Simerdip Kaur takes a look at the latest ophthalmology-related news stories and asks which are based on facts and which are 'fake news'.

Headline: *Doctor prints cornea on demand!*

Dr Hideo Kodama from the Nagoya Municipal Industrial Research Institute first conceived three dimensional (3D) printing in the early 1980s. He developed a rapid prototyping system for manufacturing through polymerisation of ultraviolet (UV) light-activated resin to form a hardened material layer-by-layer [1]. A few years later, this technique was further developed and patented by Charles Hull who formally described it as stereolithography (SLA) [2]. Essentially, 3D printing technology is a form of additive manufacturing and been widely used in the automobile industry and construction to name a few. In the medical field, it has been utilised predominantly in reconstructive surgery for its ability to build tactile models and implants. Advances in tissue engineering have led researchers to investigate the possibility of printing whole organs with this technology. This begs the question – what is 3D bioprinting and can we really print corneas and other organs?

3D bioprinting is the process of producing viable tissue and organ structures through the use of bio-inks, -materials, -printers and the appropriate digital design [3]. The initial step requires medical imaging and subsequent tomographic reconstruction to obtain segmental two dimensional (2D) images to facilitate the layer-by-layer printing process. Thereafter, the bioprinter is fed with bioink consisting of cells and nutrients to function as extracellular matrix to encourage cell proliferation and differentiation. The printing process involves depositing this bioink onto a biomaterial scaffold made of alginates and synthetic hydrogels to construct the intended tissue or organ. Post-bioprinting, further photo cross-linking is often necessary to ensure the stability and mechanical integrity of the tissue. The three main types of printers used are the inkjet, extrusion and laser-assisted, of which the latter two will be further elaborated on later in this article [3].

Whilst it is far more complicated to print certain organs like the kidney and liver, the cornea due to its lack of vascularisation and low thickness lends itself perfectly to 3D bioprinting [4]. With a global demand for corneal transplants at 12.7 million and a shortage of corneal donors worldwide, Professor Connon's research at Newcastle University brings some hope [5, 6]. His team discovered that the artificial cornea would require the distinct lamellar arrangement of stromal collagen to fortify its shape and provide strength, in addition to a symmetrical curvature to mimic the human cornea. They formulated a bioink consisting of alginate from seaweed, type I collagen and human stromal stem cells that were differentiated to form encapsulated corneal keratocytes. This bioink was deposited onto a 3D printed hollowed-out plastic mould based on the shape of the anterior donor cornea surface via an extrusion bioprinter that uses a pneumatic dispensing system. The bioprinter in use costs about $8,000 and the printing process is complete in approximately 10 minutes. The cells that were printed showed viability at day one and day seven post printing [6].

In a separate study, Sorkio et al. produced three types of cornea-mimicking tissues with the use of laser-assisted bioprinting [4]. The first, a stratified epithelium developed from human embryonic stem cell derived limbal epithelial stem cells (hESC-LESC). Secondly, a lamellar stroma using alternating human adipose tissue derived stem cells (hASC) with accellular layer of bioink containing human sourced collagen type I, recombinant human laminin and hyaluronic acid. The third was a combination between the epithelial and stromal tissue. They used pulses of energy from Nd:YAG and Er:YAG-laser to express the bioink from one donor slide onto the collector glass slide. All three tissue types were subsequently implanted into porcine corneal organ cultures. A week later, the artificial corneas formed attachments to the host tissue demonstrating cell adhesion and migration. They were also found to be viable up to 12 days later [4].

Both studies provided proof-of-concept that 3D bioprinting of artificial human cornea is not only feasible but also resembles the native corneal epithelium and stroma. Nevertheless, further studies on the durability and functionality of these 3D printed corneas both in vivo and vitro are needed. Corneal shape and structural integrity aside, its transparency is also an important factor to consider. Practically, the artificial cornea would have to be implantable and cost-effective and, finally, its safety and efficacy in human and animal studies proven.

Whilst still in its infancy, this breakthrough in cornea bioprinting is likely to pave the way for other avenues of tissue engineering within ophthalmology for printing of other ocular tissues such as conjunctiva and sclera [7]. Perhaps in the future, artificial intraocular lenses and glaucoma valves could be custom printed to each patient's anatomical specifications too.

References

1. Kodama H. Automatic method for fabricating a three-dimensional plastic model with photo-hardening polymer. *Rev Sci Instrum* 1981;**52(11)**:1770-3.
2. 3dprinting.com. https://3dprinting.com/what-is-3d-printing/ Last accessed February 2019.
3. Atala A, Shafiee A. Printing technologies for medical applications. *Trends Mol Med* 2016;**22(3)**:254-65.
4. Sorkio A, Koch L, Koivusalo L, et al. Human stem cell based corneal tissue mimicking structures using laser-assisted 3D bioprinting and functional bioinks. *Biomaterials* 2018;**171**:57-71.
5. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol* 2016;**134(2)**:167-73.
6. Isaacson A, Swioklo S, Connon CJ. 3D bioprinting of a corneal stroma equivalent. *Exp Eye Res* 2018;**173**:188-93.
7. Huang W, Zhang X. 3D printing: print the future of ophthalmology. *Invest Ophthalmol Vis Sci* 2014;**55**:5380-1.

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