATION DESIGN

The correlation of the 6-hr and 24-hr ^{131}I RAIU values of patients with Graves' disease referred to the UNMD in the Free State was investigated. The study design was two-fold (see Figure 1.2): First a literature review was carried out to determine the significance of both the 6-hr and 24-hr ^{131}I RAIU values in patients with Graves' disease. Second, a retrospective investigation was conducted to analyse and compare the 6-hr and 24-hr RAIU values of patients diagnosed with Graves' disease referred to the UNMD during 2004 and 2005.

- The investigation design implies the plan for collecting and utilising data so that the required information can be obtained with adequate accuracy to test a theory.

3.3 INVESTIGATION GROUP

The investigation group included patients with confirmed Graves' disease referred to the UNMD during 2004 and 2005. The patients included in the investigation group, both male and female, were from different race groups ranging from 15-75 years in age.

3.4 PROCEDURE

The paragraphs that follow focus on the procedure of the investigation and provide a description of the methods used. Aspects of the investigation design which include the retrospective data retrieval, the inclusion and exclusion of patient data, as well as the experimental methods used, will receive attention.

3.4.1 Retrieval of patient data

All the files of patients who had undergone ^{131}I RAIU thyroid tests to diagnose Graves' disease during 2004 and 2005 at the UNMD were obtained. At the Universitas Hospital Graves' disease is confirmed by a suppressed TSH, elevated T_4 or T_3, a diffuse increased uptake of ^{99m}Tc-pertechnetate, and an increased 6-hr and 24-hr ^{131}I RAIU value. Patients who did not meet the above criteria of diagnosis of Graves' disease were excluded from the investigation group.

3.4.2 Inclusion criteria

The investigation focused on Graves' disease specifically, not on other thyroid diseases. The inclusion criteria included patients with only Graves' disease who had undergone both a 6-hr and 24-hr ^{131}I RAIU.

3.4.3 Exclusion criteria

In order to increase the validity of the investigation, all factors that can influence the accuracy of the ^{131}I RAIU thyroid test were excluded. The exclusion criteria for the patients from the investigation were the following:

- Patients who received antithyroid medication or any other medication that could influence the RAIU values obtained.
- Patients who received an iodine-containing X-ray examination during the period of the 6- and 24-hr ^{131}I RAIU examination.
- The presence of nodules on the ^{99m}Tc-pertechnetate scintigraphy of patients who had received 6- and 24-hr ^{131}I RAIU examination during 2004 until the end of 2005.

As part of the exclusion phase of the study, it was important to determine which medication the patients used at the time of their 6- and 24-hr ^{131}I RAIU examination and whether this had an influence on the uptake values obtained. Appendix C:5 shows in table form relevant materials and medication that should be excluded for a delayed period before an RAIU examination. All the medications used by patients visiting Universitas hospital is listed on a computer file system. The Graves' disease patient list of medications used from 2 weeks before and during the time period of the RAIU test was noted on data sheets. The information used on the data sheets was used to exclude patient for investigation group.

The medication and antithyroid drugs listed in Appendix C:5 had an influence on the 6- and 24-hr ^{131}I RAIU value. A short summary of the characteristics of these antithyroid drugs and medication was made (see Appendix C:6). The medication used by some of the patients that influenced the accuracy of the ^{131}I RAIU test from the above table, included atenolol (n=1), carbimazole (n=1), propranolol (n=13) and thyroxine (n=2).

Patients who had received an iodine-containing X-ray examination two weeks prior to the 6- and 24-hr ^{131}I RAIU test were also excluded. There was only one patient who had undergone Magnetic Resonance Imaging (MRI) of the orbits with iodine contrast administration. This patient was excluded because of this examination.

Another exclusion factor was the presence of nodules on the ^{99m}Tc-pertechnetate scintigraphy. When the pertechnetate scintigraphy results were evaluated, it was found that out of the 178 patients, 33 were multi-nodular; one had Plummer's disease; one had Marine-Lenhardt syndrome; two had had lobes removed; and one had toxic autonomic adenoma. All these patients had to be excluded, as only Graves' disease patients were included and other thyroid diseases would have had an influence on the accuracy of the ^{131}I RAIU values for this specific investigation.

The original investigation group consisted of 178 patients and 54 patients were excluded. Two of the 54 patients displayed to two of the exclusion criteria.

3.5 ANALYSIS

The Department of Biostatistics of the UFS, were consulted for recommendations regarding the management of data and the processing of results. Results were summarised by means and standard deviations or medians and percentiles for continuous data and frequencies and percentages for categorical data. The 95% confidence intervals were constructed for the difference in mean and median values. The Spearman correlation coefficient was used to determine the correlation between different variables. A regression analysis was performed between the 6-hr and 24-hr

^{131}I RAIU values. An analysis was also made of the different transit patterns of Graves' disease patients at the UNMD. This analysis of the transit patterns was done to determine how many of these patients had rapid turnover of iodine in their thyroid glands.

Graves' disease is treated effectively with an absorbed intrathyroid dosage of 296 MBq (Alexander & Larsen 2002:1073). As previously mentioned, the following equation was used to determine the ^{131}I administration therapeutic activity that was given according to the 6-hr or 24-hr RAIU% (Alexander & Larsen 2002:1074):

$$\text{CAA from } ^{131}\text{I RAIU value} = \frac{\text{Aimed IAA}}{\text{\% (value) of the 6- or 24-hr } ^{131}\text{I RAIU}}$$

^{131}I thyroid treatment activity that is not absorbed in the thyroid gland should be limited, because ^{131}I is fairly expensive and should not be wasted (cost-effectiveness). Keeping cost-effectiveness in mind, it was of value to see what the difference between the administered ^{131}I activity using the 6-hr or 24-hr ^{131}I RAIU would be. It was also of value to see when the 24-hr ^{131}I RAIU value was used with the CAA by the 6-hr RAIU value if the IAA was still between the recommended range of 110 MBq to 350 MBq. Graves' disease patients showed increased 6-hr and 24-hr ^{131}I RAIU values, as well as an increased T_4 value. A comparison was also made between the 6-hr and 24-hr ^{131}I RAIU values to see if there was any correlation with the T_4 values of Graves' disease patients.

3.6 ETHICAL ASPECTS

Informed consent was obtained from the Ethics Committee of the UFS (ETOVS Nr. 40/06) and the Central University of Technology (CUT) after evaluation of the investigation protocol. Since the investigation was done retrospectively, consent was obtained from the chief specialist and the director of the Universitas Hospital. There was no need to obtain consent from the RCC, as the ^{131}I uptake measurements done at the UNMD falls within the RCC rules and regulations.

3.7 CONCLUDING REMARKS

This chapter focused on the investigation design, methods, as well as the process followed. The different aspects of the design were addressed and the method of collecting data received attention. In the next chapter, the statistical results and findings of the investigation will be presented.

CHAPTER 4

RESULTS AND FINDINGS

4.1 INTRODUCTION

In this chapter the results of the investigation group with regard to the following areas will be reported on: The transit patterns; how the 6-hr and 24-hr ^{131}I RAIU values correlate with each other and the T_4 values and the correlation between the 6-hr and 24-hr RAIU CAA (therapy dosage) and their correlation with T_4. The results of the IAA that will be received by the thyroid when the 24-hr RAIU value is used with CAA by 6-hr RAIU value and if the IAA falls between the recommended range of 110 MBq to 350 MBq are provided. The TSH values of the investigation group was analysed to see if any significant statistical information was obtained.

4.2 RESULTS

The original group investigated consisted of 178 Graves' disease patients before patients were excluded due to the specific criteria mentioned. After the exclusion criteria had been applied, the final group investigated consisted of 124 Graves' disease patients. The age of the investigation group ranged between 15 and 75 years (see Table 4.1).

Table 4.1: Summary of age

n	Lower Quartile (Q)	Median	Upper Quartile (Q)	Minimum (Min) years	Maximum (Max) years
124	30	39	48	15	75

The group mainly consisted of females, whereas the males were only 14.5% of the total investigation group. The race of the investigation group consisted of black, white and coloured (see Table 4.2).

Table 4.2: Gender and race of investigation group

	n	% of total group
Gender		
Male	18	14.5
Female	106	85.5
Race		
Black	87	70.2
White	28	22.6
Coloured	9	7.3

In the next section the results of the 6-hr and 24-hr ^{131}I RAIU values of the investigation group are provided. Comparison and analysis of the 6-hr and 24-hr ^{131}I RAIU values will also be scrutinised.

4.3 THYROID UPTAKE VALUES

This section reports on the 6- and 24-hr ^{131}I RAIU values and the related statistics of the investigation group. Figure 4.1 demonstrates the values for

the 6- and 24-hr RAIU of the investigation group (n=124). In Figure 4.1 it can be seen that the 24-hr RAIU values tended to fall more in the higher percentage range. On the other hand, the 6-hr RAIU values tended to fall in between the lower and higher % values.

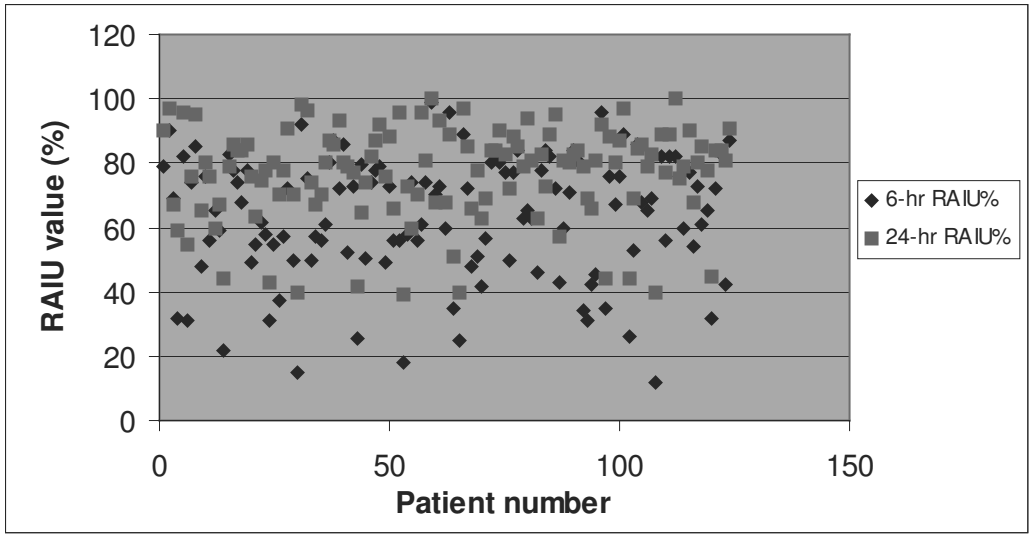


Figure 4.1: Comparison between 6-hr and 24-hr RAIU values

The analysis of the 6- and 24-hr RAIU values indicated that the median of the 6-hr RAIU values was 67.5% and the median of the 24-hr RAIU values was 80% (see Table 4.3).

Table 4.3: Summary of the 6-hr and 24-hr RAIU values

	n	Lower Q	Median	Upper Q	Min (%)	Max (%)
6-hr RAIU	124	51.5	67.5	78	11.9	99
24-hr RAIU	124	69	80	87	39	100

Regression analysis was done to see if there was any relation between the 6-hr RAIU and the 24-hr RAIU values (see Figure 4.2). Figure 4.2 shows a strong positive linear relationship between the 6-hr RAIU and the 24-hr RAIU values (Pearson correlation coefficient obtained r=0.82).

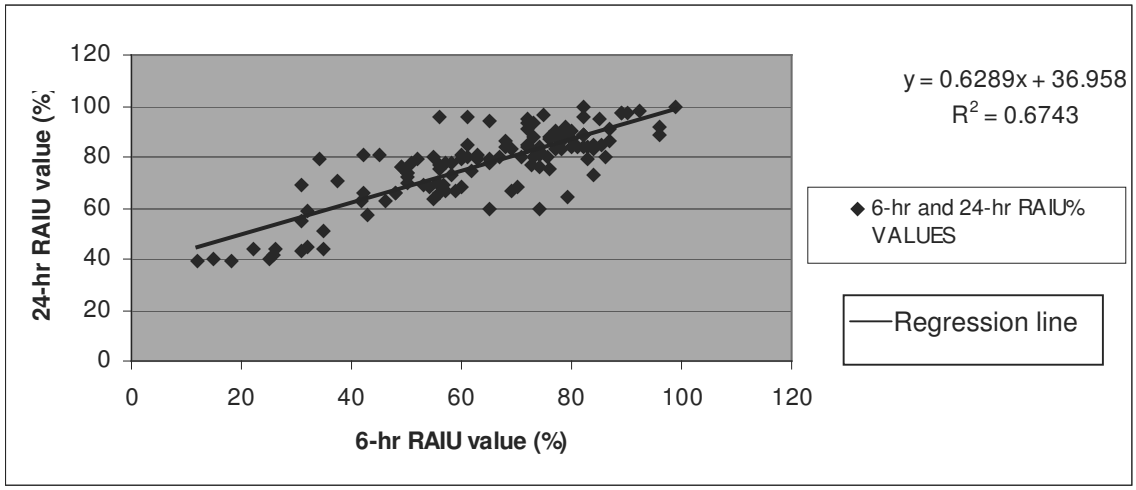


Figure 4.2: Pearson correlation analysis between the 6-hr and the 24-hr RAIU values

Table 4.4 summarises the difference between the 6-hr and 24-hr RAIU values. The limits of agreement (the range within which the central 95% of data is expected to lie) is –38 to 7.

Table 4.4: Difference between the 6-hr and the 24-hr RAIU values

n	Lower Q	Median	Upper Q	Min (%)	Max (%)
124	-20.35	-13	-7	-45	14.9

Table 4.5 demonstrates the difference between the 6-hr and 24-hr RAIU values. A -5% or smaller difference between the 6-hr and 24-hr RAIU values was only present in 11 of the 124 Graves' disease patients.

Table 4.5: Summary of the difference between the 6-hr and the 24-hr RAIU values (n=124)

Dif. between 6-hr and 24-hr RAIU values	Frequency	Percent	Cumulative Frequency	Cumulative Percent
-45.9 to -40	2	1.6	2	1.6
-39.9 to -35	4	3.2	6	4.8
-34.9 to -30	1	0.8	7	5.7
-29.9 to -25	9	7.3	16	13.0
-24.9 to -20	18	14.5	34	27.4
-19.9 to -15	19	15.3	53	42.7
-14.9 to -10	26	20.9	79	63.7
-9.9 to -5.1	20	16.1	99	79.8
-5 to 0	11	8.9	110	88.7
0 to 5	9	7.3	119	96.0
5.1 to 10	2	1.6	121	97.6
10.1 to 15	3	2.4	124	100.0

4.4 TRANSIT PATTERNS

The transit patterns give an indication whether the 6-hr RAIU value will only be effective to determine the ^{131}I therapy dosage for Graves' disease. The transit patterns of the investigation group for the 6- and 24-hr RAIU values are given in Table 4.6. In 11.3% (n=14) of the investigation group the 6-hr RAIU value was higher than the 24-hr RAIU value. The 24-hr RAIU value was higher in 88.7% (n=110) of the investigation group higher than the 6-hr RAIU. The transit patterns show that in a very few Graves' disease patients, the 6-hr RAIU values will be higher than the 24-hr RAIU values.

Table 4.6: Transit patterns 6-hr and 24-hr RAIU values

Group	Frequency (*f*)	Percent (%)
6>24	14	11.3
6<24	110	88.7

4.5 CORRELATION ANALYSIS BETWEEN 6-HR RAIU AND T_4 VALUES

Regression analysis was done to see if there was any relation between the 6-hr RAIU and the T_4 values (see Figure 4.3). Figure 4.3 shows a moderate positive linear relationship between the 6-hr RAIU and the T_4 values (Pearson correlation coefficient obtained r=0.53; Spearman correlation coefficient r=0.57).

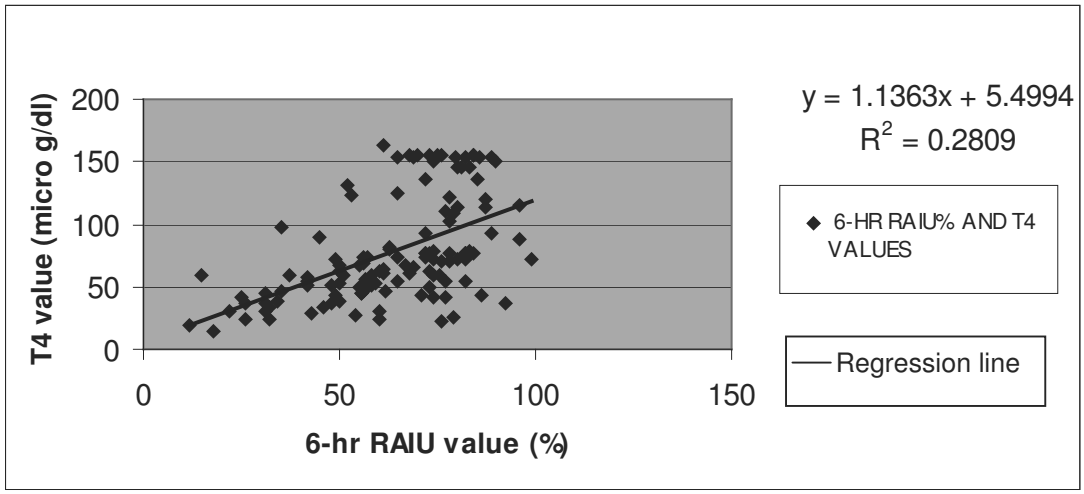


Figure 4.3: Pearson correlation analysis between 6-hr RAIU and T_4 values

The median for the 6-hr RAIU values was 67.5% and the median for the T_4 values was 67.3%. Table 4.7 shows that the median % values for the 6-hr RAIU and T_4 lie very close together.

Table 4.7: Summary of 6-hr RAIU values with T_4 values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
6-hr RAIU (%)	51.5	67.5	78	11.9	99
T_4 (µg/dl)	46.5	67.3	105.8	15	163.1

4.6 CORRELATION ANALYSIS BETWEEN THE 24-HR RAIU AND T_4 VALUES

Regression analysis was done to see if there was any relation between the 24-hr RAIU and the T_4 values (see Figure 4.4). Figure 4.4 shows a weak positive linear relationship between the 24-hr RAIU and the T_4 values (Pearson correlation coefficient obtained r=0.39; Spearman correlation coefficient r=0.46).

