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Artificial Organs

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Introduction

We, as humans, possess natural structures that can be replicated and made new in the form of an artificial network. Regenerative medicine has now expanded to creating artificial tissue, by which cells grow in a lab on technological scaffolds that defines an organs structure (Hansson, 2005), in order to replace old, diseased, or damaged organs. Tissue engineering emerged as a new field in the mid-1980's and continues to improve restoration and replacement of defective tissue (Chan & Leong, 2008). The combination of scientific and technological fields has made the engineering of organs and tissues in the lab possible. This is an irreversible hybrid system, which incorporates lab-manufactured scaffolds and natural tissues or stem cells. Artificial tissue regeneration is done by seeding artificial scaffolding made of biomaterials with stem cells or specialized cells, and then by adding a slurry of designated biochemicals to promote optimal cell growth (Stocum, 2015). Most scaffolds are technological structures that are biodegradable and bioabsorbable materials that are incorporated into the body after transplant (Park & Lakes, 2007). Roughly 120,000 people are currently waiting to receive vital allogeneic (not genetically their own) organs such as livers, hearts, kidneys, and lungs (Rojahn, 2014). Organ transplant puts the recipient at high risk of immune system rejection and the need of anti-rejection drugs (Stocum, 2015). Making artificial organs is a developing process and there are many techniques that are being used to incorporate them into our natural systems.

Biology

Our body's natural organs pump blood through our bodies, remove cellular waste and circulate oxygen needed for proper cell function; they make us human. In the case when damaged or diseased tissue is in need of repair and cannot be treated with a drug or particular therapy, tissue regeneration provides a viable option (Zhao et, al. 2013). When organs aren't performing optimally it means they could be damaged or deteriorating due to disease or injury (Chan & Leong, 2008), which can lead to total organ failure. Specifically, the kidneys, heart, liver, and lungs are high priority organs for people on the donor waiting list (Rojahn, 2014) and are therefore being targeted using the methods of artificial tissue regeneration.

Diseases rarely target just one organ, particularly because organ systems are interrelated and highly contingent on one another. For example, chronic kidney disease can lead to decreased cardiovascular function (Levey *et. al*, 2003). Bright disease, or nephritis, is a disease that causes inflammation of the kidneys; chronic nephritis is life threatening ("Bright Disease", 2015). Similarly, coronary heart disease is the most common form of cardiovascular disease and is characterized by plaque buildup in the coronary artery that causes death of living heart tissue (Weininger, 2015). Murakami et. *al*, (2015) gives evidence to support the fact that pulmonary emphysema can promote tumor metastasis. It is likely that tumors that arise from lungs with emphysema are more likely to metastasize into what is categorized as aggressive lung cancer (Murakami et. *al*, 2015). This study and the diseases mentioned, indicate that damaged or diseased tissue(s) need to be replaced by an alternative biological or technological system to not only treat, but to cure these problems.

Technology

Creating artificial organs involves the use of biomaterials to lay the foundation onto

which the patient's cells grow. This foundation is known as the "scaffold" and is combined with a person's stem cells or cells taken directly from the tissue of interest. Normally cells secrete their own extracellular matrix (ECM), or scaffolding ("Tissue Engineering", 2016). Artificial scaffolds are made and designed by researchers and then seeded with the patient's cells and growth factors or made from a 3D-Printer, in which the cells in a nutrient slurry are incorporated into the scaffold at the same time it is being printed. In order to recreate this scaffolding for stem cells or specialized cells to grow on, researchers and engineers devised a couple of solutions. The most common approach involves the seeding of cells onto a man-made porous scaffold, although the preferred method involves the use of native ECM (Chan & Leong, 2008). In a second approach, the artificial scaffolds are created using a mixture of biomaterials and biochemicals that are ideal for cell growth. Some types of scaffolds that are used in tissue engineering are highly porous sponges made of biodegradable polymers (Mooney *et. al*, 2006), bioactive glasses, made of materials composed of several oxidized minerals (Leach *et. al*, 2006), or "Bio rubber", a synthetic biomaterial that is used as scaffolding to guide early cell growth ("Can We Live Forever", 2011). Hydrogels, such as hyaluronic acid, alginate, chitosan, and collagen are more natural derivatives of scaffolding that can decompose inside the body (Drudy &Mooney, 2003). Decellularization is another artificial process of scaffold creation that involves the removal of cells by enzymatic, physical or chemical means (Gilbert, 2006). A combination of these methods proves useful with different tissues. For example, decellularization of lung matrices while keeping them intact, was accomplished by chemical and physiological means (Ott *et. al*, 2010). This is highly effective and has been used in clinical trials (Gilbert, 2006). Cells are removed from an organ or tissue of interest, leaving behind an ECM that becomes seeded with new cells. Manipulation of tissue in this way can have varying effects on the ECM and cell-scaffold

