Optimal Control of Cancer Treatment Model with an Isoperimetric Constraint: Analytical and Numerical Study

Ashraf Awadelkarim Suliman[1], Hala Abbas Badawi Laz[2], Salwa Harfy Wadie[3]

[1]Department of Mathematics, College Of Science, Sudan University of Science and Technology, Khartoum, Sudan
Corresponding Author Email: ashraf.awad1992@gmail.com

[2]Department of Mathematics, University of Bahri (Sudan) and Wadi Alshatti University (Libya)
Email: halalaz55@gmail.com

[3]Department of Mathematics, College Of Science, Sudan University of Science and Technology, Khartoum, Sudan
Email: salwaharfy1@gmail.com

Abstract

This study examines an optimal control framework for a cancer treatment model with an isoperimetric constraint representing a bounded total drug dosage. The objective is to minimize tumor burden and treatment cost using Pontryagin's Maximum Principle to derive necessary optimality conditions. An auxiliary state variable is introduced to transform the constrained problem into a standard optimal control formulation. Analytical results are supported by numerical simulations, and a comparative analysis is conducted between constrained and unconstrained control strategies. The results show that the isoperimetric constraint leads to time varying dosing policies, while the unconstrained case yields constant control, highlighting the importance of cumulative dosage limits in treatment design.

Keywords: Optimal control; Pontryagin's Maximum Principle; Isoperimetric constraint; Mathematical oncology; Chemotherapy; Tumor growth; Optimal dosing strategy; Sensitivity analysis.

1 Introduction

Many real-world processes can be described mathematically through dynamical systems, where the evolution of certain quantities over time is governed by ordinary differential equations (ODEs), partial differential equations (PDEs), or discrete-time models [1, 7].
and in many applications, some components of these systems can be influenced externally through intervention or control variables. Thus, the fundamental question that arises is: how should these controls be selected over time in order to achieve the most desirable outcome according to a specified objective? [2, 3]

Optimal control theory provides a rigorous mathematical framework to address such questions [7]. The goal is to determine a control function that optimizes a performance index while respecting the underlying system dynamics and any imposed constraints. Typically, the objective functional reflects competing priorities, such as minimizing cost, maximizing efficiency, or reducing risk. In biomedical applications, the objective functional often represents a balance between therapeutic effectiveness and treatment-related side effects [12, 14].

In the context of cancer treatment, optimal control has become an important tool for designing chemotherapy or radiotherapy protocols. Tumor growth can be modeled by differential equations that capture the proliferation of cancer cells and their response to therapeutic agents. A control variable generally represents the drug dosage or treatment intensity, while the state variable describes the tumor burden. The objective is frequently to minimize tumor size over a fixed treatment horizon while also limiting drug toxicity and cumulative exposure [13, 11].

A particularly important feature in treatment modeling is the presence of practical and physiological limitations on the total amount of drug that can be administered. This leads to the inclusion of an *isoperimetric constraint*, which restricts the integral of the control over the treatment period [9]. Mathematically, such a constraint takes the form

$$\int_0^T u(t)\, dt \leq B,$$

where $u(t)$ denotes the treatment intensity and B represents the maximum allowable total drug amount. This type of constraint reflects clinical reality: although high doses may be effective in suppressing tumor growth, cumulative toxicity imposes strict upper bounds on total exposure [10, 16].

An isoperimetric constraint significantly influences the structure of optimal control. Unlike unconstrained problems, where the control may be determined solely by instantaneous optimality conditions, the cumulative restriction couples decisions across time [15, 4]. As a result, the optimal dosing schedule must strategically allocate the limited drug supply throughout the treatment horizon. In many cases, this leads to front-loaded strategies, where stronger doses are applied early to reduce tumor burden rapidly, followed by moderated administration to remain within the total budget.

From a theoretical perspective, such problems are typically analyzed using Pontryagin's Maximum Principle, which provides necessary conditions for optimality in the presence of state equations, control bounds, and integral constraints [15, 1]. The resulting optimality system consists of the state equation, the adjoint equation, transversality conditions, and a characterization of the optimal control that incorporates both pointwise bounds and the isoperimetric multiplier [6, 11].

The integration of optimal control with isoperimetric constraints therefore offers a powerful framework for studying cancer therapy design. It captures the essential trade-off between aggressive tumor suppression and cumulative toxicity limits, providing insight into how treatment intensity should be distributed over time. This approach not only deepens the mathematical understanding of therapeutic strategies but also contributes to the development of more effective and clinically realistic treatment protocols [14, 5].

