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Modeling and Analysis of Radioactive Iodine Treatment for Hyperthyroidism: A Mathematical Approach

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ABSTRACT:
Objectives: To develop a patient-specific mathematical model to capture the dynamics of key components involved in Graves' disease and its treatment with radioactive iodine therapy.
Methods: A system of ordinary differential equations is formulated to model the interactions between uptake rate of radioactive iodine, concentration of thyroid receptor antibodies (TRAbs), concentration of thyroid stimulating hormone (TSH), concentration of free thyroxine (FT4), and thyroid volume over the course of treatment.
Findings: The mathematical model provides a framework to understand the dynamics of Graves' disease. Stability analysis and numerical simulations demonstrate the model's utility for optimizing radioactive iodine therapy on a patient-specific basis.
Novelty: The model offers a novel approach to simulate Graves' disease progression and treatment response at the individual patient level. Personalized simulations can inform treatment planning. In conclusion, the mathematical model provides clinicians and researchers with a powerful new tool for gaining insights into Graves' disease dynamics and optimizing radioactive iodine therapy. The model contributes to the growing field of personalized medicine by enabling patient-tailored treatment strategies.
KEYWORDS: *Hyperthyroidism, Radioactive iodine, Graves' disease, Ordinary Differential Equations, Stability.*

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I. INTRODUCTION

Hyperthyroidism is a medical condition characterized by an overactive thyroid gland, which results in the excessive production of thyroid hormones. Hyperthyroidism is characterized by an overproduction of thyroid hormones, which can lead to concerning health effects like unexplained weight loss, anxiety, rapid heartbeat, and other symptoms that can significantly impact a person's overall well being[1]. To manage hyperthyroidism, doctors often prescribe radioactive iodine therapy, which involves ingesting a radioactive form of iodine that accumulates in and destroys parts of the overactive thyroid gland, gradually reducing excess thyroid hormone levels. This approach proves efficacious in diminishing thyroid function and can offer alleviation to individuals experiencing hyperthyroidism[2].

Administering radioactive iodine to treat hyperthyroidism requires expertise and careful consideration, as the process involves comprehending the intricate workings of thyroid function and how radioactive iodine behaves in the body. Precisely prescribing the right radioactive iodine dose demands an in-depth understanding of the mechanisms regulating the thyroid as well as the pharmacokinetics of radioactive iodine in order to achieve the desired therapeutic effect while minimizing potential risks. Mathematical modeling offers a powerful tool for investigating these dynamics and optimizing the treatment process. This is the focus of our study, where we delve into the development of a mathematical treatment model for hyperthyroidism with radioactive iodine. In addition to analytical insights, this research includes numerical simulations that enable to explore a wide range of treatment scenarios. These simulations help in optimizing the radioactive iodine therapy process, providing valuable guidance for medical practitioners, and ultimately improving patient outcomes[3].

Modeling and analyzing radioactive iodine treatment for hyperthyroidism is a complex endeavor, seamlessly merging mathematics and medicine. It has the potential to enhance the understanding of hyperthyroidism treatment, leading to more effective and personalized approaches to managing this challenging medical condition. This research not only contributes to the field of medical mathematics but also holds the promise of making a meaningful impact on the lives of individuals living with hyperthyroidism[4]. Radioiodine-131 (RAI) therapy has gained greater prominence in the treatment of hyperthyroid Graves' disease. Several factors have contributed to its growing acceptance as both a primary and secondary treatment option, particularly in cases where Graves' disease reemerges following drug therapy. focused on the dosage

(radioactivity) used in RAI therapy was determined through trial-and-error, but over the past century, the methods for RAI treatment have evolved and improved with accumulating experience in the past[5]. Graves' disease can be managed using medications that block the production of thyroid hormones. Alternatively, treatment options include reducing the size of the thyroid gland. This can be achieved through surgical removal (thyroidectomy) or by administering radioactive iodine, which accumulates in the thyroid gland and uses radiation to destroy thyroid tissue.

A simplified differential equation model were constructed to depict the functioning of the HPT axis in individuals with Hashimoto's thyroiditis. This model comprises four variables: the functional size of the thyroid gland, the concentration of serum TSH, serum FT4, and serum thyroid peroxidase antibody[6]. Similarly, Graves' disease was addressed through a set of differential equations. The initial mechanistic model, designed to predict relapse in Graves' disease patients, was constructed using an ordinary differential equation system to capture the dynamics of the condition[7]. In 2018, Similar method was employed to formulate a treatment model for Graves' hyperthyroidism. One of the challenges in this models is the limited availability of data on the functional sizes of patients' thyroid glands, given the impracticality of conducting thyroid screen tests during every visit[8].