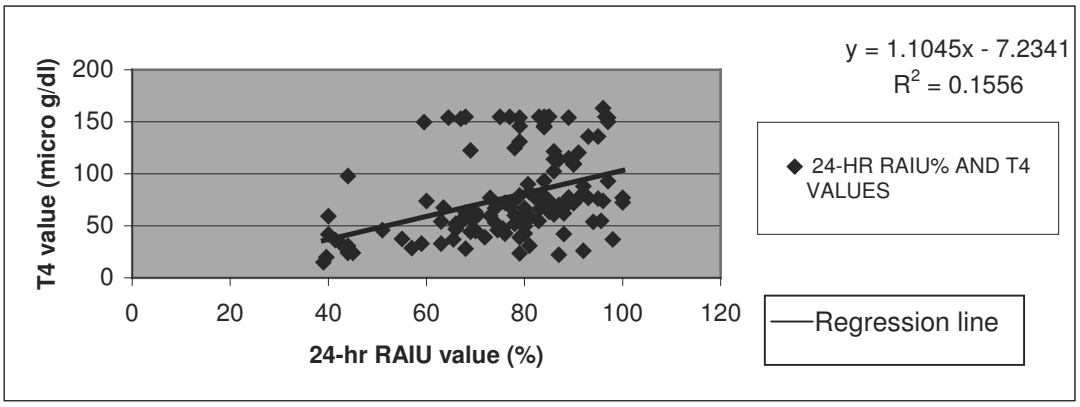


Figure 4.4: Pearson correlation analysis between 24-hr RAIU and T_4 values

The median for the 24-hr RAIU values was 80% and the median for the T_4 values of the same patients was 67.3%. Table 4.8 shows that the median % values for the 24-hr RAIU values and T_4 lie very far apart, with the median of the 24-hr RAIU values much higher.

Table 4.8: Summary of 24-hr RAIU values with T_4 values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
24-hr RAIU (%)	69	80	87	39	100
T_4 (µg/dl)	46.5	67.3	105.8	15	163.1

4.7 CORRELATING THE VALUES OF THE 6-HR AND THE 24-HR CAA VALUES

Figure 4.5 shows the different values for the 6-hr and 24-hr RAIU CAA for the investigation group (n=124). When a closer look is taken at Figure 4.5, it shows that the 6-hr RAIU CAA values are much higher than those of the 24-hr RAIU CAA values. The 24-hr RAIU CAA values lie closer together, whereas the 6-hr RAIU CAA values lie further apart. The 6-hr RAIU CAA has the highest value and the 24-hr RAIU CAA has the lowest value. Overall the 6-hr RAIU CAA has the highest values and the 24-hr RAIU CAA has the lowest values.

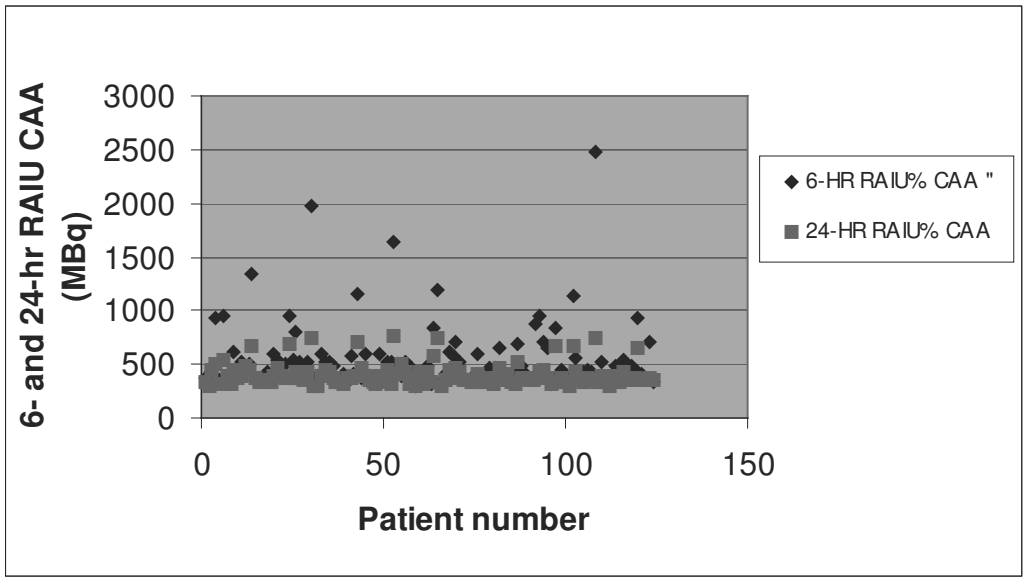


Figure 4.5: Comparison between 6- and 24-hr RAIU CAA.

Table 4.9 gives a summary of the 6-hr RAIU CAA and the 24-hr CAA values for the investigation group (n=124). Table 4.9 confirms what was seen in Figure 4.5 about the minimum and the maximum values of the 6-hr and 24-hr RAIU CAA values. The median of the 6-hr RAIU CAA values was 438.5 MBq and the median of the 24-hr RAIU CAA was 370 MBq. Table 4.9 shows that the 6-hr CAA values had a higher median than the 24-hr CAA values.

Table 4.9: Summary of 6-hr RAIU CAA values with the 24-hr RAIU CAA values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
6-hr (MBq)	380	438.5	564	299	2487
24-hr (MBq)	344	370	429	296	759

4.8 DIFFERENCE BETWEEN 6-HR AND THE 24-HR RAIU CAA

The results are given below of the difference between the 6-hr and 24-hr CAA values. Table 4.10 summarises this specific data analysis as stated in this section.

Table 4.10: Difference between the 6-hr and the 24-hr RIAU CAA values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
Dif. 6-hr and 24-hr CAA (MBq)	28	76	168.5	-98	1739

4.9 INTRATHYROID ABSORBED ACTIVITY

Figure 4.6 shows the values for the patient IAA calculated when the 24-hr RAIU values were used with the CAA by the 6-hr RAIU values.

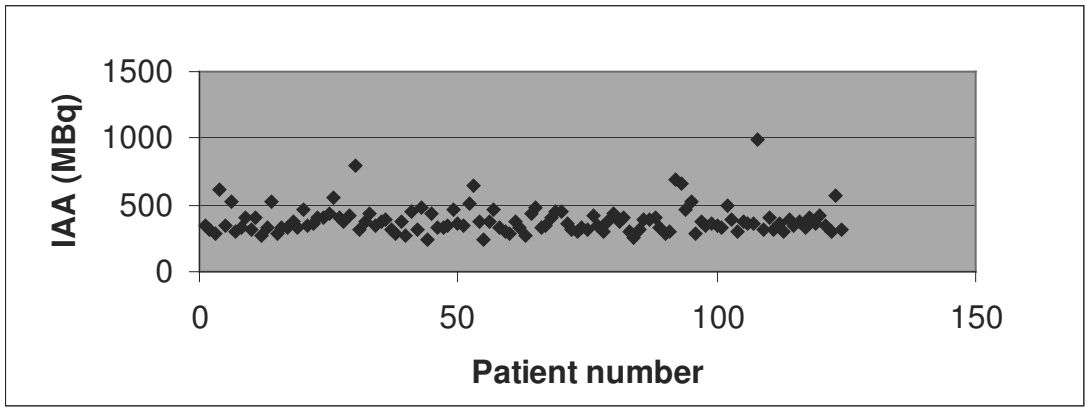


Figure 4.6: Patient calculated IAA when 24-hr RAIU value is used with CAA by the 6-hr RAIU value

The most effective intrathyroid absorbed dosage received to treat Graves' disease should be between 110 MBq and 350 MBq. Table 4.11 demonstrates the statistics when the 24-hr RAIU value is used with the CAA by the 6-hr RAIU value. The minimum value for the IAA calculated when the 24-hr RAIU value is used with the CAA by the 6-hr RAIU value is 238 MBq. The minimum IAA for this calculation therefore falls within the recommended range of 110-350 MBq. The maximum IAA on the other hand, is much higher than the most effective IAA 985 MBq. The median for this specific calculated IAA is 357.5 MBq. Therefore the median of the 24-hr value used with the CAA by the 6-hr RAIU value does not fall within the recommended range.

Table 4.11: IAA for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
IAA (MBq)	321.5	357.5	411.5	238	985

Table 4.12 illustrates how many of the investigation group (n=124) would have received more activity than the recommended range (110-350Mq). Fifty eight (46.8%) of the Graves' disease patients would receive IAA within the recommended range. More than 53.3% of the investigation group would receive a higher IAA than the recommended range if the 24-hr RAIU was used with the CAA at the 6-hr RAIU.

Table 4.12: Amount of activity (act.) exceeding the recommended range of 110-350 MBq

Amount of act. exceeding recommended range (MBq)	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	58	46.8	58	46.8
1-20	8	6.4	66	53.3
21-40	15	12.1	81	65.3
41-60	11	8.9	92	74.2
61-80	7	5.6	99	79.8
81-100	5	4.0	104	83.9
101-120	5	4.0	109	87.9
121-140	2	1.2	111	89.5
141-160	2	1.2	113	91.1
161-180	2	1.2	115	92.7
181-200	0	0	115	92.7
201-220	1	0.8	116	93.6
221-240	1	0.8	117	94.4
241-260	1	0.8	118	95.2
261-280	1	0.8	119	96.0
281-300	1	0.8	120	96.8
301-320	1	0.8	121	97.6
321-340	1	0.8	122	98.4
341-420	0	0	122	98.4
421-440	1	0.8	123	99.2
441-620	0	0	123	99.2
621-640	1	0.8	124	100

4.10 CORRELATING THE CAA BY THE 6-HR RAIU VALUES WITH T_4 VALUES

Figure 4.7 shows the regression analysis between the CAA by the 6-hr RAIU values and T_4 values. A moderate negative linear relationship was obtained (Pearson correlation coefficient obtained r=-0.43; Spearman correlation coefficient r=-0.58).

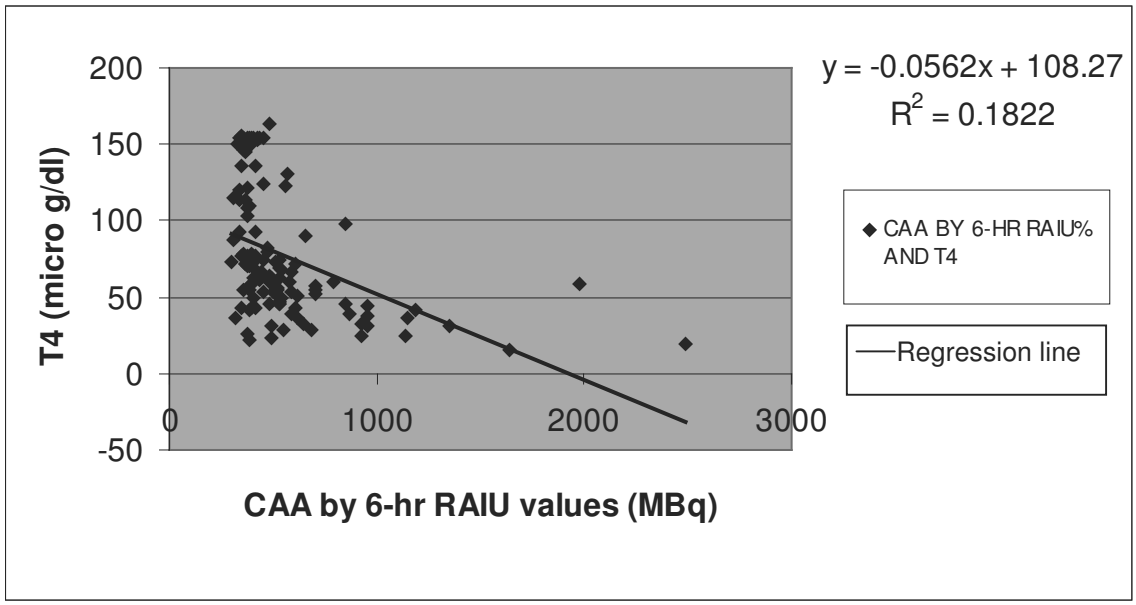


Figure 4.7: Correlating the CAA by 6-hr RAIU values with T_4 values

Table 4.13 illustrates the summary statistics between the CAA by the 6-hr RAIU values and T_4. The median of the CAA by the 6-hr RAIU was 438.5 MBq and the median of T_4 values in the same Graves' disease patients was 67.3 µg/dl. Table 4.13 also shows that the median for the CAA by the 6-hr RAIU is much higher than that of T_4.

Table 4.13: Summary of CAA by the 6-hr RAIU values with T_4 values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
6-hr CAA (MBq)	380	438.5	564	299	2487
T_4 (µg/dl)	46.5	67.3	105.8	15	163.1

4.11 CORRELATING THE CAA BY THE 24-HR VALUES WITH T_4 VALUES

Figure 4.8 shows the regression analysis between the CAA by the 24-hr RAIU value and T_4 (Pearson correlation coefficient obtained r=-0.38; Spearman correlation coefficient r=-0.45). A moderate negative linear relationship was found between the CAA by the 24-hr RAIU values and the T_4 values.

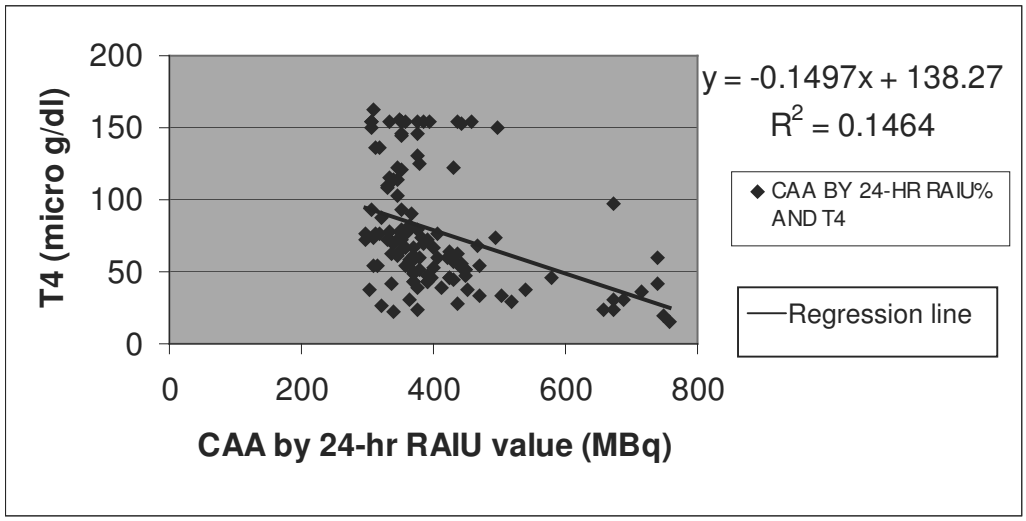


Figure 4.8: Pearson correlation analysis of the CAA by 24-hr RAIU values with T_4 values

The median of the CAA by the 24-hr RAIU was 370 MBq and the median of T_4 was 67.3 µg/dl for the same Graves' disease patients. Table 4.14 shows that the median for the CAA by the 24-hr RAIU is therefore also much higher than that of T_4.

Table 4.14: Summary of CAA by the 24-hr RAIU values with T_4 values for the investigation group (n=124)

Variable	Lower Q	Median	Upper Q	Min	Max
CAA 24-hr (MBq)	344	370	429	296	759
T_4 (µg/dl)	46.5	67.3	105.8	15	163.1

4.12 THYROID-STIMULATING HORMONES

The TSH values for the investigation group are not indicated as specific values (see Table 4.15). Therefore a correlation cannot be made between TSH and the 6-hr or 24-hr RAIU values.

Table 4.15: TSH values as obtained from the investigation group (n=124) files

TSH value	Frequency (*f*)	Percent (%)
0	1	1
<0.01	99	80
0.01	10	8
<0.02	1	1
<0.03	10	8
0.03	1	1
0.06	1	1
0.43	1	1

4.13 SUMMARY

The investigation group for the period 2004 till the end of 2005 consisted mainly of females (85.5%) and the race group that was the highest was blacks (70.2%). The comparison between the 6-hr and 24-hr RAIU median values shows that the 24-hr RAIU median values are higher than those of the 6-hr RAIU median values. There is a strong positive relationship between the 6-hr RAIU values and the 24-hr RAIU values (Pearson correlation coefficient obtained r=0.82). The limits of agreement (the range within which the central 95% of data is expected to lie) are –38 to 7.

The transit patterns showed that, in a very few (n=14) Graves' disease patients, the 6-hr RAIU values were higher that the 24-hr RAIU values. A less than 5% value difference between the 6-hr and 24-hr RAIU values was only present in 11 of the 124 Graves' disease patients.

There was a moderate positive linear relationship between the 6-hr RAIU values and the T_4 values (Pearson correlation coefficient obtained r=0.53; Spearman correlation coefficient r=0.57). A weak positive linear relationship was found between the T_4 values and 24-hr RAIU values (Pearson correlation coefficient obtained r=0.39; Spearman correlation coefficient r=0.46).

Overall, when calculating the CAA using the 6-hr RAIU value, the resultant value was higher than if the calculation was done using the 24-hr RAIU value. The median difference between the 6-hr and 24-hr CAA is 76 MBq. The CAA by the 6-hr RAIU values was used with the 24-hr RAIU values to calculate the IAA. 53.3% (n=66) of the investigation group would receive IAA higher than 350 MBq when the CAA by the 6-hr RAIU values was used with the 24-hr RAIU values to calculate the IAA.

A moderate negative linear relationship was found between the CAA by the 6-hr RAIU values and T_4 values in the same Graves' disease patients (Pearson correlation coefficient obtained r=-0.43; Spearman correlation coefficient r=-0.58). Between the CAA by the 24-hr RAIU and T_4 values a moderate negative linear relationship was found (Pearson correlation coefficient obtained r=-0.38; Spearman correlation coefficient r=-0.45).

Chapter 4 provided the results and findings of the investigation that was undertaken. In the next chapter the results and findings of the investigation will be discussed and overall recommendations regarding the investigation will be supplied.

CHAPTER 5

DISCUSSION AND RECOMMENDATIONS

5.1 INTRODUCTION

The investigation was undertaken in view of the responsibility that health workers have to reduce health care cost and improve health service. At the UNMD the 6- and 24-hour RAIU values are used to calculate the ^{131}I treatment dosages for patients with Graves' disease. According to the literature (see paragraph 1.1.9 on page 10) the highest 6- or 24-hr RAIU value will be the most effective to determine the correct ^{131}I therapy dosage for Graves' disease (Harbert & Da Rocha 1984:12). Yet, if it could be confirmed that the 6-hr RAIU value alone could be used, the hospitalisation cost and the patients' own expenses could be reduced. In order to address the problem statement, the investigation sought to answer the following questions:

- Is the 6-hr ^{131}I RAIU value alone sufficient to calculate the optimal administered therapeutic activity for ^{131}I for patients with Graves' disease?
- How do the 6-hr and 24-hr ^{131}I RAIU values correlate with the T_4 values of patients with Graves' disease?
- What information will be obtained when the transit patterns in patients with Graves' disease are analysed?

The above-mentioned questions form the essence of this endeavour and the answers were searched for in the literature as well as in the outcome of the study.

Chapter 5 is a discussion of the main findings from both the literature and the investigation done. Salient points will be argued and connections between the reviewed literature and the results of the present study will be presented. Specific recommendations regarding further research will be given and the limitations of the investigation will receive attention.

In Chapter 1 the investigation methodology and design were discussed and in Chapter 2 a literature review was carried out to determine the significance of the 6-hr and 24-hr RAIU values in patients with Graves' disease. In the next section the validity of the investigation as well as how the information provided in Chapters 1 and 2 plays a role will be discussed.

