**Advancing Biomedical 3D Printing for Healthcare Innovation**

3D BIO-PRINTED ACL

One of the most crucial components of the human knee joint, the anterior cruciate ligament (ACL), is essential for both motion and stability. ACL injuries are common, particularly in athletes and can cause discomfort, instability, and restricted function/movement. Autografts and allografts are used in traditional surgical procedures for ACL injuries; however, they have drawbacks and possible consequences. The limitations for availability, surgical complications, and the reduced function at the site of the graft are the most common disadvantages for autografts, while the risk of rejection, time-consuming research for donors, possible diseases transmission and long-term impact health challenges are some disadvantages for allografts. Researchers have shown that artificial ligaments are promising but like the allografts, have a few disadvantages as biocompatibility and long-term safety/durability, flexibility limitations, slow process, price, and risk for infections. A unique and promising method for producing ACL replacements with improved precision, mechanical qualities, and integration potential can be provided by 3D bioprinting technology. So far studies on 3D printing have been targeted on surgical implants that focus on the ankering of the graft, while some with the “enthesis region” using different materials as patients body fat printed on a hydrogel to form a tendon/ligament or the use of mixtures of collagen and bioglass as bio inks to 3d print biomimetic-gradient scaffolds (Bakirci et al. 2017, Kajave et al. 2020, Toprakhisar et al.2018).

This research project proposal aims to develop a 3D bio printed anterior cruciate ligament that can copy the biological and biomechanical properties of an original ACL. The goals of the study are stability and flexibility of the graft, customized fabrication of the ligament according to the differences in patient anatomy and injury specifics, promotion of the integration of the bio printed ligament with host tissues, durability of the graft to reduce future revisions and validation of meeting the regulatory standards for safety.

The project will combine knowledge in biomechanics, radiology, tissue engineering, material science and 3D bioprinting technologies. There are different 3D techniques that have to be tested, Vat Photopolymerization, Power Bed Fusion and Material extrusion. For the scaffold of the graft, materials as Nanocellulose, Nylon and PLA will be tested for their elasticity and tensile strength to discover which is better mimicking the mechanical properties of the native ligament. Cell sources like fibroblasts can be used to make possible the seeding approach that will help the growth of tissue in the scaffold to empower the strength of the graft and make the graft more natural, so the acceptance is easier by the body. A hydrogel might be useful, covering the graft to make the scaffold biocompatible in case there are small pieces from friction of the scaffold materials. The graft is customized for each patient after using an MRI to measure the exact length and thickness of the original ligament. The evaluation of performance and effectiveness of the graft will happen by directed testing of the biomechanical properties using in vivo and in vitro models. Large animal models will be used such as goats and pigs for having the greatest similarities with humans. Histological and immunological analyses will be conducted for the biological integration and material analysis for the assessment of the mechanical and biological properties.

This project has a new approach in the field with promising outcomes. The successful completion of this project will open the gates for future research and field advancement as it can be the base for the 3D bio printed production of all the ligaments in the human body. The development of the graft will result in reduced complications and risk failure, higher success rates and less revisions but also reduce health care costs.

The first quarter, expected deliverables are a detailed plan about methods, resources and equipment that will be needed for the project. The rest of the year till beginning of second, the team will focus on data collection and experiments that needs to be conducted. The start of the second year should be the analysis of the results and retest of any failures that has happened. By the end of the second-year conclusions must be draw and approval of all the researchers of the findings. The third year should be for the preparation of research reports and presentations to be able to publicly report the findings and get peer reviews and feedback. Closing the project by conducting final evaluations and submitting a final report. The financial resources needed for the project will cover the salaries for researchers, equipment, materials and other supplies, possible travel expenses, publishing expenses and a part of the budget should be on the side for unexpected costs.

This project can fill the gap between conventional grafts and the cutting-edge field of bioprinting short term but also has potential impact by opening the horizon for other 3D bio printed ligaments. The research project will be presented in conferences for 3D bioprinting and medicine and will be posted in respectively academic journals. All the equipment, methods and tools will be posted online so students can do further research and explore new ideas.

By understanding all the regulations, the research will follow all the federal and local laws as well as FDA regulations. The animals that will be used for research will be treated properly and according with relevant laws and ethical principles (IACUC). Compliance will be ensured with the funding agency requirements and their expectations.

Collaboration between experts in biomaterials, biomechanics, bioprinting and clinical medicine will be crucial for the success of this project. The project is a valuable investment in raising the standards of ACL reconstruction surgery because of the expected advantages for patients and the healthcare sector.