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The scientist on the stage, who says that he has a method that could eradicate transplant lists and save innumerable lives, is at once nonchalant and spellbinding. It is as though the vision he articulates—a better world where it is routine to grow bladders in a lab and to print skin grafts directly onto wounds—is already a reality for him even as his audience sits captivated by it, some chuckling in wonder at the novelty of the ideas. Their heart rates rise along with their curiosities as he finally introduces the sophisticated piece of equipment that he believes will usher in a new age in medical advancement. The 3D bioprinter—engulfed in light on the projector screen as it is unveiled—moves with fluidity, its metallic surfaces and bright pink bioink cartridge emphasizing its allure. According to the scientist, the video shows the device in the midst of printing a completely organic kidney. As proof, and as uneasiness settles over the crowd, he asks a colleague to bring him a kidney that they had printed earlier. Intrigue outweighs discomfort: the audience sits with eyes fixed on the bioprinting pioneer as he dons gloves and carefully cups his hands around the printer's product. Before their eyes, his promise of a better tomorrow has been transfigured into real, printed flesh.

The NovoGen MMX Bioprinter

The pursuit of providing organs through scientific advancements is not an uncommon theme in science fiction. For example, consider Milla Jovovich's character being bioprinted in *The Fifth Element*, or the secret behind *The Island*. Such stories can be valuable as well as exciting: they show how seemingly impossible scientific advancements could affect society, and beneath their plots usually lie questions that expose science to an ethical review that is occasionally uncomfortable but always necessary. However, since the fictional advancements often seem infeasible, an audience can ignore these ethical dilemmas easily enough. But what happens when science fiction is no longer fiction? Does the real version seem any different ethically? Such questions are now important because, in the case of organ printing, fiction has become reality. The scientist previously mentioned is Dr. Anthony Atala, a pioneer of the 3D bioprinting industry. The event that was described is a presentation Dr. Atala gave in 2011 for the popular Technology, Entertainment, Design (TED) conference series (Atala 2011).

To approach ethical questions about bioprinting, we should start by considering its history. The technology emerged on the heels of great strides in tissue engineering that occurred in the early 2000s: at the turn of the century, Atala, among others, helped catalyze its development when he successfully transplanted lab-grown bladders into several patients (Atala 2000). After this breakthrough, questions began to emerge about how tissue engineering could be improved to make more complex organs. Then, in 2003, another team of bioprinting pioneers developed one of the earliest known bioprinters by modifying an inkjet printer to print cells and gels into scaffolds (Mironov, Boland, Trusk, Forgacs, & Markwald 2003). This innovation was based on a technology developed in the 1980s called 3D printing: an additive manufacturing form of engineering that prints layers of heated plastic or other material. As a layer is finished, the print platform moves downward in preparation for the printing of the next layer, and 3D modeling software controls where the printhead will lay the material. In the case of bioprinting, the printed material consists of bioinks, which contain cells, hydrogel, and other biological factors. The incredible capabilities of 3D printing can enhance tissue engineering, making bioprinting a worthwhile alternative to conventional tissue engineering approaches.

As of now, the dominant tissue engineering method involves biodegradable scaffolds used to support the three-dimensional shape of a tissue and promote cell adhesion to the scaffold's surface. These scaffolds are usually designed out of polymers and are porous to provide space for vascularization and the seeding of cells inside the scaffold (Mironov et al. 2009). While this method has proved effective, it also has its limitations. Major issues with this method include difficulties in getting thicker tissues to vascularize thoroughly, as well as precisely seeding different cells inside the scaffold (Mironov et al. 2009). However, advancements in bioprinting have produced vascularized tissues without scaffolding (Norotte, Marga, Niklason, & Forgacs 2009). Furthermore, bioprinting obviates the time-intensive work involved in carefully seeding cells onto a scaffold. Although conventional tissue engineering can produce the same tissue constructs as

bioprinters, the speed and precision with which bioprinting occurs make it more efficient for research purposes.