TSH (Thyroid-Stimulating Hormone): TSH, which is a hormone produced by the pituitary gland in the brain. Its primary role is to regulate the activity of the thyroid gland, which is a vital part of the endocrine system. TSH acts as a messenger, instructing the thyroid gland to release thyroid hormones, primarily thyroxine (T4) and triiodothyronine (T3). When the levels of T4 and T3 in the blood are too low, the pituitary gland increases TSH production to stimulate the thyroid gland to produce more hormones[8]. Conversely, when T4 and T3 levels are too high, TSH production decreases to reduce thyroid hormone production[9]. In the context of hyperthyroidism treatment, monitoring TSH levels is important to assess the effectiveness of therapy. A reduction in TSH levels can indicate successful suppression of thyroid hormone production.

FT4 (Free Thyroxine): FT4 is one of the two primary thyroid hormones produced by the thyroid gland (the other being T3). It plays a crucial role in regulating the body's metabolism. FT4 is the unbound, active form of thyroxine in the bloodstream, and it exerts its effects on target tissues and organs. In the context of hyperthyroidism, elevated FT4 levels are a hallmark of the condition. Monitoring FT4 levels helps healthcare providers assess the severity of hyperthyroidism and evaluate the response to treatment. Treatment goal is that often to normalize FT4 levels, indicating the successful restoration of thyroid hormone balance[10].

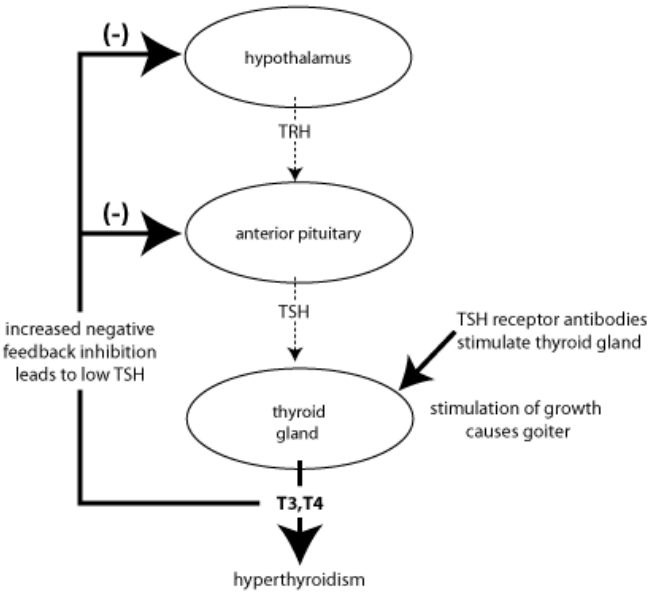
Thyroid Gland: The thyroid gland is a butterfly-shaped gland located in the neck. Its primary function is to produce thyroid hormones (T4 and T3), which play a central role in regulating various physiological processes in the body. These hormones control metabolism, energy production, and the functioning of numerous organs and systems. In hyperthyroidism, the thyroid gland becomes overactive and produces excessive amounts of thyroid hormones, leading to the characteristic symptoms of the condition. In radioactive iodine treatment, the goal is to reduce the size and activity of the thyroid gland to bring thyroid hormone levels back into the normal range. The thyroid gland role in this context is to respond to the radioacaltive iodine and undergo controlled shrinkage and reduction in hormone production[11].

TrAb (Thyroid Receptor Antibodies): TrAb, or Thyroid Receptor Antibodies, are antibodies that bind to and activate the thyroid-stimulating hormone receptor on thyroid cells. In the context of hyperthyroidism, these antibodies play a pivotal role, particularly in autoimmune forms of the condition, such as Graves' disease. When TrAb binds to the TSH receptor, it stimulates the thyroid gland to produce more thyroid hormones, leading to hyperthyroidism[8]. Monitoring TrAb levels is important for diagnosing and managing autoimmune hyperthyroidism and for assessing the efficacy of treatment. Successful treatment often leads to a decrease in TrAb levels, indicating a reduction in the autoimmune attack on the thyroid gland and the normalization of thyroid function[7].