The main objective of this study is to investigate an optimal control problem for a cancer treatment model under an isoperimetric constraint. The study derives the necessary optimality conditions using Pontryagin's Maximum Principle, characterizes the structure of the optimal control, and provides analytical and numerical solutions. In addition, a comparative analysis is carried out between the cases with and without the isoperimetric constraint to highlight its impact on the optimal treatment strategy and system dynamics.

2 Isoperimetric Constraint

2.1 Definition of the Isoperimetric Constraint

Let $f(t,x,u)$, $g(t,x,u)$, and $h(t,x,u)$ be continuously differentiable functions in all three variables. Consider the optimal control problem [12, 13, 16]:

$$\max_u \int_{t_0}^{t_1} f\left(t, x(t), u(t)\right) dt + \phi(x(t_1))$$

subject to

$$x'(t) = g\left(t, x(t), u(t)\right), \quad x(t_0) = x_0,$$

$$\int_{t_0}^{t_1} h\left(t, x(t), u(t)\right) dt = B,$$

$$a \leq u(t) \leq b.$$

This type of problem is called an *isoperimetric problem*, and the integral constraint

$$\int_{t_0}^{t_1} h\left(t, x(t), u(t)\right) dt = B$$

is called an *isoperimetric constraint* [9, 8].
The following example explains to us the idea of using the isoperimetric constraint in the optimal control problem.

Example 2.1. *Consider the simple problem involving cancer treatment:*

$$\min_u \int_0^T u^2(t)dt + x(T)$$

subject to

$$x'(t) = \alpha x(t) + \beta u(t), x(0) = x_0$$

We wished to minimize the final concentration of tumor cells and the total harmful effects of the drugs. Now, suppose we wanted to further restrict the amount of drug administered to the patient. One method would be to introduce a bound on the control, say $0 \leq u(t) \leq M$*, where* M *is an appropriately chosen constant. This method still allows some leniency in the total amount of drug. Suppose we know precisely the amount of treatment which can be given to this patient over the given time interval and still be within safety limits. Further, suppose we wish to administer precisely this amount over the time period, or stated mathematically*

$$\int_0^T u(t)dt = B$$

where B *is the known amount. Then, the problem we are now faced with is to minimize the final concentration of cancerous cells using a total drug amount of* B *over the time interval [8, 10] . This can be stated*

$$\min_u \int_0^T u^2(t)dt + x(T)$$

subject to

$$x'(t) = \alpha x(t) + \beta u(t), x(0) = x_0,$$

$$\int_0^T u(t)dt = B$$

3 Method of Solution

Pontryagin's Maximum Principle cannot be directly applied to problems with an isoperimetric constraint. To handle this, we define an auxiliary state variable [2, 7]:

$$z(t) = \int_{t_0}^{t} h(s, x(s), u(s))ds \quad \Rightarrow \quad z'(t) = h(t, x(t), u(t)), \quad z(t_0) = 0, \quad z(t_1) = B.$$

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Thus, the original problem is transformed into a standard optimal control problem with an additional state:

$$\begin{aligned} \max_u \quad & \int_{t_0}^{t_1} f(t, x(t), u(t))dt + \phi(x(t_1)) \\ \text{subject to} \quad & x'(t) = g(t, x(t), u(t)), \quad x(t_0) = x_0, \\ & z'(t) = h(t, x(t), u(t)), \quad z(t_0) = 0, \quad z(t_1) = B, \\ & a \leq u(t) \leq b. \end{aligned}$$

This transformation allows the use of standard optimal control techniques while explicitly enforcing the total integral constraint [9, 11].

