Rationale and goal of the project:

Animal models of cardiovascular disease allow to assess the feasibility of implantation and the safety of new technologies and therapies, although the predictability of their effectiveness is very limited, which is caused by the absence of the underlying disease - atherosclerosis. Having such a model, easily accessible, with occlusive lesions in a similar location as in humans would allow to study the effectiveness of new drug therapies and endovascular technologies at an early stage, reducing the risk of failure at the stage of clinical trials and predicting earlier their effectiveness. Available models, based on high cholesterol diet or genetic modifications require a long breeding time, animals are too large, the location of the lesions is unpredictable and the price is thigh. In our previous study, by local administration of LDL cholesterol directly into the vessel wall by endovascular techniques, we proved the possibility of inducing the first stages of atherosclerosis (thickening of the media, lipid infiltration), although this process did not progress due to the lack of cholesterol retention in the vessel wall. Hence, the goal of this project will be to obtain a reproducible, feasible model of atherosclerosis creating occlusive lesions in predictable locations in the model of a healthy domestic pig by administering human LDL and synthetic cholesterol in a long-releasing form.

Study description:

This goal will be achieved based on the local delivery of cholesterol in a long-release form directly to the peripheral and coronary artery wall of a domestic pig. The solution of long-release cholesterol will be obtained by encapsulation in polymeric microspheres of LDL cholesterol obtained from blood plasma apheresis of patients with hypercholesterolemia as well as the synthetic cholesterol. The test solution will then be administered by endovascular techniques directly to the wall of the coronary and peripheral arteries of a healthy domestic pig, using catheters with retractable microneedles. In the first part of the experiment, long-term LDL and synthetic cholesterol retention in the vessel wall will evaluated. This kinetic part of experiment will be studied in 24 animals, both in coronary and peripheral arteries. After proving long-term presence in the vessel wall, one of the lipids (etiher LDL or synthetic) will be chosen to deliver in the same fashion and to evaluate tissue effects and severity of atherosclerotic lesions in the coronary (15 animals) and peripheral (12 animals) artery injury model which will be subjected to 30 and 90 days of observation At terminal follow-up, intravascular imaging (intravascular ultrasound and optical coherent tomography) will be performed and the vascular segments harvested and subjected to histopathological evaluation.

Expected effects:

Based on our previous research after achieving long-term cholesterol retention in the vascular wall, we expect the progression of previously obtained pathological intimal thickenings to lesions consisting of lipid fibrous atheromas, i.e. more advanced atherosclerotic lesions.