II. NOTATIONS

k_1	:	Relative maximum uptake rate of TSH
k_2	:	rate constant of TSH increased due to TRAb
k_3	:	Relative maximum secretion rate of FT4.
k_4	:	Inhibition rate of FT4 with the effect of RAI
k_5	:	Proportional rate of TRAb to the size of thyroid gland
k_6	:	Basic growth rate of thyroid gland.
k_7	:	Inactivation rate of thyroid gland due to RAI
k_8	:	Maximum production rate of TRAb
k_9	:	Inhibition rate of TRAb in the influence of RAI.
k_{10}	:	Elimination rate of TRAb :
k_a	:	Michaelis-Menten constant for half maximal secretion of FT4
k_b	:	Michaelis-Menten constant for half maximal secretion of TSH

α : Elimination rate of TSH
β : Elimination rate of TSH



The provided figure distinctly illustrates the mechanism of Graves' disease within the endocrine gland.

III. METHODOLOGY

Construction of the Model

The system of differential equations we are about to discuss is composed of five interconnected equations, each representing a specific variable's rate of change over time. These variables are denoted as A, TSH, FT4, V, and Ab, and they represent different aspects of the system under consideration. The equations governing the rates of change for these variables are as follows:

$$\frac{\mathrm{dA}}{\mathrm{dt}} = D - \delta \mathrm{A}$$

$$\frac{\mathrm{dTSH}}{\mathrm{dt}} = k_1 - \frac{k_1 \mathrm{FT4}}{k_a + \mathrm{FT4}} + k_2 \mathrm{Ab} - \alpha \mathrm{TSH}$$

$$\frac{\mathrm{dFT4}}{\mathrm{dt}} = \frac{k_3 \mathrm{V\ TSH}}{k_b + \mathrm{TSH}} - k_4 \mathrm{FT4\ A}\text{-}\beta \mathrm{FT4}$$

$$\frac{\mathrm{dV}}{\mathrm{dt}} = k_5 \left(\frac{\mathrm{Ab}}{V} \right) + k_6 - k_7 \mathrm{AV}$$

$$\frac{\mathrm{dAb}}{\mathrm{dt}} = k_8 - k_9 \mathrm{A\ Ab}\text{-}\mathrm{k}_{10} \mathrm{Ab}$$

where $\delta = \frac{\ln(2)}{T_{eff}}$

This equation describes how the concentration of Radio Active Iodine changes over time, where D is a constant.The term represents the decay of A over time, with Teff being a constant that determines the rate of decay. This term represents the rate of change of TSH (Thyroid-Stimulating Hormone) concentration over time. k_1 is a maximum secretion rate of TSH in the absence of FT4.The next term $\frac{k_1 FT4}{k_a + \mathrm{FT4}}$ is modeled by using Michaelis_Menten Kinetics. The next term represents the influence of Ab in TSH. The last term represents the natural elimination rate of TSH.

The third equation describes how the concentration of FT4 (Free Thyroxine) changes over time. The first term $\frac{k_3 VTSH}{k_b + \mathrm{TSH}}$ represents the production of FT4, which depends on the concentration of V and TSH. The next term represents a loss of FT4 due to the interaction with A. The last term represents a decay effect on FT4.

The fourth equation represents the rate of change of Volume of thyroid gland over time. The first term $k_5\left(\frac{\mathrm{Ab}}{V}\right)$ represent the basic growth of thyroid gland. the second term represents a negative effect on V due to the interaction of A with V. The last term represents a positive effect on V, which depends on the concentration of Ab and the reciprocal of V.

This equation describes how the concentration of Ab changes over time, where represents a natural production of Ab. The second term represents a negative effect on Ab due to the interaction of A with Ab. The last term represents a loss or decay of Ab over time.

Theorem 1. Using the initial conditions given in equation (1), the solutions $A(t), TSH(t), FT4(t), V(t), Ab(t)$ are non-negative for all time $t > 0$

Proof. From the first equation of (1)

$$\frac{dA}{dt} \geq -\delta A$$

Both sides multiply by $e^{\delta t}$

$$e^{\delta t}\frac{dA(t)}{\mathrm{dt}} + \delta A(t)e^{\delta t} \geq 0$$

$$\frac{d}{\mathrm{dt}}(e^{\delta t}.A(t)) \geq 0$$

$$\int_0^t \frac{d}{\mathrm{dt}}(e^{\delta s}.A(s))ds \geq 0 \quad \text{where } \delta = \frac{\ln(2)}{T_{eff}}$$

$$A(t) \geq A(0)e^{\delta t}$$

$$A(0) > 0$$

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For Second equation

$$\frac{d(TSH)}{\mathrm{dt}} + \alpha TSH = k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 \mathrm{Ab}$$

Both sides multiply with $e^{\int \alpha dt}$

$$e^{\int \alpha dt}\frac{d\left(TSH\right)}{dt} + \alpha e^{\int \alpha dt}\, TSH = \left(k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 Ab\right)e^{\int \alpha dt}$$

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Integrate on both sides

$$TSH = \frac{1}{e^{\int \alpha dt}}\int\left[\left(k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 Ab\right)e^{\int \alpha dt}\right]dt + C$$

Integrate on both sides

$$TSH = \frac{1}{e^{\int \alpha dt}}\int\left[\left(k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 Ab\right)e^{\int \alpha dt}\right]dt + C$$

RHS of this equation is a definite Internal and the Integrand is a positive function.
TSH remains non-negative during the entire time interval. A similar approach can be used to demonstrate the validity of the remaining equation.