4 An Application: Cancer Treatment Model

Consider the above cancer treatment model using

$$\alpha = 0, \quad \beta = 1, \quad T = 1, \quad B = 1$$

Then the problem could be on the form

$$J = \min_u \frac{1}{2} \int_0^1 u^2(t)dt$$

subject to

$$x'(t) = u(t), x(0) = 0, x(1) = 1$$

$$\int_0^1 x(t)dt = 2$$

Define another state variable $z(t) = \int_0^1 x(t)dt$, such that,

$$\begin{aligned} z'(t) &= x(t) \\ z(0) &= 0 \\ z(1) &= 2 \end{aligned}$$

Then, our problem becomes

$$\min_u \frac{1}{2} \int_0^1 u^2(t)dt$$

subject to

$$x'(t) = u(t), x(0) = 0, x(1) = 1$$

$$z'(t) = x(t), z(0) = 0, z(1) = 2$$

4.1 Analysis of Optimal Control

The necessary conditions that an optimal solution must satisfy come from Pontryagin's Maximum Principle [1]. The Hamiltonian is defined as:

$$H = \frac{1}{2}u^2 + \lambda_1 u + \lambda_2 x$$

Theorem 4.1. *There exists an optimal control u^* and corresponding solution, x^* and z^*, that minimizes J. Furthermore, there exist adjoint functions, $\lambda_1(t) and \lambda_2(t)$, such that*

$$\lambda_1'(t) = -\frac{\partial H}{\partial x} = -\lambda_2$$

$$\lambda_2'(t) = -\frac{\partial H}{\partial z} = 0 \Longrightarrow \lambda_2(t) = C$$

with transversality conditions

$$\lambda_i(t_f) = 0, i = 1, 2$$

Proof

Theorem (3.2.1) gives the existence of an optimal control due to the convexity of integrand of J with respect to u. Applying Pontryagin's Maximum Principle, we obtain

$$\lambda_1'(t) = -C \Longrightarrow \lambda_1(t) = -Ct + k, \quad k \quad is \quad a \quad constant$$

By Evaluating the adjoint variables at the optimal control and corresponding state trajectories, together with the optimality condition, yields the following expression.

$$\frac{\partial H}{\partial u} = 0 \Longrightarrow u + \lambda_1 = 0 \Longrightarrow u^*(t) = -\lambda_1(t) = Ct - k$$

and solving for u^*, subject to the constraints, we get

$$x'(t) = Ct - k \Longrightarrow x(t) = \frac{1}{2}Ct^2 - kt + m, \quad m \quad is \quad a \quad constant$$

Using the condition $x(0) = 0$, we have

$$x(0) = 0 = m \Longrightarrow x(t) = \frac{1}{2}Ct^2 - kt$$

Then

$$z'(t) = x(t) = \frac{1}{2}Ct^2 - kt \Longrightarrow z(t) = \frac{1}{6}Ct^3 - \frac{1}{2}kt^2 + n, \quad n \quad is \quad a \quad constant$$

Using the condition $z(0) = 0$, we have

$$z(0) = 0 = n \Longrightarrow z(t) = \frac{1}{6}Ct^3 - \frac{1}{2}kt^2$$

Using the conditions $x(1) = 1, z(1) = 2$, we have

$$\begin{aligned} \frac{1}{2}C - k &= 1 \\ \frac{1}{6}C - \frac{1}{2}k &= 2 \end{aligned}$$

Then

$$k = \frac{1}{2}C - 1 \Longrightarrow \frac{1}{6}C - \frac{1}{2}(\frac{1}{2}C - 1) = 2 \Longrightarrow C = -18$$

Thus

$$k = -9 - 1 = -10$$

This gives the optimal solutions

$$\begin{aligned} u^*(t) &= 10 - 18t \\ x^*(t) &= 10t - 9t^2 \end{aligned}$$

Next, we discuss the numerical solutions of the optimality system and the corresponding optimal control.