5.2 VALIDITY OF THE INVESTIGATION

In Chapter 1 the investigation design was described as follows: First, a literature review was carried out to determine the significance of the 6-hr and 24-hr RAIU values in patients with Graves' disease. Second, a retrospective investigation was conducted to analyse and compare the 6-hr and 24-hr uptake values in patients with proven Graves' disease in the Free State referred to the UNMD. The literature review was provided in Chapter 2. The sources that were consulted about aspects of the 6-hr and 24-hr RAIU values in patients with Graves' disease were relevant published books and journal articles. The fact that the literature review was done by consulting published resources contributed to the validity of the retrospective research study. Prior to the final conclusion of the investigation a literature search was done again, but no new sources were found.

As previously mentioned, only patients with proven Graves' disease were included in the investigation group. The exclusion and inclusion criteria (see

paragraphs 3.4.1 and 3.4.2) for the investigation group were used to select patients with increased 6-hr and 24-hr RAIU values; increased T_4 values; decreased TSH values; and an increased uptake on ^{99m}Tc thyroid scintigraphic scan. Patients with thyroid nodules were excluded from the investigation group, as nodules affect the physiological function of the normal thyroid gland and therefore influence the RAIU values. Graves' disease patients that received medication that could have influenced the 6- and 24-hr RAIU values, as well as recent iodine-containing x-ray examinations were also excluded. The inclusion and exclusion procedure that was followed contributed to the validity of the investigation, as only proven Graves' disease patients were included in the investigation group.

5.3 LIMITATIONS OF THE INVESTIGATION

The investigation was successful in achieving its overall goal and aim in answering the investigation questions. As the investigation was done retrospectively, some limitations occurred. The first limitation was that the Graves' disease patients who had undergone the RAIU procedure might not have been done exactly under the same circumstances. An example of this inconsistency is that the radiographer who did the patient positioning might have been different, even though the same IAEA RAIU procedure was followed. The second limitation was that some of the Graves' disease patients who had undergone the RAIU examination did not undergo a T_4 blood test and had to be excluded. Third, the Graves' disease patients at the Universitas Hospital did not undergo a blood test as a standard procedure to detect antibodies. The blood test that detects antibodies contributes to the accuracy of the diagnosis of Graves' disease, even if this blood test does not assess thyroid function. Fourth, the TSH values of the Graves' disease patients received from the files were abnormally low and fitted in with the diagnosis of

Graves' disease. These values were not specific, however, and could not be used for statistical purposes. Even though the above-mentioned limitations did occur, they did not decrease the validity of the study. The limitations mentioned can be overcome by performing a prospective research study in the future.

5.4 FINDINGS

In this section the findings of the investigation will be discussed in relation to the investigation questions. After the inclusion and exclusion process, the final investigation group was made up out of 124 Graves' disease patients. All the 124 confirmed Graves' disease patients had increased T_4 values, increased 6-hr and 24-hr RAIU values, increased uptake on the ^{99m}Tc scintigram, and decreased TSH values. The age range of the investigation group was between 15 and 75 years. The investigation group consisted of 85.5% (n=106) females and 14.5% (n=18) males. The race of the investigation group consisted of 70% (n=87) blacks, 23% (n=28) whites, and 7% (n=9) coloureds.

The 6- and 24-hr RAIU values were compared. There was a large difference between the median of the 6-hr RAIU and the 24-hr RAIU values (67.5% vs. 80%). There was a strong positive linear relationship between the 6-hr and 24-hr RAIU values, but the difference between the 6-hr RAIU and 24-hr RAIU values is large (Pearson correlation coefficient obtained r=0.82). The limits of agreement (the range within which the central 95% of data is expected to lie) are –38 to 7.

The transit patterns of the 6- and 24-hr RAIU values were also evaluated to determine which of the 6- or 24-hr RAIU values was most effective to calculate the ^{131}I therapy dosage for Graves' disease. Harbert and Da Rocha

(1984:12) state that the highest RAIU value 6- or 24-hr will be the most effective to determine the correct ^{131}I therapy dosage for Graves' disease. In only 11% (n=14) of the study group the 6-hr RAIU value was higher than the 24-hr RAIU value. In 89% (n=110) of the study group the 24-hr RAIU value was higher than the 6-hr RAIU. The transit patterns show that in a very few Graves' disease patients, the 6-hr RAIU value will be higher than the 24-hr RAIU. The transit patterns therefore demonstrate that the 24-hr RAIU value will be most effective to determine the ^{131}I therapy dosage for Graves' disease. A less than 5% value difference between the 6-hr and 24-hr RAIU values was only present in 11 of the 124 Graves' disease patients.

The median of the 6-hr RAIU and the T_4 values differed only by 0.2% (67.5% vs. 67.3%). There was a moderate positive linear relationship between the 6-hr RAIU values and the T_4 values. The median of the 24-hr RAIU values was higher than the median of the T_4 values (80% vs. 67.3%). There was a weak positive linear relationship between the 24-hr RAIU values and the T_4 values.

The CAA by the 6-hr RAIU values was compared with the CAA by the 24-hr RAIU values. The median of the CAA by the 6-hr RAIU values was higher than the median of the CAA by the 24-hr RAIU values (438.5 MBq vs. 370 MBq). The difference between the CAA by the 6-hr and 24-hr RAIU values was large.

The most effective IAA that must be received to treat Graves' disease must be between 110 MBq and 350 MBq (EANM 2003:30). Van Isselt *et al.* (2000:609) state that the 24-hr ^{131}I RAIU is most effective to determine the CAA. Therefore the 24-hr RAIU values were used with the CAA by the 6-hr RAIU values to determine if the IAA would still fall within the limits of 110-350 MBq. The minimum value for the IAA calculated when the 24-hr RAIU values were used with the CAA by the 6-hr RAIU values is 238 MBq. The minimum

IAA for this calculation therefore falls within the recommended range of 110-350 MBq. The maximum IAA on the other hand, is much higher than the most effective IAA of 985 MBq. For these Graves' disease patients the median of the IAA calculated by the 24-hr RAIU values used with the CAA by the 6-hr RAIU values is 357.5 MBq. The conclusion that can be made if the 6-hr RAIU was used for the calculating the administration activity for the investigation group, the median of the IAA would not fall within the recommended range of 110-350 MBq.

The median of the CAA by the 6-hr RAIU values was higher than the median of the T_4 values (438.5 MBq vs. 67.3 µg/dl). The CAA by the 6-hr RAIU values therefore shows a moderate negative linear relationship with the T_4 values (Pearson correlation coefficient obtained r=-0.43; Spearman correlation coefficient r=-0.58). The median of the CAA by the 24-hr RAIU values was higher than the median of the T_4 values (370 MBq vs. 67.3 µg/dl). The CAA by the 24-hr RAIU values shows a moderate negative linear relationship with the T_4 values (Pearson correlation coefficient obtained r=-0.38; Spearman correlation coefficient r=-0.45).

5.5 RECOMMENDATIONS

The investigation was done retrospectively to answer the investigation questions stated in Chapter 1. As the investigation was done retrospectively, certain limitations occurred and were discussed. A recommendation can therefore be made for further future research to perform the investigation as a prospective investigation. A prospective investigation is also recommended with more than two RAIU time values to plot a graph to better evaluate the transit patterns of Graves' disease, for example 3-hr, 6-hr, 18-hr and 24-hr RAIU values. Therefore the overall recommendation that can be made is to

repeat the investigation as a prospective study to verify and contribute to the validity of the investigation.

5.6 SIGNIFICANCE OF THE INVESTIGATION

The results from this investigation answer the investigation questions that were formulated to find ways to reduce the cost in the SAHS. The hospitalisation cost, as well as the patient cost, can be reduced if a 6-hr RAIU value alone can be used to calculate the ^{131}I theraphy dosage for Graves' disease. The goal with the administration of ^{131}I therapy dosage is to treat the patient with Graves' disease so that the patient's thyroid function reaches a euthyroid state (ideal state). A too high dosage can cause the patient to become hypothyroid and to start taking thyroid medication. The accuracy with which the ^{131}I therapy dosage is therefore calculated can contribute to the question if a Graves' disease patient will be euthyroid or hypothyroid after radiation therapy. The overall implication of the investigation can therefore contribute to the well-being of the patient and justify the cost spent on the diagnosis and treatment of the Graves' disease patient.

5.7 SUMMATIVE PERSPECTIVE OF THE INVESTIGATION

The investigation that was undertaken mainly concentrated on the transit patterns of the 6-hr and 24-hr ^{131}I RAIU values in Graves' disease patients. The motivation for the investigation was to find a way to reduce health care cost at the UNMD. By utilising only a 6-hr ^{131}I RAIU value to calculate the ^{131}I therapeutic dosage of a Graves' disease patient, no overnight stay in hospital would be needed.

Hayes *et al.* (1990:519) state that the 24-hr ^{131}I RAIU value can be discarded and only a 6-hr ^{131}I RAIU value is needed to calculate the ^{131}I therapeutic dosage. On the other hand, Braunwald *et al.* (1987:1736) also state that the 24-hr RAIU value is traditionally used to calculate the ^{131}I therapeutic dosage. The highest RAIU value is the best to calculate the therapeutic dosage as this gives a true reflection of the thyroid function of a Graves' disease patient. In the investigation group the median of the 24-hr ^{131}I RAIU values was higher than the 6-hr ^{131}I RAIU values. The research thus showed that the 24-hr ^{131}I RAIU in most of the investigation group was the highest value and most effective to calculate the ^{131}I therapeutic dosage.

There is an increased T_4, 6-hr and 24-hr ^{131}I value in a patient with Graves' disease (Braunwald *et al*. 1987:1744). A correlation was done between the T_4 value and the 6-hr and 24-hr ^{131}I RAIU value to see if there is any relation between these values. The investigation found no statistical significant relationship between the T_4 values and the 6-hr and 24-hr ^{131}I RAIU values.

The recommended range of IAA that should be received to effectively treat Graves' disease should be between 110 MBq and 350 MBq (EANM 2003:30). The investigation group would receive IAA higher than 350 MBq when the CAA by the 6-hr ^{131}I values is used with the 24-hr RAIU values to calculate the IAA.

The investigation had the advantage of justifying the cost spent by the patient staying overnight for the 24-hr ^{131}I RAIU value. In the next section the conclusion of the research will be discussed.

5.8 CONCLUSION

A retrospective investigation of 124 patients with Graves' disease was undertaken and mainly concentrated on finding ways to reduce cost in the UNMD. The area that was focused on at the UNMD was the 6-hr and 24-hr RAIU values in patients with Graves' disease. An analysis of the transit patterns was done and it was found that in most of the investigation group the 24-hr ^{131}I RAIU value was higher than the 6-hr ^{131}I RAIU value.

The IAA received by a Graves' disease patient should fall within the recommended range of 110 MBq to 350 MBq. A 5% value difference between the 6-hr and 24-hr RAIU values would make a less than 1 MBq difference to the CAA for the Graves' disease patient as long as the aimed IAA stayed the same. At the UNMD a 5% value difference between the 6-hr and 24-hr RAIU values would be acceptable, as the patient radiation dosage received would not be significantly higher. In 113 of the Graves' disease patients the value difference between the 6-hr and 24-hr ^{131}I RAIU was more than 5%. Hence, 91.1% (n=113) had a more that 5% value difference between the 6-hr and 24-hr ^{131}I RAIU value.

The conclusion was made that the 24-hr ^{131}I RAIU value was more effective than the 6-hr ^{131}I RAIU value in calculating the accurate therapeutic dosage in most of the investigation group (not all) as it indicated the highest point (percentage) of ^{131}I thyroid uptake. The 24-hr ^{131}I RAIU was found to be the most effective to determine the CAA. This contradicts the findings by Hayes *et al*. (1990:519).

The 6-hr and 24-hr ^{131}I RAIU values were also compared with the T_4 thyroid diagnostic test. The conclusion that was made was that there was a moderate positive linear relationship between the T_4 values and the 6-hr ^{131}I RAIU

values, but a weak positive relationship between T_4 and the 24-hr ^{131}I RAIU values in Graves' disease patients.

The ^{131}I intrathyroid treatment dosage received determines what the outcome of a Graves' disease patient will be. The median of the IAA calculated by the administration activity of the 6-hr ^{131}I RAIU values with the 24-hr ^{131}I RAIU value did not fall within the limits of 110-350 MBq. The conclusion that was drawn from this investigation was that the 24-hr ^{131}I RAIU value is more effective to determine the ^{131}I therapy dosage for Graves' disease.

The transit patterns of the ^{131}I RAIU was abnormally rapid in only 11% (n=14) of the Graves' disease patients. The 6-hr RAIU values were higher than the 24-hr ^{131}I RAIU values. In summary, it is concluded that - according to the investigation done at the UNMD - the transit pattern shows that the 24-hr ^{131}I RAIU value is more accurate to determine the CAA. At a time when research-based practice is taking on an important role, it is essential for nuclear medicine departments to make evidence-based recommendations. The investigation into the correlation between the 6-hr and 24-hr RAIU clearly justified the cost spent on Graves' disease patients that must stay overnight for the 24-hr ^{131}I RAIU procedure. It should also be remembered that the higher the measurement of the ^{131}I RAIU value the lower the therapeutic dosage needed, thus cost saving in its own right.

REFERENCES

Alexander, E.K. & Larsen, P.R. 2002. High Dosage ^{131}I Therapy for the Treatment of Hyperthyroidism Caused by Graves' disease. *The Journal of Clinical Endocrinology & Metabolism* 87(3):1073-1077.

Anderson, K.N. 1998. *Mosby's medical, nursing & allied health dictionary*. 5th ed. U.S.A., St. Louis: Mosby. 1-1752.

Becker, D.V., Charkes, N.D., Hurley, J.R., McDougall, I.R., Price, D.C., Royal, H.D., Sarkar, S.D & Dworkin, J. 2003. *Society of Nuclear Medicine Procedure Guideline for Thyroid Uptake Measurement*. Society of Nuclear Medicine Procedure Guidelines Manual 2.0:33-36.

Berkow, R. 1992. *The Merck Manual*. 16th ed. U.S.A, New Jersey: Merck Research Laboratories. 4-2715.

Bernier, D.R., Christian, P.E. & Langan, J.K. 1994. *Nuclear Medicine Technology and Techniques*. 3rd ed. U.S.A., St Louis: Mosby. 225-241.

Braunwald, E., Isselbacher, K.J., Petersdorf, R.G., Wilson, J.D., Martin, J.B. & Fauci, A. 1987. *Harrison's Principles of Internal Medicine*. 11th ed. U.S.A., New York: McGraw-Hill. 1736-1745.

Chapman, E.M. 1983. History of the discovery and early use of radioactive iodine. *JAMA* 250(15):2042-2044.

Chapman, E.M. & Maloof, F. 1955. The use of radioactive iodine in the diagnosis and treatment of hyperthyroidism: ten years' experience. *Medicine* 34:261-270.

Datz, F.L. 1993. *Handbook of Nuclear Medicine*. 2nd ed. U.S.A., St. Louis: Mosby. 1-23.

De Bruin, T.W.A., Croon, C.D.L., De Klerk, J.M.H. & Van Isselt, J.W. 1994. Standardized radioiodine therapy in Graves' disease: the persistent effect of thyroid weight and radioiodine uptake on outcome. *Journal of Internal Medicine* 263:507-513.

Dworkin, H.J., Meier, D.A. & Kaplan, M. 1995. Advances in the Management of Patients with Thyroid Disease. *Seminars in Nuclear Medicine* 25(3):205-220.

EANM. 2003. EANM Procedure Guidelines for Therapy with Iodine-131. *European Journal of Nuclear Medicine* 30(3):27-31.

Early, P.J. & Sodee, D.B. 1995. *Principles and Practice of Nuclear Medicine*. 2nd ed. U.S.A., St. Louis: Mosby. 627-630.

Freitas, J.E. 1999. The role of nuclear medicine in the management of Graves' disease. *The Quarterly Journal of Nuclear Medicine* 43(4):297-306.

Ganong, W.F. 1995. *Review of Medical Physiology*. 7th ed. U.S.A., Connecticut: Appelton & Lange. 290-305.

Gibbon, C.J. 1997. *South African Medicines Formulary (SAMF)*. 5th ed. Western Cape: INCE Cape. 1-509.

Glennon, J.A., Gordon, E.S. & Sawin, C.T. 1972. Hypothyroidism After Low-Dosage ^{131}I Treatment of Hyperthyroidism. *Annals of Internal Medicine* 76(5):721-723.

Grayson, R.R. 1960. Factors Which Influence the Radioactive Iodine Thyroidal Uptake Test. *American Journal of Medicine* 28:397-415.

Gunasekera, R.D., Hesslewood, S.R., Notghi, A. & Harding, L.K. 2000. Hypothyroidism following 400 MBq vs 200 MBq radioiodine therapy for thyrotoxicosis. *Nuclear Medicine Communications* 21:209.

Hamburger, J.I. 1971. Application of Radioiodine Uptake to the Clinical Evaluation of Thyroid Disease. *Seminars in Nuclear Medicine* 1(3):287-300.

Harbert, J. & Da Rocha, A.F.G. 1984. *Textbook of Nuclear Medicine*. Vol. 2, 2nd ed. U.S.A., Philadelphia: Lea & Febiger. 9-35.

Hayes, A.A., Akre, C.M. & Gorman, C.A. 1990. Iodine-131 Treatment of Graves' Disease Using Modified Early Iodine-131 Uptake Measurements in Therapy Dosage Calculations. *The Journal of Nuclear Medicine* 31(4):519-522.

Hennemann, G., Krenning, E.P. & Sankaranarayanan, K. 1986. Place of Radioactive iodine in treatment of thyrotoxicosis. *The Lancet* 35:1369-1372.

Holm, L.E., Lundell, G., Israelsson, A. & Dahlqvist, I. 1982. Incidence of Hypothyroidism Occurring Long After Iodine-131 Therapy for Hyperthyroidism. *Journal of Nuclear Medicine* 23(2):106.

IAEA (International Atomic Energy Agency). 1961. *The Calibration and Standardization of Thyroid Uptake Measurements*.
<www.iop.org/EJ /article/00319155/6/4/302/pbv6i4p533.pdf>
Retrieved on 17 February 2006.

Iruxol Mono Leaflet. 2001. S.A., Pinetown: Smith & Nephew Pharmaceuticals (Pty) Ltd. 1.

Kaplan, M.D. 1985. Clinical and Laboratory Assessment of Thyroid Abnormalities. *Medical Clinics of North America* 69(5):863-881.

Kasper, D.L., Fauci, A.S., Longo, D.L., Braunwald, E., Hauser, S.L. & Jameson, J.L. 2005. *Harrison's Principles of Internal Medicine*. 16th ed. U.S.A., New York: McGraw-Hill. 2104-2117.

KLOREF Leaflet. 1998. S.A., Constantia Kloof: Abbott Laboratories S.A. (Pty) Ltd. 1.

Lind, P. 2002. Strategies of radioiodine therapy for Graves' disease. *European Journal of Nuclear Medicine* 29(2):453-455.

Maisey, M.N., Britton, K.E. & Gilday, D.L. 1991. *Clinical Nuclear Medicine*. 2nd ed. U.K., London: Chapman & Hall Medical. 198-213.

