ABSTRACT

INTRODUCTION

Previous Work

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1. From research [1], it has been investigated that in 70% of the cancer cases, the cancer cells suffer a distortion in the survival and features of the cells that are specialized to regulate/ eradicate the dead and degenerative cells – known as Macrophage [2].[3].
2. And it has been explored from following papers [4], [5] that the macrophage can be populated the antigens and the immune system can be rejuvenated once affected with cancer cells via therapies.
3. In various resources, it has been illustrated that the therapies based on macrophage – and modelling based on equations – depict a method of using the process of diffusion after infiltrating the tumour with macrophage [6], [7], [8] using the mechanism of gliding motility but in using such therapies can also result in increasing the tumour size [7].

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1. As suggested and evaluated [1], [2], [3], [4], [5], [6], [7], [8], [9], [10], [11], [12], [13] with the administration of drug dose along with the Chemotherapy is a healthy alternative to radio therapies which show side-effects and tends to destroy the healthy cells along with the cancer cells.
2. Furthermore, the approach of optimal control therapy [9], [11], [13], [12] is required to have an optimal administration with the Chemotherapy [3], [2], which is observed by using a cost/ loss function to minimize the cost of model [6], [7] and resources for a favourable result with linear and quadratic modelling expressions.

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1. Pharmacokinetics is used for administration of drug using a linear model once, the intake of drug concentration is given.
2. For the administration of a drug, the scheme suggest that the dose is infused followed with a low maintenance of drug dose at a stable infusion rate [1] which tends to be easy.
3. But it holds the drawback that the administration of data is a rough approximation especially for the induction step and neither there is a sync between drug administration time and the pharmacodynamic phase, solution to this was given by synchronizing the time interval for the induction phase.
4. A linear model also solves the problem of corresponding time intervals between a compartment and the management of drug within it [2]
5. The scheme of infusion can get more plausible using the Microprocessor Controlled Infusion for simultaneously infusion of drug with a programmed microprocessor.

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1. Another type of pharmacokinetic model which is based on physiological attributes is known as the Physiological-based Pharmacokinetic (PBPK) approach of modelling and make predictions on the chemical concentrations for the unexplored regions or for the regions without data based on ADME approach. [1].
2. [2] showcase the simulation for the PBPK modelling, and [3], [4], [5], [6] gives walk through over the influencing factors in pharmacokinetics.
3. Papers (Barton et al., 2007; Beaudouin et al., 2010; Bois et al., 2010; Fierens et al., 2016) gave the insights to make predictions with uncertainty and variability using the approach of Bayesian and Monte Carlo.
4. The following work also shows the work on the drug administration considering the environmental chemicals (Kenyon et al., 2016; Kim et al., 2007).
5. Even after the manifold of benefits of the PBPK (USEPA, 2006; WHO, 2010) approach and in reporting templates (EMA, 2019; Shebley et al., 2018; USFDA, 2018), it is not wholly accepted due to formal and informal factors (Chiu et al., 2007; McLanahan et al., 2012; Tan et al., 2018, McLanahan et al., 2012, Paini et al., 2017).

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1. To control of problem of closed loop in the administration of a drug, compartmental and non-negative model are found to be quite useful as they contain interconnected subsystems. [1]
2. The following papers illustrate that the systems of non-negative adaptive control [8], [9], [10], [11].
3. Alternatively, the Adaptive algorithms shows a diverse behaviour in different subject due to a healthy correlation between the dose of the drug dose and the concentration of the blood as well as (pharmacokinetics) and between amount of blood and the physiological effect (pharmacodynamics). [6]
4. Previously, based on Pharmacokinetic/ Pharmacodynamic models and on control algorithms for linear adaptivity and proportional-integral-derivative. [2], [3], [4], [5]
5. Previous model-based algorithms have assumed either a fixed pharmacokinetic model or a fixed pharmacodynamic model [4], [5].
6. In another approach, more flexible linear framework built on adaptive control compartment models is used with diverse implications from non-linear pharmacodynamic and pharmacokinetic criticalities of patients using compartmental model and non-negative model but in a non-linear environment. [This paper]
7. Quite similar approach can also be seen from the paper [11], [7].

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Aim

METHODOLOGIES

1. Design and building framework for modelling and optimization for medical/ healthcare system.
2. Components of framework:
   1. Build models, optimize parameters, and test build models.
   2. Simulating the biological mechanism for the models and optimization
   3. Collecting significant patient-specific features to find the outcome.
   4. Hybrid method
3. Benefits of building a model for bio-medical: analysis over distinct values of scales and influencing factors (i.e., clearance, absorption rate, dose, time interval, etc). [1]

[1] Hall et al., 2011 C. Hall, E. Lueshen, A. Mošat’, A.A. Linninger Interspecies scaling in pharmacokinetics: a novel whole-body physiologically based modeling framework to discover drug biodristribution mechanisms in vivo J Pharm Sci, 101 (3) (2011), pp. 1221-1241

1. Understanding the influencing of changing parameters based on observations and interpretations to analysis the behaviour and biological of the characteristics within the body. [2], [3], [4], [5]

[2] Androulakis, 2014 I.P. Androulakis A chemical engineer's perspective on health and disease Comput Chem Eng, 71 (2014), pp. 665-671

[3] Chen et al., 2012 T. Chen, N.F. Kirkby, R. Jena Optimal dosing of cancer chemotherapy using model predictive contro and moving horizon state/parameter Estimation Comput Methods Programs Biomed, 108 (3) (2012), pp. 973-983

[4] Harrold and Parker, 2009 J.M. Harrold, R.S. Parker Clinically relevant cancer chemotherapy dose scheduling via mixed-integer optimization Comput Chem Eng, 33 (12) (2009), pp. 2042-2054

[5] Ho et al., 2013 T. Ho, G. Clermont, R.S. Parker A model of neutrophil dynamics in response to inflammatory and cancer chemotherapy challenges Comput Chem Eng, 51 (2013), pp. 187-196

1. It is complex to decipher the impact of dose within a biological body and the further implications but with the study of personalized medication possible from getting deeper insights of protein and molecules in a large-scale help in gaining precise, cost-effective and patient-specific diagnostic details. [6].

[6] Saha et al., 2014 R. Saha, A. Chowdhury, C.D. Maranas Recent Advances in the reconstruction of metabolic models and integration of omics data Curr Opin Biotechnol, 29 (2014), pp. 39-45

1. Challenges:
   1. The authenticity and the validity of the methodologies used.
   2. Incorporation of 3 vital elements:
      1. Patient-specific information
      2. Disease-specific information
      3. Building adaptive/ dynamic model for the patient of better treatment.

Optimization

Ordinary Differential Equations

DATA

RESULT and CONCLUSION

Existing Results

New Results

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Methodologies

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