Research Diary

3D Bioprinting for Tissue Engineering and In Vitro Tissue Modelling

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The demand for engineered tissues has increased greatly owing to the shortage of donor tissues and organs for transplantation. Though there were some promises, tissue engineering has been able to provide functional implantable tissue constructs except in a few cases. Additive manufacturing, also popularly known as 3D printing, is a cutting-edge technology in almost all the fields of day-to-day life to create 3D objects. It is a process of depositing materials layer upon layer to join materials to make 3D objects from a virtual 3D model. 3D printing has also been applied to print cells into 3D tissue constructs. Studies revealed that it has the potential for creating complex composite tissue constructs through the precise placement of cells and matrix materials in a layer-by-layer fashion. Our BioFabTE lab at IITH focuses on the development of different tissues using synthetic and tissue-derived natural polymer hydrogels using scaffold-based and 3D printing technologies. We are working on many aspects of this technology starting from formulating bioinks (3D printable polymer formulations), developing a 3D printing protocol targeted to a particular tissue, and in vitro maturation using our customized 3D printed bioreactors. While we have demonstrated 3D printing of a few tissues like cornea, esophagus, liver, and bone, a few more like skin tissue models, kidney glomerulus model, breast and esophagus cancer models are in the developmental stages as shown in **Figure 1**.

In a first attempt, we developed corneal extracellular matrix hydrogels from discarded bovine and human corneas and proved their potential to prevent corneal scarring (Chameettachal et al. 2020) and thicken the ectatic cornea (Chameettachal et al. 2021). Recently, we have been awarded the Sree Padmavathi Foundation Translation Research Grant in Biomedical Sciences 2022 for starting a clinical trial of our cornea hydrogel.

We also could make a major advance in generating the corneal construct with complexities such as human corneal size and shape using 3D bioprinting with fibril orientation and cell homeostasis. We demonstrated that the technique using SLA 3D printing was dependable to create cornea or tissues with curvature. Another interesting in vitro study explored the feasibility of engineering esophageal tissue. The main theme of the study was to develop technology to fabricate tubular tissues and organs by using mechano-compromised biomaterials (Yeleswarapu et al., 2021).

One of our studies focuses on the value addition of synthetic polymer, Polycaprolactone (PCL) which has been extensively utilized for bone tissue engineering. The application of PCL is limited because of poor cellular interaction and tissue integration. We have optimized a PCL- Silk composite to strike a balance among the cellular response, biodegradation, and mechanical strength of the materials. The results indicate that the PCL-silk fibroin microfiber composite could be an efficient biomaterial not only for conventional bone tissue engineering applications (Bojedla et al., 2022). We have also developed a 3D printable composite formulation out of these and demonstrated the fabrication of patient-specific mandible implants.

Apart from the development of viable tissues for transplantation, in vitro tissue models are also a major contribution to 3D printing for tissue engineering. Tissue models are promising tools for drug development to predict the possibilities and adverse events during clinical application. In a study using a decellularized liver matrix, we could prove its potential to serve as a liver model to screen the drugs. The liver tissue model with extracellular matrix helps in maintaining the tissue-specific microenvironment and thereby retaining the hepatic cellular phenotypes, functionality, and a more realistic drug response compared to the normal native liver (Sasikumar et al., 2021). The developed liver model has huge prospects for drug and toxicity screenings.

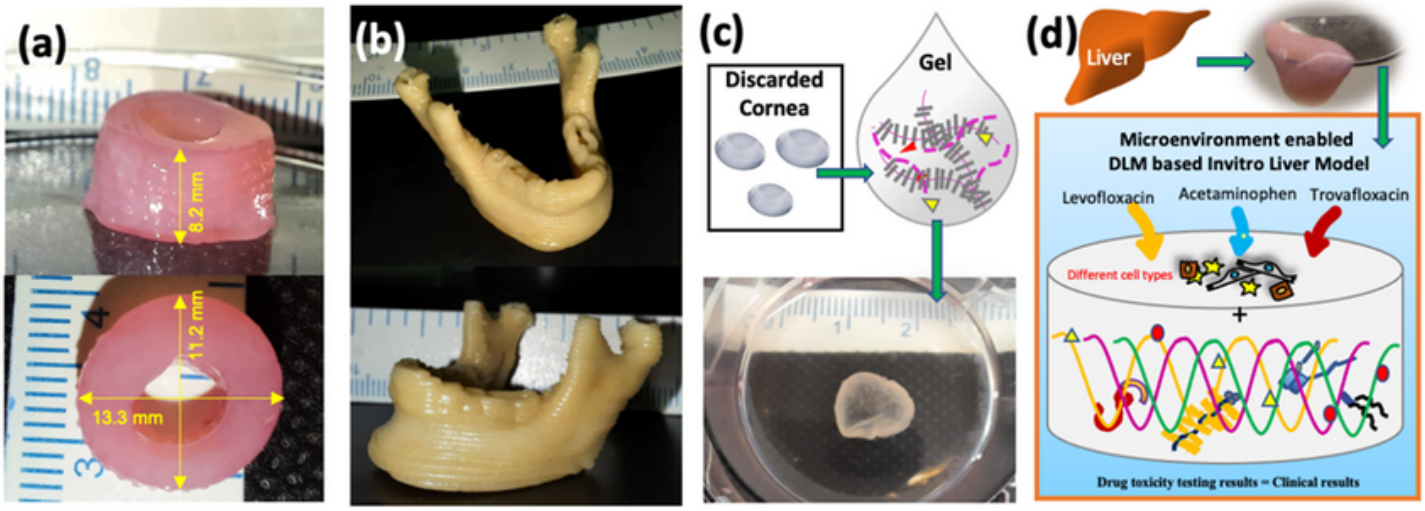

Figure 1: (a) 3D bioprinted tubular structure with smooth muscle matrix hydrogel for esophageal repair, (b) 3D printed patient-specific mandible from CT data for restoration of defect/damage, (c) 3D bioprinting of corneal stroma with decellularized cornea matrix hydrogel for partial keratoplasty, and (d) 3D bioprinted liver model for drug and toxicity screening