

The main goal of the project is to develop original models and methods, which support analysis of clinical and imaging data and aim at better prediction of spread and colonization of tumor cells to distant organs, with emphasis on the most common subtype of lung cancer - non-small-cell lung carcinoma (NSCLC). Lung cancer is one of the most commonly diagnosed cancer and is the leading cause of cancer-related deaths. The most common histological subtype is non-small-cell lung carcinoma, accounting for 85% of all lung cancer cases. Advanced NSCLC is more likely to metastasize, leading to severe symptoms and a decrease in overall survival. The presence of distant metastases is one of the most predictive factors of poor prognosis.

Distant metastases (distant cancer) refer to cancers that have spread via blood or lymphatic vessels from the original location (the primary tumor) to distant organs or lymph nodes. The main cause of cancer death is associated with metastases, which are mainly incurable. Thus, distant cancer is resistant to treatment intervention. Even though cancer researchers have made a lot of effort to understand the appearance of metastases, few preclinical studies about metastases were translated to clinical practice. Metastasis is a complex process that involves the spread of a cancer to distant parts of the body from its original site. In order to become clinically detectable lesions, it must complete a series of steps at multiple temporal and spatial scales.

The deterministic description of this process is based on either ODE or PDE models. The proposer has developed a stochastic model of non-small cell lung cancer progression and dissemination to local lymph nodes and distant sites. The model proposed by us considers two ways of metastatic dissemination: through blood vessels (hematogenous route) and through lymphatic vessels (lymphatic route). The project aims at tackling metastases in the most common type of lung cancer. If successful, the project outcome will be information about the dynamics of tumor metastases in lung cancer, i.e., when, where, and how the primary tumor will metastasize. Information will be extracted using a non-invasive PET/CT imaging techniques. The conversion of digital medical images into mineable high-dimensional data is known as radiomics. Radiomics is designed to develop decision support tools; therefore, it involves combining radiomic data with other patient characteristics (clinical, molecular etc.), if available, to increase the power of the decision support models. This information will be incorporated in different types of known and original models using machine learning tools.

The proposed project includes interdisciplinary research employing methods from machine learning, data analysis, biomathematical modeling, image processing, bioinformatics and systems biology, with strong support from clinical and biomedical images data. It will provide a new framework of data integration and analysis and novel algorithms that will support interdisciplinary research. The results of the project could bring us knowledge about the dynamics and origin of metastatic dissemination of lung cancer. By dynamics, we understand when and where a tumor will disseminate, and by origin we mean dissemination path (directly from original tumor or through lymphatic nodes). This information is very valuable for clinicians, as it could guide the personalized treatment of lung cancer patients. Results obtained in the project will elucidate important issues concerning prediction of individual progress of cancer and treatment outcome in oncology. They will provide both theoretical and simulation tools to support decision making and diagnostics in oncology, on the basis of individual patient state.

Although the first attempt to use mathematical modeling to study quantitatively metastases of untreated lung cancer had more than sixty years of history, there are currently no mechanistic models incorporating biomarkers, which could play a role of prognosis tools that could predict when and where NSCLC may metastasize.