McDougall, I.R. 1991. Graves' Disease. *Medical Clinics of North America* 75(1):79-95.

Meier, D.A., Brill, D.R., Becker, D.V., Clarke, S.E.M., Silberstein, E.B., Royal, H.D. & Balon, H.R. 2002. Procedure Guideline for Therapy of Thyroid Disease with ^{131}Iodine. *The Journal of Nuclear Medicine* 43(6):856-857.

MIRD Dosage Estimate Report No. 5. 1975. Dosage Estimate Report No.5: Summary of current radiation dosage estimates to humans from ^{123}I, ^{124}I, ^{125}I, ^{126}I, ^{130}I, ^{131}I and ^{132}I as sodium iodide. *Journal of Nuclear Medicine* 16(9):857-860.

Nordyke, R.A. & Gilbert, F.I. 1991. Optimal Iodine-131 Dosage for Eliminating Hyperthyroidism in Graves' Disease. *Journal of Nuclear Medicine* 32(3):411-416.

Peters, H., Fischer, C., Bogner, L., Reiners, C. & Schleusener, H. 1995. Radioiodine therapy of Graves' hyperthyroidism: standard vs. calculated ^{131}iodine activity. Results from a prospective, randomized, multicentre study. *European Journal of Clinical Investigation* 25:186.

Riccabona, G. 1994. *^{131}I Therapy of Thyroid Disease: Why? When? How?* EANM-continuing education, Germany, Dusseldorf.

Robbins, S.L. & Kumar, V. 1987. *Basic Pathology*. 4th ed. U.S.A., Philadelphia: W.B. Saunders Company. 681-682.

Safa, A.M. & Skillern, P.G. 1975. Treatment of Hyperthyroidism With a Large Initial Dosage of Sodium Iodide I-131. *Arch. Internal Medicine* 135:673-676.

Solomon, B., Glinoer, D., Lagasse, R. & Wartofsky, L. 1990. Current Trends in the Management of Graves' Disease. *Journal of Clinical Endocrinology and Metabolism* 70(6):1518-1519.

Van Isselt, J.W., De Klerk, J.M.H., Koppeschaar, H.P.F. & Van Rijk, P.P. 2000. Iodine-131 uptake and turnover rate vary over short intervals in Graves' disease. *Nuclear Medicine Communication* 21:609-616.

Volpé, R. 1977. Treatment of Graves' Disease. *Thyroid Today* 1(1):2.

Wagner, H.N., Szabo, Z. & Buchanan, J.W. 1995. *Principles of Nuclear Medicine*. 2nd ed. U.S.A., St. Louis: Mosby. W.B. Saunders Company. 598-600.

APPENDIX A

DATA SHEETS

1. **Patient ^{131}I uptake percentages and biochemistry information (numbers missing are patients that were excluded from the investigation group)**

PATIENT STUDY NUMBER	PATIENT HOSPITAL NUMBER	6-HR ^{131}I UP-TAKE (%)	24-HR ^{131}I UP-TAKE (%)	T_4	TSH	^{99m}TC-PERTECH-NETATE THYROID SCAN (↑ INCREAS-ED OR ↓ DECREAS-ED)
1	UM321825 530503	79	90	109.0	0.01	↑
2	UM326493 630909	90	97	150	<0.01	↑
4	UM321390 550625	69	67	153	<0.01	↑
5	UM210826 890930	32	59	33	<0.01	↑
6	UM323198 650529	82	95,6	54.7	<0.01	↑
7	UM322491 560918	31	55	37.4	<0.01	↑
8	UM322694 740901	74	76	42.4	<0.01	↑
10	UM323897 670927	85	95	135.9	<0.01	↑
11	UM049979 510523	48	65,5	37	<0.01	↑
12	UM324847 730407	75,7	80	58.7	0.00	↑
13	UM109632 610706	55,9	75,6	47.4	<0.01	↑
15	UM324708 891219	65	60	73.9	<0.01	↑
16	UM326348 521020	59	67	53.4	<0.01	↑
17	UM326628 620425	22	44	30.8	<0.01	↑

22	UM328554 740320	83	79	145.8	<0.01	↑
23	UM328615 651201	78	86	102.5	<0.01	↑
24	UM328553 810219	74	84	71.9	<0.01	↑
26	UM328598 720206	68	84	154.8	<0.01	↑
27	UM329201 820103	78	86	121.6	<0.01	↑
29	UM329172 751225	49	76	72.2	<0.01	↑
31	UM331115 780616	55	63,5	67.5	0.055	↑
32	UM330652 561012	61,7	74,5	46	0.03	↑
33	UM304837 610927	58	78	52	<0.01	↑
34	UM332017 291229	31	43	31	0.01	↑
36	UM332201 451129	55	80	50	<0.01	↑
37	UM270611 550322	37,3	70,4	60	<0.01	↑
41	UM333093 540310	57,7	77,7	73.3	<0.01	↑
42	UM334716 591201	72	91	77	<0.03	↑
49	UM335951 420810	50	70	63.2	<0.01	↑
50	UM330657 791205	15	40	59.2	<0.01	↑
51	UM336765 520714	92,3	98	37	<0.01	↑

52	**UM336960 690914**	**75**	**96,5**	**154.8**	**0.01**	↑
53	**UM337405 620824**	**50**	**74**	**53.2**	**0.43**	↑
54	**UM337310 710813**	**57**	**67**	**55**	**<0.02**	↑
55	**UM336754 660529**	**55,7**	**70**	**45.3**	**<0.01**	↑
56	**UM338415 531020**	**61**	**80**	**60.5**	**<0.01**	↑
57	**UM339695 840704**	**80**	**87**	**113.8**	**<0.01**	↑
58	**UM339830 640525**	**87**	**86**	**114.0**	**<0.01**	↑
59	**UM226136 700629**	**72**	**93**	**135.8**	**<0.01**	↑
62	**UM341553 691008**	**86**	**80**	**42.6**	**<0.03**	↑
64	**UM343576 660112**	**52**	**79**	**131**	**<0.01**	↑
65	**UM344221 740330**	**72,9**	**77**	**154.8**	**<0.01**	↑
67	**UM315130 721215**	**25,8**	**41,4**	**36.3**	**<0.01**	↑
68	**UM342428 691015**	**79,4**	**64,5**	**154**	**<0.01**	↑
69	**UM342428 420604**	**50,2**	**74**	**67**	**<0.01**	↑
70	**UM345534 570522**	**74**	**82**	**78**	**<0.01**	↑
72	**UM343608 700128**	**78**	**87**	**70**	**<0.01**	↑
75	**UM343605 601023**	**79**	**92**	**26**	**<0.01**	↑
77	**UM176724 550710**	**49**	**76**	**43.1**	**0.01**	↑
78	**UM343002 550122**	**73**	**88**	**62**	**<0.01**	↑
79	**UM328615 651201**	**56**	**66**	**47**	**<0.01**	↑
80	**UM351211 570502**	**56**	**96**	**74**	**<0.01**	↑

83	**UM351909 710415**	**18**	**39**	**15.0**	**<0.01**	↑
85	**UM354052 510906**	**58**	**73**	**59.6**	**<0.01**	↑
86	**UM067246 841029**	**74**	**59,5**	**149.7**	**<0.01**	↑
87	**UM336754 660529**	**55,7**	**70**	**45.3**	**<0.01**	↑
88	**UM353714 840216**	**61**	**96**	**163.14**	**<0.03**	↑
90	**UM356740 521107**	**74**	**81**	**59**	**<0.01**	↑
91	**UM357892 780505**	**99**	**100**	**72.5**	**<0.01**	↑
94	**UM351536 550624**	**70**	**68**	**154.8**	**<0.01**	↑
96	**UM360149 600315**	**73**	**93**	**76.8**	**<0.03**	↑
98	**UM359929 700907**	**60**	**68**	**63**	**<0.01**	↑
99	**UM362578 691105**	**96**	**89**	**115**	**<0.01**	↑
100	**UM362527 550726**	**35**	**51**	**45.8**	**<0.01**	↑
101	**UM288586 640818**	**25**	**40**	**41.8**	**<0.01**	↑
102	**UM364785 580412**	**89**	**97**	**154**	**0.01**	↑
103	**UM234979 630409**	**72**	**85**	**74**	**0.01**	↑
105	**UM339836 640525**	**48**	**66**	**51.4**	**<0.01**	↑
106	**UM364217 880111**	**51**	**78**	**60**	**<0.01**	↑
107	**UM342105 770128**	**41,9**	**63**	**54.2**	**<0.01**	↑
108	**UM335307 660505**	**56,7**	**69**	**56.6**	**<0.01**	↑
109	**UM367708 610424**	**80**	**84**	**146.0**	**<0.01**	↑
110	**UM367382 790813**	**82**	**84**	**77.2**	**<0.03**	↑
111	**UM368464 710309**	**80**	**90**	**71.7**	**<0.01**	↑

112	UM368475 671231	77	82,9	54.8	<0.01	↑
113	UM336839 671119	50	71,9	39.1	<0.01	↑
116	UM368578 580211	77	88	42.1	<0.01	↑
118	UM369229 680808	84	85	155.0	<0.01	↑
119	UM369194 710215	63	79	79.3	<0.01	↑
121	UM364098 541130	65	94	53.8	<0.03	↑
124	UM864859 681002	63	81	82.2	0.01	↑
125	UM372113 420101	46	63	33	<0.01	↑
126	UM364841 521027	78	83	77	<0.01	↑
127	UM373232 600101	84	73	77	<0.03	↑
129	UM373375 880623	82	89	72	<0.01	↑
130	UM372935 561220	72	95	76.1	<0.03	↑
133	UM315902 431113	43	57	28.6	<0.01	↑
134	UM375892 600405	60	81	30.9	<0.01	↑
135	UM375922 670702	71	80	42.8	<0.01	↑
136	UM374247 691120	84	83	154.8	<0.01	↑
137	UM307324 580228	81	84	145	<0.01	↑
138	UM378119 441220	34	79	39	0.01	↑
141	UM368463 750526	31	69	44.3	<0.01	↑
142	UM378673 890703	42	66	52	<0.01	↑
143	UM380026 750314	45,1	80,7	90	<0.01	↑

144	**UM379591 331023**	**96**	**92**	**88**	**<0.01**	↑
145	**UM379543 550815**	**35**	**44**	**97.8**	**0.01**	↑
147	**UM380489 530403**	**76**	**88**	**71**	**<0.01**	↑
148	**UM380661 630128**	**67**	**80**	**67.1**	**<0.03**	↑
149	**UM379929 570719**	**76**	**87**	**22.1**	**<0.01**	↑
150	**UM382201 661013**	**89**	**97**	**93**	**<0.01**	↑
151	**UM382228 561204**	**26**	**44**	**24**	**<0.01**	↑
152	**UM381542 620130**	**53**	**69**	**122.5**	**<0.01**	↑
153	**UM383118 720317**	**85,5**	**84,7**	**154**	**<0.01**	↑
154	**UM325613 800916**	**68**	**86**	**61**	**<0.01**	↑
155	**UM383824 821226**	**65**	**79**	**154**	**<0.01**	↑
158	**UM384020 560221**	**69**	**83**	**66**	**<0.01**	↑
159	**UM380598 680522**	**11,9**	**39,6**	**19.8**	**<0.01**	↑
161	**UM385424 830806**	**82**	**89**	**154**	**<0.01**	↑
162	**UM386007 770301**	**56**	**77**	**69**	**<0.01**	↑
163	**UM377005 760703**	**82**	**89**	**77.2**	**<0.03**	↑
164	**UM386591 791201**	**82**	**100**	**77**	**<0.01**	↑
165	**UM386592 890825**	**76**	**75**	**154.8**	**<0.01**	↑

166	**UM382397 581203**	**60**	**79**	**23.6**	**<0.01**	↑
168	**UM384292 821115**	**77**	**90**	**110**	**<0.01**	↑
169	**UM358122 730924**	**54**	**68**	**28**	**0.01**	↑
171	**UM388630 870601**	**73**	**80**	**49.3**	**<0.01**	↑
172	**UM388673 670327**	**61**	**85**	**63.6**	**<0.01**	↑
173	**UM388675 720814**	**65**	**78**	**124.7**	**<0.01**	↑
174	**UM388059 801109**	**32**	**45**	**24.0**	**<0.01**	↑
175	**UM389145 770908**	**72**	**84**	**93.2**	**<0.01**	↑
176	**UM389157 821014**	**83**	**84**	**78.5**	**<0.01**	↑
177	**UM056242 620515**	**42**	**81**	**57.5**	**<0.01**	↑
178	**UM389148 661213**	**87**	**91**	**120.3**	**<0.01**	↑

APPENDIX A

DATA SHEETS

2. Patient information form

PATIENT STUDY NUMBER	PATIENT HOSPITAL NUMBER	AGE	GENDER	RACE
1	UM321825 530503	51	F	W
2	UM326493 630909	41	F	B
3	UM321679 611219	43	F	B
4	UM321390 550625	49	F	B
5	UM210826 890930	15	F	W
6	UM323198 650529	39	F	B
7	UM322491 560918	48	F	B
8	UM322694 740901	30	F	B
9	UM322478 780412	26	F	B
10	UM323897 670927	37	F	B
11	UM049979 510523	53	F	W
12	UM324847 730407	31	F	W
13	UM109632 610706	43	F	W
14	UM324793 620808	42	F	B
15	UM324708 891219	15	F	W
16	UM326348 521020	52	F	B
17	UM326628 620425	42	F	C
18	UM327301 740815	30	F	B
19	UM327795 710507	33	F	B

20	**UM294443 800710**	**24**	**F**	**B**
21	**UM326265 470626**	**57**	**F**	**W**
22	**UM328554 740320**	**30**	**F**	**W**
23	**UM328615 651201**	**39**	**F**	**B**
24	**UM328553 810219**	**23**	**F**	**B**
25	**UM259758 681209**	**36**	**F**	**B**
26	**UM328598 720206**	**32**	**F**	**B**
27	**UM329201 820103**	**22**	**F**	**B**
28	**UM327913 400210**	**64**	**F**	**B**
29	**UM329172 751225**	**29**	**F**	**B**
30	**UM070867 740409**	**30**	**F**	**B**
31	**UM331115 780616**	**26**	**M**	**W**
32	**UM330652 561012**	**48**	**F**	**B**
33	**UM304837 610927**	**43**	**F**	**B**
34	**UM332017 291229**	**75**	**F**	**W**
35	**UM331943 690601**	**35**	**F**	**B**
36	**UM332201 451129**	**59**	**F**	**B**
37	**UM270611 550322**	**49**	**F**	**B**
38	**UM291739 580907**	**46**	**F**	**B**
39	**UM331716 660516**	**38**	**F**	**B**
40	**UM332733 651225**	**39**	**F**	**B**
41	**UM333093**	**50**	**F**	**B**

	540310			
42	UM334716 591201	45	M	B
43	UM334202 680508	36	F	W
44	UM310877 560325	48	F	B
45	UM072715 481031	56	F	B
46	UM335307 660505	38	F	B
47	UM335768 440310	60	F	B
48	UM335473 630724	41	F	B
49	UM335951 420810	62	F	W
50	UM330657 791205	25	F	B
51	UM336765 520714	52	F	B
52	UM336960 690914	35	F	B
53	UM337405 620824	42	F	B
54	UM337310 710813	33	F	B
55	UM336754 660529	38	F	B
56	UM338415 531020	51	F	B
57	UM339695 840704	20	F	B
58	UM339830 640525	40	F	B
59	UM226136 700629	34	F	B
60	UM339712 670604	37	F	B
61	UM336647 730721	31	F	B
62	UM341553 691008	35	F	C

63	UM286958 410729	63	F	W
64	UM343576 660112	38	F	B
65	UM344221 740330	30	F	W
66	UM189492 600125	44	F	B
67	UM315130 721215	33	F	B
68	UM342428 691015	35	M	B
69	UM344748 420604	62	F	B
70	UM345534 570522	47	F	W
71	UM345969 250304	79	M	W
72	UM343608 700128	34	F	B
73	UM346380 360312	68	F	B
74	UM347526 650425	39	F	C
75	UM343605 601023	44	M	B
76	UM348743 500101	54	F	B
77	UM176724 550710	49	F	C
78	UM343002 550122	49	F	B
79	UM328615 651201	39	F	B
80	UM351211 570502	47	F	B
81	UM352210 670409	37	F	B
82	UM352187 461111	58	F	B
83	UM351909 710415	33	F	C
84	UM353438	54	F	W

	510409			
85	UM354052 510906	54	F	B
86	UM067246 841029	21	M	W
87	UM336754 660529	39	F	B
88	UM353714 840216	21	F	B
89	UM356411 520315	53	F	B
90	UM356740 521107	53	F	W
91	UM357892 780505	27	F	B
92	UM358122 730924	32	M	B
93	UM124769 261119	79	F	W
94	UM351536 550624	50	M	B
95	UM360513 640102	41	F	B
96	UM360149 600315	45	F	B
97	UM336736 630819	42	F	B
98	UM359929 700907	35	F	B
99	UM362578 691105	36	F	C
100	UM362527 550726	50	M	W
101	UM288586 640818	41	M	W
102	UM364785 580412	47	F	W
103	UM234979 630409	42	F	B
104	UM360009 401230	65	F	W
105	UM339836 640525	41	F	B
106	UM364217	17	F	B

	880111			
107	**UM342105 770128**	**28**	**F**	**W**
108	**UM335307 660505**	**39**	**F**	**B**
109	**UM367708 610424**	**44**	**F**	**B**
110	**UM367382 790813**	**26**	**F**	**B**
111	**UM368464 710309**	**34**	**F**	**B**
112	**UM368475 671231**	**38**	**M**	**B**
113	**UM336839 671119**	**38**	**F**	**W**
114	**UM365294 510709**	**54**	**F**	**C**
115	**UM367966 310319**	**74**	**M**	**W**
116	**UM368578 580211**	**47**	**F**	**B**
117	**UM368815 770805**	**28**	**F**	**B**
118	**UM369229 680808**	**37**	**F**	**B**
119	**UM369194 710215**	**34**	**F**	**B**
120	**UM369258 680821**	**37**	**M**	**W**
121	**UM364098 541130**	**51**	**M**	**B**
122	**UM369947 650524**	**40**	**F**	**C**
123	**UM186157 731120**	**32**	**F**	**W**
124	**UM864859 681002**	**37**	**M**	**B**
125	**UM372113 420101**	**63**	**F**	**W**
126	**UM364841 521027**	**53**	**F**	**B**
127	**UM373232 600101**	**45**	**F**	**B**
128	**UM372125**	**63**	**F**	**B**

	420218			
129	UM373375 880623	17	F	B
130	UM372935 561220	49	F	B
131	UM222312 240507	81	F	W
132	UM356462 790101	26	F	B
133	UM315902 431113	62	M	W
134	UM375892 600405	45	F	B
135	UM375922 670702	38	F	C
136	UM374247 691120	36	F	B
137	UM307324 580228	47	M	B
138	UM378119 441220	61	F	B
139	UM375999 390802	66	F	B
140	UM378561 591214	46	F	B
141	UM368463 750526	30	F	B
142	UM378673 890703	16	M	B
143	UM380026 750314	30	F	C
144	UM379591 331023	72	F	B
145	UM379543 550815	50	M	B
146	UM380049 760606	29	F	B
147	UM380489 530403	52	F	B
148	UM380661 630128	42	F	C
149	UM379929 570719	48	F	B
150	UM382201	39	F	C

