Manufacturing of Biological Tissues: Standardisation and Automation

The manufacturing of biological tissues responds to major societal challenges, but it also faces major issues, especially those related to the standardisation of manufacturing processes and scale-up. Bearing these challenges in mind, the French start-up Poietis has developed the Next Generation Bioprinting (NGB) platform, equipped with a Stäubli TX2-40 robotic arm to perform 4D bioprinting of biological tissues in a faster, more affordable and more functional way. The world's first clinical trial of a bioprinted skin graft will start in 2022 at the University Hospital of Marseille.

Issue

In the past decade, a first generation of tissue-engineered products has been brought to market, mainly for cartilage, skin or corneal indications. These products have shown good clinical results and opened the regulatory pathway, but they have also highlighted a number of issues related to the standardisation of manufacturing processes, product repeatability and scale-up, i.e. the ability to produce them in a massive and cost-effective way.

According to Fabien Guillemot, CEO & Scientific Director of Poietis, "this is due to the traditional manufacturing method used for this first generation of products. These are cell cultures that depend on operators and require an extremely large number of technicians and engineers. To overcome these problems, there was a real need for automation but also for the replacement of operators by robotics."

Solution

In this context and based on its expertise in high-resolution laser-assisted bioprinting, Poietis has developed the NGB modular platform which is designed to give tissue engineers and researchers greater freedom in the selection of biomaterials and hydrogels as well as greater versatility in their research and development.

Poietis launches two bioprinters based on the NGB platform: the NGB-R, marketed for research applications, and the NGB-C, a GMP-compliant clinical quality system for medical applications. Fabien Guillemot specifies that the purpose of this platform is not only to get more affordable treatments (today a bioprinted cornea is marketed at a price of around 100,000 euros for a patient) but also to increase the functionality of the implanted tissues by controlling their composition and their architecture. Highly inspired by the principles of the 4.0 Industry, this new platform integrates automation and robotics technologies, coupled with numerous online sensors and Artificial Intelligence processing. It also includes all bioprinting techniques (laser-assisted bioprinting, bioextrusion, micro-valve bioprinting) and is based on four single-cell resolution technologies: computer-assisted design, automated and robotic bioprinting, in-line control and tissue formation modelling.

Customer Use

The platform includes a TX2-40 6-axis robot since the end of 2017, when Poietis launched its printers automation programme. The Stericlean version of the TX2-40 is fully cleanable and sterilisable and is designed for medical and pharmaceutical applications.

What is the function of the TX2-40? The tissues are constructed on a cell culture plate within the platform isolator. The latter is composed of different print heads, one of which can print cells and the others can print materials that are also part of the tissue. The Stäubli robot is in charge of moving the tissue being constructed from one print head to another. The robot works with the different bioprinting modes embedded in the system (laser and extrusion) and its software can be easily implemented for an industrial solution.

The platform equipped with the Stäubli robot allows to produce a substitute composed of both dermis and epidermis, and not only of epidermis (the most superficial layer of the skin) as it was the case until now with cell culture manufacturing techniques. The printing itself now takes only three to four hours for a 40cm2 square of skin, compared to eight to nine hours previously with traditional manufacturing methods.

Benefits

Stäubli identified Poietis' needs in terms of biomanufacturing right from the start. "The main reason we chose Stäubli for the automation of our printers is that they are able to supply robots in both configurations, one for R&D and one for clinical applications. Besides, their robots are GMP-compatible and are already used in pharmaceutical production, which was an extremely important and differentiating factor for us," explains Fabien Guillemot from Poietis.

The robot's accuracy and speed were also convincing factors. "The TX2-40 robot from Stäubli allows us to reach the different print heads with a very high degree of precision, while at the same time meeting our needs in terms of speed and repeatability. Moreover, and this is very important for therapeutic applications, its action generates infinitely few particles likely to contaminate the tissue," continues Fabien Guillemot. Tissue contamination is a key issue as the isolator in which the printer is placed must be a Class A aseptic environment.

"The robot, just like the rest of the isolator, must be cleanable with detergents and sterilisable. The Stericlean robot meets these requirements, as well as having the right dimensions since our printers should not be too large in order to be deployed in hospital cell therapy centres," concludes Fabien Guillemot.

The Next Generation Bioprinting (NGB) platform, equipped with a Stäubli TX2-40 robotic arm to perform 4D bioprinting of biological tissue..

Future Developments

The platform automation was completed in 2019 and the NGB platform went to market in 2020. The platform was installed at the University Hospital of Marseille at the end of 2021 with the intention of starting the world's first clinical trial of a bioprinted skin graft this year, with different indications regarding healing, small burns and traumatic wounds.

Poietis also works on other applications, showing the versatility of its platform. "We have more upstream projects on the bioprinting of cartilage, pancreas or neurons," explains Bruno Brisson, co-founder and Director Business Develoment. "Some applications will require an adaptation of the platform's modules but its components will remain the same: a laser head to print cells, extrusion to print biomaterials and Stäubli robotic arm to move samples from one print head to another".

Biological tissue sample. © Poietis

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