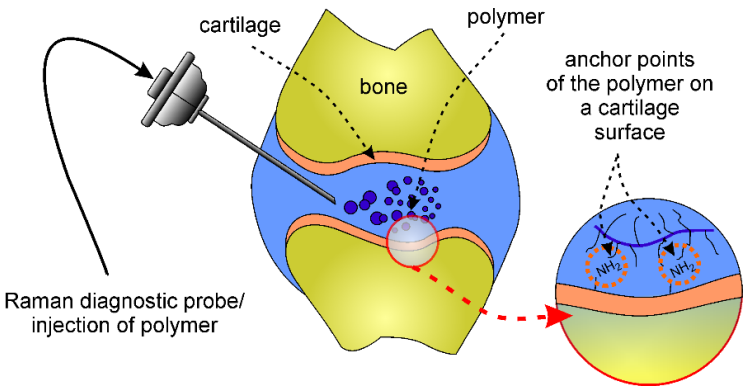
Osteoarthritis poses a contemporary epidemiologic problem of unknown etiology hitting more than 20% of global population. It is a main reason of physical disability of aging population. There are no effective methods to diagnose this disease at its earlier stage, thus in most cases a surgical intervention and prosthetic is necessary. Mechanisms of functioning of mammals (including human) joints described in literature indicate the crucial role of lubricin – natural amino acid with special spatial structure. The proposed research hypothesis assumes that the medical problems related to osteoarthritis are preceded by a change in the chemical structure of the cartilage and the loss of lubricin, that subsequently leads to the changes in the mechanism of joint functioning, including tribological properties, causing the joint degeneration. The key issue is to understand the phenomena and identify the elements responsible for the specific properties of cartilage. It is a fundamental problem, which could only be solved if the knowledge from various scientific fields, such as medicine, synthesis and chemical analysis as well as materials engineering will be fused. The aim of the proposed study is to determine the relationship between the structure of articular cartilage and the degree of development of osteoarthritis. This will aid to understand a mechanism of cartilage degeneration and to diagnose disease at the earlier stage. As a result, the design and synthesis of new copolymers with a molecular bottlebrush topology and their applications at various levels of advancement of the degenerative disease will be possible. Obtained polymers will serve as synthetic models of lubricin. The project tasks include also the elaboration of novel methodology useful to determine the interactions between synthesized copolymers and cartilage tissue, characterization of the properties of obtained systems (including study on an influence of polymers introduced to the joint on cartilage etiology).

Molecular bottlebrushes will be synthesized using atom transfer radical polymerization, ATRP. It is one of the most effective reversible-deactivation radical polymerizations methods, providing a new synthetic route to various polymeric materials with precisely defined architecture, composition and functionality. Molecular brushes with different chemical compositions, backbone length, number and length of side chains and blocks that allow interaction with the surface will be synthesized. It is also proposed to introduce novel functional groups that will interact with cartilage surface at different stage of osteoarthritis development.

Presence of appropriate functional groups, for example acidic, epoxy, ketone, thiol, introduced directly or by the post-polymerization modification processes, will help to anchor bottlebrush polymers onto the cartilage surface via interactions with functional groups of the tissues (for example amino groups).

Determination of the changes in the chemical structure of the articular cartilage at different stages of disease development will be performed by Raman spectroscopy, which is a potential diagnostic method allowing to detect osteoarthritis at the earlier phase. The novel analytical procedures will be developed based on broad range of spectral parameters (full width at half maximum, peak positions, integral intensities, etc.). The next step will be a deposition of the selected copolymers onto the cartilage surface under *ex vivo* conditions and determination how the polymer chains are anchored at the cartilage surface. The sample surface will be investigated before and after tribological tests in order to estimate the efficiency of synthesized copolymer as lubricant and the changes in degree of surface covering induced by friction.

The preliminary studies showed that, the copolymers with the chemical structure similar to proposed in the project enhanced the human fibroblast cell vitality at the level of 27% at the polymer concentration 55 ppm and 10% at 98 ppm concentration. In a similar way, the influence of polymers on the activity of human leucocytes (mononuclear cells selected from peripheral blood) was determined. 20% cells proliferation was detected at up to 100 ppm polymer concentration.



The main idea of the project is to elaborate new diagnostic method based on an analysis of Raman spectra of articular cartilage collected through the special probe. It is proposed that the copolymer will be delivered to the degenerated joint directly as it is demonstrated in the figure. This approach can potentially lead to development of a combined therapy, including simultaneous diagnosis and medical treatment within one medical operation procedure with potentially significant societal and economic impacts.