The Classification of Bioprinted Organs and Its Legal and Societal Consequences

A Research Paper submitted to the Department of Engineering and Society

Presented to the Faculty of the School of Engineering and Applied Science
University of Virginia • Charlottesville, Virginia

In Partial Fulfillment of the Requirements for the Degree
Bachelor of Science, School of Engineering

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Spring, 2021

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Introduction

3D bioprinting technology is edging closer to fully realizing its capabilities for manufacturing synthetic organs at a large scale. This merge of autologous cells and additive manufacturing is beginning to blur the line between artificial and natural as bioprinting techniques continue to advance with more biological components that mimic native tissue. As the possibility of wide-spread use in the coming decades in hopes to address the organ donor shortage becomes more visible, questions are raised about how legal bodies will interpret this new technology. This is closely intertwined with social and cultural meaning of the human body, and what constitutes a human and a human organ. One issue that has become evident as the concept of biofabricated organs emerges is how this technology will be regulated, specifically in patenting and ownership of the technology and resultant product, and this is where the classification of biofabricated tissues and organs becomes an important aspect of this sociotechnical system.

For this paper, the framework of classifications and standard will be discussed in the scope of legal language to discuss how it affects social norms and perspectives on synthetic organs. This will address the main question of how bioprinted organs should be classified and defined in a way that incorporates both the technical and societal definitions of a human organ and human body part. Then, I will be analyzing how legal and societal groups categorize something that crosses the conventional boundaries of life and non-life; as patentable machines or non-patentable human organs.

Prior Scholarship on The Ethics of Synthetic and Bioprinted Organs

It is well-established that the current legal and regulatory frameworks cannot keep up with the rapid rate of technological development in 3D bioprinting. This technology encompasses a broad group of stakeholders and ethical implications that have not been addressed in recent years by regulatory bodies. This broad range of stakeholders includes scientists, engineers, clinicians, businesses, policymakers, and laymen with ethical considerations in access to treatment, cost, cell-sourcing, manufacturing practices, patenting and ownership, and social attitudes (Vijayavenkataraman et al., 2016). For the purposes of this research paper, I will be analyzing these last two aspects, ownership of bioprinted organs and social perspectives on this technology, since classifications play a substantial part. However, legal and regulatory frameworks also encompass and have direct effects on all these ethical issues as they all need to be regulated in some way.

This is important to address because there is currently no specific FDA regulation on 3D printing with biological, cellular, and tissue-based materials (Gilbert et al., 2018) And even globally, these regulations are extremely limited and broad. But, as we work towards standardizing and scaling up production of this medical technology, it becomes increasingly difficult to regulate from every single step of clinical trials to manufacturing and marketing, since it doesn't neatly fit into any current regulatory category. As of now, it is considered a combination treatment, neither fully machine nor fully biologics. Without clear and specific regulatory frameworks, a huge regulatory vacuum can cause major consequences in quality and use of the technology (Gilbert et al., 2018). People could technically print an organ in their homes with the right bioprinter, bioink, and computer. Clinical studies, good manufacturing practices, and risk-benefit analyses are also loosely defined and generalized. But, most

importantly with patents, the increasing value of bioprinted products by manufacturers and companies requires regulatory oversight and guidelines to prevent abuse or ethical problems.

However, no matter how technical this definition of a synthetic or bioprinted organ becomes in the language of policymakers, societal attitudes play a part in these ethical debates and are important to address when classifying. Though highly contested, emotions and reactions such as 'yuck' and 'disgust' may have basis in moral judgement and consequently, how society will view synthetic organs (Vermeulen et al., 2017) With the advancements in technology and manufacturing, humans have become more opinionated with the concept of "natural" and what is acceptable for use in society. Despite this, society has not had such analytical discussions on the naturalness of our own bodies and the consisting parts.

Classification Framework

The framework for this discussion will be derived from the book, *Sorting Things Out: Classifications and Its Consequences* (Bowker & Star, 1999). Since the classification of synthetic organs is going to be analyzed in the context of legal bodies, standardization is inevitably an important sub-framework. Two works will be utilized to transition from the notion of classifications to its use in regulations and society, which are *Standards and Their Stories: How Quantifying, Classifying, and Formalizing Practices Shape Everyday Life* (Lampland & Star, 2009) and *Standards: Recipes for Reality* (Busch, 2011). These three resources provide the scholarly definitions of classification and standards, which will aid in explaining the complexities of regulating synthetic organs and what they represent to society.

