

Will 3D Bioprinting Turn Disruptor in Healthcare?

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3D bioprinting has come to the limelight recently and a lot of research activities have been undertaken for the same. Creating organ models that can be used for preclinical testing of drugs and other interventional molecules and creating organ scaffolds for clinical transplantation can become a breakthrough in the healthcare domain. Though the technology is yet to be accepted fully among India's medical sector, current efforts by academics and research labs will ensure that 3D bioprinting provides personalised solutions for individual patients.

3D bioprinting has been in focus these days with healthcare professionals, researchers taking interest on how the technology can impact the overall healthcare scenario. It is an application of additive manufacturing techniques to live cells, growth factors and/or biomaterials to fabricate biomedical parts, to mimic natural tissue characteristics. 3D bioprinting covers a broad range of bioprinting techniques and biomaterials. Currently, bioprinting can be used to print tissue and organ models to help research drugs and potential treatments.

According to various bioprinting market reports, the global 3D bioprinting market is currently valued at \$1.3 billion as of 2022 and is projected to reach \$3.3 billion by 2027. And there is a huge demand seen in the pharmaceutical and cosmetology industries.

The technology is being used to create living tissues such as blood vessels, bones, hearts, skin etc. It is anticipated that 3D bioprinting is likely to revolutionise the healthcare space in two main ways. Firstly by creating organ models which can be used for preclinical testing of drugs and other interventional molecules. Secondly by creating organ scaffolds that can be

used for clinical transplantation. Additionally, 3D bioprinting is a step towards personalised medicine because, unlike conventional organ transplantation, the 3D printed tissue substitutes can be customised for the individual case.

Role of academics and research activities

The concept of 3D is slowly gaining momentum in India and most of the current efforts in the country are being pursued in academic and research labs such as the Indian Institute of Science (IISc), Indian Institutes of Technology (IITs), National Institutes of Technology (NITs), Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST) and other universities such as Shanmugha Arts, Science, Technology & Research Academy (SASTRA), Vellore Institute of Technology (VIT), etc. These efforts are still in the research stage.

A major boost to the 3D bioprinting technology ushered in when CELLINK, a global leader in developing 3D bioprinters and IISc partnered to establish a Centre of Excellence (CoE) for 3D bioprinting in Bengaluru. The CoE, the first-of-its-kind in the sub-continent, will be housed in the Centre for BioSystems Science and Engineering (BSSE) at IISc. The CoE will provide access to 3D bioprinting systems, enabling researchers to accelerate their work across critical applications with the ultimate goal of improving health outcomes.

The new CoE will house several state-of-the-art 3D bioprinters from CELLINK and will serve as a hub for several research initiatives and training activities within this emerging and exciting technology. IISc and CELLINK will work together to conduct workshops aimed at providing researchers within the institute, and elsewhere, the skills necessary to utilise 3D bioprinting within their work and reap the benefits of 3D cell culture. The two groups will undertake and advise on research projects across multiple applications spanning the fields of tissue engineering, drug discovery, material science and regenerative/personalised medicine. The CoE will have a keen focus on work around the heart, bone, cartilage and cancer.

Apart from this, IISc has taken initiatives when it comes to innovation in 3D bioprinting. The institute has taken efforts to regenerate tissues using 3D bioprinting, particularly, for bone, cartilage and skin tissues. Another area of work undertaken is to create tissue models such as breast cancer and fibrotic lung tissue models. These models, which hold promise as alternatives to animal models, can help the biotech and biopharma industries in testing the efficacy and toxicity of drugs. There are efforts to prepare deployable medical devices. Through a combination of smart choice of materials and design, it is possible to fabricate shape-changing 3D printed parts widely, a theme of technology called 4D printing. These 4D printed parts can facilitate minimally invasive surgery and reduce the complexity of surgeries.

Kaushik Chatterjee, Professor, Department of Materials Engineering, Indian Institute of Science mentions, "As a new technology, there is limited penetration in the country. Many researchers are unaware of how this technology can help their work. The centre has started conducting workshops and will continue to conduct them for researchers from academia and industry. Many new technologies are being introduced in the market. We can look forward to many developments with respect to new printing technology and also their applications in medicine. In terms of technology development in the country, there are other companies in India that are working to launch 3D bioprinters or have recently launched."

Making inroads in medicine

Hospitals and startups are taking baby steps to make 3D printing a reality in the country. The team at Raegene Biosciences lead by Dr Subrahmaniyam Vangala, Founder & CEO and Dr Uday Saxena, Co-Founder & Chief Ideator have developed several first-in-class models - the 3D bioprinted human vascular lung model which mimics some features relevant to human COVID and not seen in animal models of this disease. In total, to date, four such models have been developed. The startup is currently looking to offer these tools to others to foster drug discovery and will also use these for launch of products. It is open to developing any model that its collaborators would need and is useful in drug discovery and development.