Realizing that bioprinters could revolutionize large-scale tissue manufacturing, many researchers have moved quickly to take advantage of these devices. Some of the early developers of bioprinting founded a company called Organovo to commercialize their bioprinters and 3D printed tissue models. Recently, Organovo achieved one of its major goals: to develop printed liver tissue products, which it is now selling to drug companies to make toxicology testing more accurate (Organovo Holdings, Inc. 2014). Other bioprinting experts, for their part, have been researching ways to mass-produce organs and tissues, and have published papers outlining elaborate systems of automated tissue engineering assembly lines (Mironov, Kasyanov, & Markwald 2011).

While the long-term goal of bioprinting is to print transplantable organs, Organovo and other research groups also focus on short-term goals that, when accomplished, have so far had a remarkable impact on the field of regenerative medicine. In the area of stem cell research, bioprinting has become a good option for engineering microenvironments that encourage a particular pathway of stem cell differentiation (Tasoglu & Demirci 2013). Also, stem cell printing is now sophisticated enough to print various kinds of stem cells that function normally and have a high rate of survival (Tasoglu & Demirci 2013). However, bioprinting seems to be most useful for engineering basic tissues. Already, bioprinted bones and cartilage can be used in various clinical applications, and extensive work on other bioprinted tissues, such as aortic valves, is underway to provide more kinds of transplants (Seol, Kang, Lee, Atala, & Yoo 2014). Unfortunately, even as the technology of bioprinting advances, the field of organ manufacturing turns complicated once the tissues leave the printers.

While the transplantation of a lab-grown bladder is a great feat in regenerative medicine, the ability to print a variety of transplantable organs seems far off. First, a bladder is a very simple organ composed of only two cell types; a kidney, by comparison, consists of many cell types and requires a complex vasculature. In fact, the kidney that Atala presented during his talk is a model with limited survival time (Atala 2011). The difficulty lies in the development of the tissue after printing. Seeking clues from nature to bypass the current developmental barriers of printed organs, some bioprinting researchers are exploring aspects of tissue formation in embryonic development (Mironov et al. 2009). Another barrier, however, is difficulty in printing tissues with complex vasculature systems. Organovo was successful in generating viable liver tissue models, but a full-sized liver is thicker than their models, and thus requires more vasculature. Although bioprinting has significantly improved tissue engineering, transplantable organ regeneration is still bound, for now, to the realm of science fiction. However, this does not mean that the ethical debate surrounding the idea of bioprinted transplantable organs should pause to wait for the technology.

Recently, a group of information technology experts at the research firm Gartner predicted that advancements in 3D bioprinting will catalyze a major ethical debate within a few years (Gartner, Inc. 2014). Currently, many tissue engineers are starting to talk extensively about bioprinting as they become interested in integrating the technology into their work. But to most of the public, bioprinting still sounds like science fiction. One can imagine how the public would react to news that clinical trials for 3D printed organs had begun: having heard almost nothing about the science, they would be faced with innumerable ethical questions to answer and little information to go on. Some of the questions that come to mind deal with availability of use and regulatory precautions. If 3D printers are now inexpensive enough for the common man, is it not plausible that bioprinters could eventually become inexpensive enough as well? Regulations would be required to delineate who is responsible enough to utilize the technology. Also, in the case that printed organs make it to clinical use, who would receive the benefits of this technology? Would the benefits of expanding access to lifesaving tools outweigh the dangers of providing the technology to regions with poor baseline healthcare and weak regulatory abilities? And would abuse of the technology lead to an increase in patients receiving unnecessary body modifications? For transplantable printed organs to cross the boundary between science fiction and reality, society must first consider the ramifications of releasing this technology to the public.

Dr. Atala brings his presentation to a close by showing a video of a previous patient (Atala 2011). Luke, an early test subject who received a lab-grown bladder, explains how Atala's work changed Luke's childhood. Once the video ends, the talk's host invites Luke on stage. The audience tries to maintain composure as Dr. Atala humbly receives accolades from the host and a healthy dose of gratitude from his now twenty-something former patient. Although most people are more comfortable with science fiction stories remaining fiction, there are aspects of ethically challenging advancements that make compromises seem justified. Bioprinting pioneers like Atala are probably aware of the ethical issues that will arise as they get closer to achieving their long-term goals. However, successes like Luke's transplantation are probably what drive researchers deeper into an ever-evolving field that promises to be full of both complexities and triumphs.

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