Baltic Biomaterials Centre of Excellence

Baltic Biomaterials Centre of Excellence (BBCE) project´s main objective is to establish a joint Centre for development of advanced biomaterials based on the long-term strategic cooperation between AO Research Institute Davos, Switzerland (ARI) and Friedrich-Alexander University of Erlangen-Nuremberg, Germany (FAU) on the one hand and Riga Technical University, Faculty of Natural Sciences and Technology Institute of Biomaterials and Bioengineering (RTU IBB), Latvian, Institute of Organic Synthesis (LIOS) and Riga Stradins University (RSU) and Riga Stradins University Institute of Stomatology (RSU IS) on the other hand.

DEVELOPMENT OF BBCE

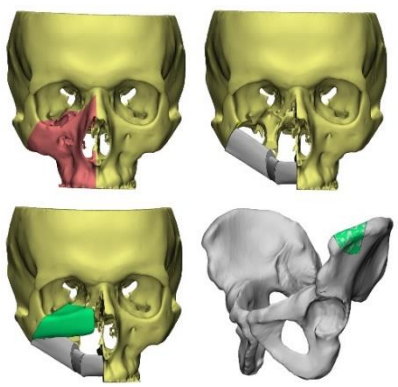
BBCE had a very successful 2023 year! We had **12** internal consortium meetings for planning the visits and events, and also for discussing the research directions, upcoming articles and overall cooperation. During this year BBCE members participated in **19** conferences (60 oral/poster presentations), published **25** manuscripts with acknowledgement to BBCE and submitted **31** research grant applications. Consortium members were also active in disseminating project goals and results towards industry members, mainly through participating in exhibitions and meetings with enterprises. We could hear and see BBCE members on the TV and radio interviews, opening new possibilities for further cooperation with other organizations in Latvia. Highlights of the events during the year 2023 are:

1. Five short-term outgoing visits to FAU and ARI and eight short-term advanced partner incoming visits to Riga;
2. Summer school organized by FAU, which provided a lot of new knowledge for Early Stage Researchers;
3. Seven long-term visits to ARI and FAU.

BBCE Collaboration Enables Groundbreaking Surgery

Latvian TV news Panorama aired a story with an interview of surgeon Jānis Zariņš about a unique Head and neck reconstruction operation was performed thanks to the cooperation with BBCE members RSU IS. Their expertise helped in the planning of the operation using 3D planning and printing technologies. This operation is unique in Latvia and all over the world, and widely disseminated in National TV news. An oncological patient underwent 15-hours-long reconstructive operation during which the tumor was removed, and the damaged areas were reconstructed by transplanting tissues from other areas of the body.

After the operation surgeon Jānis Zariņš added: "What we remove, we try to restore as much as possible. One of the main challenges is dealing with large tissue defects, which require reconstruction to maintain facial symmetry. Proper preoperative planning is crucial. Today, the focus is on quality of life, making it essential to reconstruct everything that is removed during surgery. However, the recovery process is not easy." The surgeon explained why 3D technology was used: "If everything is planned correctly and on time, the surgery becomes more precise, and the duration is shortened." He emphasized that this is a significant multidisciplinary effort. Looking to the future, he noted: "It's hard to predict because perfect outcomes aren't always possible without good planning. Every patient is unique, and sometimes the surgeon needs to improvise. "Various bones, such as the fibula, lateral femoral condyle, and pelvic bone, are used for reconstruction during these surgeries. "



This project has received funding from European Union's Horizon 2020 research and innovation programme under agreement No 857287

SUCCESS OF 2023

BBCE Facilities are Growing

On March 31, 2023, at Konsula Street 21, the Rīga Stradiņš University's Pharmaceutical Education and Research Centre was officially opened. It is the home and the working space for the SFG4 team. The research center was created thanks to the funding of the BBCE project. Within the six-story building, there are the Departments of Pharmaceutical Chemistry, Pharmacology, and Applied Pharmacy, as well as the crucial Finished Dosage Form Laboratory (FDF), vital for scientific advancements. This laboratory is designed according to the principles of the pharmaceutical industry, including clean rooms compliant with ISO 8 standards. FDF is equipped with infrastructure for solid dosage form preparation (tablets, capsules, granules) and their subsequent analysis with instruments like UHPLC-MS/MS, ICP/MS, RAMAN, XRD, and others. The provided infrastructure and equipment will allow the research directions of SFG4 (novel drug delivery systems and their pharmacokinetics) to reach new heights.