4.2 Numerical Solution

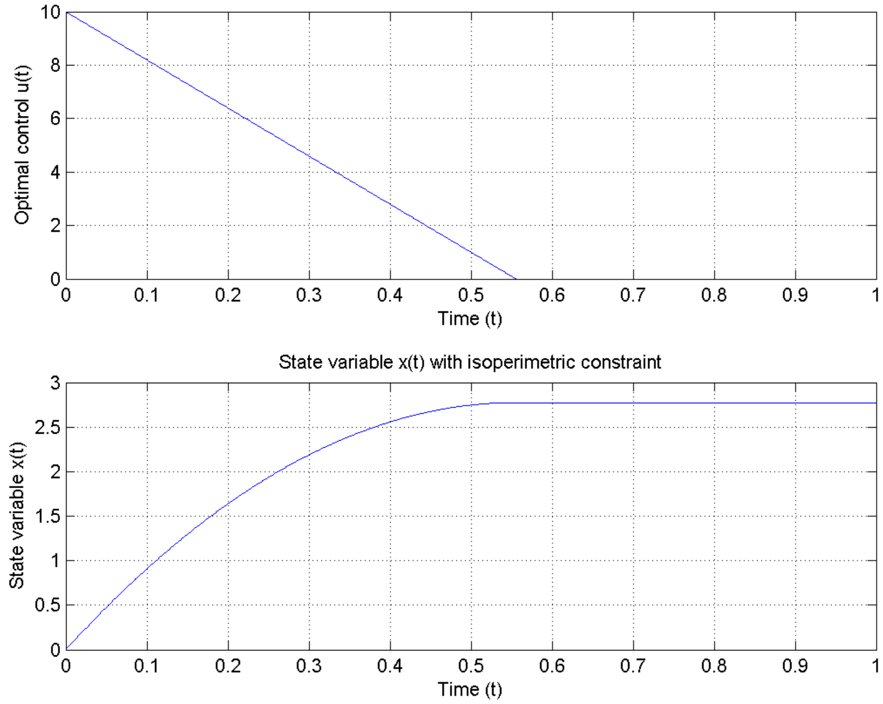

Figure 4.1: state variable and optimal control for the problem with isoperimetric constraint.
We want to exclude the isoperimetric constraint and reconstruct the code to solve the problem without isoperimetric constraint and compare between the controls in both cases.

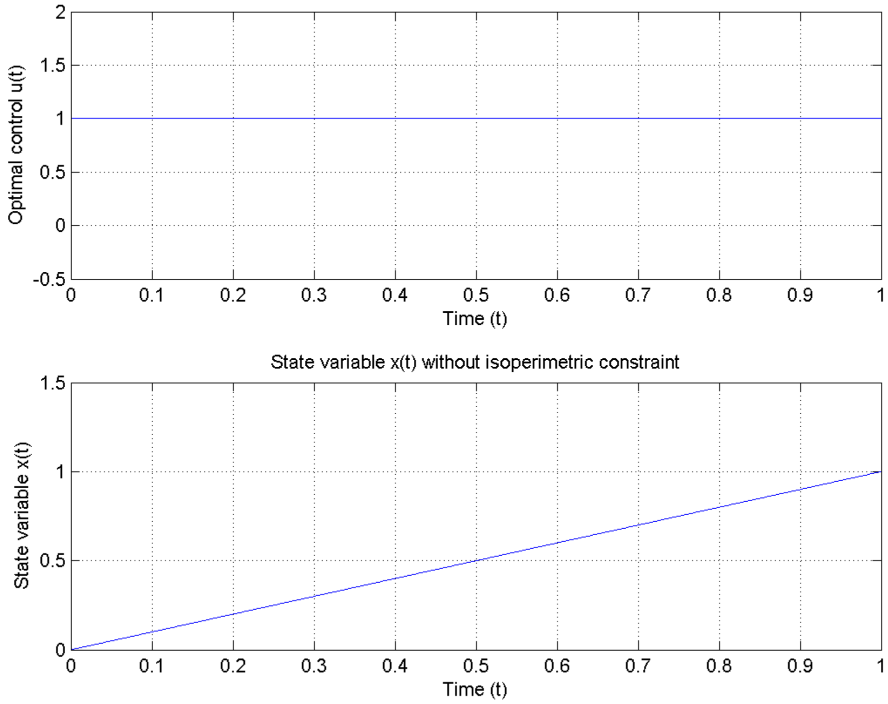

Figure 4.2: state variable and optimal control for the problem without isoperimetric constraint.

It is observed that the optimal control for the problem without isoperimetric constraint is a constant function, and that means the control should be distributed by a same magnitude in all the interval, but on the other hand the optimal control for the problem with isoperimetric constraint is a decreasing function and that means the control be should distributed highly at first and then decrease till arrive or to be closed to zero and that because in this case we have an exact or bounded a mount of control.

5 Conclusion

This study presents an optimal control formulation for a cancer treatment model under an isoperimetric constraint that limits total drug dosage. By applying Pontryagin's Maximum Principle and introducing an auxiliary state variable, the constrained problem is transformed and solved analytically. The results indicate that the presence of a cumulative dosage constraint leads to time dependent control strategies, in contrast to constant dosing in the unconstrained case. Numerical simulations support the analytical findings and demonstrate the practical relevance of incorporating dosage limits in treatment design. These results highlight the importance of constrained optimization in developing realistic and effective therapeutic strategies.

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