	661013			
151	**UM382228 561204**	**49**	**F**	**W**
152	**UM381542 620130**	**43**	**F**	**W**
153	**UM383118 720317**	**33**	**F**	**B**
154	**UM325613 800916**	**25**	**M**	**W**
155	**UM383824 821226**	**23**	**F**	**B**
156	**UM301010 881231**	**17**	**M**	**B**
157	**UM383887 511108**	**54**	**F**	**B**
158	**UM384020 560221**	**49**	**F**	**W**
159	**UM380598 680522**	**37**	**F**	**W**
160	**UM221884 371223**	**68**	**F**	**W**
161	**UM385424 830806**	**22**	**F**	**B**
162	**UM386007 770301**	**28**	**M**	**B**
163	**UM377005 760703**	**29**	**F**	**B**
164	**UM386591 791201**	**26**	**F**	**B**
165	**UM386592 890825**	**16**	**F**	**B**
166	**UM382397 581203**	**47**	**F**	**B**
167	**UM329437 511228**	**54**	**F**	**W**
168	**UM384292 821115**	**23**	**F**	**B**
169	**UM358122 730924**	**32**	**M**	**B**
170	**UM189492 600125**	**45**	**F**	**B**
171	**UM388630 870601**	**18**	**F**	**W**

172	**UM388673 670327**	**38**	**F**	**B**
173	**UM388675 720814**	**33**	**F**	**B**
174	**UM388059 801109**	**25**	**F**	**W**
175	**UM389145 770908**	**28**	**F**	**B**
176	**UM389157 821014**	**23**	**F**	**B**
177	**UM056242 620515**	**43**	**F**	**B**
178	**UM389148 661213**	**39**	**F**	**B**

APPENDIX A

DATA SHEETS

3. Patient 6- and 24-hour therapeutic dosage information

PATIENT HOSPI-TAL NUMBER	PATIENT HOSPI-TAL NUMBER	6-HR ADMI-NISTERED ACTIVITY (MBq)	24-HR ADMINI-STERED ACTIVITY (MBq)	DIFFE-RENCE BETWEEN ADMINI-STERED ACTIVITY CALCULA-TED WITH THE 6-HR AND 24-HR RAIU (MBq)	CALCU-LATED ABSORBED ACTIVITY TO THYROID WHEN USING 6-HR ADMINISTE-RED ACTIVITY FROM RAIU WITH THE 24-HR RAIU % (MBq)	HOW MUCH MORE ACTIVITY THAN RECOM-MENDED WITHIN THE LIMITS OF 110 MBQ – 350 MBQ (MBq)
1	UM321825 530503	375	329	46	338	0
2	UM326493 630909	329	305	24	319	0
3	UM321679 611219	740	493	247	444	94
4	UM321390 550625	429	442	-13	287	0
5	UM210826 890930	925	502	423	620	270
6	UM323198 650529	361	310	51	345	0
7	UM322491 560918	955	538	417	525	175
8	UM322694 740901	400	390	10	304	0
9	UM322478 780412	277	277	0	296	0
10	UM323897 670927	348	312	36	331	0
11	UM049979 510523	617	452	165	404	54
12	UM324847 730407	391	370	21	313	0
13	UM109632 610706	530	392	138	401	51
14	UM324793	357	344	13	307	0

	620808					
15	UM324708 891219	455	493	-38	273	0
16	UM326348 521020	502	442	60	336	0
17	UM326628 620425	1346	673	673	529	242
18	UM327301 740815	559	462	97	358	8
19	UM327795 710507	846	617	229	406	56
20	UM294443 800710	759	477	282	470	120
21	UM326265 470626	1057	658	399	476	126
22	UM328554 740320	357	375	-18	282	0
23	UM328615 651201	380	344	36	327	0
24	UM328553 810219	400	352	48	336	0
25	UM259758 681209	519	423	96	363	13
26	UM328598 720206	435	352	83	374	24
27	UM329201 820103	380	344	36	327	0
28	UM327913 400210	779	395	384	584	234
29	UM329172 751225	604	390	214	459	109
30	UM070867 740409	1346	580	766	687	337
31	UM331115 780616	538	466	72	342	0
32	UM330652 561012	480	397	83	358	8
33	UM304837 610927	510	380	130	398	48
34	UM332017 291229	955	688	267	411	61
35	UM331943 690601	356	298	58	353	3

36	**UM332201 451129**	**538**	**370**	**168**	**430**	**80**
37	**UM270611 550322**	**794**	**421**	**373**	**559**	**209**
38	**UM291739 580907**	**673**	**455**	**218**	**438**	**88**
39	**UM331716 660516**	**510**	**390**	**120**	**388**	**38**
40	**UM332733 651225**	**580**	**519**	**61**	**331**	**0**
41	**UM333093 540310**	**513**	**381**	**132**	**399**	**49**
42	**UM334716 591201**	**411**	**352**	**59**	**374**	**24**
43	**UM334202 680508**	**705**	**455**	**250**	**458**	**8**
44	**UM310877 560325**	**0**	**348**	**-**	**0**	**0**
45	**UM072715 481031**	**0**	**538**	**-**	**0**	**0**
46	**UM335307 660505**	**0**	**370**	**-**	**0**	**0**
47	**UM335768 440310**	**538**	**455**	**83**	**350**	**0**
48	**UM335473 630724**	**604**	**630**	**-26**	**284**	**0**
49	**UM335951 420810**	**529**	**423**	**106**	**414**	**64**
50	**UM330657 791205**	**1973**	**740**	**1233**	**789**	**439**
51	**UM336765 520714**	**321**	**302**	**19**	**315**	**0**
52	**UM336960 690914**	**395**	**307**	**88**	**381**	**31**
53	**UM337405 620824**	**592**	**400**	**192**	**438**	**88**
54	**UM337310 710813**	**519**	**442**	**77**	**348**	**0**
55	**UM336754 660529**	**531**	**423**	**108**	**372**	**22**
56	**UM338415**	**485**	**370**	**115**	**388**	**38**

	531020					
57	UM339695 840704	370	340	30	322	0
58	UM339830 640525	340	344	-4	292	0
59	UM226136 700629	411	318	93	382	32
60	UM339712 670604	411	370	41	329	0
61	UM336647 730721	298	296	2	298	0
62	UM341553 691008	344	370	-26	275	0
63	UM286958 410729	779	470	309	491	141
64	UM343576 660112	569	375	194	450	100
65	UM344221 740330	406	384	22	313	0
66	UM189492 600125	375	348	27	319	0
67	UM315130 721215	1147	715	432	475	125
68	UM342428 691015	373	459	-86	241	0
69	UM344748 420604	590	400	190	437	87
70	UM345534 570522	400	361	39	328	0
71	UM345969 250304	1057	442	615	708	358
72	UM343608 700128	380	340	40	331	0
73	UM346380 360312	502	329	173	452	102
74	UM347526 650425	740	510	230	429	79
75	UM343605 601023	375	322	53	345	0
76	UM348743 500101	477	411	66	343	0

77	UM176724 550710	604	390	214	459	109
78	UM343002 550122	406	336	70	357	7
79	UM328615 651201	529	449	80	349	0
80	UM351211 570502	529	308	221	508	158
81	UM352210 670409	740	519	221	422	72
82	UM352187 461111	336	311	25	319	0
83	UM351909 710415	1644	759	885	641	291
84	UM353438 510409	1345	569	776	699	349
85	UM354052 510906	510	406	104	372	22
86	UM067246 841029	400	498	-98	238	0
87	UM336754 660529	531	423	108	372	22
88	UM353714 840216	485	308	177	466	116
89	UM356411 520315	871	510	361	505	155
90	UM356740 521107	400	365	35	324	0
91	UM357892 780505	299	296	3	299	0
92	UM358122 730924	423	384	39	326	0
93	UM124769 261119	1021	529	492	572	222
94	UM351536 550624	423	435	-12	288	0
95	UM360513 640102	281	274	7	304	0
96	UM360149 600315	406	318	88	378	28
97	UM336736 630819	1233	740	493	493	143
98	UM359929	493	435	58	335	0

	700907					
99	UM362578 691105	308	333	-25	274	0
100	UM362527 550726	846	580	266	432	82
101	UM288586 640818	1184	740	444	474	124
102	UM364785 580412	333	305	28	323	0
103	UM234979 630409	411	348	63	349	0
104	UM360009 401230	493	406	87	360	10
105	UM339836 640525	617	449	168	407	57
106	UM364217 880111	580	380	200	452	102
107	UM342105 770128	706	470	236	445	95
108	UM335307 660505	522	429	93	360	10
109	UM367708 610424	370	352	18	311	0
110	UM367382 790813	361	352	9	303	0
111	UM368464 710309	370	329	41	333	0
112	UM368475 671231	384	357	27	318	0
113	UM336839 671119	592	412	180	426	76
114	UM365294 510709	1021	559	462	541	191
115	UM367966 310319	3288	1139	2149	855	505
116	UM368578 580211	384	336	48	338	0
117	UM368815 770805	430	318	112	400	50
118	UM369229 680808	352	348	4	299	0
119	UM369194 710215	470	375	95	372	21
120	UM369258	477	325	152	434	84

	680821					
121	UM364098 541130	455	315	140	428	78
122	UM369947 650524	380	375	5	300	0
123	UM186157 731120	673	455	218	437	87
124	UM864859 681002	470	365	105	381	31
125	UM372113 420101	644	470	174	406	56
126	UM364841 521027	380	357	23	300	0
127	UM373232 600101	352	406	-54	257	0
128	UM372125 420218	395	312	83	375	25
129	UM373375 880623	362	333	29	321	0
130	UM372935 561220	411	312	99	391	41
131	UM222312 240507	560	529	31	319	0
132	UM356462 790101	502	435	67	341	0
133	UM315902 431113	688	519	169	392	42
134	UM375892 600405	493	365	128	399	49
135	UM375922 670702	417	370	47	334	0
136	UM374247 691120	352	357	-5	292	0
137	UM307324 580228	365	352	13	307	0
138	UM378119 441220	871	375	496	688	338
139	UM375999 390802	779	548	231	421	71
140	UM378561 591214	617	444	173	411	61
141	UM368463 750526	955	429	526	659	309
142	UM378673	705	449	256	465	115

	890703					
143	UM380026 750314	656	367	289	529	179
144	UM379591 331023	308	322	-14	283	0
145	UM379543 550815	846	673	173	372	22
146	UM380049 760606	None	336	-	None	None
147	UM380489 530403	390	336	54	343	0
148	UM380661 630128	442	370	72	354	4
149	UM379929 570719	390	340	50	339	0
150	UM382201 661013	333	305	28	323	0
151	UM382228 561204	1139	673	466	501	151
152	UM381542 620130	559	429	130	386	36
153	UM383118 720317	346	350	-4	293	0
154	UM325613 800916	435	344	91	374	24
155	UM383824 821226	455	375	80	360	10
156	UM301010 881231	449	349	100	381	31
157	UM383887 511108	705	380	325	550	200
158	UM384020 560221	429	357	72	356	6
159	UM380598 680522	2487	748	1739	985	635
160	UM221884 371223	1410	925	482	451	101
161	UM385424 830806	361	333	28	321	0
162	UM386007 770301	529	384	145	407	57
163	UM377005 760703	361	333	28	321	0
164	UM386591	361	296	65	361	11

	791201					
165	UM386592 890825	390	395	-5	293	0
166	UM382397 581203	493	375	118	392	42
167	UM329437 511228	1139	538	601	627	277
168	UM384292 821115	384	329	55	346	0
169	UM358122 730924	548	435	113	373	23
170	UM189492 600125	493	384	109	380	30
171	UM388630 870601	406	370	36	325	0
172	UM388673 670327	485	348	137	412	62
173	UM388675 720814	455	380	75	355	5
174	UM388059 801109	925	658	267	416	66
175	UM389145 770908	411	352	59	345	0
176	UM389157 821014	357	352	5	300	0
177	UM056242 620515	705	365	340	571	221
178	UM389148 661213	340	352	-12	309	0

APPENDIX B

MEASUREMENT

4. Example of ^{131}I percentage form

APPENDIX C

ADDITIONAL INFORMATION

5. Table summary of the medication used by the 178 Graves' disease patients and if it had an influence on thyroid function

Medication name	**Medication group**	**Influence on thyroid function (Yes/No)**
Amikacin	Aminoglycosides	No
Amoxycillin	Penicillins	No
Aqueous cream	Emollients and protectants	No
Aspirin	Salicylic acid and derivatives	No
Atenolol	Beta-blocking agents	Yes
Betaine hydrochloride	Mineral substitutes	No
Budesonide	Corticosteroids	No
Calcium carbonate	Calcium compounds	No
Captopril	Angiotensin-converting enzyme	No
Carbimazole	Sulphur-containing imidazole derivatives	Yes
Cefepime	Cephalosporins	No
Ciprofloxacin	Quinolones	No
Collagenase clostrid	Ointment	No
Dextran	Blood substitutes and plasma fractions	No
Dilitiazem	Benzothiazepine derivatives	No
Enalapril	Angiotensin-converting enzyme (ACE) inhibitors	No
Fenoterol	$Beta_2$-adrenoceptor agonists	No
Furosemide	Diuretics	No

Hydrochlorothiazide	Diuretics	No
Hydroxyzine	Diphenylmethane derivatives	No
Hyoscine butylbromide	Belladonna alkaloids semisynthetic	No
Isosorbride dinitrate	Organic nitrates	No
Methyl salicylate	Salicylic acid derivatives and capsicum	No
Nystatin	Antibiotics	No
Omeprazole	Proton pump inhibitors	No
Paracetamol	Anlides	No
Propranolol	Beta blocking agents	Yes
Resrepine	Rauwalfia alkoids	No
Thiamin	Vitamin B	No
Thyroxine	Thyroid hormones	Yes
Verapamil	Phenylalkylamine derivatives	No

APPENDIX C

ADDITIONAL INFORMATION

6. Summary of medications that can interfere with RAIU

AMIKACIN

Group:

Amikacin belongs to the group aminoglycosides (Gibbon 1997:262).

Indications:

Amikacin is used as part of the anti-infectives and antibacterials for systemic purposes and has already been used in medical practice for many years (Gibbon 1997:262). Amikacin has demonstrated outstanding lack of resistance problems, partly due to its resistance to the aminoglycoside-inactivating enzymes to which other aminoglycosides are more vulnerable. Gibbon (1997:262) recommends that amikacin only be used in situations where resistance to gentamicin and tobramycin presents a problem. Amikacin can play an important role in the management of infections caused by gram-negative bacilli that is resistant to drugs such as gentamicin and to bromycin (Berkow 1992:36).

Pharmacokinetics:

Quickly and entirely absorbed from the injection sites and dispersed to extracellular fluid and body tissues; high concentrations found in urine and highly perfused organs (Gibbon 1997:263). Diffusion into the cerebrospinal fluid (CSF) is poor even when the meninges are inflamed.

Half-life (elimination): Usually two to three hours, except in the cases of renal impairment and in neonates that can prolong its elimination.

Adverse effects:

The following adverse effects may occur from the use of amikacin:

- Nephrotoxicity (Gibbon 1997:263).
- Ototoxicity.
- Deterioration of renal function.
- Damage to the eighth cranial nerve, characterised by dizziness, nystagmus, vertigo and ataxia.
- Cochlear toxicity resulting in hearing loss.

- CNS adverse effects include neuromuscular blockade, headache, tremor, lethargy and sometimes organic brain syndrome.
- Other adverse effects that can occur include blood dyscrasias, electrolyte disturbances, hepatic damage, rashes, urticaria and fever.

Conclusion:

Amikacin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used amikacin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

AMOXYCILLIN

Group:

Amoxycillin belongs to the group of penicillins with an extended spectrum (Gibbon 1997:249).

Indications:

Amoxycillin is used as part of the anti-infectives and antibacterials for systemic purposes (Gibbon 1997:249). An important characteristic of amoxycillin is its broad-spectrum activity against a number of Gram-positive, Gram-negative cocci and bacilli. Amoxycillin is used for infections of the respiratory tract, GIT, urinary tract, soft tissue infections, as well as for cholecystitis and typhoid.

Pharmacokinetics:

Amoxycillin when taken orally is absorbed 85% and penetrates well into most body fluids (Gibbon 1997:250). It is metabolised in the liver and elimination mainly be renal tubular secretion.

Half-life: In the case of renal impairment prolonged, but usually 1-1.3 hours.

Adverse effects:

The following adverse effects may occur from the use of amoxycillin:

- Skin rash
- Diarrhoea

- Gastrointestinal irritation.

Conclusion:

Amoxycillin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used amoxycillin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

AQUEOUS CREAM

Group:

Aqueous cream belongs to the group of soft paraffin and fat products classified under emollients and protectants (Gibbon 1997:163).

Indications:

Aqueous cream is used to rehydrate and soothe the skin, especially in conditions of dryness, scaling and cracking of skin (Gibbon 1997:163).

Pharmacokinetics:

Emulsifying ointment 30 g, phenoxyethanol 1 g, purified water 69 g (Gibbon 1997:164).

Adverse effects:

Aqueous cream has no adverse effects.

Conclusion:

Aqueous cream therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used aqueous cream during the 6- and 24-hr ^{131}I RAIU examination need not to be excluded from the study group.

ASPIRIN

Group:

Aspirin belongs to the group salicylic acid and derivatives classified under analgesics of the CNS (Gibbon 1997:368).

Indications:

Aspirin is used for the following:

- Relief from mild pain symptoms
- Pyrexia
- Prophylaxis of platelet aggregation
- Rheumatic fever
- Acute and chronic inflammatory disorders (Gibbon 1997:368).

Pharmacokinetics:

Aspirin is quickly hydrolysed to the active metabolite, salicylate, which is then bound to albumin in serum (Gibbon 1997:368). Excreted by the kidneys.

Half-life: 15-20 minutes.

Adverse effects:

Aspirin may cause the following adverse effects when used:

- Gastric irritation causing abdominal pain, vomiting, nausea and even occult or overt mucosal bleeding.
- Gastric erosion and haemorrhage.
- Pseudo-allergic reactions.
- Tinnitus.
- Decreased hearing.
- Impairment of renal function.
- Renal papillary necrosis (Gibbon 1997:368).

Conclusion:

Aspirin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used aspirin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

ATENOLOL

Group:

Atenolol belongs to the group of beta blocking agents classified under beta-blocking agents used for the cardiovascular system (Gibbon 1997:138).

Indications:

Atenolol is indicated for the following conditions:

- Angina
- Arrhythmias
- Hypertension (Gibbon 1997:139).

Pharmacokinetics:

Atenolol is a lipophilic beta blocker and does not easily enter the CNS (Gibbon 1997:139). Excreted by the kidneys.

Half-life: 6-9 hours.

