C.1. DESCRIPTION FOR THE GENERAL PUBLIC

Over the last decade the number due to cancer significantly increased, despite the rapid progress in diagnosis of even small, early stage of cancerous transformations. In some type of tumours, such as glioma multiforme, a median patient survival does not exceed 14 months from the diagnosis. Similar situation exists also for other aggressive tumours, such as HER2-positive breast cancers. Currently, surgery, next external radiotherapy, and systemic chemotherapy relying on administering of cytostatic drugs are the most common conventional therapy options. Unfortunately, therapeutic effects of cytostatic drugs are usually hindered by serious side-effects due to their toxic influence on healthy tissues. Moreover, many types of cancer cells show inherited or acquired resistance to the administered drugs and ionizing radiation.

Recently, better results in the treatment of such tumours are achieved with use of the targeted radionuclide therapy, in which the active targeting molecules are labeled with the emitters of corpuscular radiation. The preliminary clinical trials of aggressive glioma tumours at Warsaw Medical University, a substantial lifetime increase was achieved for the treated patients. The second, and very promising method, is the so-called magnetic hyperthermia, particularly in connection with the external radiotherapy. In such treatment, a colloidal suspension of superparamagnetic nanoparticles is administered to the patient to locally heat the tumour tissue under the influence of alternating magnetic field. Also in this case the first clinical trials reported spectacular therapeutic effects for the case of glioma tumours and breast cancers.

In our application we propose to combine these two methods by using superparamagnetic iron oxide-based nanoparticles (SPIONs) with radioisotopes incorporated in their magnetic core and surface-modified with covalently bound biomolecules, actively targeting selected cancer cells. The multiplied therapeutic effect of the proposed radiobioconjugate results both from the radioisotope radiation and from the local heating of cancer cells.

The interdisciplinary consortium responsible for the project will be formed between the University of Warsaw (UW), Chemistry Department and the Institute of Nuclear Chemistry and Technology (IChTJ) in Warsaw. The research team at UW an innovative concept of application of superparamagnetic iron oxide-based nanoparticles as a new generation of carriers that can be used in diagnosis and targeted chemotherapy, while the research team at IChTJ for 5 years develops the concept of the use of nanoparticles with bound radioisotopes and addressing biomolecules for targeted therapy of, e.g., brain tumours.

In our research we propose to use the superparamagnetic ferrites containing paramagnetic Tb(III) or Ho(III) ions in their core. Terbium and holmium cations should enhance the magnetic behaviour of nanocarriers and therefore increase their capability of heat generation in an alternating magnetic field. What is more important for the targeted radiotherapy, the stable Tb(III) and Ho(III) ions can be partially substituted with ^{161}Tb and ^{166}Ho isotopes, emitting β^- radiation. Thus, the magnetic nanoparticles containing ^{161}Tb or ^{166}Ho become the sources of β^- radiation, and being targeted to the tumour tissue by biologically active addressing molecule (trastuzumab or substance P) will enable the radiotherapy "from inside" of the tumour, without affecting healthy tissues, contrary to the commonly used "external" radiotherapy. Additionally, the external alternating magnetic field will induce heating of the cancer tissue.

This way we will obtain the multifunctional action of bioconjugate resulting from the ionizing radiation emitted by the radionuclide and the possibility of therapeutic effect due to the localized magnetic hyperthermia. Based on the literature of tumour biology, we expect that the so-called synergetic effect achieved due to the simultaneous action of both methods will substantially enhance the therapeutic result compared to both methods applied separately.