In total, the building features 4 lecture halls, 11 classrooms, 10 laboratories for students, and 7 research laboratories. This environment, equipped with state-of-the-art technology, functions as a foundation for students and researchers to pursue their scientific ambitions.

BBCE Headquarters

The construction of the new building is still in progress, and it will serve as the flagship headquarters for BBCE. Scientists will research and synthesize implant materials made from calcium phosphates to replace damaged tissues and organs. Upon completion of the building, scientists from the Biomaterials and Bioengineering Institute of the RTU Faculty of Natural Sciences and Technology (DTF) will relocate there. Institute scientists focus on developing materials and technologies for personalized medicine - personalized drug delivery systems, shaping implant materials, and adjusting their chemical composition. The new BBCE building will provide a modern environment for research, studies, and transferring products from the lab to the market. It will feature well-equipped chemistry labs, a clean room, laboratories for *in vitro* research and implant prototype production. Additionally, there will be workspaces for scientists and facilities for conferences.

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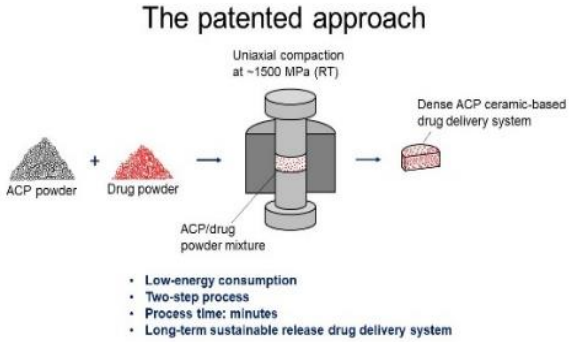
SUCCESS OF 2023

SFG1 - Calcium phosphates and composites

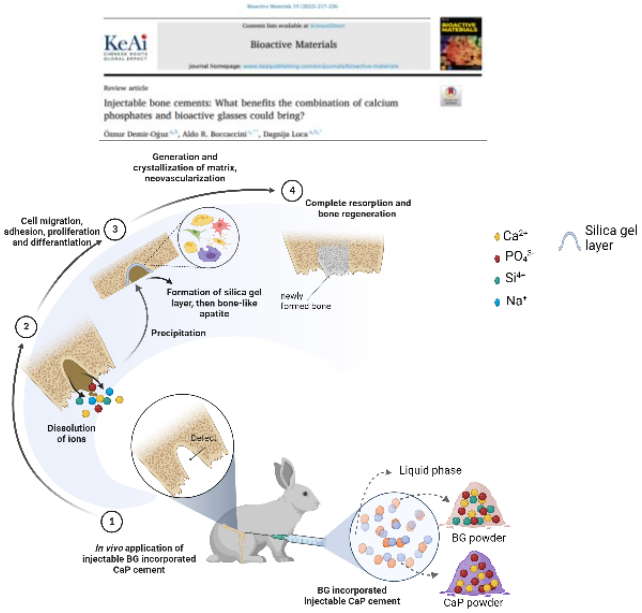
BBCE has pioneered a cutting-edge method to enhance how medicines are delivered over time through a ceramic-based system. This innovative approach involves integrating drugs into a special kind of ceramic known as amorphous calcium phosphate (ACP) during a process called sintering, which traditionally requires high temperatures. However, patented technique (PCT/IB2022/056873) can achieve this at room temperature, simplifying the process and retaining the material's high effectiveness. The major benefit of this technology is its simplicity and speed. Drugs are mixed with ACP, known for its high bioactivity and ability to be absorbed by the body. The drug delivery system created can control how quickly drugs are released, which can be adjusted depending on how the ceramic is processed. Both dense and porous forms of this ceramic can be produced, catering to different medical needs. In practical terms, the ACP powder is combined with a drug in a specified ratio and compacted under high pressure to form the ceramic. This not only ensures the ceramic's structural integrity—comparable to those processed at over 1000 °C—but also its capability to release medication over an extended period. This method could revolutionize how treatments are administered for various medical conditions, making it an exciting development in medical technology.