As defined by Bowker and Star (1999), classification is a spatio-temporal segmentation of the world, and an ideal classification system should exhibit three requirements. First, they should be consistent and unique, which means origin and descent are often used to classify

things. Second, the categories are mutually exclusive; and third, these systems are complete. Standards, on the other hand, are any set of agreed-upon rules for the production of objects. They also have a temporal reach that persists over time and span multiple communities. And most importantly, legal bodies often enforce these standards.

Classification Are Imperfect

It is clearly stated by the authors, that real-world classification systems never meet these three ideal requirements, which will be evident when applying them to bioprinted organs. With the infinite complexities of the world, classifications cannot encompass all the aspects of a certain object. There's overlap and a mix of different principles that produce contradictions. For example, Bowker and Star analyzes the International Classification of Disease (ICD), which is the classification scheme for different diseases created in the late 1800s and still used today. For such an important tool for medicine and medical infrastructure, the ICD has become increasing tangled in crisscrossing classification schemes. Bowker and Star attribute this to global public health systems, discrepancies in Western and Eastern medicine and practices, corporate entities such as insurance companies, large health organizations, and religion. There are so many stakeholders that require their own views and input into this classification scheme and so many uncertainties that still remain in medicine that even classifying death becomes a complicated and unresolvable topic of debate for the ICD. This flawed classification scheme demonstrates how, if unclearly defined, the global and local distribution of information and services could be riddled with ambiguity, uncertainty, and overlap, and shows just how difficult it is to overcome these issues when classifying.

Lampland and Star (2009) and Busch (2011) further discuss the implications of these boundary objects by stating that standards are never completely adequate and are relative to

different sociotechnical landscapes. They bring some aspects into view, while making others invisible. While certain standards and classification can be benign or irrelevant to an individual or group, it can be life-threatening to others. However, standards still represent and embody the morals and values of society. And the legal procedures that standardize these objects directly embeds itself and integrates into many layers of social and cultural infrastructure. It is human nature to classify various aspects of life, such as technoscientific artifacts, into distinctly defined and mutually exclusive categories. However, with the innovation of these artifacts comes greater complexity, which makes it even more difficult to classify them into a clear category that meets the needs and views of legal and cultural entities.

Current Debates on the Classification of Synthetic Organs

As 3D bioprinting is edging closer to fully realizing its capabilities for manufacturing synthetic organs at a large scale, it is becoming evident that regulatory bodies are not prepared for its testing and introduction to the public. Scientific innovations are constantly changing and morphing into different or larger versions of itself, and the regulatory body's job to keep up with such changes and produce up-to-date standards for the public. However, legislature and regulations cannot keep up with the evolving definition of 3D bioprinted body parts. Once considered purely medical devices, due to its more synthetic polymeric material, and main use for regenerative medicine, bioprinting is now becoming more naturally derived with the goals of tissue engineering complete replacements for entire body parts (Gebelein, 1984). As regulations deal with classification and standardizations, the language in which it describes synthetic organs are no longer conforming with the current state of the innovation. As legal bodies, whether in professional organizations, manufacturers, or the government, adapt to these rapid changes, they

may need to reassess how they have classified and categorized synthetic organs because it will play an important part in the decisions and views that society will have on this novel medicine.

The fundamental question surrounding current negotiations about the classification of 3D bioprinted organs is whether they are actual biological tissue or a medical device. Currently regulators for the FDA, and regulatory bodies in other countries, are posed with the difficult decision of categorizing 3D bioprinting under medical devices or as biologics (Mendis & Rutschman, 2020). Most legal entities still consider bioprinting as a medical device, but as more cellular and bioactive factors are added into the manufacturing process, these two classifications are starting to overlap. 3D bioprinting no longer fits neatly into current regulatory frameworks, and regulatory agencies around the globe are trying to address these uncertainties and lack of uniformity in dealing with bioprinting (Gilbert et al., 2018). The article by Mendis and Rutschman (2020) also introduces the possibility of creating a completely new framework for which bioprinting would be regulated by, if neither category is well-suited to encompass the major aspects 3D bioprinting. Whether through existing or new regulatory frameworks, this will shape the way the public can interact with the products. As mentioned earlier, classifications and standards embody moral and ethical values of society. So, another major area of contention in regulation is if manufacturers are allowed to patent bioprinted material (Mendis & Rutschman, 2020). As 3D bioprinted products increasingly resemble human organs and tissues, the legality of patenting these materials would become a great moral issue. As the innovations in 3D bioprinting are evolving, so are the conversations pertaining to its regulation. In the process of defining synthetic organs, certain voices in society will be heard, while others silenced, so it's important to analyze how these classifications come about and how they are changing with the emergence of new information and ethical questions.