Adverse effects:

The following adverse effects can occur with the use of atenolol:

- Reduction in serum HDL
- Triglycerides increases
- Glucose utilisation impaired
- Bronchospasm
- Gastrointestinal disturbances
- Skin reactions.

Conclusion:

Atenolol therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used atenolol during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

BETAINE HYDROCHLORIDE

Group: Belongs to the group of mineral substitutes (*KLOREF Leaflet* 1998:1).

Indications: Indicated for hypokaemia.

Pharmacokinetics: Betaine hydrochloride pharmacological classification is electrolytes.

Adverse effects:

The following adverse effects can occur with the use of betaine hydrochloride:

- Hyperkalaemia
- Paraesthesia of the extremities
- Muscle weakness
- Paralysis
- Hypotension
- Cardiac arrhythmias.

Conclusion:

Betaine hydrochloride therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used betaine hydrochloride during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

BUDESONIDE

Group:

Budesonide is classified under corticosteroids for local use (Gibbon 1997:61).

Indications:

Budesonide is used for inflammatory conditions in the case of ulcerative colitis or Crohn's colitis (Gibbon 1997:60).

Pharmacokinetics:

Retention enema 3 mg and sodium chloride 2 mg/100ml (Gibbon 1997:61). Budesonide has a first-pass hepatic clearance of higher than 90% (Gibbon 1997:60).

Adverse effects:

The high first-pass hepatic clearance of budesonide reduces the risk of systemic adverse effects (Gibbon 1997:60).

Conclusion:

Budesonide therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used budesonide during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

CALCIUM CARBONATE

Group:

Calcium carbonate belongs to the calcium compounds group (Gibbon 1997:37).

Indications:

Calcium carbonate is indicated for patients with renal failure (Gibbon 1997:37).

Pharmacokinetics:

Calcium carbonate (Gibbon 1997:37).

Adverse effects:

The adverse effects associated with calcium carbonate include hypercalcaemia and 'milk-alkali' syndrome (Gibbon 1997:37).

Conclusion:

Calcium carbonate therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used calcium carbonate during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

CAPTOPRIL

Group:

Captopril is classified under the group of angiotensin-converting enzyme (ACE) inhibitors (Gibbon 1997:147).

Indications:

Captopril is indicated for the following medical conditions:

- Cardiac failure
- Hypertension (adults)
- Post infarction
- Nephropathy (Gibbon 1997:147).

Pharmacokinetics:

Captopril's protein binding is mainly to albumin. Captopril is to a degree metabolised in the liver and excreted by the renal system (Gibbon 1997:146). Half-life: Can be prolonged in the case of renal failure, but mostly between two to three hours.

Adverse effects:

The following adverse effects may be experienced when using Captopril:

- Hypotension
- Skin rashes
- Angioneurotic oedema
- Neutropenia, accompanied by thrombocytopenia and pancytopenia
- Proteinuria
- Renal failure (Gibbon 1997:147).

Conclusion:

Captopril therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used captopril during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

CARBIMAZOLE

Group:

Carbimazole belongs to the group of sulphur-containing imidazole derivatives that are classified under antithyroid preparations for thyroid therapy (Gibbon 1997:234).

Indications:

Carbimazole is indicated for hyperthyroidism (Gibbon 1997:234). The characteristics of carbimazole inhibit thyroid hormone synthesis by inhibiting the incorporation of iodide into tyrosine. Carbimazole also inhibits the coupling of iodotyrosines.

Pharmacokinetics:

Readily absorbed and converted into methimazole (Gibbon 1997:234). Carbimazole is metabolised in the liver and excreted by the renal system.

Half-life: Between four to 14 hours.

Adverse effects:

The following adverse effects may be experienced when using carbimazole:

- Pruritus
- Skin rashes
- Gastrointestinal disturbances
- Headache
- Mild arthralgia
- Urticaria
- Alopecia
- Drug-induced agranulocytosis
- Cholestatic hepatitis with jaundice
- Blood dyscrasias
- “Drug-fever” reactions (Gibbon 1997:235).

Conclusion:

Carbimazole therefore has characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used carbimazole during the 6- and 24-hr ^{131}I RAIU examination need be excluded from the study group.

CEFEPIME

Group:

Cefepime belongs to the group cephalosporins (fourth generation) and is classified under beta-lactam antibacterials (Gibbon 1997:252).

Indications:

Cefepime is effective for the use against Gram-positive and Gram-negative infections and this also includes *Ps. aeruginosa* (Gibbon 1997:252).

Pharmacokinetics:

Broad-spectrum semisynthetic beta-lactam antibiotics (Gibbon 1997:252).

Adverse effects:

No adverse effects indicated for cefepime (Gibbon 1997:255).

Conclusion:

Cefepime therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used cefepime during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

CIPROFLOXACIN

Group:

Ciprofloxacin belongs to the group quinolones classified under antibacterials for systemic use (Gibbon 1997:267).

Indications:

Ciprofloxacin is indicated for the treatment of infections caused by sensitive organisms (Gibbon 1997:267).

Pharmacokinetics:

Distributed effective throughout the body especially to the bones and soft tissue (Gibbon 1997:267). Metabolised in the liver. Small amounts excreted in the bile and in the faeces.

Half-life: Usually four to five hours and might be a little longer in the case of renal failure.

Adverse effects:

The following adverse effects may be experienced when using ciprofloxacin:

- Gastrointestinal disturbances such as abdominal pain, nausea, vomiting and diarrhoea
- Pseudomembranous colitis
- Central nervous system effects
- Skin rashes
- Urticaria
- Pruritus
- Vasculitis
- Stevens-Johnson syndrome
- Anaphylaxis
- Raised liver enzymes
- Hepatic necrosis
- Interstitial nephritis
- Blood disorders
- Reversible arthralgia (Gibbon 1997:267).

Conclusion:

Ciprofloxacin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used ciprofloxacin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

COLLAGENASE CLOSTRID

Group: Collagenase clostrid is an ointment (*Iruxol Mono Leaflet* 2001:1).

Indications: Collagenase clostrid is mainly used for wound cleaning.

Pharmacokinetics: Collagenase clostrid is pharmacokinetically classified as collagenase clostridiopeptidase.

Adverse effects: Local irritation or a burning sensation may be experienced with the use of collagenase clostrid.

Conclusion: Collagenase clostrid therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used collagenase clostrid during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

DEXTRAN

Group:

Dextran belongs to the group of blood substitutes and plasma fractions and is a branched-chain polysaccharide (Gibbon 1997:105).

Indications:

Dextran is indicated for the restore of intravascular volume in the emergency treatment of shock (Gibbon 1997:105). Dextran is also indicated to restore intravascular volume impending shock resulting from burns or haemorrhage.

Pharmacokinetics:

Metabolised mainly in the liver and excreted by the kidneys (Gibbon 1997:105).

Adverse effects:

The following adverse effects may be experienced when using dextran:

- Antigenicity
- Rash
- Pruritus
- Hypotension
- Anaphylaxis
- Bleeding
- Renal failure (Gibbon 1997:105).

Conclusion:

Dextran therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used dextran during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

DILTIAZEM

Group:

Diltiazem belongs to the group of benzothiazepine derivatives classified under calcium-channel blockers for the cardiovascular system (Gibbon 1997:145).

Indications:

Diltiazem is indicated for the following medical conditions:

- Angina
- Hypertension
- Supraventricular arrhythmias (Gibbon 1997:145).

Pharmacokinetics:

Diltiazem has a high first-pass hepatic metabolism (Gibbon 1997:145).

Half-life: Four to seven hours.

Adverse effects:

Diltiazem may cause the following adverse effects when used:

- Nausea
- Gastrointestinal upset
- Hypotension
- Dizziness
- Lightheadedness
- Ankle swelling
- Exfoliative dermatitis
- Lupus-like syndrome
- Gastrointestinal bleeding (Gibbon 1997:145).

Conclusion:

Diltiazem therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used diltiazem during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

ENALAPRIL

Group:

Enalapril belongs to the group of ACE inhibitors (Class II) classified under agents acting on the renin angiotensin system (Gibbon 1997:147).

Indications:

Enalapril is indicated for hypertension (Gibbon 1997:146).

Pharmacokinetics:

Enalapril is an angiotensin-converting enzyme inhibitor (Gibbon 1997:146) and contains enalapril maleate (Gibbon 1997:147).

Adverse effects:

No adverse effects indicated. The initial dosage for patients at risk of first-dosage hypotension and the elderly should be reduced to 5 mg (Gibbon 1997:147).

Conclusion:

Enalapril therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used enalapril during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

FENOTEROL

Group:

Fenoterol belongs to the group of $beta_2$-adrenoceptor agonists for systemic use and is classified under antiasthmatics of the respiratory system (Gibbon 1997:455).

Indications:

Fenoterol is indicated for asthma (Gibbon 1997:452).

Pharmacokinetics:

Fenoterol hydrobromide (Gibbon 1997:455).

Adverse effects:

No adverse effects indicated. Should only be used when needed, not on a regular basis (Gibbon 1997:452).

Conclusion:

Fenoterol therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used fenoterol during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

FUROSEMIDE

Group:

Furosemide belongs to the group of high-ceiling (loop) diuretics and is classified under diuretics for the cardiovascular system (Gibbon 1997:132).

Indications:

Furosemide is indicated for the following medical conditions:

- Oedema
- Hypertension
- Oliguria
- Hypercalcaemia (Gibbon 1997:132).

Pharmacokinetics:

Metabolised in the liver and excreted by the renal system (Gibbon 1997:133).
Half-life: 0.5-1 hour.

Adverse effects:

The following adverse effects may be experienced when furosemide is taken:

- Hypokalaemia
- Hypomagnesaemia
- Hyponatraemia
- Hypocalcaemia
- Hyperuricaemia
- Hypochloaemic alkalosis
- Dehydration

- Hypotension
- Hypovolaemic shock
- Gastro-intestinal disturbances
- Transient azotaemia
- Gout
- Hearing impairment
- Allergic vasculitis
- Rash
- Pruritus
- Photo-sensitivity
- Blood dyscrasias
- Hyperglycaemia
- Pancreatitis
- Jaundice (Gibbon 1997:133).

Conclusion:

Furosemide therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used furosemide during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

HYDROCHLOROTHIAZIDE

Group:

Hydrochlorothiazide belongs to the group of low-ceiling diuretics (thiazides) and is classified under diuretics (Gibbon 1997:130).

Indications:

Hydrochlorothiazide is indicated for the following medical conditions:

- Oedema
- Hypertension
- Cardiac failure (Gibbon 1997:130).

Pharmacokinetics:

Excreted by the renal system (Gibbon 1997:130).

Half-life: Can be as high as 15 hours.

Adverse effects:

The following adverse effects may be experienced when using hydrochlorothiazide:

- Hypokalaemia
- Hypochloraemic alkalosis
- Hyponatraemia
- Hypomagnesaemia
- Hyperuricaemia
- Gout
- Diabetes
- Increased serum calcium
- Hypercalcaemia
- Influences glomerular filtration rate
- Volume depletion
- Hypotension
- Gastro-intestinal reactions
- Haematological reactions
- Pancreatitis
- Photo-sensitivity
- Sulphonamide-type hypersensitivity reactions (Gibbon 1997:131).

Conclusion:

Hydrochlorothiazide therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used hydrochlorothiazide during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

HYDROXYZINE

Group:

Hydroxyzine belongs to the group of diphenylmethane derivatives and is classified under psycholeptics for the CNS (Gibbon 1997:408).

Indications:

CNS, for example anxiety (Gibbon 1997:408).

Pharmacokinetics:

The properties of hydroxyzine include antidopamine, antihistaminic, anxiolytic and hypnotic (Gibbon 1997:408).

Adverse effects:

No adverse effects indicated.

Conclusion:

Hydroxyzine therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used hydroxyzine during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

HYOSCINE BUTYLBROMIDE

Group:

Hyoscine butylbromide belongs to the group of belladonna alkaloids semisynthetic (quarternary ammonium compounds) and is classified under antispasmodic and anticholinergic agents and propulsives (Gibbon 1997:44).

Indications:

Hyoscine butykbromide is used because of the antispasmodic action on the gastrointestinal, biliary and genitourinary tract (Gibbon 1997:44).

Pharmacokinetics:

Properties similar to those of atropine (Gibbon 1997:44).

Adverse effects:

Adverse effects are very rarely experienced when taking hyoscine butylbromide, but the following may be experienced:

- Dry mouth
- Visual disturbances

- Tachycardia
- Central nervous system effects, for example fatigue and drowsiness
- Paradoxical stimulation
- Excitation (Gibbon 1997:44).

Conclusion:

Hyoscine butylbromide therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used hyoscine butylbromide during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

ISOSORBRIDE DINITRATE

Group:

Isosorbride dinitrate belongs to the group of organic nitrates and is classified under vasodilators used in cardiac disease (Gibbon 1997:120).

Indications:

Isosorbride dinitrate is indicated for the following medical conditions:

- Congestive cardiac failure
- Relief and prophylaxis of angina (Gibbon 1997:121).

Pharmacokinetics:

Metabolites less active in the urine and is excreted by the renal system (Gibbon 1997:21).

Half-life: One hour.

Adverse effects:

The following adverse effects may be experienced when using isosorbride dinitrate:

- Headache
- Tachycardia
- Nausea
- Vomiting
- Postural hypotension wit dizziness, weakness and syncope

- Bradycardia
- Methaeglobinaemia
- Blurred vision
- Dry mouth (Gibbon 1997:21).

Conclusion:

Isosorbride dinitrate therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used isosorbride dinitrate during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

METHYL SALICYLATE

Group:

Methyl salicylate belongs to the group of preparations with salicylic acid derivatives and capsicum and is classified under topical products for joints and muscle pain (Gibbon 1997:336).

Indications:

Methyl salicylate is indicated for pain of the muscles and joints (Gibbon 1997:336).

Pharmacokinetics:

Ointment (Gibbon 1997:336).

Adverse effects:

Adverse effects as for systemic agents (Gibbon 1997:336).

Conclusion:

Methyl salicylate therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used methyl salicylate during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

NYSTATIN

Group:

Nystatin belongs to the group of antibiotics and is classified as antifungals for dermatological use (Gibbon 1997:158-159).

Indications:

Nystatin is mainly used for the treatment of cutaneous and mucocutaneous infections (Gibbon 1997:159).

Pharmacokinetics:

Antimyotic antibiotic (Gibbon 1997:159).

Adverse effects:

Sensitisation or skin irritation is the only adverse effects stated by Gibbon (1997:159).

Conclusion:

Nystatin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used nystatin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

OMEPRAZOLE

Group:

Omeprazole belongs to the group of proton pump inhibitors (Gibbon 1997:41).

Indications:

Omeprazole is indicated for the following medical conditions:

- Gastric and duodenal ulcers
- Reflux oesophagitis
- Zollinger-Ellison syndrome (Gibbon 1997:41).

Pharmacokinetics:

Absorption takes place in the small intestine and is metabolised in the liver (Gibbon 1997:41). Omeprazole is excreted in the urine and the faeces.

Adverse effects:

The adverse effects associated with the use of omeprazole is gastrointestinal related and include diarrhoea, nausea, flatulence and constipation (Gibbon 1997:41). Headache and rashes can also be experienced.

Conclusion:

Omeprazole therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used omeprazole during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

PARACETAMOL

Group:

Paracetamol belongs to the group anlides and is classified under analgesics for the CNS (Gibbon 1997:369).

Indications:

Paracetamol is mainly indicated for pyrexia or mild to moderate pain (Gibbon 1997:369).

Pharmacokinetics:

Half-life: One to four hours (Gibbon 1997:369).

Paracetamol is conjugated in the liver and excreted renally.

Adverse effects:

The adverse effects that can occur with the use of paracetamol include the following:

- Skin reactions
- Neutropenia
- Thrombocytopenia
- Hepatic necrosis
- Renal necrosis (Gibbon 1997:369).

Conclusion:

Paracetamol therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that

used Paracetamol during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

PROPRANOLOL

Group:

Propranolol is classified under beta blocking agents (Gibbon 1997:137).

Indications:

Propranolol is indicated for the following medical conditions:

- Hypertension
- Angina
- Arrhythmia
- Hyperthyroidism
- Hypertrophic cardiomyopathy
- Prevention of cyanotic spells due to Fallot's tetralogy
- Anxiety
- Thyrotoxicosis
- Tremor
- Migraine prophylaxis (Gibbon 1997:137).

Pharmacokinetics:

Metabolised in the liver and eliminated in the urine and in faeces (Gibbon 1997:137).

Half-life: Three to six hours.

Adverse effects:

The adverse effects associated with the use of propranolol include:

- Bradycardia
- CNS effects
- Gastrointestinal disturbances
- Sleep disturbances
- Bronchospasm
- Hypotension

- Acute cardiac failure
- Skin reactions
- Nail changes
- Alopecia
- Transient eosinophilia (Gibbon 1997:137).

Conclusion:

Propranolol therefore has characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used propranolol during the 6- and 24-hr ^{131}I RAIU examination need to be excluded from the study group.

RESERPINE-0.25MG

Group:

Reserpine belongs to the group rauwalfia alkoids and is classified under antihypertensives (Gibbon 1997:124-125).

Indications:

Reserpine is indicated for mild to moderate hypertension (Gibbon 1997:124).

Pharmacokinetics:

Metabolised in the liver and excreted in the faeces (Gibbon 1997:124).

Half-life: 45-168 hours.

Adverse effects:

The following adverse effects can occur when using reserpine:

- Dizziness
- Drowsiness
- Lethargy
- Bradycardia
- Hypotension
- Decreased libido
- Nasal congestion
- Dry mouth

- Headache
- Depression
- Fluid retention
- Diarrhoea
- Nausea
- Vomiting
- Skin rashes
- Pruritus
- Thrombocytopenia (Gibbon 1997:124).

Conclusion:

Reserpine therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used reserpine during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

THIAMIN

Group:

Thiamin belongs to the group of vitamin B and is classified under vitamins (Gibbon 1997:80-81).

Indications:

Thiamin is indicated for any condition where a deficiency thereof has occurred (Gibbon 1997:81).

Pharmacokinetics:

Thiamin hydrochloride (Gibbon 1997:81).

Adverse effects:

Thiamin has been associated with the following adverse effects when intravenously used:

- Angioedema
- Respiratory distress
- Hypotension

- Vascular collapse (Gibbon 1997:81).

Conclusion:

Thiamin therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used thiamin during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

THYROXINE-0.05MG

Group:

T_4 is also known as levothyroxine sodium (Gibbon 1997:233).

Indications:

T_4 is indicated for hypothyroidism (Gibbon 1997:233).

Pharmacokinetics:

A low percentage of thyroxine is deiodinated in peripheral tissues to T_3 and some of T_4 is metabolised in the liver (Gibbon 1997:233). T_4 is excreted in the bile.

Half-life: Six to seven days.

Adverse effects:

The following adverse effects can occur when T_4 is used:

- Hyperthyroidism
- Skin reactions (Gibbon 1997:233).

Conclusion:

T_4 therefore has characteristics that can affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used T_4 during the 6- and 24-hr ^{131}I RAIU examination need to be excluded from the study group.