IV. STABILITY ANALYSIS

In order to gain a deeper comprehension of the system's dynamics, our initial approach involves examining the system in the absence of drug input (where A(t) equals zero for all instances of time). Then the equation becomes

$$\frac{dTSH}{dt} = k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 Ab - \alpha TSH$$

$$\frac{dFT4}{dt} = \frac{k_3 V\ TSH}{k_b + \mathrm{TSH}} - \beta FT4$$

$$\frac{dV}{dt} = k_5\left(\frac{Ab}{V}\right) + k_6$$

$$\frac{dAb}{dt} = k_8 - k_{10}Ab$$

The model has an non-negative equilibrium namely $\bar{E} = \left(\overline{\text{TSH}}, \overline{FT4}, \bar{V}, \overline{\text{Ab}}\right)$ These are obtained by solving the algebraic equations

$$k_1 - \frac{k_1 FT4}{k_a + FT4} + k_2 Ab - \alpha TSH = 0$$

$$\frac{dFT4}{\text{dt}} = \frac{k_3 \text{V TSH}}{k_b + TSH} - \beta FT4 = 0$$

$$k_5\left(\frac{\text{Ab}}{V}\right) + k_6 = 0$$

$$k_8 - k_{10}\text{Ab} = 0$$

The equilibrium points are

$$\overline{\text{TSH}} = \frac{1}{\alpha}\left(\frac{k_1 k_a}{\left(k_a + FT4\right)} - k_2 \text{Ab}\right)$$

$$\overline{FT4} = \frac{1}{\beta}\left(\frac{k_3 \text{V TSH}}{k_b + \text{TSH}}\right)$$

$$\bar{V} = -k_5\left(\frac{\text{Ab}}{k_6}\right)$$

$$\overline{\text{Ab}} = \frac{k_8}{k_{10}}$$

Theorem 2. The equilibrium E^* is locally asymptotically stable without any condition.

Proof. To study the local stability character of E^* we need the following Jacobian matrix for the model (2), about E^*

$$\bar{J} = \begin{vmatrix} -\alpha & -\frac{k_1 k_a}{(k_a + \overline{FT4})^2} & 0 & k_2 \\ \frac{k_b k_3 \bar{V}}{(k_b + \overline{\text{TSH}})^2} & -\beta & \frac{k_3 \overline{\text{TSH}}}{k_b + \overline{\text{TSH}}} & 0 \\ 0 & 0 & -\frac{k_5 \overline{\text{Ab}}}{\bar{V}^2} & \frac{k_5}{\bar{V}} \\ 0 & 0 & 0 & -k_{10} \end{vmatrix}$$

$$J = \begin{vmatrix} -\alpha - \lambda & -\frac{k_1 k_a}{(k_a + \overline{FT4})^2} & 0 & k_2 \\ \frac{k_b k_3 \bar{V}}{(k_b + \overline{\text{TSH}})^2} & -\beta - \lambda & \frac{k_3 \overline{\text{TSH}}}{k_b + \overline{\text{TSH}}} & 0 \\ 0 & 0 & -\frac{k_5 \overline{\text{Ab}}}{\bar{V}^2} - \lambda & \frac{k_5}{\bar{V}} \\ 0 & 0 & 0 & -k_{10} - \lambda \end{vmatrix}$$

$$= (-k_{10} - \lambda)\begin{vmatrix} -\alpha - \lambda & -\dfrac{k_1 k_a}{(k_a + \overline{FT4})^2} & 0 \\ \dfrac{k_b k_3 \bar{V}}{(k_b + \overline{\mathrm{TSH}})^2} & -\beta - \lambda & \dfrac{\overline{\mathrm{TSH}}\, k_3}{k_b + \overline{\mathrm{TSH}}} \\ 0 & 0 & -\dfrac{k_5 \overline{\mathrm{Ab}}}{\bar{V}^2} - \lambda \end{vmatrix}$$

