Every drop counts: from liquid drop to solid bone. Injectable, biomimetically mineralized microgels as a next-generation platform for minimally invasive bone repair

Nowadays, bone defects represent a significant challenge for medicine. This stems from factors such as an aging society, an increase in the number of injuries and accidents, and the limitations of traditional treatment methods such as grafts. Bone defects, understood as the absence of bone tissue where it should normally be present, can arise from injuries, tumor resections, infections, or surgical operations. Tissue regeneration in such locations depends, among other things, on the size of the defect. Defects larger than 2.5 cm are considered critical. They require additional medical intervention so that the tissue can regenerate and the patient can return to full functionality. The key is to create an environment at the defect site that mimics the natural structure of bone, namely the extracellular matrix. In the case of bone, this matrix consists of water (10-20%), an organic phase (20-25%), and an inorganic phase (60-70%), the main component of which is hydroxyapatite. Currently, the gold standard treatments are autologous grafts (originating from the patient's body) or allogenic grafts (originating from a donor). A significant problem with this standard is the limited availability of graft material. In the case of autologous transplantation, additional surgery is necessary, and there is a risk of complications at the tissue harvesting site. On the contrary, in the case of allogenic transplantation, the quality of the available material is variable and there is a risk of immunological rejection or disease transmission. The solution to these problems is the use of synthetic fillers that are biocompatible, replace the structure of natural bone by mimicking the extracellular matrix, and create favorable conditions for the growth of new tissue.

One potential solution to this problem is the development of mineralized hydrogel microparticles, that is, microgels. Such microgels can combine many desirable properties required for bone tissue regeneration material. First, they can be produced from polymers that are simultaneously biocompatible, biodegradable, and bioresorbable, such as gellan gum or sodium alginate. As a result, they will be well tolerated by the patient's body and gradually give way to new, regenerated bone. Secondly, because of their hydrogel nature, they allow for the binding of water within their structure and the formation of combinations with the inorganic phase, thereby closely mimicking the natural extracellular matrix and promoting osteoconductivity, which means passively supporting cell migration. Third, due to their micron size, they can be injected into the bone defect. This allows the developed material to be used in minimally invasive therapies, ensuring less tissue damage, faster recovery, lower risk of infection, and better patient quality of life after the procedure.

In this project, the development and creation of a microfluidic chip is planned, a system for obtaining mineralized microgels of reproducible micrometer sizes. The resulting materials will find application in minimally invasive therapies for treating bone defects, mimicking the natural extracellular matrix, and providing support for newly created bone tissue.

During the 3-year project, aided by Finite Element Method (FEM) computer simulations, we will design a microfluidic device for generating microgels to create a chip with the most optimal parameters for particle production. Subsequently, the chip will be created using 3D printing technology. Next, we will conduct studies to select the appropriate material composition for the efficient production of mineralized microgels that are also characterized by injectability. In the final stage of the project, the prepared materials will be tested using bone cells and stem cells to ensure that they do not have toxic effects and to assess their potential to support bone tissue regeneration (Fig. 1).

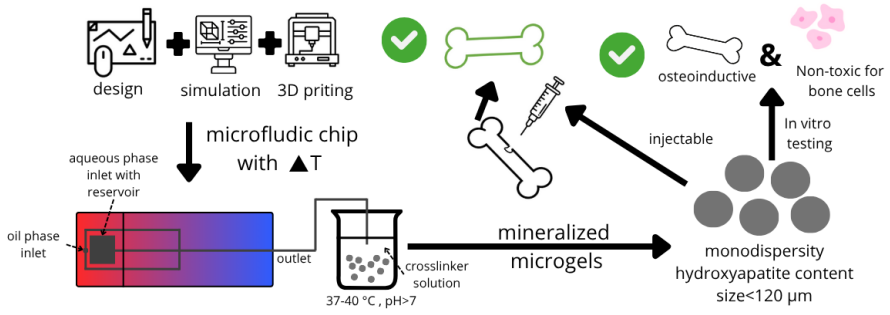

Fig. 1 Schematic representation of the project.