Hyderabad-based L V Prasad Eye Institute is working on 3D bioprinting of corneas, in collaboration with Indian Institute of Technology (IIT) Hyderabad, and Centre For Cellular And Molecular Biology (CCMB). According to **Sayan Basu, Network Director, L V Prasad Eye Institute**, "corneal diseases are a major cause of blindness worldwide and particularly in the developing world. The shortage of donor tissues is also most acute in these geographies. With 3D bioprinted corneas we hope to bridge the gap in demand and supply, provide personalised solutions for individual patients, and new innovations in corneal surgery through refractive lenticules and biological contact lenses. Our focus is not just on the material or the product, but also on the method of delivery/application and the cost."

Apart from this, Amrita Hospital, Kochi has developed a first-of-its-kind Extended Reality (XR) Supported ecosystem in healthcare which leverages augmented reality (AR), virtual reality (VR), and mixed reality (MR) technologies to significantly enhance capabilities in patient care, medical training, and research.

The integration of this advanced technology in clinical practice marks a major milestone in the healthcare industry of India, according to experts. The hospital's paediatric cardiac unit has been utilising 3D printing and extended reality (AR/VR) technologies for the clinical benefit of patients. These state-of-the-art 3D+ technologies enable doctors to create precise replicas of real or actual heart or any organ, facilitating in-depth study and preparation before actual surgery. The hospital houses India's first "point of care" medical 3D printing and virtual reality laboratory.

Says Dr Mahesh Kappanayil, Professor, Paediatric Cardiologist and Lead at 3D Labs, Amrita Hospital, Kochi "We have handled numerous rare and unique cases using the 3D imaging system. Many of the cases we have undertaken have been either first in the world or in India. Despite the advanced nature of the technology, only a handful of centres worldwide have adopted it on a large scale. We are now able to treat patients who have been rejected by other hospitals due to doctors' constraints to understand the structural complexities of organs and plan the surgeries effectively. The process involves converting a patient's real CT scan into a digital 3D file, allowing doctors to examine each case in three dimensions using 3D printing technology or AR/VR."

Australia-based biotech company Inventia Life Science has announced a new distribution agreement with Mumbai-based Biotron Healthcare, for Inventia Life Science's flagship RASTRUM platform to enter the Indian market. The RASTRUM platform helps researchers accelerate the quest to investigate and cure debilitating diseases such as cancer, neurodegenerative and fibrotic diseases. RASTRUM is designed specifically for cell biology and is a world-first technology. The platform is highly automated which creates complex, miniaturised 3D cell cultures quickly by printing hydrogels and cells in a highly controlled way.

Bengaluru-based startup Avay Biosciences has launched 'Mito Plus,' an indigenous state-of-the-art 3D bioprinter that can print human tissues. The first prototype of Mito Plus was installed at IISc. Mito Plus can be used for pharmaceutical drug discovery and drug testing applications, It can also be used in cancer biology and cosmetology applications. Avay Biosciences has developed the bio printers in-house with around 70 per cent of manufacturing undertaken in Chennai and Bengaluru.

Safety & Efficacy

One of the major challenges is to source the right material followed by to procure the right combination of strength and other tissue properties. Another challenge is to develop a tissue substitute that has the right physical and structural properties, is easy to handle, can be transported over long distances, is bio integrable, and most importantly is affordable.

A key challenge to adopting these technologies in the clinic is to establish the efficacy and safety of the technologies for tissue regeneration through animal and, eventually, human trials. As a new and disruptive technology, the regulatory process also needs to be updated to enable translation.

Also with any emerging technology, 3D bioprinting raises ethical and regulatory questions. Issues such as patient safety, quality control, intellectual property rights, and the equitable distribution of bioprinted products need to be carefully addressed.

Increased acceptance & adoption

Dr Uday Saxena, Co-founder & Chief Ideator, Raegene Biosciences, is upbeat and thinks that every major city will potentially have 3D bioprinting clusters very shortly. He adds, "The uptick in the use of 3D bioprinting is tremendous and the Indian government agency Department of Biotechnology/ Biotechnology Industry Research Assistance Council (BIRAC) has recently launched a grant dedicated to alternate tools such as 3D bioprinting, which shows the need and excitement of this type of technologies."

According to Dr Ajay Kaul, Chairman-Cardiac Science, Fortis Noida, India would need to develop robust regulations and guidelines to ensure the responsible and ethical use of this technology. While 3D bioprinting has the potential to make a significant impact on healthcare in India, it's important to note that the technology is still evolving and faces several

challenges. The scalability, long-term viability, and regulatory framework are among the key factors that will determine the extent of its impact. However, with ongoing research and development, 3D bioprinting could play a transformative role in improving healthcare outcomes and driving innovation in India.

The strong existing R&D community base and massive scope of 3D bioprinting in medical services will drive demand for 3D bioprinting, thus reducing the time and cost of bioconvergence R&D, leading to bringing the innovation early. Though only a handful of centres worldwide have adopted 3D bioprinting on a large scale, a lot of research needs to be undertaken to make its impact being felt on the healthcare sector.

As 3D bioprinting technology advances and becomes more accessible, it has the potential to lower the costs associated with organ transplantation and prosthetics. This affordability factor can be particularly beneficial in a country like India, where a large population lacks access to expensive medical treatments.

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