SFG 2 - Drug/ion/cell delivery

SFG2 most notable and influential publication was an open-access review article titled **"Injectable bone cements: What benefits the combination of calcium phosphates and bioactive glasses could bring?"** by O.Demir-Oguz, A.R. Boccaccini and D.Loca in the journal *Bioactive Materials*. (IF=18.9, CiteScore 28).

Calcium phosphate bone cements (CPCs) are a type of material used in medicine, especially noted for their ability to support bone growth and repair. Discovered in the 1980s, these materials stand out because they can be easily molded and injected into the body, where they harden at low temperatures, matching the surrounding bone structure.



Although CPCs have been beneficial, they do have some weaknesses, such as their limited strength which can be problematic in parts of the body that bear a lot of weight. Moreover, how these cements break down and are replaced by natural bone is still somewhat unclear, and improvements are needed for their use in medical treatments.

An exciting development in this field has been the use of bioactive glasses (BGs) in combination with CPCs. BGs are friendly to the body and promote the growth of new bone while they themselves dissolve. Over the past few decades, researchers have explored adding BGs to CPCs. They've found that BGs can enhance the bone cements' properties, such as improving their strength and how they interact with the body, encouraging bone formation and better integration with the surrounding tissue. This combination holds promise for better and more effective bone repair materials in the future.

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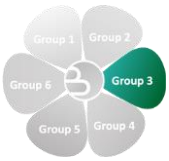
SFG3 – Materials *in vitro*

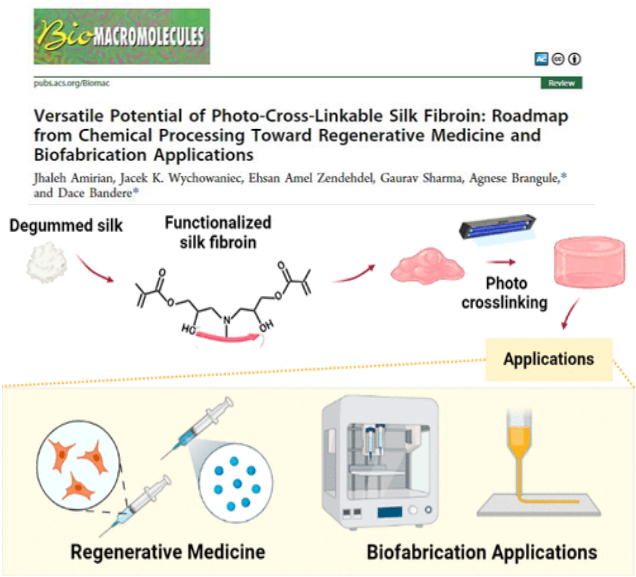


In 2023, SFG3 members advanced their knowledge and expertise in innovation commercialization. A highlight of their year was that the team of several SFG3 members, including scientific focus group leader Dr. Kristaps Klavins, was accepted into the UniLab incubator program. Unilab is a leading startup incubator in Latvia, founded by the top four Latvian universities. Over the four-month program, the team received training in assessing the commercialization potential of their technological inventions. The incubator program included training in several key areas, including investment acquisition, intellectual property strategy, and effective pitching techniques. The program also offered individual consultations with experts on topics such as IP protection, team building, and launching science-driven businesses. Additionally, the SFG3 team actively participated in several startup and business summits and trade shows, including Boston BioTech Week, Nordeep, and Nordic Life Science Days. These events provided opportunities to network with industry leaders, present the scientific advancements of BBCE, and explore further commercialization opportunities. The knowledge and connections gained throughout these experiences have increased the SFG3 team's expertise for effectively transitioning their innovations from the lab to the marketplace.

