

Taking the leap into a future of 3D-printed joints

Shanghai Jiao Tong University (SJTU), supported by its affiliated hospital and School of Translation Medicine, is spearheading **BIOPRINTING RESEARCH ON JOINT DISEASES**.

Traditional synthetic joint prostheses can fail within 10 years. They are prone to loosening, fracture, and to causing infection, according to the chief of orthopaedics, Jinwu Wang, at the Shanghai Ninth People's Hospital (SNPH), an affiliated hospital of the School of Medicine at Shanghai Jiao Tong University (SJTU).

With his mentor, Kerong Dai, a member of the Chinese Academy of Engineering, Wang has been examining every stage of biological 3D printing, from 3D models, surgical guides and implants, to bioprinted joint prostheses. Their work aims to improve outcomes in the estimated 140 million patients with joint diseases in China, and the 700,000 joint replacement surgeries each year.

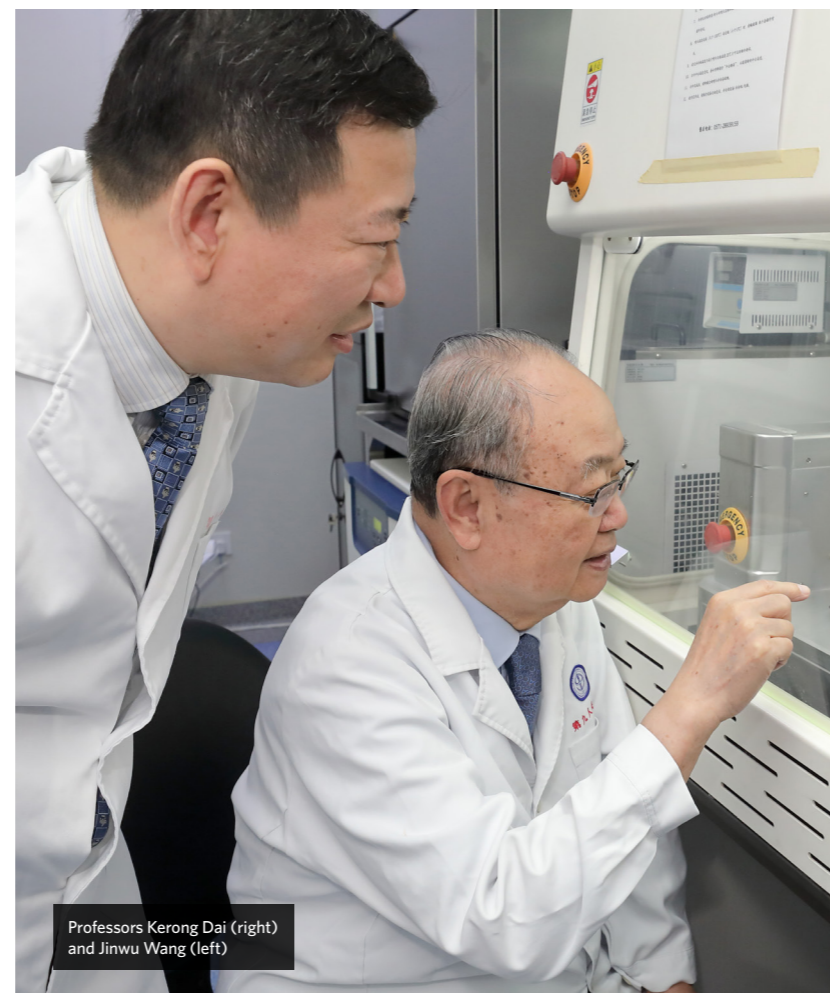
"3D bioprinting has emerged as an attractive tool to create tissues and organs with natural physiological structures which

replicate biological functions and are able to self-heal," says Wang. "Yet there are great challenges. Apart from high precision printing technology, they demand biocompatible ink with the right biochemical and biophysical properties, as well as the reconstruction of a bioactive microenvironment."

One of their latest projects is investigating vascularized bionic artificial joints, and is set to move into further clinical studies. Gathering experts in biomaterial, printing equipment and clinical medicine, this national project includes five investigation teams from 16 institutes across China.

THE RISE OF BIOLOGICAL PROSTHESES

SNPH obtained China's first personalized artificial joint prosthesis registration in 2003. Since then, new iterations of personalized joint implants have sought to improve



Professors Kerong Dai (right) and Jinwu Wang (left)

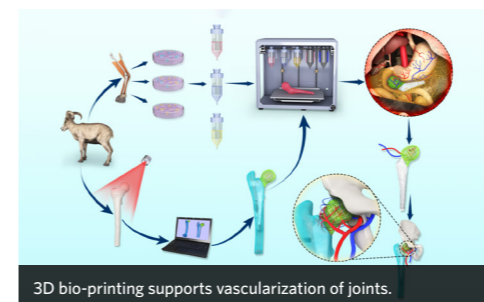
durability and bioactivity. The biggest difficulty is supporting 3D-printed joints with blood vessels, the absence of which can lead to cell death, one of the most common reasons behind the failure of biological printing joint prostheses.