Fitting Into Existing Classifications

There have been considerations in fitting 3D printed organ within current legal and regulatory frameworks. Again, the question of whether 3D bioprinted organs are considered human organs arises in discussions. From the legal language of the National Organ Transplant Act of 1984 (NOTA), human organs seem to imply "from a human being", a factor that the author presumes means 3D bioprinted organs do not fall under (Kelly, 2018). This is where the first requirement of classifications comes into play; what is the origin of a synthetic organ and how is that different or unique from human organs. From the perspective of Kelly (2018), these two entities are distinctly different and prefers to view synthetic organs as biologics, "a virus, therapeutic serum, toxin, antitoxin, vaccine, blood, blood component or derivative, allergenic product, protein (except any chemically synthesized polypeptide), or analogous product, . . . applicable to the prevention, treatment, or cure of a disease or condition of human beings." The key word that the author points out is "protein", which is the component that makes up the bioink used for printing. Medical devices are defined as "an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related article" under FDA guidelines and should achieve it intended purpose without chemical action. It makes sense logically that part of our human biology would fall within the scope of biological product and be regulated as such. With this notion, 3D bioprinted organs should be regulated with market rates consistent of other health care services to provide the incentives to innovate. This includes commodifying and patenting these products. This author argues that classification should be determined by the intended use, mode of action, and ingredients of the 3D bioprinted organs.

Completely New Classification and Regulatory Framework

However, there are other scholars that find this classification much more complex. First, the definition is slightly different in how they view artificial organs. They are "manufactured, fully implantable devices that are a destination therapy for organ failure and fulfill the essential functions of the replaced organ for an extended period" (Hutchison & Sparrow, 2016). The main difference, is that while Kelly (2018) views artificial organs as the complete manipulation of biological tissues and cells, Hutchison and Sparrow (2016) view artificial organs as a combination of mechanical parts with human tissue to fulfill the essential functions of the organ. They assume that most of these future tissue-based organ replacements will have nontissue-based components, such as composites and polymers. As the line between body and machine blurs, they do not believe artificial organs can fit under any current FDA regulations, nor do they believe that these current regulations can address the ethical challenges associated with the use of artificial organs. Additionally, they also question the ethics of ownership and patentability of artificial organs. Are they part of the patient's body or a piece of property that was purchased? Where do those rights change as they are implanted into the body?

Legal and Moral Ideas on the Ownership of Human Biological Parts

Despite the general consensus of commercialization and marketing of future synthetic organ products, there are still ethical and societal considerations to take into account when constructing a new classification and framework for the technology.

Patents and the Legality of Ownership

One of the main values of patenting is promoting and incentivizing technological development. It pushes scientists to invent and create novel and useful processes, materials, or devices with the added value of a patent along with it. But as policymakers strive to incentivize scientific progress in bioprinted organs, they also need to prevent unethical practices with human

subjects and products. Congress has determined that "no patent may issue on a claim directed to or encompassing a human organism" (Goodman, 2017) However, they failed to define or clarify what the term "human organism" means, especially in the world of biotechnology. Patentable subject matter technically includes any process, machine, manufacture, or composition of matter that is made by man, except for subject matters pertaining to a law of nature, natural phenomena, and abstract idea (Goodman, 2017). A subject matter pertaining to a law of nature is only patentable if it is substantially different from what exists in nature. So, the creation of an artificial equivalent of an existing natural product, such as a human organ, may possibly not be a patentable object. However, there is clear distinction between the types of claims that can be submitted for patents. One is the actual tangible product, and the other is the process to create that product. There have been many patents granted for methods of creating and growing artificial tissue, however, patents on the actual tissue itself, which is a more valuable patent for infringement and collecting damages, have not been granted.

Though there have been no claims on artificial organs, living creatures are patentable, but have been limited to "non-human" subject matter. This includes bacteria, genetically engineered animals, cloning techniques, and *in vitro fertilization*. There have also been some landmark decisions in court pertaining to the patentability of certain subject matter. *Diamond v. Chakrabarty*, which ruled that genetically modified bacterium was patentable because the modified bacterium possessed properties that no naturally occurring bacteria had, established that living matter is patentable if manmade (Goodman, 2017). However, in *Pathology v. Myriad Genetics*, isolated DNA sequences were determined not to be patentable because the sequences already existed in nature. Despite these rulings, the courts have yet to discuss if synthetically-derived mimics of naturally occurring substances, such as bioprinted organs, are patentable.

