Bioinks and bioprinting in dentistry

Dan Shaffer discusses bioinks and bioprinting and the applicability of these technologies to printing bone and tooth

It is doubtless that technology has touched most industries. None more so than 3D bioprinting technology. Bioinks and bioprinting are set to become the technologies of tomorrow's reality, today.

This article will explore the use of bioprinting technologies in relation to differentiated biological tissue generation. The aim is to give an overview of some of the current, most promising technologies and methods as well as discussing how this will impact modern dental practice.

THE DIGITAL AGE

We find ourselves in the fourth industrial revolution; we live in the digital age. Ever since my father brought home the Sinclair ZX81 (that admittedly didn't do much), my mindset changed to considering things from a digital perspective.

This is no more applicable than to issues of world over-population, food farming and biological solutions to therapeutic body tissue generation.

These issues have become increasingly pressing and the solutions that are being generated increasingly advanced.

BIOINKS AND BIOPRINTING

Back in 2017, a team of researchers from the Pohang University of Science and Technology developed so-called 'bio-blood-vessels' using material extracted from the human body as a template for 3D printing. The blood vessels functioned very well, exhibiting no problems in performing their desired function when implanted.

While researchers from Harvard University, just a year earlier, developed a new type of bioink specifically for building kidneys, allowing the team to recreate vital parts of the kidney.

A team from the bioprinting start-up Organovo in San Diego has already gone on to demonstrate that it can print human liver patches and implant them into mice. Human trials for liver transplants could start as early as next year.

The idea of bioprinting human organs is clearly no longer some far-off science fiction dream. Researchers from private companies and leading universities have printed ears, corneas, lungs, and even a heart.

Researchers from Carnegie Mellon University recently created the first full-size 3D bioprinted human heart digital model using their freeform reversible embedding of suspended hydrogels (FRESH) technique.

The model, created from MRI data using a specially built 3D printer, realistically mimics the elasticity of cardiac tissue and sutures. This novel additive manufacturing method utilises a needle to inject bioink into a bath of soft hydrogel, which supports the object as it prints.

Once finished, a simple application of heat causes the hydrogel to melt away, leaving only the 3D bioprinted object.

The technique allows for the creation of complex organ features and characteristics.

Printing a heart, a kidney, a cornea or even brain tissue might be some way off from coming to a hospital near you due to problems printing the intricate vascularisation networks. Printing bioinks is presently difficult at more than 200 microns resolution.

The microstructure of blood supply required by living cells in these sorts of organs exceeds the practical capabilities in all but the most expensive and advanced technologies currently available.

TISSUE GENERATION

3D printing is set to become the technology that revolutionises biological tissue generation for humankind's therapeutic benefit.

Presently, biological tissues are mainly provided by generous post-mortem donation from human and animal donors. Many synthetic mineral-based alternatives are widely available for bone augmentation, including mineral and metal-based products.

Let's consider these materials in terms of their advantages and drawbacks.

Mineral-based and cadaver bone substitutes have enabled us to augment and replace missing tissues.