SFG4 - Kinetics and stability of drug delivery systems

SFG4 most successful and impactful publication was an Open Access review article entitled "**Versatile Potential of Photo-Cross-Linkable Silk Fibroin: Roadmap from Chemical Processing Toward Regenerative Medicine and Biofabrication Applications**" by Jhaleh Amirian, Jacek K. Wychowaniec, Ehsan Amel Zendehdel, Gaurav Sharma, Agnese Brangule and Dace Bandere in the journal *Biomacromolecules* (IF 6.5, CiteScore 11.1).

This review was an excellent collaboration between SFG4 and our partners at AO Research Institute, Davos. The publication focused on the transformative role of hydrogels in tissue engineering and regenerative medicine, highlighting the last two decades of innovation. In this comprehensive review, we explored the unique properties of silk fibroin (SF), a biopolymer that has garnered significant attention for its biocompatibility and tunable mechanical properties. The publication detailed how chemical modifications, specifically the addition of methacrylate groups, have broadened SF's applications, enhancing its processing capabilities and suitability for 3D printing. We provided in-depth analyses of the functionalization techniques, cross-linking methods, and versatile applications of SF hydrogels in the fields of biofabrication, tissue engineering, and regenerative medicine. This publication has not only been a cornerstone of our research efforts but has also significantly contributed to advancing the field by outlining future directions for the development of SF hydrogels and their composites.



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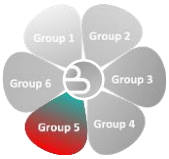
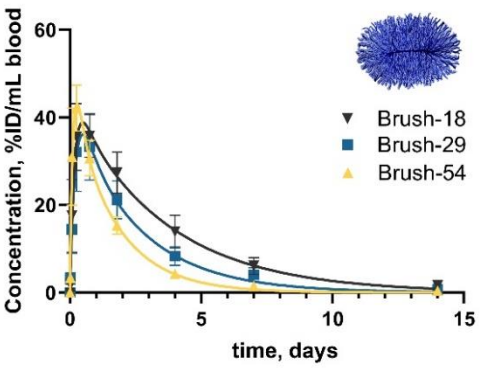
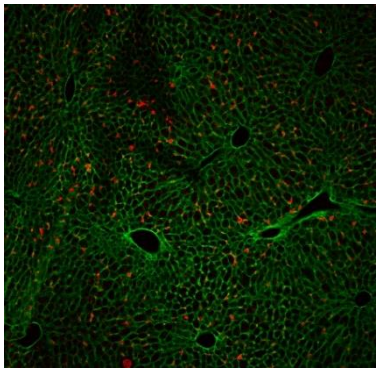
SFG5 - Preclinical biomaterial evaluation

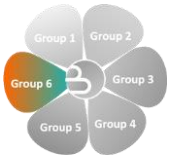


In 2023, members of SFG5 were active in participating and presenting their research at various conferences including RSU International Congress, World Congress of Basic and Clinical Pharmacology, and Annual Conference of the European Society for Biomaterials. SFG5 welcomed a new postdoctoral member – Dr. Victor Palarie, an experienced oral and maxillofacial surgeon who will be leading Group efforts in preclinical evaluation of biomaterials in vivo, developing new protocols and educating other members of SFG5 and BBCE on various aspects of in vivo experiments. The research in the group continues in two major directions, namely, improvement of fracture healing and development of nanoparticles for cancer therapy. We have completed the study where developed non-opsonizing nanomaterials demonstrated exceptionally long circulation times and were used to reveal the limits of enhanced permeation-retention effect in triple-negative breast cancer. The manuscript describing our findings is currently under review, but the results of the study are available at bioRxiv. New equipment was installed in LIOS-FFL, home of SFG5 – the in-line fluorescence detector, that will enable us to better quantify nanomaterials and macromolecules based on their fluorescence and further our research in nano biomaterials.