In general, the United States Patent and Trademark Office (USPTO) has policy that does not allow human beings, at any stage of development, to be patentable subject matter. This affects human organisms, human embryos, human fetuses, and human beings (Goodman, 2017). This again leads into the question of how to define and classify a human organism and its constituent parts?

Moral and Societal Considerations of Ownership

As stated before, how individuals and society perceive their own bodies plays an integral part in the classification of synthetic organs. Human organs play such a big part of our everyday lives, yet we rarely think about what exactly a human body part is and how closely intertwined it is with personal identity. Let us consider the philosophical dilemma of the Ship of Theseus. The ship where Theseus and his crew returned to Athens was preserved in the city for years. But as the wood decayed, they were replaced with newer and stronger timber until the entire ship was replaced. Is the ship still the same or completely different once all the pieces were replaced one by one? If not the same, at which point was the ship no longer the same? Human beings are an aggregate of different hierarchal parts; organs are made of tissue, which are made of cells, which are made of proteins, and so on, until subatomic particles. Does society perceive humans as aggregate of biological tissue, or individual cells, or atoms? Depending on how society views the aggregate of their human parts, synthetic organs could still be considered human parts, made of the same basic biological components (Rea, 1995).

Additionally, the sense of ownership of a human body part is very much left to the experience of the individual. The rubber hand illusion, a study of the condition of embodiment of an object, demonstrates this concept. Many participants consciously do not perceive the rubber hand as their own. But once a stimulus is added, a slight brushing of a feather or the slam of a

hammer, the illusion of ownership is induced. Experiences and sensations play a big part in our perceptions and judgements about our human body parts and organs (de Vignemont, 2011).

Discussion

To discuss this further, let us delve into the aforementioned technology of *in vitro* fertilization. The process for *in vitro* fertilization and for growing a fetus is patentable, but the actual fetus is not. This is because 1) it already exists in nature, and 2) it is highly unethical to patent another human being. The fertilized egg has not been modified, with the exception of the fertilization process, but the product, the fetus itself, is no different than any other naturally-derived fetus or human being that exists in society. No matter how unnatural *in vitro* fertilization was perceived when it was first patented, the product is still considered a full human organism and human being. Currently, bioprinted organs may not have reached the complexity to completely produce an accurate and whole imitation of naturally-derived organs, but it has the possibility to do so. As of today, scientists and industries can obtain patents for both the methodology and artificial tissue itself, even if it is comprised of living, human cells. Synthetic tissues can be commoditized and produced in industry, which technically allows for patents, since it pertains to a business and business practices. Synthetic tissue is still considered significantly different from naturally occurring tissues, but scientists are still working towards fully replicating the natural product. The closer scientist get to replicating a natural product, the further they get from being able to patent and commodify the product. But, even if it fully replicates a natural product, the concept of "natural" plays an important part in societal norms and acceptance of synthetic organs. "Yuck" is a human reaction that condemns a confusing or contradictory object or idea which is classified as out of place (Kelly, 2018). Society has yet to accept synthetic organs as natural or normal, and at the same time, many find distaste in

commodifying organs, even if they are manufactured. However, there have been many instances of slow, widespread acceptance and understanding of new, 'unnatural' technologies, such as *in vitro* fertilization.

Furthermore, although the creation of an artificial equivalent of an existing natural product, such as a human organ, is not a patentable object, there are possibilities of 3D bioprinting organs that exceed the limits of natural organs. Both sides of the argument on how to classify synthetic organs do agree that they will be commodified and should be regulated as such. The market for synthetic organs will drive rapid development and advancements in the technology, which is good for consumers. However, it is a challenge for regulators and policymakers to anticipate these types of developments in synthetic organ technology. But, if we want people to accept these synthetic organs as a norm, policies should anticipate and not be reactionary to poor outcomes. Regulatory frameworks influence the behavior of commercial entities at all stages of development and commercialization of the product, which have consequences in society.

Conclusion

Throughout this paper and discussion, it clear that most of the challenges in classifying 3D bioprinted organs require an extremely high level of foresight into the future of this technology. Though this analysis of several arguments and viewpoints may present the essential struggle in classifying, it is nearly impossible to clearly present an ideal framework to classify bioprinted organs with the rapid changes that the technology is currently undergoing. In conclusion, a new regulatory framework is needed to encompass the developments in 3D bioprinting, which is distinct from medical devices or biologics. To successfully classify

synthetic organs, insights from the scientific community, policymakers and laymen need to be included in the discussion to redefine what a human organism and human body part is.

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