A study published by Wang's team in *Advanced Functional Materials* in 2021 combined polyamide (PNIPAM), and gelatin methacrylate (GelMA) to generate thermo-responsive scaffolds. The in-vivo study in mice demonstrated a cost-saving and less labour-intensive alternative for fabricating artificial micro-scale vasculature.

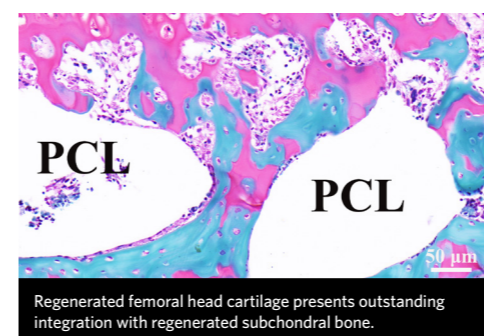
"The scaffolds' volume shrinkage at 37°C effectively triggers the creation of micro-scale vasculature, with a minimum diameter achieved of 50 µm. Such high precision can ensure the delivery of oxygen and nutrients," Wang explains.

Also underlying such success is his team's ongoing research into bioreactors, which supports the regeneration of tissues and organs. In vivo bioreactors, he explains, can simulate the internal environment of the tissues and organs to a greater extent, especially in vascularizing target joints.

"As our technologies evolve,



3D bio-printing supports vascularization of joints.



Regenerated femoral head cartilage presents outstanding integration with regenerated subchondral bone.



A robot developed at the 3D bioprinting centre in a SNPH laboratory

the integration of materials science and cell biology drives exploration to create the ideal scaffold which optimizes the physical microenvironment for cells and promotes blood-vessel growth."

OVERCOMING TRANSLATION CHALLENGES

At SNPH, Dai's team has established China's first patient consultation centre for 3D printing.

The researchers have independently built and achieved world-leading technologies on various fronts: bio-ink adaptable for different tissues, modelling software for

digital bionic models, as well as 3D printing and maintenance system supporting cellular viability bone and cartilage cells.

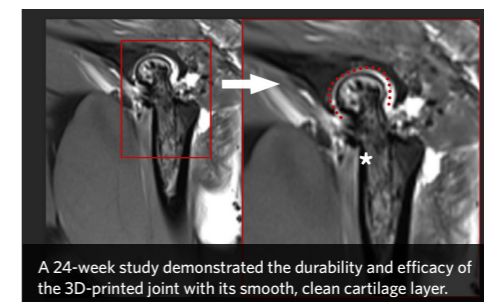
"Based on mechanical tests and clinical trials, we formulated China's first expert consensus and standards in 2018, covering the design, manufacturing, and use of 3D-printed medical devices," says Wang. "Many of them, patented in China, are based on load reduction principles to enhance clinical effect."

Yet, as Wang conceded, the last mile in clinical translation has been tough, not just because of technological

obstacles, but also registration regulations for medical devices.

"In 2019, our team became the first in China as a university-affiliated company designated as a marketing authorization holder to directly commission manufacturers for their 3D-printed medical devices," he says.

"We have also become the first to initiate the provision of registration services for scientific research teams, after we co-established an innovative device registration centre with the Shanghai Municipal Review and Verification Center for Medical Devices and Cosmetics."



A 24-week study demonstrated the durability and efficacy of the 3D-printed joint with its smooth, clean cartilage layer.



This 3D bioprinter is equipped with various nozzles targeting diverse tissue types.



National Facility for Translational Medicine (Shanghai)

SETTING A BLUEPRINT FOR THE FUTURE

"Having synergized collaboration between government, university, hospital and industry, we are building a cloud platform driven by data from 3D-printed personalized medical devices. It's expected to serve at least 25,000 patient cases to obtain national approval," says Wang.

Apart from the designs of printers and robots, they have also looked at real-time cell activity monitoring, bio-ink to support cell development, and bioprinted tissue models used for in vitro drug screening.

These ambitious projects are supported by the National Facility for Translational Medicine (Shanghai), which is a comprehensive research facility for the transformation of key technologies of large-scale high-end medical equipment. The facility is able to simultaneously host 100 research groups on site, supporting research and development of drugs and devices.

"While we want our research to be innovation-driven, it must always be ethical, and clinically safe," says Wang. "We have already released various national standards on customized 3D-printing, including for bioprinted medical devices, which can become international reference in safety and efficacy management. These standards will also have to be futureproof to accommodate rapid technological growth." ■



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