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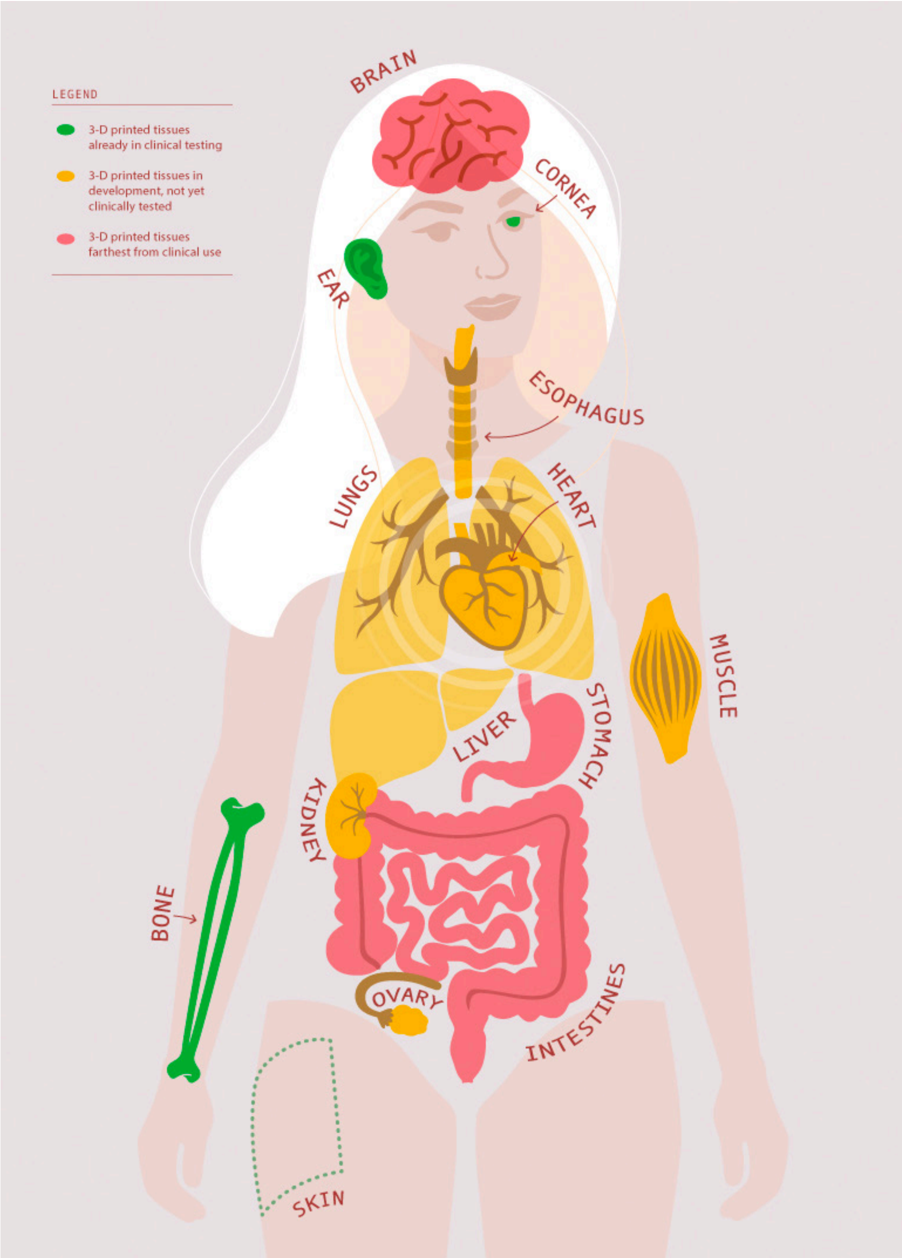

FIGURE 1: *Researchers have been using 3D printing techniques in hopes of developing tissues that can be transplanted into humans. Some printed tissues, such as skin and bone, are already being tested in humans, while many others are early in development (image copyright: The Scientist)*

WHAT IS BIOINK?

A bioink is a hydrogel biomaterial that can be used to produce engineered (artificial) live tissue using 3D printing technology. It can be composed only of cells, but in most cases an additional carrier material that envelopes the cells is also added. This carrier material is usually a biopolymer gel, which acts as a 3D molecular scaffold. Cells attach to this gel, and enables them to spread, grow and proliferate. An important characteristic of the biopolymer in bioink is its capability to retain water, making it a hydrogel (Rehman, 2019).

Controversy has long surrounded the provision of animal and human cadaver bone, with ethically indignant patients opting for completely synthetic and sometimes less effective, mineral-based alternatives.

It makes sense that the most effective bone substitutes would be closely matched to human tissue types. Human cadaver bone can be processed to enable its use without rejection due to incompatible tissue typing. It is used by the body as a framework for the host to colonise the graft with osteoblasts (bone generating cells) to form new bone.

Completely synthetic mineral-based products are widely available but are generally less effective than biological alternatives.

Wouldn't it make more sense to 3D print a bio framework with a suitably intricate substructure for cell colonisation?

Lately, we have seen the emergence of bioinks that are suitable for printing bone and the ability to print intricate architecture has developed in 3D printing technology. This has enabled industrial manufacture of the intricate substructure favourable for effective cell colonisation. This should enable us to economically manufacture generic bone substitute materials on a commercial scale for use in bone augmentation.

Using CT scanning and accurate visible light scanners, a bony defect can be precisely augmented in terms of size, shape and volume to enable printing of a bone implant that would fit the defect more precisely, enabling enhanced integration.

WHAT ABOUT TEETH?

Teeth are highly differentiated structures made up of mixed mineral and organic components. Theoretically possible to print, their therapeutic integration with recipients is fraught with difficulty.

Growth factors and stem cells have been implicated to aid biological integration. This area of research appears to be promising.

Presently, replacing missing teeth has been dominated by the use of titanium-based screw type implants. Zirconia is a material that also looks encouraging. Recently, scanning of the recipient site and custom, recipient specific 3D print manufacture has shown a lot of promise. This customisation of the implant dimensions (based on CT and intraoral scans) has enabled more precise fitting of the implant into the recipient site, enhancing effective of integration.

CONCLUSION

Bioprinting is an industry in its infancy and warrants further attention. Could it be that we should be looking at this technological advance when we consider tooth replacements with the dentistry of tomorrow?

The real question is not whether this will happen but when this prospect will become a commercially viable therapeutic option for our patients. CD