VERAPAMIL

Group:

Verapamil belongs to the group phenylalkylamine derivatives and is classified under calcium-channel blockers (Gibbon 1997:144).

Indications:

Verapamil is indicated for the following medical conditions:

- Angina
- Paroxysmal
- Supraventricular arrhythmias
- Atrial fibrillation
- Hypertension (Gibbon 1997:144).

Pharmacokinetics:

Verapamil is excreted in the urine (Gibbon 1997:144).

Half-life: Two to eight hours.

Adverse effects:

The following adverse effects may be experienced when using verapamil:

- Serious cardiovascular reactions
- Hypotension
- Bradycardia
- Asystole
- Congestive heart failure
- Pulmonary oedema
- Elevation of the liver enzymes
- Nausea
- Headache
- Dizziness
- Fatigue
- Facial flushing
- Gynaecomastia
- Gastrointestinal bleeding (Gibbon 1997:144).

Conclusion:

Verapamil therefore has no characteristics that affect the uptake of ^{131}I by the thyroid gland during the 6- and 24-hr ^{131}I RAIU examination. Patients that used verapamil during the 6- and 24-hr ^{131}I RAIU examination need not be excluded from the study group.

APPENDIX D

STATISTICS

7. Outprint of statistical data from the University of the Free State

NUMBER	HOSP_NUMBER	AGE	GENDER	RACE	HR6_UPTAKE_Perc	HR24_UPTAKE_Perc	T4	TSH	THYROID_SCAN	HR6_ACTIVITY	HR24_ACTIVITY	DIFFERENCE_6_24_RAIU	ABSORBED_ACTIVITY_Perc	MORE_ACTIVITY
1	UM321825	51	F	W	79.00	90.00	109.00	0.01	Increase	375	329	46	338	0
2	UM326493	41	F	B	90.00	97.00	150.00	<0.01	Increase	329	305	24	319	0
4	UM321390	49	F	B	69.00	67.00	153.00	<0.01	Increase	429	442	-13	287	0
5	UM210826	15	F	W	32.00	59.00	33.00	<0.01	Increase	925	502	423	620	270
6	UM323198	39	F	B	82.00	95.60	54.70	<0.01	Increase	361	310	51	345	0
7	UM322491	48	F	B	31.00	55.00	37.40	<0.01	Increase	955	538	417	525	175
8	UM322694	30	F	B	74.00	76.00	42.40	<0.01	Increase	400	390	10	304	0
10	UM323897	37	F	B	85.00	95.00	135.90	<0.01	Increase	348	312	36	331	0
11	UM049979	53	F	W	48.00	65.50	37.00	<0.01	Increase	617	452	165	404	54
12	UM324847	31	F	W	75.70	80.00	58.70	0	Increase	391	370	21	313	0
13	UM109632	43	F	W	55.90	75.60	47.40	<0.01	Increase	530	392	138	401	51
15	UM324708	15	F	W	65.00	60.00	73.90	<0.01	Increase	455	493	-38	273	0
16	UM326348	52	F	B	59.00	67.00	53.40	<0.01	Increase	502	442	60	336	0
17	UM326628	42	F	C	22.00	44.00	30.80	<0.01	Increase	1346	673	673	529	242
22	UM328554	30	F	W	83.00	79.00	145.80	<0.01	Increase	357	375	-18	282	0
23	UM328615	39	F	B	78.00	86.00	102.50	<0.01	Increase	380	344	36	327	0
24	UM328553	23	F	B	74.00	84.00	71.90	<0.01	Increase	400	352	48	336	0
26	UM328598	32	F	B	68.00	84.00	154.80	<0.01	Increase	435	352	83	374	24
27	UM329201	22	F	B	78.00	86.00	121.60	<0.01	Increase	380	344	36	327	0
29	UM329172	29	F	B	49.00	76.00	72.20	<0.01	Increase	604	390	214	459	109
31	UM331115	26	M	W	55.00	63.50	67.50	0.055	Increase	538	466	72	342	0
32	UM330652	48	F	B	61.70	74.50	46.00	0.03	Increase	480	397	83	358	8
33	UM304837	43	F	B	58.00	78.00	52.00	<0.01	Increase	510	380	130	398	48
34	UM332017	75	F	W	31.00	43.00	31.00	0.01	Increase	955	688	267	411	61
36	UM332201	59	F	B	55.00	80.00	50.00	<0.01	Increase	538	370	168	430	80
37	UM270611	49	F	B	37.30	70.40	60.00	<0.01	Increase	794	421	373	559	209
41	UM333093	50	F	B	57.00	77.70	73.30	<0.01	Increase	513	381	132	399	49
42	UM334716	45	M	B	72.00	91.00	77.00	<0.03	Increase	411	352	59	374	24
49	UM335951	62	F	W	50.00	70.00	63.20	<0.01	Increase	529	423	106	414	64
50	UM330657	25	F	B	15.00	40.00	59.20	<0.01	Increase	1973	740	1233	789	439
51	UM336765	52	F	B	92.30	98.00	37.00	<0.01	Increase	321	302	19	315	0
52	UM336960	35	F	B	75.00	96.50	154.80	0.01	Increase	395	307	88	381	31
53	UM337405	42	F	B	50.00	74.00	53.20	0.43	Increase	592	400	192	438	88
54	UM337310	33	F	B	57.00	67.00	55.00	<0.02	Increase	519	442	77	348	0
55	UM336754	38	F	B	55.70	70.00	45.30	<0.01	Increase	531	423	108	372	22
56	UM338415	51	F	B	61.00	80.00	60.50	<0.01	Increase	485	370	115	388	38
57	UM339695	20	F	B	80.00	87.00	113.80	<0.01	Increase	370	340	30	322	0
58	UM339830	40	F	B	87.00	86.00	114.00	<0.01	Increase	340	344	-4	292	0
59	UM226136	34	F	B	72.00	93.00	135.80	<0.01	Increase	411	318	93	382	32
62	UM341553	35	F	C	86.00	80.00	42.60	<0.03	Increase	344	370	-26	275	0
64	UM343576	38	F	B	52.00	79.00	131.00	<0.01	Increase	569	375	194	450	100
65	UM344221	30	F	W	72.90	77.00	154.80	<0.01	Increase	406	384	22	313	0
67	UM315130	33	F	B	25.80	41.40	36.30	<0.01	Increase	1147	715	432	475	125
68	UM342428	35	M	B	79.40	64.50	154.00	<0.01	Increase	373	459	-86	241	0
69	UM344748	62	F	B	50.20	74.00	67.00	<0.01	Increase	590	400	190	437	87
70	UM345534	47	F	W	74.00	82.00	78.00	<0.01	Increase	400	361	39	328	0
72	UM343608	34	F	B	78.00	87.00	70.00	<0.01	Increase	380	340	40	331	0
75	UM343605	44	M	B	79.00	92.00	26.00	<0.01	Increase	375	322	53	345	0

77	UM176724	49 F	C	49.00	76.00	43.10	0.01	Increase	604	390	214	459	109
78	UM343002	49 F	B	73.00	88.00	62.00	<0.01	Increase	406	336	70	357	7
79	UM328615	39 F	B	56.00	66.00	47.00	<0.01	Increase	529	449	80	349	0
80	UM351211	47 F	B	56.00	96.00	74.00	<0.01	Increase	529	308	221	508	158
83	UM351909	33 F	C	18.00	39.00	15.00	<0.01	Increase	1644	759	885	641	291
85	UM354052	54 F	B	58.00	73.00	59.60	<0.01	Increase	510	406	104	372	22
86	UM067246	21 M	W	74.00	59.50	149.70	<0.01	Increase	400	498	-98	238	0
87	UM336754	39 F	B	55.70	70.00	45.30	<0.01	Increase	531	423	108	372	22
88	UM353714	21 F	B	61.00	96.00	163.14	<0.03	Increase	485	308	177	466	116
90	UM356740	53 F	W	74.00	81.00	59.00	<0.01	Increase	400	365	35	324	0
91	UM357892	27 F	B	99.00	100.00	72.50	<0.01	Increase	299	296	3	299	0
94	UM351536	50 M	B	70.00	68.00	154.80	<0.01	Increase	423	435	-12	288	0
96	UM360149	45 F	B	73.00	93.00	76.80	<0.03	Increase	406	318	88	378	28
98	UM359929	35 F	B	60.00	68.00	63.00	<0.01	Increase	493	435	58	335	0
99	UM362578	36 F	C	96.00	89.00	115.00	<0.01	Increase	308	333	-25	274	0
100	UM362527	50 M	W	35.00	51.00	45.80	<0.01	Increase	846	580	266	432	82
101	UM288586	41 M	W	25.00	40.00	41.80	<0.01	Increase	1184	740	444	474	124
102	UM364785	47 F	W	89.00	97.00	154.00	0.01	Increase	333	305	28	323	0
103	UM234979	42 F	B	72.00	85.00	74.00	0.01	Increase	411	348	63	349	0
105	UM339836	41 F	B	48.00	66.00	51.40	<0.01	Increase	617	449	168	407	57
106	UM364217	17 F	B	51.00	78.00	60.00	<0.01	Increase	580	380	200	452	102
107	UM342105	28 F	W	41.90	63.00	54.20	<0.01	Increase	706	470	236	445	95
108	UM335307	39 F	B	56.70	69.00	56.60	<0.01	Increase	522	429	93	360	10
109	UM367708	44 F	B	80.00	84.00	146.00	<0.01	Increase	370	352	18	311	0
110	UM367382	26 F	B	82.00	84.00	77.20	<0.03	Increase	361	352	9	303	0
111	UM368464	34 F	B	80.00	90.00	71.70	<0.01	Increase	370	329	41	333	0
112	UM368475	38 M	B	77.00	82.90	54.80	<0.01	Increase	384	357	27	318	0
113	UM336839	38 F	W	50.00	71.90	39.10	<0.01	Increase	592	412	180	426	76
116	UM368578	47 F	B	77.00	88.00	42.10	<0.01	Increase	384	336	48	338	0
118	UM369229	37 F	B	84.00	85.00	155.00	<0.01	Increase	352	348	4	299	0
119	UM369194	34 F	B	63.00	79.00	79.30	<0.01	Increase	470	375	95	372	21
121	UM364098	51 M	B	65.00	94.00	53.80	<0.03	Increase	455	315	140	428	78
124	UM864859	37 M	B	63.00	81.00	82.20	0.01	Increase	470	365	105	381	31
125	UM372113	63 F	W	46.00	63.00	33.00	<0.01	Increase	644	470	174	406	56
126	UM364841	53 F	B	78.00	83.00	77.00	<0.01	Increase	380	357	23	300	0
127	UM373232	45 F	B	84.00	73.00	77.00	<0.03	Increase	352	406	-54	257	0
129	UM373375	17 F	B	82.00	89.00	72.00	<0.01	Increase	362	333	29	321	0
130	UM372935	49 F	B	72.00	95.00	76.10	<0.03	Increase	411	312	99	391	41
133	UM315902	62 M	W	43.00	57.00	28.60	<0.01	Increase	688	519	169	392	42
134	UM375892	45 F	B	60.00	81.00	30.90	<0.01	Increase	493	365	128	399	49
135	UM375922	38 F	C	71.00	80.00	42.80	<0.01	Increase	417	370	47	334	0
136	UM374247	36 F	B	84.00	83.00	154.80	<0.01	Increase	352	357	-5	292	0
137	UM307324	47 M	B	81.00	84.00	145.00	<0.01	Increase	365	352	13	307	0
138	UM378119	61 F	B	34.00	79.00	39.00	0.01	Increase	871	375	496	688	338
141	UM368463	30 F	B	31.00	69.00	44.30	<0.01	Increase	955	429	526	659	309
142	UM378673	16 M	B	42.00	66.00	52.00	<0.01	Increase	705	449	256	465	115
143	UM380026	30 F	C	45.10	80.70	90.00	<0.01	Increase	656	367	289	529	179
144	UM379591	72 F	B	96.00	92.00	88.00	<0.01	Increase	308	322	-14	283	0
145	UM379543	50 M	B	35.00	44.00	97.80	0.01	Increase	846	673	173	372	22
	UM380489	52 F	B	76.00	88.00	71.00	<0.01	Increase	390	336	54	343	0

148	UM380661	42 F	C	67.00	80.00	67.10	<0.03	Increase	442	370	72	354	4
149	UM379929	48 F	B	76.00	87.00	22.10	<0.01	Increase	390	340	50	339	0
150	UM382201	39 F	C	89.00	97.00	93.00	<0.01	Increase	333	305	28	323	0
151	UM382228	49 F	W	26.00	44.00	24.00	<0.01	Increase	1139	673	466	501	151
152	UM381542	43 F	W	53.00	69.00	122.50	<0.01	Increase	559	429	130	386	36
153	UM383118	33 F	B	85.50	84.70	154.00	<0.01	Increase	346	350	-4	293	0
154	UM325613	25 M	W	68.00	86.00	61.00	<0.01	Increase	435	344	91	374	24
155	UM383824	23 F	B	65.00	79.00	154.00	<0.01	Increase	455	375	80	360	10
158	UM384020	49 F	W	69.00	83.00	66.00	<0.01	Increase	429	357	72	356	6
159	UM380598	37 F	W	11.90	39.60	19.80	<0.01	Increase	2487	748	1739	985	635
161	UM385424	22 F	B	82.00	89.00	154.00	<0.01	Increase	361	333	28	321	0
162	UM386007	28 M	B	56.00	77.00	69.00	<0.01	Increase	529	384	145	407	57
163	UM377005	29 F	B	82.00	89.00	77.20	<0.03	Increase	361	333	28	321	0
164	UM386591	26 F	B	82.00	100.00	77.00	<0.01	Increase	361	296	65	361	11
165	UM386592	16 F	B	76.00	75.00	154.80	<0.01	Increase	390	395	-5	293	0
166	UM382397	47 F	B	60.00	79.00	23.60	<0.01	Increase	493	375	118	392	42
168	UM384292	23 F	B	77.00	90.00	110.00	<0.01	Increase	384	329	55	346	0
169	UM358122	32 M	B	54.00	68.00	28.00	0.01	Increase	548	435	113	373	23
171	UM388630	18 F	W	73.00	80.00	49.30	<0.01	Increase	406	370	36	325	0
172	UM388673	38 F	B	61.00	85.00	63.60	<0.01	Increase	485	348	137	412	62
173	UM388675	33 F	B	65.00	78.00	124.70	<0.01	Increase	455	380	75	355	5
174	UM388059	25 F	W	32.00	45.00	24.00	<0.01	Increase	925	658	267	416	66
175	UM389145	28 F	B	72.00	84.00	93.20	<0.01	Increase	411	352	59	345	0
176	UM389157	23 F	B	83.00	84.00	78.50	<0.01	Increase	357	352	5	300	0
177	UM056242	43 F	B	42.00	81.00	57.50	<0.01	Increase	705	365	340	571	221
178	UM389148	39 F	B	87.00	91.00	120.30	<0.01	Increase	340	352	-12	309	0

n = 14 patients 4 hr > 24 hr RNJH

The FREQ Procedure

Diff_Uptake_Perc	Frequency	Percent	Cumulative Frequency	Cumulative Percent
-45	1	0.81	1	0.81
-40	1	0.81	2	1.61
-39	1	0.81	3	2.42
-38	1	0.81	4	3.23
-35.6	1	0.81	5	4.03
-35	1	0.81	6	4.84
-33.1	1	0.81	7	5.65
-29	1	0.81	8	6.45
-27.7	1	0.81	9	7.26
-27	5	4.03	14	11.29
-25	2	1.61	16	12.90
-24	4	3.23	20	16.13
-23.8	1	0.81	21	16.94
-23	1	0.81	22	17.74
-22	1	0.81	23	18.55
-21.9	1	0.81	24	19.35
-21.5	1	0.81	25	20.16
-21.1	1	0.81	26	20.97
-21	4	3.23	30	24.19
-20.7	1	0.81	31	25.00
-20	3	2.42	34	27.42
-19.7	1	0.81	35	28.23
-19	3	2.42	38	30.65
-18	5	4.03	43	34.68
-17.5	1	0.81	44	35.48
-17	1	0.81	45	36.29
-16	4	3.23	49	39.52
-15.6	1	0.81	50	40.32
-15	3	2.42	53	42.74
-14.3	2	1.61	55	44.35
-14	4	3.23	59	47.58
-13.6	1	0.81	60	48.39
-13	6	4.84	66	53.23
-12.8	1	0.81	67	54.03
-12.3	1	0.81	68	54.84
-12	3	2.42	71	57.26
-11	3	2.42	74	59.68
-10	5	4.03	79	63.71
-9	3	2.42	82	66.13
-8.5	1	0.81	83	66.94
-8	7	5.65	90	72.58
-7	7	5.65	97	78.23
-5.9	1	0.81	98	79.03
-5.7	1	0.81	99	79.84
-5	1	0.81	100	80.65
-4.3	1	0.81	101	81.45

The FREQ Procedure

Diff_Uptake_Perc	Frequency	Percent	Cumulative Frequency	Cumulative Percent
-4.1	1	0.81	102	82.26
-4	2	1.61	104	83.87
-3	1	0.81	105	84.68
-2	2	1.61	107	86.29
-1	3	2.42	110	88.71
0.8	1	0.81	111	89.52
1	3	2.42	114	91.94
2	2	1.61	116	93.55
4	2	1.61	118	95.16
5	1	0.81	119	95.97
6	1	0.81	120	96.77
7	1	0.81	121	97.58
11	1	0.81	122	98.39
14.5	1	0.81	123	99.19
14.9	1	0.81	124	100.00

The MEANS Procedure

Analysis Variable : AGE

N	Lower Quartile	Median	Upper Quartile	Mean	Std Dev
124	30.0000000	39.0000000	48.0000000	38.8629032	12.1917836

Analysis Variable : AGE

Minimum	Maximum
15.0000000	75.0000000

The FREQ Procedure

GENDER	Frequency	Percent	Cumulative Frequency	Cumulative Percent
F	106	85.48	106	85.48
M	18	14.52	124	100.00

RACE	Frequency	Percent	Cumulative Frequency	Cumulative Percent
B	87	70.16	87	70.16
C	9	7.26	96	77.42
W	28	22.58	124	100.00

The FREQ Procedure

TSH	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	1	0.81	1	0.81
0.01	10	8.06	11	8.87
0.03	1	0.81	12	9.68
0.055	1	0.81	13	10.48
0.43	1	0.81	14	11.29
<0.01	99	79.84	113	91.13
<0.02	1	0.81	114	91.94
<0.03	10	8.06	124	100.00

THYROID_ SCAN	Frequency	Percent	Cumulative Frequency	Cumulative Percent
Increase	124	100.00	124	100.00

The MEANS Procedure

Variable	N	Lower Quartile	Median	Upper Quartile
HR6_ACTIVITY	124	380.0000000	438.5000000	564.0000000
HR24_ACTIVITY	124	344.0000000	370.0000000	429.0000000
DIFFERENCE_6_24_RAIU	124	28.0000000	76.0000000	168.5000000
ABSORBED_ACTIVITY_Perc	124	321.5000000	357.5000000	411.5000000

