Pancreatic cancer is one of the most hypoxic human neoplasms. At the same time, it is also one of the worst-off ones - the five-year survival rate after diagnosis is around 10%. In order to better understand why the currently most common anti-cancer therapies have such low effectiveness, it is necessary to understand better their mechanisms of action in the context of changes in the environment in which the tumor cells are located, particularly tumor tissue hypoxia (oxygen deficiency).

This project assumes that changes in tumor oxygen levels following anti-cancer therapy may provide a better answer to why pancreatic cancer is connected to poor prognosis. The research will be carried out on various mouse and human pancreatic tumor models, including injectable and spontaneous tumors. What is more, all studied tumors will have a physiologically correct localization (which determines the appropriate tumor microenvironment). Two of the most recommended therapies will be performed as an anti-cancer treatment—chemotherapy, which uses three different drugs, and second - surgery. Three non-invasive imaging techniques will be used to study tumor oxygenation (by electron paramagnetic resonance), hemoglobin saturation and collagen (by photoacoustic imaging - PAI), and functional vasculature and perfusion (by – ultrasonography), followed by tumor biopsies and biological analysis. Next, all collected data will be registered with each other, and we will try to extract, with advanced image analysis, unique markers which can be helpful for therapy planning. The image-guided therapy on the selected protocol will be performed in the last step of the current proposal.

Diversified methodologically, oxygen measurements before, during, and after the therapy will assess the role of oxygen in the organism's vascular, cellular, and immune response to the performed treatment. As a result, an answer will be given to the question - is the increase of pancreatic tumor oxygenation after antitumor therapy possible, and if yes – when and how big is it? In the end, we could answer the question if tumor tissue reoxygenation is a sign of cure or an indication of a progressive neoplastic disease? This proposal aims to plan chemotherapy and monitor animal response to treatment to improve therapy outcomes.

Significant effects of the project implementation are expected on various levels. First, the translational plane - the role of pancreatic cancer reoxygenation in predicting treatment response will be learned. Secondly - in the methodological aspect - three independent techniques for evaluating tissue oxygenation, their sensitivity to changes in oxygen partial pressure, and ease of implementation will be compared. Thirdly - on the biological plane - the late and early effects of PDAC tumor therapy in mice will be investigated, resulting in the selection of biomarkers of treatment efficacy. Subsequently, the mechanism and kinetics of pancreatic tumor tissue reoxygenation in mouse models will be explored in the biophysical aspect. The social dimension of the project should also be emphasized, which will empower the promotion of knowledge about the role of oxygen in the treatment of cancer and publicized the problem of pancreatic cancer treatment.