

Low tissue oxygenation is associated with many disease states, such as cancer, wound healing, and cardiovascular disease. It is very difficult to improve the oxygenation of such tissues. In cancerous tumors, the lack of oxygen is associated with a worse response to therapies, especially to radiotherapy. In recent years, ultrasound-sensitive oxygen microbubbles have been shown to be an effective way to overcome hypoxia in tumors in animals. Once administered to the body, they can be broken down by means of an ultrasound pulse in the selected tissue, selectively supplying oxygen. However, our previous research has shown that this approach leads to increased metastasis.

To prevent this and, at the same time, provide oxygen to the tumor and thus improve the effects of oxygen-dependent cancer therapies, such as radiotherapy or sonodynamic therapy, we propose the use of much smaller nanobubbles. Our goal will be to check whether oxygen-containing nanobubbles will be equally effective in increasing the level of oxygenation of cancerous tumors in mice, but above all to investigate how nanobubbles affect the biology of tumor tissue, its metabolism, immune profile, and metastasis process. Oxygen nanobubbles can also be used as contrast agents for ultrasound imaging, so they fulfill a dual, theranostic role, acting both as a therapeutic and diagnostic agent at the same time.

Our team has extensive experience in studying the microenvironment of neoplastic tissue using noninvasive imaging methods. In the project, we will use ultrasound imaging to visualize the structure of the tissue, vascularity, and, using nanobubbles, its perfusion. Another method, electron paramagnetic resonance imaging, will be used to map the oxygen and metabolic rate of the tumor. Such precise and quick measurements will allow us to track the changes that occur in tumors in real time.

In the next stages of the project, we will check the distribution of oxygen in solutions and tissue models and in animal tumors. We will check whether the administration of nanobubbles is safe, i.e., it does not cause toxicity and how it affects metastasis. If the administration of nanobubbles turns out to be effective and safe, then in the last step we will examine whether radiotherapy and sonodynamic therapy with nanobubbles will be more effective than without them. The conclusions of these studies will be relevant both for our understanding of the functioning of the neoplastic tissue environment and for the practical application of oxygen nanobubbles in cancer and other diseases related to tissue hypoxia.