The project goal: The goal of this project is the elaboration of new non-invasive imaging methods for positron emission tomography of the whole human body which would enable fast and real-time diagnose of cancer and cardiovascular diseases. The resulting methods will be verified by clinical trials with healthy subjects as well as patients with cancer and cardiovascular diseases.
Positron emission tomography (PET) is a well-established diagnostic method enabling the detection of tissue pathology on a molecular level before it evolves to the functional or morphological abnormalities. Currently, routine PET diagnosis with scanners of about 20 cm length, in a single bed position, enables for the simultaneous diagnosis of individual organs only, and the diagnosis of the whole body requires a combination of a series of sequential images obtained for many patient positions in the scanner. With the advent of the total-body PET, a PET with a length of 200 cm, precision medicine has been enhanced with a new tool that allows for the simultaneous molecular imaging of the whole human body. Thanks to the high sensitivity, total-body PET enables the significant reduction of the whole-body imaging duration or the reduction of the dose of the radiopharmaceutical, thus opening perspectives for the application of PET to the wider group of patients also those having systemic diseases. PET is most often used for the diagnosis of cancer diseases, however, in the case of the total-body covering it may be also effectively used for the diagnosis of cardiovascular diseases.

Reasons for attempting a proposed research topic: According to the World Health Organization, cardiovascular and cancer diseases are the first and the second cause of death globally. Therefore, it is important to conduct scientific experiments that may lead to a better understanding of the background and mechanisms of these diseases, leading to more accurate diagnosis and effective treatment. For this purpose, the Total-Body Jagiellonian Positron Emission Tomograph (TB-J-PET) is being developed at the Jagiellonian University and its construction will be completed in the year 2023. It will be a first of this kind research instrument in Europe and the first in the world enabling total-body multi-photon imaging based on the nuclear and particle physics originating methods, invented at the Jagiellonian University. This Maestro project concerns the pioneering experiments which will be conducted by means of this unique research facility.

Description of research: The proposed project is interdisciplinary, intertwining experimental particle and nuclear physics with medicine. On the physics side, it concerns processes such as nuclear decay, positron-electron annihilation, formation and annihilation of positronium atoms, modeling of photons' interaction inside patient and detectors, advanced simulations, and signal analysis of multi-modular detector response, analysis, and filtration of big data streams and image reconstruction methods. While from a medical point of view, it concerns the diagnosis and treatment of oncological and cardiological patients, basic studies with patients, and testing correlations between molecular, metabolic or histopathological parameters and image-based assessments. In this project, we hypothesized that the combination of (i) dynamic standard PET image, (ii) kinetic parametric image, and (iii) positronium image may serve as *image-biomarker* enabling detection of diseased tissues and quantitative enhancement of specificity in cancer and vascular diseases (infarct and stroke) assessment. In order to verify the project working hypothesis, we will design, construct, take into operation and calibrate modular and extendable Frontal Detector, which combined with the TB-J-PET will enable high sensitivity imaging of the brain and body. Next, we will elaborate, test, and validate image reconstruction methods for dynamic 2-photon metabolic imaging, kinetic model-based parametric imaging, and positronium imaging. The positronium images will be reconstructed based on the method developed by the J-PET group using both 2-photon and 3-photon positronium decay modes. The reconstruction procedures will be tested using phantoms. Next, the dynamic scans will be performed with patients. We will enroll healthy subjects as well as patients with cancer and cardiovascular diseases (atherosclerosis, thrombosis). In the final stage of the research, the statistical analysis will be performed in order to establish correlations between the standard diagnostic parameters presently used for the disease assessment (e.g. grade of cancer malignancy from histopathological studies) and information available from the combined dynamic, parametric, and positronium images.

Expected results: The realization of this interdisciplinary project will open new perspectives in medical diagnostics by paving the way for the in-vivo assessment of tissue pathology in the whole patient body. It will be an example of the transfer of particle and nuclear physics methods to medicine for the qualitatively new medical experimentation with a promising perspective of establishing a new field in medical diagnostics. The successful implementation of this project will provide unique in the global scale facility for the simultaneous high sensitivity positronium-, dynamic- and kinetic model-based parametric imaging of all organs of the patient, simultaneously (including body and brain). Such facility and methods, which will constitute results of this project, will open utterly new, not yet explored, possibilities to study metabolism rate correlation between near and distant organs in the body, and simultaneously the structure of cells at the molecular level and concentration of bio-active molecules in the tissue in-vivo.