The main goal of the project is to develop original system engineering models and methods which support analysis of clinical data and aim at better prediction of anticancer therapy outcome and possible improvement of this outcome when combined therapies are used

Usually, patient data used to evaluate efficiency of planned oncological treatment concerns time until reoccurrence or time until death for patients with a particular type of disease . So called survival analysis, a widely used statistical method, is a typical approach to analysis of such data. **However, it provides conclusions only with respect to average response to treatment in some patient population and does not allow to take into account individual patient state and, consequently, does not provide accurate prognosis of therapy outcome for specific patients.** As a result, it is difficult to determine advantages of using adjuvant therapy in individual cases.

The proposed project will focus on systemic analysis of data and available mathematical methods aimed at development of computational models that support prognosis of personalized therapies outcomes and thus support decision making in oncology.

So far, development of adjuvant anticancer therapies have been largely empirical, based on the outcome of a prospectively designed randomized clinical trials. One of the most intensively explored areas in the clinic is comparison of the effectiveness of postoperative (or preoperative) radiotherapy to the effectiveness of postoperative (or preoperative) radiotherapy combined with chemotherapy and these will be the main areas of the proposed studies. The proposed research team has access to the original databases from the prospectively designed randomized clinical trials that explore the effectiveness of postoperative radiochemotherapy in cancer of the oral cavity and preoperative radiochemotherapy in locally advanced rectal cancer. They contain not only the data on overall survival, loco-regional tumor control and distant metastases rate, but also description of tumor site, stage, extent of surgery, general performance of the patient, age, gender, time interval surgery-radiotherapy and the parameters estimated from the pretreatment and post-treatment automated blood-cell counter. These databases have not been yet systematically explored from the point of view proposed in this project. While the methods developed in the project will be tested on these data, the conclusions and computational tools developed will be easily adaptable to other types of cancer as well.

The project consists of three tasks that will be run simultaneously but with clear dependencies among them:

1. Development of mathematical models of cancer response to different forms of treatment and verification of their usefulness from the clinical viewpoint using available data
2. Development of original methods for classification of patients with respect to predicted therapy outcome and their validation using clinical data and expert's knowledge
3. Application of tools of evolutionary game theory to analyze the role of interaction between different treatments in effects of combined therapy

The proposed project includes pioneer, interdisciplinary research including methods from statistical inference, system engineering, systems biology, optimization, modeling and simulation with strong support from clinical data. Ability to use the methods developed in the project both for predicting therapy outcome for a patient undergoing personalized treatment and for search for better general treatment protocols will be their main advantage over existing solutions. When completed, the project will indicate factors that can be used to predict therapy outcome and point out possible changes in currently used treatment protocols that may increase cure probability. Combining these two project results is a step toward a personalized medicine. The proposed class of models will contribute to the system engineering development.