Clearly, one eigenvalue of E^* (i.e. $-k_{10}$) is negative. The other three eigen values of Jacobian matrix J corresponding to E^* are given by the following characteristic polynomial,

$$\lambda^3 + a_1\lambda^2 + a_2\lambda + a_3 = 0$$

$$a_1 = \frac{k_5 \overline{\mathrm{Ab}}}{\bar{V}^2} + \frac{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 \alpha + (k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 \beta}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2}$$

$$a_2 = \frac{\alpha\beta (k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 + \bar{V} k_1 k_3 k_a k_b}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2} + \frac{\overline{\mathrm{Ab}} k_5 (\alpha (k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2) + \beta (k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2)}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 \bar{V}^2}$$

$$a_3 = \frac{(\alpha\beta (k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 + \bar{V} k_1 k_3 k_a k_b)(\overline{\mathrm{Ab}} k_5)}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2 \bar{V}^2}$$

$$a_1 a_2 - a_3 = \alpha\beta^2 + \alpha^2\beta + \frac{k_5 \alpha^2 \overline{\mathrm{Ab}}}{\bar{V}^2} + \frac{k_5 \beta^2 \overline{\mathrm{Ab}}}{\bar{V}^2} + \frac{\overline{\mathrm{Ab}}^2 \alpha k_5^2}{\bar{V}^4} + \frac{\overline{\mathrm{Ab}}^2 \beta k_5^2}{\bar{V}^4} + \frac{2 k_5 \alpha\beta \overline{\mathrm{Ab}}}{\bar{V}^2}$$
$$+ \frac{\bar{V}\alpha k_1 k_3 k_a k_b}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2} + \frac{\bar{V}\beta k_1 k_3 k_a k_b}{(k_a + \overline{FT4})^2 (k_b + \overline{\mathrm{TSH}})^2}$$

$$\dot{U} = m_1 \left(A - A^*\right)^2 \delta - \frac{k_1 k_a}{(k_a + F)^2} m_2 \left(T - T^*\right)\left(F - F^*\right) - m_3 \left(F - F^*\right)^2 (k_4 A^* + \beta)$$
$$+ k_2 m_2 \left(T - T^*\right)\left(B - B^*\right) + \frac{k_b k_3 V^*}{\left(k_b + T^*\right)^2} m_3 \left(F - F^*\right)\left(T - T^*\right)$$
$$+ \frac{k_3 T^*}{k_b + T^*} m_3 \left(F - F^*\right)\left(V - V^*\right) - m_4 k_7 V^* \left(A - A^*\right)\left(V - V^*\right)$$
$$- \left(\frac{k_5 B^*}{V^{*2}} + k_7 A^*\right) m_4 \left(V - V^*\right)^2 - m_4 \frac{k_5}{V^*}\left(B - B^*\right)\left(V - V^*\right)$$
$$- k_9 B^* m_5 \left(A - A^*\right)\left(B - B^*\right) - m_5 \left(k_9 A^* + k_{10}\right)\left(B - B^*\right)^2$$

$\dot{U}$ will be negative definite

$$m_4 (k_7 V^*)^2 < \frac{1}{3} m_1 m_4 \delta \left(\frac{k_5 B^*}{V^{*2}} + k_7 A^*\right)$$

$$m_5 (k_9 B^*)^2 < \frac{4}{9} m_1 \delta \left(\frac{k_5 B^*}{V^{*2}} + k_7 A^*\right)$$

$$m_2 \left(\frac{k_1 k_a}{(k_a + F)^2}\right)^2 < \frac{4}{9} m_3 \alpha (k_4 A^* + \beta)$$

$$m_3\left(\frac{k_b k_3 V^*}{\left(k_b+T^*\right)^2}\right)^2 < \frac{4}{9} m_2 \alpha (k_4 A^* + \beta)$$

$$m_2 (k_2)^2 < \frac{4}{9} m_5 \alpha \left(k_9 A^* + k_{10}\right)$$

$$m_3 (\frac{k_3 T^*}{k_b + T^*})^2 < \frac{4}{9} m_4 \left(\frac{k_5 B^*}{V^{*2}} + k_7 A^*\right)(k_4 A^* + \beta)$$

$$m_4\left(\frac{k_5}{V^*}\right)^2 < \frac{4}{9} m_5 \left(\frac{k_5 B^*}{V^{*2}} + k_7 A^*\right)\left(k_9 A^* + k_{10}\right)$$

Now,

$$m_1 = m_4 = 1$$

$$m_2 < \frac{4k_{10}}{9(k_2)^2} \alpha m_5$$

$$m_5 < \frac{2\delta k_{10}}{3(k_9 B^*)^2}$$

$$m_3 < \frac{\alpha \beta m_2 k_b^2 k_3^2 V^{*2}}{(k_b + T^*)^2}$$

$\dot{U}$ will be negative definite provided the above conditions are satisfied and hence E^* is globally asymptotically stable.

