

# The Role of the Vasculature and the Immune System in Optimal Protocols for Cancer Therapies

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## Abstract

A systematic study of cancer treatment requires that we take into account not only the cancerous cells and their growth, but also aspects of the tumor microenvironment. Its elements include various types of cancer cells, sensitive and resistant to the treatment, healthy cells, tumor vasculature, immune system and more. We shall discuss mathematical models that describe the dynamics of tumor growth in relation to its supporting vasculature under reciprocal angiogenic signaling [1]. For such models, in addition to standard direct treatments that kill cancer cells, one can introduce a second indirect treatment by means of angiogenic inhibitors that target the tumor vasculature. Another indirect approach is to consider the interactions between the tumor and the immune system, including tumor surveillance [4]. These approaches generate challenges in the mathematical analysis when a multi-state dynamics is coupled with the multi-input controls which represent the combination therapies [3]. These challenges will be addressed from the dynamical systems point of view leading to the optimal control problems of designing protocols for these treatments [2]. The role of models for the pharmacokinetics of the drug will also be addressed. We outline some future work on a more complex model which encompasses more elements of the microenvironment and multi-target therapies.

**Keywords:** tumor microenvironment, angiogenic signaling, immune system, multi-target therapies, multi-input control systems, optimal protocols.

## References

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