

## **DESCRIPTION FOR THE GENERAL PUBLIC (IN ENGLISH)**

Breast cancer accounts for 20% of all cancer cases in our country and is also the most common malignant tumor occurring in women. Based on the expression of specific receptors there are several types of breast cancer: estrogen receptor-positive, progesterone receptor-positive, HER2-positive and triple-negative (no expression of receptors). The main treatment for early stage of breast cancer is conservative surgical excision of tumor (quadrantectomy) with postoperative whole breast radiotherapy. Numerous studies have shown that 80-90% recurrence arises mostly within the scar. The dominance of metastases within the scar initiated a series of scientific research, and their consequences in clinical trials, aimed to assess whether localized radiotherapy, such as intraoperative radiotherapy (IORT), will be more effective in inhibiting the possibility of local recurrence than the standard postoperative whole breast radiotherapy. Intraoperative radiotherapy involves irradiating of diseased tissue directly during surgery within the tumor bed. The rationale for this approach is that an increase in the radiation dose increases local tumor control. It is known that ionizing radiation (IR) directly affects the cells by damaging DNA and consequently changes the phenotype of the cell. In addition to a direct action, the effect of IR may also be observed in cells that were not irradiated but being in a high proximity of the irradiated cells. This phenomenon is called the "bystander effect" (RIBE, radiation induced bystander effect). RIBE contributes either to induce death in unirradiated cells (through cell-cell contact or by production of cytokines), or to the changes in the tumor microenvironment. Moreover it has been shown that RIBE is associated with changes in the plasma membrane and production of soluble immune signals that initiate an effective immune response - the immune response to IR-induced stress. Results from clinical studies using intraoperative radiotherapy (TARGIT and ELIOT) indicate a low toxicity of intraoperative radiotherapy and a decreased recurrence of the disease in follow-up. In addition, Belletti et al. have demonstrated that post-operative fluid obtained from patients after IORT inhibits the proliferating and migrating properties of cells in the culture conditions as compared to fluid of patients who underwent the standard operation without IORT. The researchers showed that this effect was related to the biological activity of serum collected from the drain after surgery. These studies confirmed that IORT not only sterilizes the cancer cells, but also modifies the wound microenvironment by modeling them as hostile to the growth of cancer cells and metastasis. According to the authors of the project, the drain fluid collected from a patient after intraoperative radiation therapy is a fluid acting as so-called "bystander effect". The researchers assume that, as the RIBE medium, the IORT fluid will change the properties of cancer cells by inducing their death and by the production of soluble immune signals which affects the radiation-induced immune response. The results of the project can serve as a starting point for further analysis and to create an opportunity to identify and test new therapeutic agents. Research results will be presented in the form of oral presentations and poster at conferences at national and international levels. Due to the innovative approach of the research, the results will be published in international journals with high impact factor.