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Original Article

Predicting Therapeutic Radioiodine Activity in Graves' Disease Using Thyroidal Technetium-99m (Tc-99m) Uptake Values

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ABSTRACT

Objective: To estimate 24-hour radioiodine uptake in patients with Graves' disease using 20-minute Tc-99m uptake values for calculating radioiodine therapeutic dose.
Study Design: Prospective observational study.
Place and Duration of Study: Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from Mar 2022 to Mar 2023.
Methodology: A total of 131 patients with Graves' disease who were referred to our center for radioiodine therapy (RAIT) were selected prospectively. Patients were explained pre-requisites, procedure, and precautionary measures in detail, and informed written consent was obtained. All patients underwent 24-hour radioiodine uptake (RAIU24hrs) and 20-minute Tc-99m uptake (TcU20min) measurements after oral ingestion of radioiodine (RAI) and intravenous injection of Tc-99m, respectively. Logarithmic regression analysis was done to correlate RAIU24hrs and TcU20min values. A *p*-value of less than 0.05 was considered significant.
Results: Of 131 patients, 89(67.9%) were female, while 42(32.1%) were male, with a mean age of 46.93±13.39 years. The mean TcU20min was 18.93±12.08% while the mean RAIU24hrs was 62.68±13.93%. Logarithmic regression analysis showed a significant correlation ($p<0.001$) between RAIU24hrs and TcU20min, which is described by following equation: Estimated RAIU24hrs = 13.99 x ln (TcU20min) + 25.93; R2 = 0.898.
Conclusion: RAIU24hrs can be predicted from TcU20min, thus providing an alternative, simple, cost-effective, and convenient method for therapeutic radioiodine dose calculation.

Keywords: Graves' Disease, Radioiodine Uptake, Radioiodine Therapy, Tc-99m Uptake.

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INTRODUCTION

Graves' disease (GD) is a common autoimmune thyroid disorder causing excessive hormone production and is a leading cause of hyperthyroidism, affecting about 1% of the global population.[1] Its incidence varies by age, gender, ethnicity, and location, with women in their 30s and 40s most affected. Robert James Graves first described the condition, which arises from immune system breakdown leading to constant stimulation of the thyroid by TSH receptor antibodies.[2] GD has significant health impacts, especially in older adults, including cardiovascular and mental health risks.[3] Undiagnosed cases increase patient and healthcare costs, making early detection and treatment critical.[4]

There are three main treatments: antithyroid medications, radioactive iodine therapy (RAIT), and surgery. Treatment choice depends on clinical factors and patient preferences.[5] RAIT is effective, particularly when medical therapy fails, and has become first-line in the US per NICE guidelines due to its cost-effectiveness; however, it remains a second-line option in the UK and parts of Asia.[6]

Selecting suitable patients and calculating the appropriate dose are crucial for RAIT's success, though optimal dosing remains debated. The conventional method uses radioactive iodine uptake tests at 3 and 24 hours, but exposes patients to radiation and requires lengthy assessments.[7] Technetium Pertechnetate (Tc-99m), used since 1971 for thyroid imaging, offers advantages such as lower radiation, shorter half-life, and quicker uptake measurement (20 minutes).[8] Because Tc-99m uptake parallels that of iodine in GD, it could potentially replace RAI uptake for therapeutic dosing. This study aims to correlate TcU20min with RAIU24hrs to develop a faster, safer, and more convenient dosing method for patients.

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The primary objective of this study is to investigate the relationship between the 20-minute technetium-99m thyroid uptake (TcU20min) and the conventional 24-hour radioiodine uptake (RAIU24hrs) in patients diagnosed with Graves' disease. By establishing a reliable correlation between these two measurements, the study seeks to introduce a novel approach for calculating the therapeutic radioiodine dose required for treatment. This method is intended to be faster, as it significantly reduces the waiting time from 24 hours to just 20 minutes, safer by potentially minimising radiation exposure and associated risks, and more convenient for both patients and healthcare providers.

METHODOLOGY

This prospective study was conducted at Nuclear Medical Centre, Armed Forces Institute of Pathology, Rawalpindi Pakistan, from March 2022 to March 2023 over a period of one year. The study protocols were approved by the Institutional Review Board of the Armed Forces Institute of Pathology before the start of study (IRB no. FC-NMC21-11/READ-IRB/22/1454). The WHO sample size calculator was used to calculate the sample size with a prevalence of GD 24.8%, a margin of error 5%, and a confidence interval 95%, sample size came out to be 131 patients.[9] All patients were selected by a non-probability consecutive sampling technique. Informed written consent was obtained from all the patients.