	description	**values**	**Units**
k_1	Relative maximum uptake rate of TSH	55	$mU/L * day$
k_2	rate constant of TSH increased due to TRAb	0.5	$mU/L * day$
k_3	Relative maximum secretion rate of FT4	0.821	$pg/(ml^2 * day)$
k_4	Inhibition rate of FT4 with the effect of RAI	2.0	$pg/(ml^2 day)$
k_5	Proportional rate of TRAb to the size of thyroid gland	0.00033	
k_6	Basic growth rate of thyroid gland Difficulty breathing	$1x10^6$	$ml^3/Uday$
k_7	Inactivation rate of thyroid gland due to RAI	0.0035	
k_8	Maximum production rate of TRAb	0.875	$U/mL * day$
k_9	Inhibition rate of TRAb in the influence of RAI	0.0045	$U/mL * day$
k_{10}	Elimination rate of TRAb	0.075	$1/day$
k_a	Michaelis-Menten constant for half maximal secretion of FT4	0.0434	pg/ml
k_b	Michaelis-Menten constant for half maximal secretion of TSH	0.0021	mU/L
α	Elimination rate of TSH	16.6355	$1/day$
β	Elimination rate of FT4	0.09021	$1/day$

V. RESULTS AND DISCUSSION

Hyperthyroidism exhibits distinct stages characterized by varying TSH and FT4 levels, as outlined in the study[5]. The primary factor driving the progression of Graves' disease from its early stage to overt hyperthyroidism is the level of TRAb (Thyrotropin Receptor Antibodies) in the bloodstream. In the case of a patient with an initial euthyroid state, their FT4 level would increase by 1.55 pg/mL over time, even when their TRAb value is set to be 0.05 units higher than the normal value of 1.75 IU/L. However, if the TRAb value is elevated to 5 IU/L, the FT4 value of the same patient with the same initial conditions would undergo a further increase, reaching 6.97 units above 18 pg/mL, which is the upper limit of the normal FT4 range.

In summary, the level of TRAb plays a critical role in the progression of Graves' disease and its impact on FT4 levels in patients, with higher TRAb values leading to more pronounced increases in FT4 levels over time. In Graves' disease, the progression from a state of normal thyroid function (euthyroidism) to overt hyperthyroidism commonly involves a typical pattern characterized by a reduction in TSH levels and an elevation in FT4 levels. The decrease in TSH levels occurs due to the negative feedback resulting from the heightened levels of circulating thyroid hormones (FT4 and FT3), whereas the rise in FT4 levels is a result of the excessive production of thyroid hormones by the overactive thyroid gland.

Physicians typically strive to re-establish a balance in thyroid hormone levels by carefully monitoring and adjusting medication dosages. However, it's important to clarify that Radioactive Iodine (RAI) treatment, rather than RAI as mentioned in your previous statement, is commonly employed to treat Graves' disease by intentionally reducing the activity of the overactive thyroid gland. RAI treatment works by using radioactive iodine, which is taken up by the thyroid gland and selectively destroys the overactive thyroid cells without affecting other tissues. By reducing the thyroid's activity, this treatment aims to normalize thyroid hormone levels, including TSH and FT4, and bring them within the normal range.

Regular assessments and close monitoring of thyroid hormone levels are indeed crucial to ensure that the treatment is effective in normalizing thyroid function. By regulating and stabilizing TSH and FT4 levels within the normal range, this approach helps to alleviate the symptoms and mitigate potential complications associated with hyperthyroidism in Graves' disease. To enhance dosing strategies for Graves' disease treatment while reducing patient risk, a predictive model is utilized. Figures 3, 4, and 5 depict an optimized strategy, which is influenced by the effects of Radioactive Iodine (RAI) therapy. RAI treatment has several beneficial effects, including the improvement of TSH values and the reduction of FT4 levels and TRAb levels.

RAI therapy has a positive impact on TSH levels, leading to their improvement over time. This is important for bringing the thyroid hormone levels into a more controlled range.It results in a reduction of FT4 levels. Lower FT4 levels are desired in the treatment of hyperthyroidism associated with Graves' disease, as it indicates a decrease in the overproduction of thyroid hormones. It also leads to a decrease in Thyrotropin Receptor Antibody (TRAb) levels, which are associated with the autoimmune response in Graves' disease. Lower TRAb levels signify a reduction in the autoimmune attack on the thyroid gland.