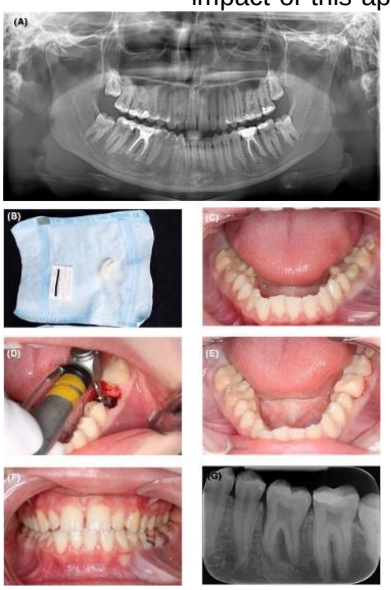


SFG6 - Clinical evaluation of the materials and personalized implant development



The SFG6 Publication of the Year 2023 was an article titled “Effect of 3D Printed Replicas on the Duration of Third Molar Autotransplantation Surgery: A Controlled Clinical Trial” by Miks Lejnieks, Ilze Akota, Gundega Jākobsone, Laura Neimane, Oskars Radzins, and Sergio E. Uribe, published in the journal Dental Traumatology (IF=2.5, CiteScore 6.4).

This study aimed to develop a protocol that combines cone-beam computed tomography, software, and 3D printing to design 3D replicas for tooth autotransplantation. The goal was to evaluate the impact of this approach on the extraoral time of the donor teeth and the total surgical time, thereby enhancing surgical efficiency and outcomes. A trial enrolled 46 patients, 13–22 years old, who required molar extraction and possessed a non-erupted third molar. The primary outcome measured was the extra-alveolar time of the donor tooth, and the secondary outcome was the total duration of surgery. The effect of using 3D replicas was not statistically significant and was associated with a decrease in the extraoral time of the donor tooth in. For the total surgical time in minutes, the use of 3D replicas had a statistically significant impact, reducing the operation duration in minutes. No early complications were observed in either group, with all teeth present at 3–4 weeks post-surgery. The study proved that integration of 3D printing technology can enhance the efficiency of autotransplantation surgeries, primarily by reducing surgical time.



ORIGINAL ARTICLE

Dental Traumatology WILEY

Effect of 3D printed replicas on the duration of third molar autotransplantation surgery: A controlled clinical trial

Miks Lejnieks[1,2] | Ilze Akota[1] | Gundega Jākobsone[3] | Laura Neimane[2,4] | Oskars Radzins[2,4] | Sergio E. Uribe[2,4,5]

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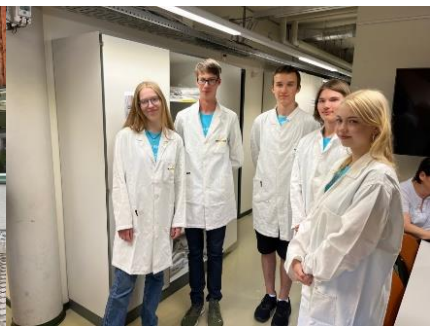
BBCE erudition competition «BIO-GO-Higher»

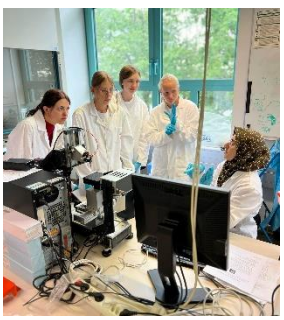
20 teams began the battle for victory in the competition, but the interest in participating was even higher - 33 teams (2022/2023) and 56 teams (2023/2024) entering the selection round.

The most successful team of 2023 – "Pērkons" from Cesu State Gymnasium, visited AO Research Institute in Davos, Switzerland. And for 2024- «Ozoliņi» from Sigulda State Gymnasium, they will visit FAU in Erlangen



Winners of 2024

This year`s winners- «Ozolini» from Sigulda State Gymnasium went to BBCE Partners at the University of Friedrich-Alexander Erlangen-Nuremberg and the Biomaterials Center in Erlangen, Germany



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What are we looking for:

- Cooperation with other institutions
- Cooperation with industry
- New project applications
- Staff mobility and training

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