Inclusion Criteria: Patients of either gender or age, diagnosed with Graves' Disease, who were referred to our center for RAIT were included in the study.

Exclusion Criteria: Individuals with a history of functional thyroid disorders, patients who have been taking Thionamide or iodine-containing drugs like Amiodarone, having a history of radioiodine uptake, or having undergone iodine contrast studies in the last 6 months were excluded from the study. Pregnancy and lactation are absolute contraindications for RAIT.

The diagnosis of GD was made by the referring physician based on clinical features, thyroid functions, autoimmune profile, and thyroid scan (Tc-99m) in required cases. All patients were evaluated by thorough history and relevant clinical examination. Information regarding any contrast procedure in the last 6 months, use of iodine-containing drugs like amiodarone, or use of antithyroid drugs, and any diseases interfering with thyroid uptake was obtained. The majority of the patients were on antithyroid medications before reporting to our center. All patients were advised to discontinue antithyroid medications and a high iodine content diet for at least 7 days before therapy. All females were specifically asked for pregnancy status, and in doubtful cases, a urine pregnancy test was advised. Informed written consent was obtained from all patients, and patients were informed of the procedure, its outcome, complications, risk of hypothyroidism, delaying pregnancy for 4-6 months, and radiation safety measures to prevent unnecessary exposure to surrounding people.

All patients underwent RAI uptake studies and Tc-99m thyroid scintigraphy to determine Tc-99m uptake in accordance with Society of Nuclear Medicine procedural guidelines.[12] RAI uptake was done at 1, 3, and 24 hours after oral administration of RAI (0.1 – 0.3 mCi). The RAI percentage uptake was calculated as the ratio of background corrected count rate of thyroid gland to the background count rate of the neck phantom using Captus ® 4000e Thyroid Uptake System. The Tc-99m thyroid scintigraphy was done 20 min after intravenous administration of Tc-99m (2 – 10 mCi) using Cor Cam Gamma Camera System (DDD-Diagnostic Denmark) with a 128 x 128-pixel matrix and 1.0 zoom. The Tc-99m percentage uptake was calculated as the ratio of background-corrected count rate over thyroid relative to pre-scan injected activity counts.

All the data, including patient demographic data, duration of symptoms, use of antithyroid medications, baseline thyroid functions, RAIU, and Tc-99m uptake, were recorded on a pre-designed proforma. Data was entered and analyzed using Statistical Package for the Social Sciences (IBM SPSS) version 21. Mean±SD was computed for continuous variables, while categorical variables were presented as frequency and percentages. Logarithmic regression analysis was done to correlate RAIU and Tc-99m uptake values. A p-value of less than 0.05 was considered significant.

RESULTS

Of 131 patients, 89(67.9%) were female, while 42(32.1%) were male, with a female-to-male ratio of 2.11:1. The mean age of the patients was 46.93±13.39 years, with an age range of 21 to 85 years. The mean duration of hyperthyroid symptoms was 37.84±38.57 months (range: 01–180 months) while mean duration of antithyroid medication was 33.80±35.35 months (range: 0–120 months). The mean TcU20min was 18.93±12.08% (range: 0.30–44.60) while mean RAIU3hrs was 40.14±20.76% (range: 8.90–102.90).

RAIU24hrs was 62.68±13.93% (range: 26.70–85.10) as shown in Table.

Table: Baseline characteristics of patients (n=131)

Characteristics	Values
Age (years) (Mean±SD)	46.93±13.39
Gender n(%)	
Male	42(32.1%)
Female	89(67.9%)
Symptoms Duration (Mean±SD), months	37.84±38.57
ATD duration (Mean±SD), months	33.80±35.35
TSH (Mean±SD), mIU/l	0.17±0.52
Tc-99m Uptake at 20 min (Mean±SD in %)	18.93±12.08
RAI Uptake (Mean±SD in %)	
At 3 hours	40.14±20.76
At 24 hours	62.68±13.93

ATD= Antithyroid drugs, TSH=Thyroid Stimulating Hormone, Tc-99m= Technetium-99m, RAI=Radioactive Iodine

