The project goal: Positron Emission Tomography (PET) is used regularly in hospitals e.g. for cancer diagnostics. During PET imaging a positron emitted by the radionuclide annihilates with the electron in the patient's body, directly or via formation of the metastable positronium atom. In the human body, positronium atoms are formed in up to about 40% of cases of positron-electron annihilations. Positronium is an atom composed of an electron and a positron. As an object made of matter and antimatter, it is not stable, but annihilates mainly into two or three photons. The mean lifetime of positronium and the ratio of its decay rate into two and three photons depends on the molecular environment in which positronium is produced.

Positronium imaging can be defined as a method for the position-sensitive reconstruction of positronium properties (such as mean lifetime, formation probability, and 3-photon/2-photon rate ratio) within the imaged object. The two or three photons from the positronium decay are used for the reconstruction of the annihilation density distribution. However, the positronium lifetime may be determined only when the administered radionuclide emits additional gamma quantum (three photon emitter) carrying information of the time of positronium formation. Information comprised in positronium images concerns the size of intramolecular voids and concentration in them of bio-active molecules and it is qualitatively different from the anatomical and morphological images obtainable by computed tomography (CT) and magnetic resonance imaging (MRI).

The main goal of the proposed project is the verification and development of the positronium imaging method by application of elaborated ^{44}Sc, ^{44m}Sc and ^{72}As labeled receptor radiopharmaceuticals for three-photon positron emission tomography, as well as the elaboration of methods of data selection and analysis that will enable multi-photon and positronium imaging with the newly developed modular J-PET detector.

Reasons for attempting a proposed research topic: According to the World Health Organization, cancer diseases is the second cause of death globally. Positronium imaging is a promising method for improving the diagnosis specificity by enabling assessment of the tissue pathology in-vivo. There are investigations demonstrating differences of the positronium lifetime between normal and cancerous cells. These results indicate that positronium imaging may be useful for the assessment of tissue alterations at the molecular level before they lead to the functional and morphological changes. Moreover, it was recently shown that positronium lifetime is changing linearly with the concentration of oxygen in organic liquids indicating its potential for detecting and quantifying hypoxia. The diagnosis of the degree of tumor hypoxia is of key importance in the planning of the cancer therapy. The first positronium images were created in the laboratory with the Jagiellonian PET prototype using ^{22}Na radionuclide. ^{22}Na radionuclide after emission of positron transfers to excited nucleus of ^{22}Ne which subsequently deexcites via emission of gamma quantum. ^{22}Na is a relatively long living isotope (with half-life of 2.6 years), and therefore it is not well suited for administration into the human body. Therefore, there is a need of elaboration of nuclear physics methods for creation of beta-plus isotopes characterized with mean lifetime in the order of hours, which in addition emits an deexcitation gamma quantum, and which can be attached to bio-ligands with high affinity to receptors expressed at cancer cells. We have identified Scandium-44 and Arsenic-72 as the most promising isotopes for the development of three-photon imaging.

Description of research: The research will be carried out at the University of Warsaw (UW), the Institute of Nuclear Chemistry and Technology (INCT), and at the Jagiellonian University (JU): UW will develop methods for the efficient production of ^{44}Sc, ^{44m}Sc, and ^{72}As isotopes. UW will also produce and supply these isotopes for research carried out at the INCT and JU. INCT will develop methods for the effective attachment of ^{44}Sc, ^{44m}Sc, and ^{72}As isotopes to ligands (e.g. PSMA, DOTATATE, trastuzumab, ANTI-HER affibody) and work on the determination of receptor affinity and internalization of the synthesized radio-bioconjugates. INCT will also produce and supply radiopharmaceuticals to perform 3-photon imaging with phantoms by means of the modular J-PET tomograph at JU. JU will develop three-photon image reconstruction methods and will perform tests on phantoms filled with tracers labeled with isotopes ^{18}F, ^{22}Na, ^{44}Sc, ^{44m}Sc, and ^{72}As.

Expected results: The expected scientific effect will be the development of methods of the targets preparation used for the production of Scandium and Arsenic radioisotopes, as well as target holders and targets heads suitable for it, enabling their long-term irradiation with currents measured in tens of microamperes of the ion beam delivered by so-called medical cyclotrons. The chemical studies carried out under the project will allow the synthesis of new radio-bioconjugates based on innovative radionuclides ^{44}Sc, ^{44m}Sc, and ^{72}As. Apart from their applications in the 3-photon PET method, they can also be used in standard 2-photon PET systems. The methods for positronium imaging will be developed and tested with new three-photon traces labeled with Scandium-44 and Arsenic-72 isotopes.