DESCRIPTION FOR THE GENERAL PUBLIC

In the modern world new areas of research continue to excite the public and have societal impact, one of these is nanotechnology. With this branch of science, it has become possible to product particles smaller than the diameter of a single human hair. An example of such systems are nanoparticles combining diagnostic and therapeutic functions. There has been particular interest in liposomes – bubble-shaped particles composed of lipids that are both hydrophilic and hydrophobic in structure. Because of their extraordinary construction, liposomes can carry in the interior therapeutic substances that are readily soluble in water (hydrophilic) as well as those that do not dissolve in water (hydrophobic). The latter group includes a number of anticancer drugs, including photosensitizing agents used in photodynamic therapy. Placement of such drugs in liposomes improves their propagation in the body and reduces side effects of the treatment. This provides hope for improvement in the quality of treatment and reduction of costs.

Currently medical diagnostics is largely based on imaging. One of the most common methods is Magnetic Resonance Imaging (MRI), a non-invasive technique to obtain images of internal organs in two and three dimensions. During the MRI, the patient may receive contrast agents - non-therapeutic substances that allow better visualization of examined structures by inducing changes in the image contrast. The most commonly used are compounds contain gadolinium ions, which are toxic in the body when chemically unbound. One way to significantly reduce the toxicity of gadolinium is to build it into a liposome. If such a liposome also comprises a drug, the additional benefit is ability to track the propagation of this drug in the body using MRI. Several studies support the lack of negative impact on tissue (biocompatibility) of liposomes that contain contrast agent and therapeutics. Moreover, these investigated systems have a high contrasting efficiency, needed for MRI imaging. The use of nanoparticles that combine diagnostic and therapeutic functions would permit one to monitor treatment progress from the moment of administration of the complex till the end of the medical procedure. Current literature indicates that the presence of a contrast agent does not adversely affect drug function, and gadolinium compounds incorporated in therapeutics-containing nanoparticles continue to exhibit contrasting properties. However, it is unclear as to whether the presence of a drug in a liposome affects the contrasting efficiency and, if so, how? This question is what we propose to address in this research.

This project will use liposomes composed of basic lipids and gadolinium-containing lipids. Additionally, into the liposome membranes, one of the three photosensitizing substances will be incorporated: zinc phthalocyanine (ZnPc, a model photosensitizer for scientific research) and temoporfin or verteporfin (therapeutic agents used in clinical practice). The contrasting properties of many types of liposomes, differing in therapeutic substance present in the composition and proportions of their components, will be compared. For each type of liposomes standard parameters used to evaluate the efficiency of contrast agents in MRI (the longitudinal relaxivity (r1) and the transverse relaxivity (r2)) will be determined. Analysis of the parameters changes depending on magnitude of the applied magnetic field (in the range of clinical and scientific use) will allow us to observe the physical basis of the contrasting effect. The next stage of research will be MRI examination of selected liposome types in a tissue-imitating gel. This experiments will demonstrate the movement of the liposomes in an environment with a density comparable to that of human tissue. It will also allow evaluation of the quantity of delivered drug for future clinical applications.

Preliminary studies conducted at the NanoBioMedical Center AMU revealed that the contrasting effect may be increased not only by incensement of the gadolinium amount in the liposome, but also by incorporation of ZnPc into its membrane. This is an important discovery as detailed knowledge of this phenomenon will enable optimization of the ratio between the various components of diagnostic-therapeutic liposomes (as far as medical applications are not precluded), leading to the best properties for MRI. The proposed approach to the problem is innovative, it draws attention to the possibility of reducing the amount of potentially harmful gadolinium-based contrast agents by taking into account the contrast increasing effect generated by other components of the complex. The applicants assume that this effect can be seen not only in the case of liposomes but for other diagnostic-therapeutic nanoparticles with gadolinium and of photosensitizers in general. In addition, the results obtained will be of use for the design of next-generation contrast media.