interaction (Gilbert, 2006), which is why a printing method is more commonly used. Scaffolding is now being made by 3D bio-printers in a process called additive manufacturing, or three-dimensional (3D) printing (Murphy & Atala, 2014). The purpose of 3D printing is to fabricate a scaffold that is made with the precision and accuracy of a printer. During printing, layer by layer of biomaterial, cells, and biochemicals are positioned in the shape of the desired tissue or organ to produce an accurate 3D scaffold with cells implanted that closely mimics the natural ECM (Murphy & Atala, 2014). Jung, Lee & Cho (2016) demonstrated the 3D printing of an ear, kidney and tooth fabricated by a computer-aided design and manufacturing system (Figure 1 & 2). This creates a more complex scaffold, with cells incorporated within and throughout as opposed to the other methods where cells are injected and spread over the outer surface of the scaffold. The synthetic scaffolding paired with the body's cells is what makes artificial organs a unique hybrid system, with many variations. This triad is shown is best represented in Figure 3 (Park & Lakes, 2007).

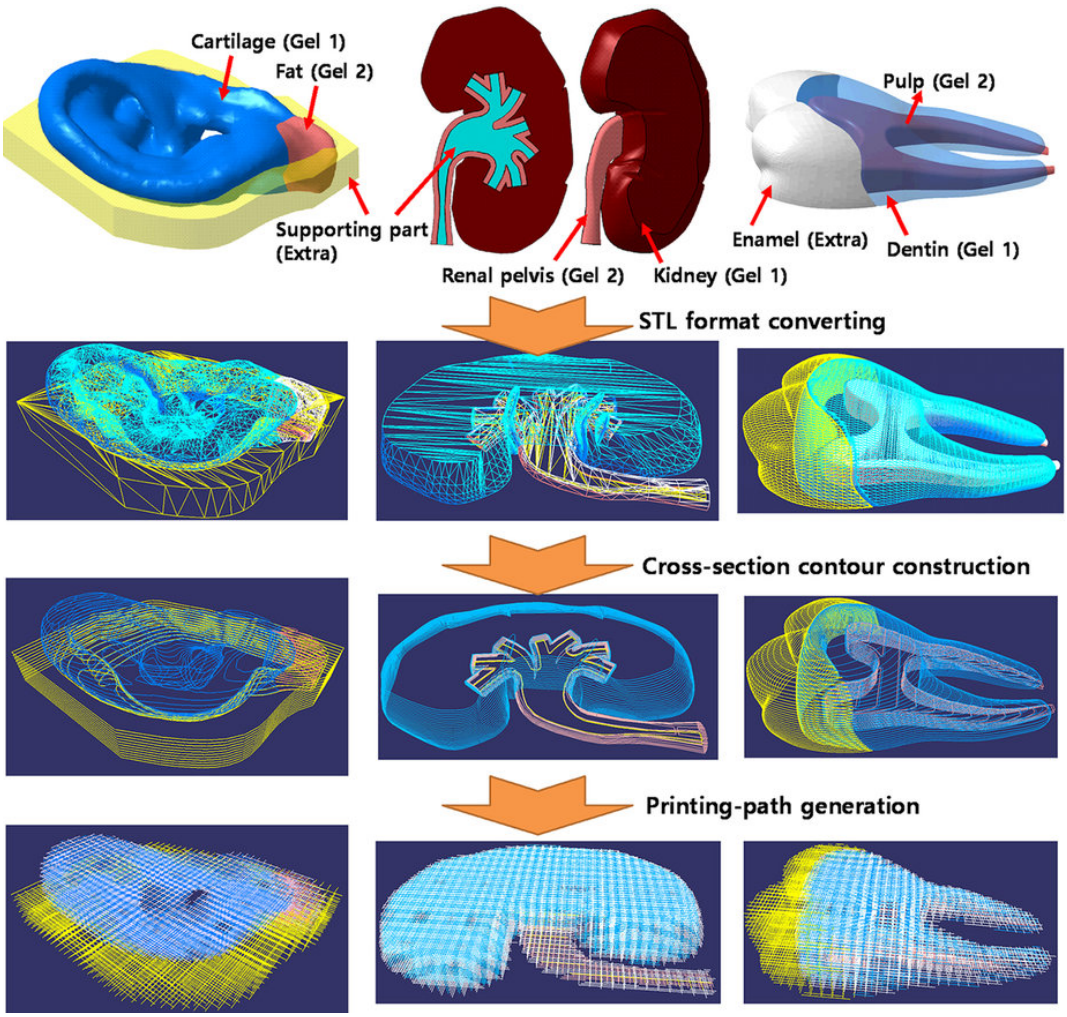

Figure 1. *The Process of Generating Printing Paths*. From left to right, outer ear, kidney and tooth images that are the results of slicing algorithm and the algorithm to generate printing paths. The frame is shown in white, hydrogel 1 in blue, hydrogel 2 in red, and the support in yellow. Figure adapted from Jung, Lee & Cho, 2016.