The values of TSH, FT4, the volume of the thyroid gland, and TRAb become stable after 70 days of RAI treatment, indicating that the therapy has successfully controlled the condition. This dosing strategy is developed based on modeling and simulations, allowing for a more calculated and controlled approach to treatment, reducing the need for trial-and-error adjustments. By implementing this predictive model and dosing strategy, healthcare providers can aim for more effective management of thyroid hormone levels while minimizing the risks associated with trial-and-error approaches. Ultimately, this approach can lead to improved patient outcomes and a better quality of life for individuals with Graves' disease.

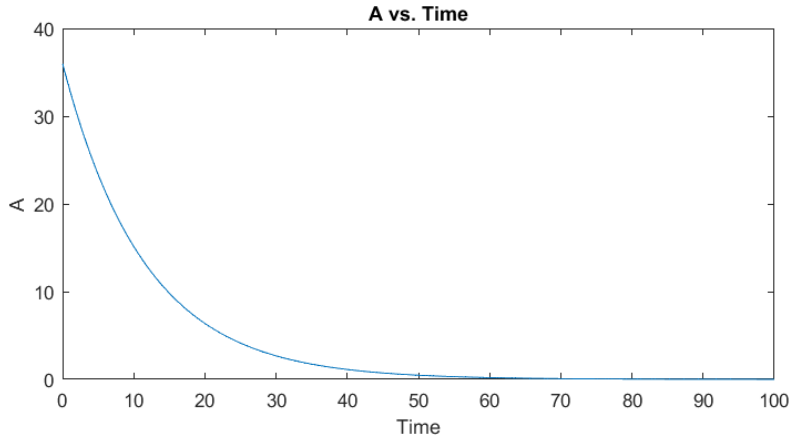

Figure 1 : Progression of the concentration of Radioactive iodine in thyroid gland for the Graves' disease patient treated with radioactive iodine. The dosage of the drug set as 38 (mCi) and the value of δ is 0.0866 1/day.

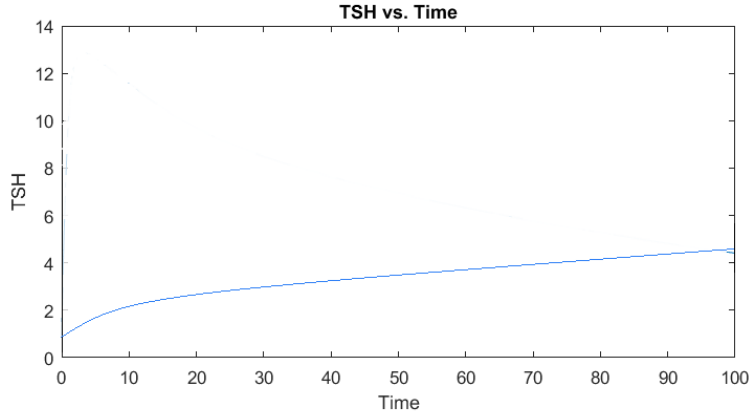

Figure 2 : Evolution of Thyroid stimulation hormone (TSH) in effect of Radioactive Iodine (RAI) Treatment on individuals with Graves' disease. In the graph, x depicts the time in days and y depicts the concentration of TSH in mU/L. Considering the Dosage value of the drug as 39 mCi. By setting, the initial value of TSH as 0.906 mU/L, FT4 as 24.97 pg/mL, V as 30 mL and TRAb as 5 IU/L. The parameter values are taken from the above table.

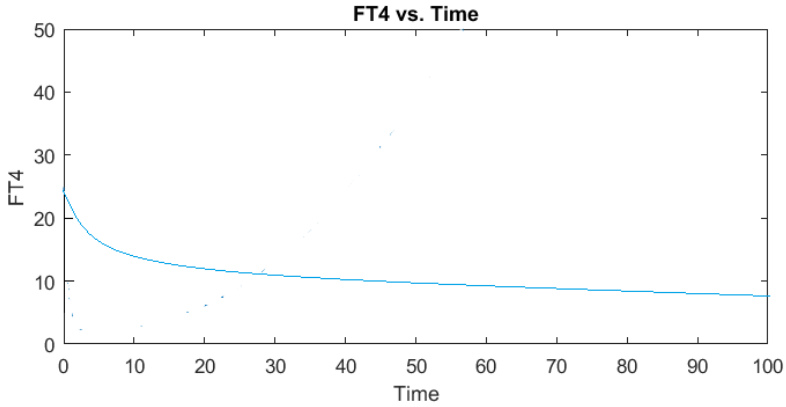

Figure 3 : Behavior of Free thyroxine (FT4) in effect of Radioactive Iodine (RAI) Treatment on individuals with Graves' disease. In the graph, x depicts the time in days and y depicts the concentration of FT4 in pg/mL. Let the Dosage value of the drug is taken as 39 mCi. By Assuming, the initial value of TSH as 0.906 mU/L, FT4 as 24.97 pg/mL, V as 30 mL, TRAb as 5 IU/L. The parameter values are taken from the above table.

