The head and neck cancer (HNC) patients constitute the sixth largest group of cancer patients. Factors that increase the risk of developing this type of cancer are exposure to tobacco smoke, alcohol, or infection with HPV. Despite the development of diagnostic and therapeutic techniques only every second patient will survive more than five years and in many patients distant metastases will appear after treatment. In this aggressive disease fight for life is carried out using aggressive treatment techniques – these are the techniques using ionizing radiation, such as radiotherapy and chemo-radiotherapy, in which the patient also gets highly toxic anti-cancer drugs.
These techniques kill the cancer cells, but normal cells are damaged too – and because HNC involves different squamous cell carcinomas located in larynx, pharynx, oral cavity, and tongue, which play crucial roles in respiratory, nutritional, social and communicative functions, treatment-induced toxicity in these organs often leads to a considerable impairment and seriously affects the patient's quality of life.

Researches have long been searching for molecular markers that will facilitate insight into the tumor, the course of its treatment and will help predict the individual response of the body to a toxic therapy. These explorations are important because it is expected that the knowledge on the molecular state of the body should translate into faster diagnosis and more precise monitoring of treatment. For the patient, this means a better tolerability and the higher efficiency of his/her therapy. Molecular marker or, more likely, a set of markers – so-called biomarker, is the key to the treatment, opening the possibility of adapting it to the real needs of the patient’s organism. In the search for a biomarker it is also important that the procedure for its determination was not invasive and embarrassing for patients. This is why peripheral blood has for years remained the "gold standard" as a source of new diagnostic factors.

The quest for biomarkers is more effective for certain types of cancer, and for others there are still no verified candidates – as it is in case of the head and neck cancers. But while the search for biomarkers of tumor activity – thus for the biomarkers answering the question of the cancer presence in the body – evidently speeds in recent years, the question of biomolecular monitoring of treatment toxicity and the patient’s response to the treatment remains open. There are very few works on such issues concerning human therapy. In contrast, the results of animal biological material (urine, blood serum) indicate that the current state of molecular biological system (its phenotype) can be linked to the severity and intensity of the “toxic event” like radiation dose. Meeting this challenge requires the use of technologically advanced research methods, known as "omics": genomics, transcriptomics, proteomics and the youngest of the "omics" – metabolomics. The latter has been developed intensively for last ten years and is based on the idea that each type of cell and tissue has a unique metabolic “fingerprint”, called metabolome – a complete set of metabolites (in a cell or a tissue), and metabolomics is one means to determine this metabolic fingerprint, which reflects the balance of all the forces influencing an individual's metabolism. Thus, it is an excellent tool for determining the phenotype. The analysis of the changes in the metabolic profile should, in turn, facilitate identification of the factors determining and/or reflecting key processes involved in the response to treatment.
In the metabolomics studies two spectroscopic techniques are of crucial importance: nuclear magnetic resonance spectroscopy and mass spectrometry. These techniques generate huge amount of complex data and in order to analyze such big datasets specialized statistical techniques are required, the so-called multivariate methods.
In our project these techniques are planned to be used to analyze a unique set of data, which will be built from a combination of molecular information derived from the spectroscopic and spectrometric blood serum analyzes of the HNC patients with a comprehensive set of clinical data, such as the results of endoscopy, imaging, laboratory and psychological tests. The final model will involve the data collected in many points in time from a large group of patients.

The project relies on two hypotheses:
I. The response of organisms to anticancer treatment is mirrored in morphological, functional and molecular changes observed both in the treated tissue and as general response of human body (including systemic and psychological alterations). Moreover, such response affects composition and concentrations of metabolites in body fluids, like blood serum and plasma, which may be evaluated by HR NMR and MS analytical approaches.
II. The combination of clinical and molecular approaches could deliver comprehensive information of treatment response, allowing monitoring and/or prediction of tolerance/toxicity of therapy as well as its short- and long-term outcome. Such approach gives a step forward into personalized treatment medicine.

Our pilot results, both on applications of nuclear magnetic resonance spectroscopy and mass spectrometry, show that these techniques can efficiently provide molecular information on the response of HNC patients to radiotherapy. But if we want to explain the metabolic consequences of prolonged and complex cancer therapy, we have to go a step further – it is necessary to join the spectroscopic techniques with full clinical data – because only on this basis metabolomics modeling using multidimensional data analysis is able to model the response to radiotherapy in terms of tumor regression and tolerance/toxicity of treatment.
The model based on a combination of clinical and molecular parameters (reflecting the changes in the metabolic blood profiles induced by treatment – is expected to allow us to predict individual response to treatment) it is expected to personalize the treatment. Finally, it will be possible to identify cancer biomarkers and biomarkers of the treatment efficacy and tolerability. Moreover, after collecting data on the long-term effects of treatment (long-term survival and late radiation reactions), the relationships between early and late effects of treatment and the metabolic changes observed in the spectroscopic blood profiles will be studied.
We believe that the knowledge accumulated in the proposed project will contribute to the development of tools and research models for possible application in other studies in the life sciences, and potential use in diagnostics.