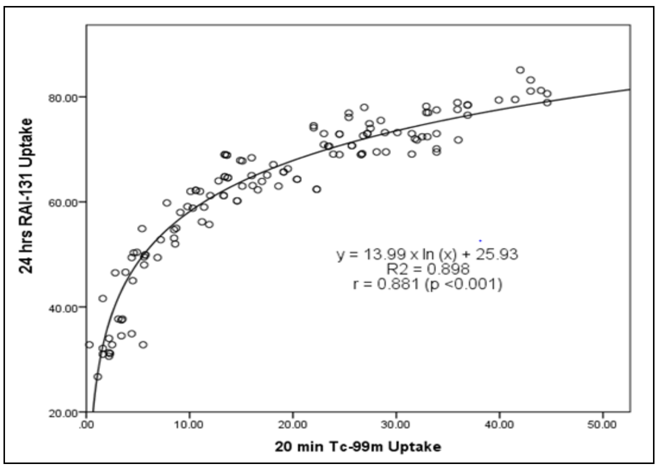

Figure-1: Scatter graph for TcU20min vs RAIU24hrs along with regression equation

A logarithmic regression analysis was done to generate a mathematical equation that would describe relationship between TcU20min values and RAIU24hrs values using RAIU24hrs value as dependent variable and natural log of TcU20min as independent variable. The relationship between TcU20min and RAIU24hrs is shown in Figure-1 and is given by formula:

Estimated RAIU24hrs = 13.99 x ln (TcU20min) + 25.93

[R2 = 0.898, r (correlation coefficient) = 0.881, p<0.001]

This equation can be used to estimate the value of RAIU24hrs, which can be used to calculate therapeutic RAI dose. The Scan showing uptake of Tc-99 m RAI images is shown in Figure-2.

DISCUSSION

The study demonstrates that 20-minute TcU-99m uptake strongly correlates with 24-hour RAIU, serving as a reliable predictor for radioiodine dose calculation. This approach eliminates the need for delayed 24-hour measurements, significantly streamlining the clinical workflow for Graves' disease management. By reducing patient visits and logistical overhead, the method offers a more convenient, cost-effective, and time-efficient alternative to traditional protocols. Consequently, these findings support utilizing Tc-99m uptake as a simplified yet accurate tool for optimizing therapeutic activity.

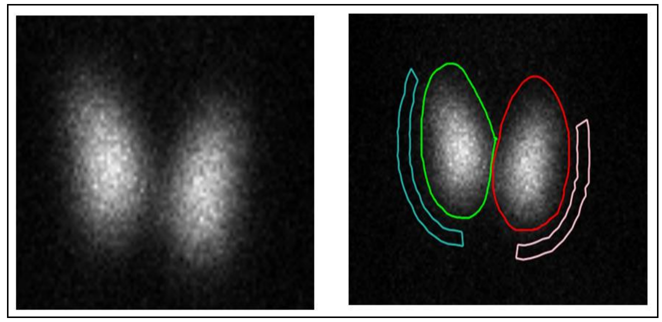

Figure-2: (A) Tc-99m Thyroid Scan, Anterior View (B) Region of Interest For Right Lobe, Left Lobe and Background

Radioiodine has remained one of the most useful and rewarding radionuclides in nuclear thyroidology for the past eight decades. The concept of RAIT emerged in the 1940s-1950s, parallel to the development of antithyroid drugs. Over time, both modalities became effective treatments for GD, substituting thyroidectomy.10 RAIT yields better therapeutic outcomes than other modalities. The initial documented success rate with RAIT in GD is >90% within the first year after treatment was reported by Yu *et al.*[11] The goal of RAIT is to achieve therapeutic outcomes with minimal residual radiation dose to the patient. Therapeutic outcomes are predicted by multiple factors, including age, gender, thyroid mass, pre-treatment serum free hormone levels, and use of ATD, etc., have been reported by Salman *et al.*[12] Optimizing the RAI dose to achieve the required therapeutic outcome with minimal radiation exposure is the cornerstone of treatment. However, the optimal method for dose calculation remains controversial, and many regimens are used depending on regional guidelines and physician preference, as concluded by Xing *et al.*[13]

According to 2025 American Thyroid Association guidelines, the therapeutic outcome of RAIT is to render the patient hypothyroid, which can be achieved either by administering a fixed dose of radioiodine or a personalized dose based on the size of gland and iodine uptake.[14] The fixed dose regimen was also described by Madu *et al.,* as a simple and effective method with a dose range from 370-550 MBq, leading to therapeutic success in 86% of the patients.[15] The European Association of Nuclear Medicine (EANM) recommends the Marinelli formula for personalized dose calculation based on thyroid volume, maximum radioiodine uptake, and effective half-life as referred by Campenni *et al*.[16]