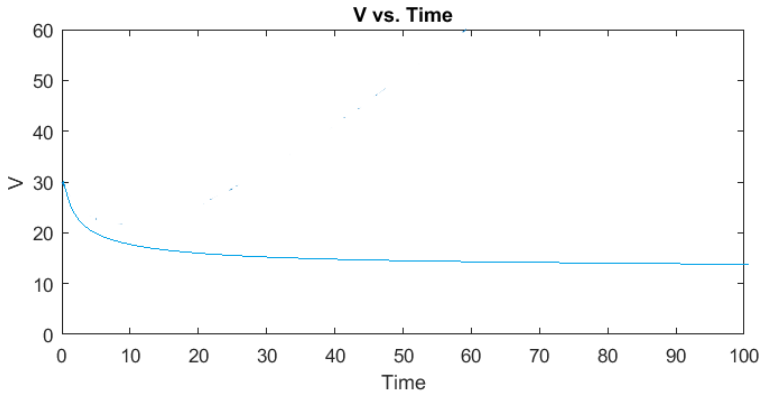

Figure 4 : Graph representing the thyroid gland shrinkage curve in effect of Radioactive Iodine (RAI) Treatment, with the X axis representing the time in days and the Y axis representing the volume of thyroid gland (V).The Dosage value of the drug was assumed as 39 mCi. By setting, the initial value of TSH as 0.906 mU/L, FT4 as 24.97 pg/mL, V as 30 mL, TRAb as 5 IU/L and the parameter values are taken from the above table.

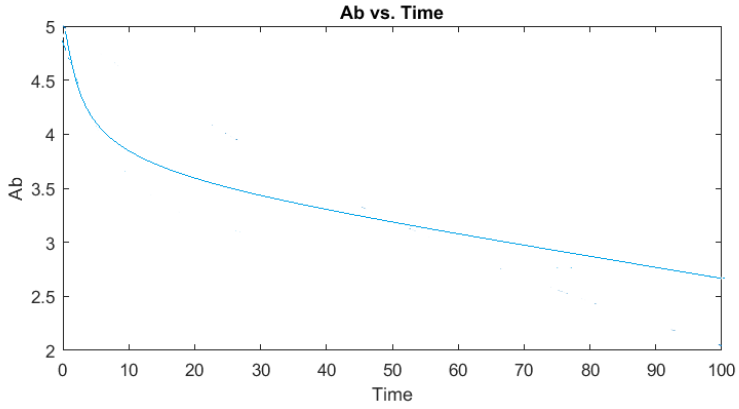

Figure 5: Progression of Thyroid Receptor Antibodies (TRAb) in effect of Radioactive Iodine (RAI) treatment on individuals with Graves' disease. The X axis represents the time in days and the Y axis represents the TRAb in IU/L. Considering the Dosage value of the drug as 39 mCi. Let initial values of the variables as follows: TSH = 0.906 mU/L, FT4 = 24.97 pg/mL, V = 30 mL, TRAb as 5 IU/L and values of the parameter are given in the table.

VI. CONCLUSION

The development of a patient-specific mathematical treatment model for Graves' disease, incorporating a system of ordinary differential equations (ODEs) involving Radioactive Iodine, TSH, FT4, and thyroid volume, Thyroid receptor antibodies (TRAb) stands as a promising and innovative approach in personalized medicine. The inclusion of Michaelis-Menten kinetics allows for a more accurate representation of the complex interplay between hormone levels, treatment impact, and thyroid function. The stability analysis of the model ensures that the treatment approach is not only personalized but also safe and effective. By examining the equilibrium points and their stability, we can better understand the dynamics of the disease and the potential outcomes of treatment, helping clinicians make informed decisions. Furthermore, the numerical simulations carried out using this model allow for a thorough exploration of different treatment scenarios and their implications on patient outcomes. This computational approach enables healthcare providers to fine-tune treatment plans, optimize dosages, and predict patient responses more accurately. In summary, the development of a patient-specific mathematical treatment model for Graves' disease, along with stability analysis and numerical simulations, represents a significant advancement in the quest for personalized and effective treatment strategies. This model holds the promise of improving patient care and outcomes in the management of Graves' disease with Radioactive Iodine, ultimately leading to better quality of life for individuals affected by this condition.

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