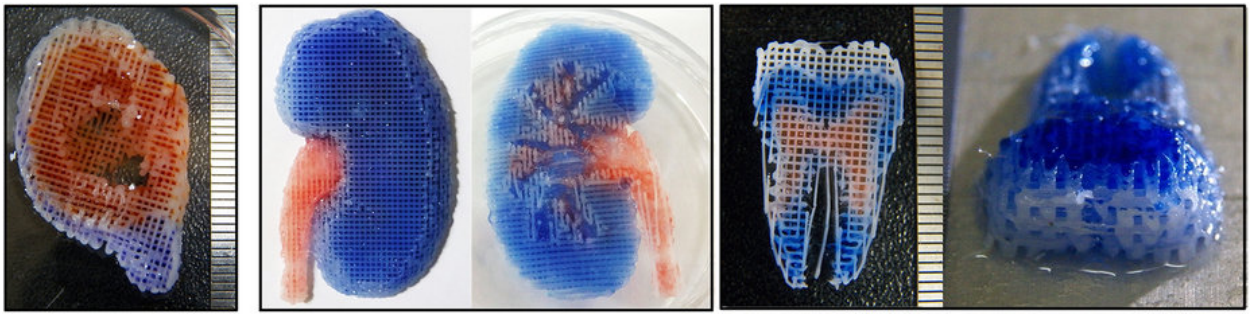

Figure 2. *3D printed heterogeneous tissue constructs*. From left to right, outer ear, kidney and tooth constructs. Tissue construct frames were partially stained by the colored alginate solutions during printing. Figure adapted from Jung, Lee & Cho, 2016.

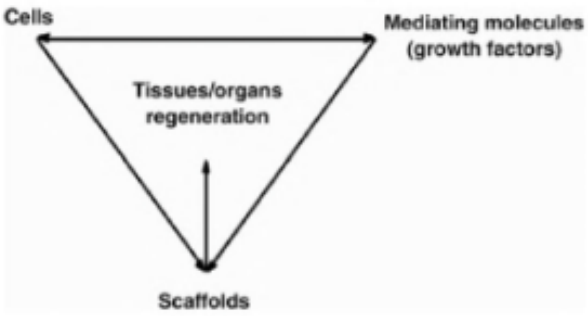

Figure 3. *Tissue Engineering Diagram*. Representation of the role of scaffolds in tissue engineering, and how its role is assisted by growth factors and cells. Adapted from Park & Lakes (2007), (pg. 491).

Neurobiology/Technology Hybrid System

The creation and implantation of artificial organs was intended to give patients a higher chance of survival while waiting for an organ or perhaps spontaneous recovery (Watanabe, *et. al*, 1997). Similarly, creating organ substitutes out of artificial tissue can also be an excellent and successful alternative to patients with operable tumors that have low resection rates, and are unable to be fully removed (Jungebluth *et. al*, 2011). Decellularization of tissue and reintroduction into the body is a more natural way of making artificial organs, while bioabsorbable scaffolding is also relatively natural. This system incorporates the ECM of whole organs as scaffold material, pluripotent stem cells, capable of anchoring to substrate, and growth factors which allow maturation and regeneration of tissues. Maturing and regenerating connections to the brain. Stem cells can specify and differentiate which make them optimal for synthetic scaffold creation; incorporating biology and technology.

However, this new research has many negatives. While new organs can save many lives and help cut back on the donor waiting list, the construction of new organs takes 6-8 weeks before implantation, this can be a costly and can arrive too late to the patient. In a rat-based

clinical trial, embryonic stem cells formed stable intramyocardial grafts when incorporated into a ventricular pouch made of bio-artificial mixture (Kofidis *et. al*, 2005). Although, there may be serious implications when it comes to human trials because of ethical boundaries (Ott & Mathisen, 2011). There is also a concern of artificial organs being used for enhancement, for humans to go beyond normal, therefore implant ethics must deal with this issue as the research progresses (Hansson, 2005). Crossing these boundaries in human trials is something we have to abide by, and in return, may not gain the research necessary to improve this system (Ott & Mathisen, 2011).

Future Predictions

Research shows a promising future for this field in a near 10-15 years. In 2002, Van De Kerkhove *et, al*. published their results of a phase I study on transplanted bioartificial liver (BAL) systems in 7 human patients, with only 2 deaths. The BAL system was a device that was transplanted to act as a bioreactor in patients with acute liver failure to bridge the waiting time for a liver-graft. The evolution of this device has become more closely related to the natural ECM that is implanted an incorporated fully into our bodies and is a long-term treatment. However, we must take caution and study the long-term effects of replacement organs and look closely at idea scaffold choice, cell source and tissue culture conditions (Ott & Mathisen, 2011). Many other countries are attempting to generate artificial organs and tissues; this arms race could help stimulate faster production of artificial organs, possibly cutting the time in half. The future may arise sooner for regenerative medicine, as research is rapidly underway to replicate tissue to replace old, diseased or damaged organs.

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Figure 2. *3D printed heterogeneous tissue constructs.* Adapted from Jung, Lee & Cho, 2016. http://www.nature.com/srep/2016/160222/srep21685/full/srep21685.html

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I have abided by the Wheaton College Honor Code in this work

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