Determining the maximum RAI uptake to calculate therapeutic RAI dose. Although it is considered that maximum iodine uptake happens 24 hours after ingestion. Still, Madu *et al.,* conducted a study to estimate 24-hour thyroid uptake values from 4- and 6-hour measurements.[17] The discrepancy between anticipated uptake values after 4- and 6-hours and actual measurements after 24-hours was 10% and 5.9%, respectively.[17] Similarly, Hammes *et al.,* demonstrated that there is a strong correlation between actual 24-hour uptake values and 4- and 6-hour estimations (r=0.94). The study also presented another method of estimating maximum iodine uptake (RAIU24hrs) using TcU20min in patients with GD, like our study.[18] They generated an algorithm to estimate RAIU24hrs based on TcU20min with statistical significance of <0.05. Contrary to our study, they took TRAb titers as a significant factor affecting RAI uptake. They also found a statistical correlation between RAIU24hrs and TcU20min with p-value <0.05 and r=0.09. Alvi *et al.,* conducted a similar study in hyperthyroid patients to develop an algorithm to estimate RAIU24hrs using TcU20min measurements and found a significant correlation (R2 = 0.708, r=0.842, p<0.001).[19] The study concluded by Roque *et al.,* that treating TMNG with a 15 mCi fixed RAI dose is effective for long-term reduction of thyroid volume and curing hyperthyroidism, resulting in low, manageable rates of hypothyroidism.[20]

However, Tc-99m uptake depends on computation and acquisition protocols used, and each camera may have a unique spectrum depending on the type of collimator, window width settings, and operation of the pulse height analyzer, etc. So, it is wise that each center should analyze and find an algorithm based on its parameters, used to obtain better and more accurate results.

LIMITATIONS OF STUDY

The limitations of our study are twofold. First, the small sample size, and second, we did not follow up patients to determine the therapeutic effectiveness of the dosage calculated by the new algorithm. Hence, a large study including patient follow-up and evaluating the therapeutic outcome is suggested.

CONCLUSION

RAIU24hrs can be predicted from TcU20min, thus providing an alternative, simple, cost-effective, and convenient method for therapeutic radioiodine dose calculation. This approach eliminates the need for time-consuming 24-hour uptake measurements by leveraging the strong correlation between early TcU-99m uptake and traditional RAIU values. By streamlining the workflow, it reduces patient visits and resource utilization while maintaining accuracy in determining the appropriate therapeutic dose for Graves' disease management.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

MA & FH: Data acquisition, data analysis, critical review, approval of the final version to be published.

ZSD & MA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MA & NUK: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

REFERENCES

1. Antonelli A, Ferrari SM, Ragusa F, Elia G, Paparo SR, Ruffilli I, et al. Graves' disease: Epidemiology, genetic and environmental risk factors and viruses. Best Pract Res Clin Endocrinol Metab 2020; 34(1): 101387. https://doi.org/10.1016/j.beem.2020.101387
2. Wiersinga WM. Graves' disease: can it be cured? Endocrinol Metab 2019; 34(1): 29-38. https://doi.org/10.3803/enm.2019.34.1.29
3. Subekti I, Pramono LA. Current diagnosis and management of Graves' disease. Acta Med Indones 2018; 50(2): 177-182.
4. Kim MJ, Cho SW, Kim YA, Choi HS, Park YJ, Park DJ, et al. Clinical Outcomes of Repeated Radioactive Iodine Therapy for Graves' Disease. Endocrinol Metab 2022; 37(3): 524-532. https://doi.org/10.3803/enm.2022.1418
5. El Kawkgi OM, Ross DS, Stan MN. Comparison of long-term antithyroid drugs versus radioactive iodine or surgery for Graves' disease: a review of the literature. Clin Endocrinol 2021; 95(1): 3-12. https://doi.org/10.1111/cen.14374
6. Okosieme OE, Taylor PN, Dayan CM. Should radioiodine now be first-line treatment for Graves' disease? Thyroid res 2020 Dec; 13(1): 1-7. https://doi.org/10.1186/s13044-020-00077-8
7. Mengistu HS, Getahun KT, Alemayehu L, Gezahign S. Cost-Effectiveness Analysis of Antithyroid Drug (Propylthiouracil) Compared to Radioactive Iodine for the Treatment of Graves' Disease in Ethiopia. Clinicoecon Outcomes Res 2022; 14: 221-229. https://doi.org/10.2147/ceor.s350984