Variable	Mean	Std Dev	Minimum	Maximum
HR6_ACTIVITY	543.5725806	312.0323147	299.0000000	2487.00
HR24_ACTIVITY	404.3387097	104.9395402	296.0000000	759.0000000
DIFFERENCE_6_24_RAIU	139.2338710	229.9263972	-98.0000000	1739.00
ABSORBED_ACTIVITY_Perc	383.9032258	105.8538968	238.0000000	985.0000000

The FREQ Procedure

MORE_ACTIVITY	Frequency	Percent	Cumulative Frequency	Cumulative Percent
0	58	46.77	58	46.77
4	1	0.81	59	47.58
5	1	0.81	60	48.39
6	1	0.81	61	49.19
7	1	0.81	62	50.00
8	1	0.81	63	50.81
10	2	1.61	65	52.42
11	1	0.81	66	53.23
21	1	0.81	67	54.03
22	4	3.23	71	57.26
23	1	0.81	72	58.06
24	3	2.42	75	60.48
28	1	0.81	76	61.29
31	2	1.61	78	62.90
32	1	0.81	79	63.71
36	1	0.81	80	64.52
38	1	0.81	81	65.32
41	1	0.81	82	66.13
42	2	1.61	84	67.74
48	1	0.81	85	68.55
49	2	1.61	87	70.16
51	1	0.81	88	70.97
54	1	0.81	89	71.77
56	1	0.81	90	72.58
57	2	1.61	92	74.19
61	1	0.81	93	75.00
62	1	0.81	94	75.81
64	1	0.81	95	76.61
66	1	0.81	96	77.42
76	1	0.81	97	78.23
78	1	0.81	98	79.03
80	1	0.81	99	79.84
82	1	0.81	100	80.65
87	1	0.81	101	81.45
88	1	0.81	102	82.26
95	1	0.81	103	83.06
100	1	0.81	104	83.87
102	1	0.81	105	84.68
109	2	1.61	107	86.29
115	1	0.81	108	87.10
116	1	0.81	109	87.90
124	1	0.81	110	88.71
125	1	0.81	111	89.52
151	1	0.81	112	90.32
158	1	0.81	113	91.13
175	1	0.81	114	91.94

82	1	0.81	100	80.65
87	1	0.81	101	81.45
88	1	0.81	102	82.26
95	1	0.81	103	83.06
100	1	0.81	104	83.87
102	1	0.81	105	84.68
109	2	1.61	107	86.29
115	1	0.81	108	87.10
116	1	0.81	109	87.90
124	1	0.81	110	88.71
125	1	0.81	111	89.52
151	1	0.81	112	90.32
158	1	0.81	113	91.13
175	1	0.81	114	91.94

The FREQ Procedure

MORE_ACTIVITY	Frequency	Percent	Cumulative Frequency	Cumulative Percent
179	1	0.81	115	92.74
209	1	0.81	116	93.55
221	1	0.81	117	94.35
242	1	0.81	118	95.16
270	1	0.81	119	95.97
291	1	0.81	120	96.77
309	1	0.81	121	97.58
338	1	0.81	122	98.39
439	1	0.81	123	99.19
635	1	0.81	124	100.00

n = 58 (46,7 %) binne perke 110 MBq - 350 MBq

The MEANS Procedure

Variable	N	Lower Quartile	Median	Upper Quartile	Mean
HR6_UPTAKE_Perc	124	51.5000000	67.5000000	78.0000000	63.5782258
HR24_UPTAKE_Perc	124	69.0000000	80.0000000	87.0000000	76.9395161
T4	124	46.5000000	67.3000000	105.7500000	77.7430645

Variable	Std Dev	Minimum	Maximum
HR6_UPTAKE_Perc	19.1500093	11.9000000	99.0000000
HR24_UPTAKE_Perc	14.6656327	39.0000000	100.0000000
T4	41.0592328	15.0000000	163.1400000

The CORR Procedure

2 Variables: HR6_ACTIVITY T4

Simple Statistics

Variable	N	Mean	Std Dev	Median
HR6_ACTIVITY	124	543.57258	312.03231	438.50000
T4	124	77.74306	41.05923	67.30000

Simple Statistics

Variable	Minimum	Maximum
HR6_ACTIVITY	299.00000	2487
T4	15.00000	163.14000

Spearman Correlation Coefficients, N = 124
Prob > |r| under H0: Rho=0

	HR6_ ACTIVITY	T4
HR6_ACTIVITY	1.00000	-0.57574 → correlation coefficient.
		P <.0001
T4	-0.57574	1.00000
	<.0001	

The CORR Procedure

2 Variables: HR24_ACTIVITY T4

Simple Statistics

Variable	N	Mean	Std Dev	Median
HR24_ACTIVITY	124	404.33871	104.93954	370.00000
T4	124	77.74306	41.05923	67.30000

Simple Statistics

Variable	Minimum	Maximum
HR24_ACTIVITY	296.00000	759.00000
T4	15.00000	163.14000

Spearman Correlation Coefficients, N = 124
Prob > |r| under H0: Rho=0

	HR24_ ACTIVITY	T4
HR24_ACTIVITY	1.00000	-0.45253 <.0001
T4	-0.45253 <.0001	1.00000

The CORR Procedure

2 Variables: HR6_UPTAKE_Perc T4

Simple Statistics

Variable	N	Mean	Std Dev	Median
HR6_UPTAKE_Perc	124	63.57823	19.15001	67.50000
T4	124	77.74306	41.05923	67.30000

Simple Statistics

Variable	Minimum	Maximum
HR6_UPTAKE_Perc	11.90000	99.00000
T4	15.00000	163.14000

Spearman Correlation Coefficients, N = 124
Prob > |r| under H0: Rho=0

	HR6_UPTAKE_Perc	T4
HR6_UPTAKE_Perc	1.00000	0.57427 <.0001
T4	0.57427 <.0001	1.00000

The CORR Procedure

2 Variables: HR24_UPTAKE_Perc T4

Simple Statistics

Variable	N	Mean	Std Dev	Median
HR24_UPTAKE_Perc	124	76.93952	14.66563	80.00000
T4	124	77.74306	41.05923	67.30000

Simple Statistics

Variable	Minimum	Maximum
HR24_UPTAKE_Perc	39.00000	100.00000
T4	15.00000	163.14000

Spearman Correlation Coefficients, N = 124
Prob > |r| under H0: Rho=0

	HR24_UPTAKE_Perc	T4
HR24_UPTAKE_Perc	1.00000	0.45557 <= <.0001
T4	0.45557 <.0001	1.00000

The MEANS Procedure

Analysis Variable : Diff_Uptake_Perc

Lower Quartile	Median	Upper Quartile	Mean	Std Dev
-20.3500000	-13.0000000	-7.0000000	-13.3612903	10.9806904

Analysis Variable : Diff_Uptake_Perc

Minimum	Maximum
-45.0000000	14.9000000

The FREQ Procedure

Group		Frequency	Percent	Cumulative Frequency	Cumulative Percent
1	6>24	14	11.29	14	11.29
2	6≤24	110	88.71	124	100.00

Transit patterns

APPENDIX F

ETHICS

8. Letter of approval from the ethics committee of the University of the Free State

UNIVERSITEIT VAN DIE VRYSTAAT
UNIVERSITY OF THE FREE STATE
YUNIVESITHI YA FREISTATA

Direkteur: Fakulteitsadministrasie / Director: Faculty Administration
Fakulteit Gesondheidswetenskappe / Faculty of Health Sciences

Research Division
Internal Post Box G40
☎(051) 4052812
Fax nr (051) 4444359

E-mail address: gndkhs.md@mail.uovs.ac.za

Ms H Strauss

2006-03-17

MS J HORN
DEPT OF NUCLEAR MEDICINE
FACULTY OF HEALTH SCIENCES
UFS

Dear Ms Horn

ETOVS NR 40/06
RESEARCHER: MS J HORN
PROJECT TITLE: THE ANALYSIS OF 6- AND 24 HOUR IODINE-131 THYROID UPTAKE IN PATIENTS WITH GRAVES' DISEASE AT UNIVERSITAS HOSPITAL.

You are hereby kindly informed that the Ethics Committee approved the above-mentioned study at their meeting held on 14 March 2006. Please note that a signed copy of the permission letter obtained from Prof Otto, Dept of Nuclear Medicine has to be submitted to the Ethics Committee for record purposes.

Your attention is kindly drawn to the following:

- A progress/final report have to be submitted after completion of the study or within a year after approval of the project
- That all extentions, amendments, serious adverse events, termination of a study etc have to be reported to the Ethics Committee
- These documents have been accepted as complying with the Ethics Standards for Clinical Research based on FDA, ICH GCP and Declaration of Helsinki guidelines as well as the Clinical Trials Guidelines 2000: Dept of Health RSA and MRC Guidelines on Ethics for Medical Research

Will you please quote the Etovs number as indicated above in subsequent correspondence to the secretariat.

Yours faithfully

DIRECTOR: FACULTY ADMINISTRATION
CC PROF AC OTTO, DEPT OF NUCLEAR MEDICINE, FACULTY OF HEALTH SCIENCES, UFS

ETHICS COMMITTEE

OF THE FACULTY OF HEALTH SCIENCES

ATTENDANCE LIST OF THE MEETING HELD ON 14 MARCH 2006

FACULTY MEMBERS (CLINICAL)

Prof BB Hoek	Chairperson M.B. Ch.B. (Pret) M.Med. (Paed.)(UOFS), D.G.G. (UOFS) Department: Paediatrics and Child Health	Present
Prof R Barry	Vice-chairperson M.B. Ch.B. (Stell.), M.Med. (Surgery)(UOFS) Department: Surgery	Present
Prof L Goedhals	M.B. Ch.B. (U.C.T.) M.Med (Rad.T.) UOFS Department: Oncotherapy	Present
Prof PH Wessels	MB. Ch.B; M.Med.(O. et G.) (UFS), L.K.O.G. (SA); MD (UOFS) Department: Obstetrics and Gynaecology	Present
Dr WJ Steinberg	MBBch (Wits) DPH; DTM & H (Wits) M.Fam.Med (UOFS) Dip. Obst (SA) Dept of Family Medicine	Absent
Prof WH Kruger	M.B. Ch.B (UOFS) M.Med. (Community Health) (UOFS), MBA (PU for CHE) Dept of Community Health	Present
Dr ND van der Merwe	M.B. Ch.B (UOFS) Dip. Av Med. M.Med (Internal Medicine) FCP (SA) Add. Qualification: Cardiology Dept of Cardiology	Absent
Ms M Nel	B.A. (Urbanology) B.A. Hons. (Statistics) M.Med (Biostatistics) (UOFS) Dept of Biostatistics	Present

SCHOOL OF NURSING REPRESENTATIVE		
Prof Y Botma (lady)	B. Soc.Sc (Nursing) Honn, M. Soc.Sc., Ph.D. (UFS) IRENSA Diploma in International Research Ethics 2005 School of Nursing	Present
Ms DE Botha (lady)	M. Soc.Sc (Nursing) (UOFS) School of Nursing	Present
REPRESENTATIVE OF SCHOOL OF ALLIED HEALTH PROFESSIONS		
Dr S van Vuuren (lady)	B. Occupational Therapy (Stell.) Head: School of Allied Health Professions	Present
Ms SM van Heerden (lady)	M. Occupational Therapy (UOFS) Dept of Occupational Therapy	Present
REPRESENTATIVE OF THE CENTRAL UNIVERSITY OF TECHNOLOGY, FREE STATE		
Prof L de Jager	Director: School of Health Technology Faculty of Health and Environmental Sciences Central University of Technology, Free State Bloemfontein	Present
RELIGIOUS/LAY MEMBER		
Rev MJ Kofa (Coloured)	MA Practical Theology (UOFS) Department: Biblical Studies	Present
Ms KM Jingosi (Lady)	Social Auxiliary Work (SA Council for Social Service Professions) Child and Family Welfare Society	Present
LEGAL MEMBER		
Prof H Oosthuizen	B.Iur., LL.B., LL.D. (UOFS) Department: Criminal Law	Present
Adv R-M Jansen (secundus) (lady)	B.Soc.Sc. (Nursing) Honn. B.Iur., LL.B., LL.M. (UOFS) Department: Private Law	Absent

14/03/06

EX OFFICIO MEMBERS *(not entitled to vote)*

Dr S Kabane	M.B. Ch.B. (Medunsa) Chief Executive Officer Universitas Hospital Bloemfontein	Absent
Dr NRJ van Zyl	M.Med. (UOFS) Business MBL (UNISA) Clinical Head: Universitas Hospital Bloemfontein	Absent
Ms MA Mabandla	Representative Universitas Hospital Bloemfontein	Absent
Mr ST Mohapi	Senior Executive Officer Free State Psychiatric Complex Bloemfontein	Absent
Dr BM Masitha	M.B.Ch.B. B.Sc Hons Health Sciences IFE - Nigeria B.Sc NBLS – ROMA H.O.C.S. – Chief Medical officer Free State Psychiatric Complex Bloemfontein	Absent
Ms MA Madolo	Senior Executive Officer Pelonomi Hospital Bloemfontein	Absent
Ms AS Sesing	M.Soc.Sc. (Nursing) (UFS) Chief Executive Officer National District Hospital Bloemfontein	Absent

DIRECTOR: FACULTY ADMINISTRATION
/hs

APPENDIX F

ETHICS

9. Letter requesting permission to perform research project

THE UNIVERSITY OF THE ORANGE FREE STATE

Department of Nuclear Medicine
Faculty of Medicine
Universitas Hospital

✉ 339 BLOEMFONTEIN 9300 REPUBLIC OF SOUTH AFRICA
☎ (051) 4053487/8

22 November 2005

PERMISSION TO PERFORM RESEARCH PROJECT

Dear Dr. Kabane

I, Jenine Horn hereby ask permission to perform a retrospective analytical study in the Nuclear Medicine Department (NMD) at Universitas Hospital, where I am a NM radiographer. This project will consist of the use of patient files of the NMD at Universitas Hospital. All patient information will be kept confidential. I will need this information to complete my Magister in Nuclear Medicine at the Central University of Technology. The project details and a short description of the advantages of this project will be described below.

Title: THE ANALYSIS OF THE 6- AND 24 HOUR IODINE-131 THYROID UPTAKE IN PATIENTS WITH GRAVES' DISEASE FOR THERAPY DOSE CALCULATIONS

Rationale: The 6hr and 24 hr ^{131}I uptake measurements for patients with Graves' disease require a costly prolonged stay in hospital or the return to the clinic on an outpatient basis. If the 6 hr ^{131}I uptake measurement alone proves to be sufficient to calculate the therapeutic dose for Graves' disease patient cost and hospital stay could be reduced significantly.

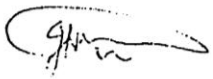
Methodology: A retrospective study will be done to analyse and compare the 6 hr and 24 hr uptake measurements in patients with Graves' disease in the Free State. The sample will include plus minus 100 patients, male and female varying in ages clinically diagnosed with Graves' disease. The sample will be obtained from patient files at the Nuclear Medicine department Universitas Hospital from 2004 to the end of 2005.

Expected outcomes: An only 6 hr RAIU will lead to a decrease in hospitalisation time of the patient as the patient will not have to stay overnight or return the next day for the 24 hr ^{131}I uptake measurement. On the other hand the 6 hr ^{131}I uptake value might not correlate with the 24 hr ^{131}I uptake, the 24 hr ^{131}I thyroid uptake

will be justified to calculate the correct ^{131}I therapeutic dose. The disparty between the 6 hr and 24 hr ^{131}I uptake values will also justify the extra cost with regards to prolonged hospitalisation or additional outpatient visits.

These results will establish more economically effective future radioactive iodine treatment approaches and protocols of Graves' disease in the Free State. Attached to this document is a letter from Prof. A.C. Otto supporting this project. I hope to hear from you soon with regards to permission about my research project.

Your sincerely



Je'nine Horn
Department of Nuclear Medicine
(051) 405 3487

APPENDIX F

ETHICS

10. Consent letter from the director of Universitas Hospital

FREE STATE PROVINCE

Ref. no.: H4/3/2

29 November 2005

Me Je'nine Horn
Department Nuclear Medicine
Universitas Hospital

Dear Me Horn

RESEARCH PROJECT: THE ANALYSIS OF THE 6- AND 24 HOUR IODINE-131 THYROID UPTAKE IN PATIENTS WITH GRAVES' DISEASE FOR THERAPY DOSE CALCULATIONS.

Your letter dated 22 November 2005 regarding the abovementioned is relevant.

Herewith permission for the mentioned project to be done at Universitas Academic Hospital on condition that approval is obtained from the Ethics Committee.

No findings can be published without permission of the Chief Executive Officer.

Yours sincerely

DR NIC R J VAN ZYL
HEAD: CLINICAL SERVICES

HEAD: CLINICAL SERVICES: **DR N R J VAN ZYL**, UNIVERSITAS TERTIARY HOSPITAL ● Private Bag X20660, Bloemfontein,9300 ● Tel. no.: 051-4052866 ● Fax: 051-4440792 ● Room 1129, First Floor, Universitas Tertiary Hospital ● E-mail: vanzylnr@doh.ofs.gov.za

APPENDIX F

ETHICS

11. Consent and support letter from the chief specialist of the Nuclear Medicine Department of the Universitas Hospital

THE UNIVERSITY OF THE ORANGE FREE STATE

Department of Nuclear Medicine
Faculty of Medicine
Universitas Hospital
✉ 339 BLOEMFONTEIN 9300 REPUBLIC OF SOUTH AFRICA
☎ (051) 4053487/8

To Whom It May Concern

It is general knowledge that there is various patterns in iodine metabolism in different patients with Grave's disease. Therefore, it is necessary that every patient should be evaluated individually to determine the radio-active dose for therapy.

This analysis gives an overview of the appearance of the iodine metabolism and therefore emphasizes the importance thereof. It is an important contribution among others endocronologists, radiotherapist and Nuclear Medicine radiologists. Not only locally but also elsewhere in the world. This study will probably arouse interest not only nationally, but internationally as well. Due to the general application of radio-active iodine therapy for Grave's disease which almost completely replaces surgery.

Prof AC Otto

LANGUAGE EDITING CERTIFICATE

I hereby declare that the protocol entitled "THE ANALYSIS OF 6- AND 24-HOUR IODINE-131 THYROID UPTAKE IN PATIENTS WITH GRAVES'S DISEASE AT UNIVERSITAS HOSPITAL" by JE'NINE HORN was edited for language usage by me. It was proofread according to the Oxford English language. The protocol is submitted in fulfilment of the requirements for the degree Magister Technologiae in Radiography (Nuclear Medicine) (NVP50AT) in the FACULTY OF HEALTH AND ENVIRONMENTAL SCIENCES, CENTRAL UNIVERSITY OF TECHNOLOGY, FREE STATE (CUT).

NAME: Mrs S.C.J. Liebenberg
12 Coligny Road
Park West
Bloemfontein
9301

TEL. NO.: 083 394 0093/(051) 444 1010/

DATE: 28 November 2007

SIGNATURE: S.C.J. Liebenberg