8. Ohiduzzaman, Md Khatun, Ruhani R, Sheikh K, M Akter, Shumaiya U, et al. Thyroid Uptake of Tc-99m and Its Agreement with I-131 for Evaluation of Hyperthyroid Function. Uni J Pub Health 2019; 7: 201-206. https://doi.org/10.13189/ujph.2019.070502
9. Kornelius E, Yang YS, Huang CN, Wang YH, Lo SC, Lai YR, Chiou JY. The Trends Of Hyperthyroidism Treatment In Taiwan: A Nationwide Population-Based Study. Endocr Pract 2018; 24(6): 573-579. https://doi.org/10.4158/EP-2017-0266
10. Iqbal A, Rehman A. Thyroid Uptake and Scan. [Updated 2022 Oct 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK555978/
11. Yu F, Zhang R, Zhang G, Meng Z, Liu X, He Y, Tan J, Wang R. Predictive Value of a Thyroid-Absorbed Dose with a Shorter Effective Half-Life on Efficacy in Graves Disease Patients Receiving Iodine-131 Therapy. Med Sci Monit 2021; 27: e928796. https://doi.org/10.12659/msm.928796
12. Salman MA, Assal MM, Salman A, Elsherbiney M. Outcomes of Radioactive Iodine Versus Surgery for the Treatment of Graves' Disease: a Systematic Review and Meta-analysis. Indian J Surg 2023; 1: 18-26. https://doi.org/10.1007/s12262-023-03692-5
13. Xing YZ, Zhang K, Jin G. Predictive factors for the outcomes of Graves' disease patients with radioactive iodine (131I) treatment. Bioscience Reports. 2020; 40(1): BSR20191609. https://doi.org/10.1042/bsr20191609
14. Ringel MD, Sosa JA, Baloch Z, Bischoff L, Bloom G, et al. 2025 American Thyroid Association Management Guidelines for Adult Patients with Differentiated Thyroid Cancer. Thyroid 2025; 35(8): 841-985. https://doi.org/10.1177/10507256251363120
15. Sellem A, Elajmi W, Mhamed RB, Oueslati N, Ouertani H, Hammami H. Irathérapie dans la maladie de Basedow: place et efficacité [Role and effectiveness of radioactive-iodine therapy for the treatment of Grave's disease]. Pan Afr Med J 2020; 36: 341. https://doi.org/10.11604/pamj.2020.36.341.21623
16. Campennì A, Avram AM, Verburg FA, Iakovou I, Hänscheid H, et al. The EANM guideline on radioiodine therapy of benign thyroid disease. Eur J Nucl Med Mol Imaging 2023; 50(11): 3324-3348. https://doi.org/10.1007/s00259-023-06274-5
17. Madu NM, Skinner C, Oyibo SO. Cure Rates After a Single Dose of Radioactive Iodine to Treat Hyperthyroidism: The Fixed-Dose Regimen. Cureus 2022; 14(8): e28316. https://doi.org/10.7759/cureus.28316
18. Hammes J, van Heek L, Hohberg M, Reifegerst M, Stockter S, Dietlein M, Wild M, Drzezga A, Schmidt M, Kobe C. Impact of different approaches to calculation of treatment activities on achieved doses in radioiodine therapy of benign thyroid diseases. EJNMMI Phys 2018; 5(1): 32. https://doi.org/10.1186/s40658-018-0231-x
19. Alvi AM, Azmat U, Shafiq W, Ali Rasheed AH, Siddiqi AI, et al. Efficacy of Radioiodine Therapy in Patients With Primary Hyperthyroidism: An Institutional Review From Pakistan. Cureus 2022; 14(5): e24992. https://doi.org/10.7759/cureus.24992
20. Roque C, Santos FS, Pilli T, Dalmazio G, Castagna MG, Pacini F. Long-term Effects of Radioiodine in Toxic Multinodular Goiter: Thyroid Volume, Function, and Autoimmunity. J Clin Endocrinol Metab 2020; 105(7): dgaa214. https://doi.org/10.1210/clinem/dgaa214

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