17. Envisioning 3D Bioprinting
Scenarios of Organs 'on Demand'

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1. Introduction

The oft-cited game-changing potential of 3D bioprinting in transplantation medicine tends to focus on its promissory power – its capability to 'solve' several key problems associated with traditional organ transplantation and revolutionize modern medicine. Whilst the nascent technology could indeed have some clear benefits, it also brings social and ethical issues regarding its embedding in health care systems, including regulation, ownership and access. Organs become exchangeable alienable objects, subject to the market forces of supply and demand. Thereby, organ bioprinting may risk further commodification of our bodies, increase existing health inequalities, while heightening expectations and desires for 'ideal health'.

In the context of emerging ethical debates on bioprinting, this chapter combines bioethics with insights from Science and Technology Studies (STS) to explore some of these issues further. Building on current ethical and legal scholarship, we are particularly interested in questions regarding ownership of bioprinted organs, e.g. who would be entitled to a bioprinted organ, whether they could be sold, and issues of liability. As real-life examples are not yet available, we use hypothetical narratives as heuristics for thinking through emerging ethical and regulatory issues, in order to provoke questions and stimulate debate. We will argue that the ways bioprinted organs become classified for legal, regulatory and economic purposes has important implications, and must be dealt with as part of the technology's further development and potential use in health care.

2. Bioprinting: Process and Overview

2.1 3D Bioprinting 101

Bioprinting, also referred to as additive manufacturing (Murphy/Atala 2014), or biofabrication (Groll et al. 2016), involves the three-dimensional printing of biological materials: printing living human cells into desired patterns and structures. The field has widely been described as 'coming of age' (Guillemot et al. 2010), incorporating

regenerative medicine and tissue engineering (Mironov et al. 2011, 2003). At present, technical capabilities only allow for printing smaller tissues, but there are hopes and expectations that scientists will one day be able to bioprint whole functioning organs. The process involves "layer by layer precise positioning of biological materials, biochemicals and living cells" to produce functional 3D structures (Murphy/Atala 2014: 773). An essential component of the bioprinting process is bioink (Gungor-Ozkerim et al. 2018), which contains a mixture of living cells and a form of 'hydrogel' (usually made from natural polymers which can be broken down once inside the body). Researchers are exploring a number of different approaches for the production of these tissues, and a variety of different printers, bioinks, cell types, and modelling software.

At present, two likely options exist for the types of cells used in bioprinting: differentiated primary cells (heart cells, lung cells, liver cells), or autologous Induced Pluripotent Stem Cells (IPSCs) (Murphy/Atala 2014).[1] The idea is that cells would come from the patient who is to receive the bioprinted organ. IPSCs are deemed the most promising, because they can be derived from adult cells but are still able to reproduce and develop into almost any type of cell. The bioprinting process as applied in a clinical setting would likely involve the following basic steps:

1. A physician takes a cell sample, likely in the form of a biopsy; or this may be a simple skin-scraping
2. The cells are cultured in a laboratory to produce IPSCs and reproduced and combined with other biomaterials to form the bioink
3. 3D images are taken of the organ (MRI, CT scan etc.) and any faults corrected using modelling software
4. The printer is programmed to print the bioink in layers into the organ structure, based on the model provided
5. Possibly, the bioprinted organ is matured for a period of time in a 'bioreactor' before surgical implantation into the patient.

Whilst this process is based on the current discussions of the state of the art, it is a simplified version, still hypothetical, and subject to change. It cannot be emphasized enough that significant technical barriers remain: keeping the cells alive post-printing, vascularization of the organ, timing the scaffold degradation, and scalability of the printing process and the materials – to name but a few (Murphy/Atala 2014). These technical barriers must be overcome before 'on demand' organ printing can be realized, if indeed it ever will be.

2.2 Framing Ethical Issues

Because the potential development of bioprinted organs is not only a technical issue, it is important to think proactively about the social and ethical aspects of this technology, including the embedding of bioprinting in health care practices. The expectations of 3D

1 This chapter focusses specifically on IPSCs and not hiPSCs (heterologous induced pluripotent stem cells – taken from cell banks or donors), as their use would not remove the risk of rejection (which is one of the leading causes of transplant failure). However, we acknowledge that there are a number of ethical issues associated with using hiPSCs in bioprinting.

bioprinting are high, and among the numerous benefits cited are its potential to revolutionize the medical industry by removing the need for organ donation (Lewis 2017; Williams 2014; Savage 2017). 3D bioprinting, it is claimed, will eliminate a number of ethical issues around difficulties in sourcing (youth) organs, black-market organ sales, and the many issues associated with xenotransplantation and animal testing. However, the science and research being conducted in 3D bioprinting is still very speculative, and as Gilbert et al. (2017) have highlighted, the overly positive and promissory media narratives of the technology create ethical implications of their own, especially for patients who need organ replacement. Against this background, we explore some of the ethical issues and potential risks of bioprinting, not aiming to be exhaustive or complete but rather to stimulate discussion.

In an earlier article, Vermeulen and colleagues (2017) provide a horizon scan of ethical issues, including expectations, safety, social stratification, and ownership. Because the technological capabilities for bioprinting are still relatively novel, scientists are unable to provide realistic development timeframes, which means that public and patients' expectations need to be managed. With regards to safety, the significant risks and likely irreversibility of transplanting living IPSCs into humans are still insufficiently tested, and no significant long-term studies exist to date. The issue of social stratification (see also Kass 2012; Squier/Waldby 2005) is becoming increasingly prevalent because increasing reliance on complex and expensive health solutions means that they are often only available to a privileged few.

Bioprinting presents new legal challenges regarding the ownership of biological materials, and how we categorize them may have a significant impact on future users/patients. Other issues, such as those relating to intellectual property (Li 2014; Li et al. 2017), are also paramount because they are associated with different stages of the bioprinting process. Intellectual property issues extend to the software, hardware and biomaterials used, as well as access/ownership of the data used in the bioprinting process, and whether aspects of bioprinting could be patented. Finally, it is possible that the technology could be used for human enhancement, not just repair. The potential for humans to bioprint body parts with greater abilities raises a whole other raft of ethical issues (Boucher 2018).

Consequently, the idea of organ printing 'on demand' presents risks because organs are seen as 'spare parts' rather than essential components of peoples' bodies; they become exchangeable alienable objects, subject to the market forces of supply and demand. Thus framed, biotechnological knowledge and innovation coincide with the creation of a paradigm in which every human health problem can be fixed or influenced. Grunwald (2007) calls this shift an increased contingency in the 'conditio humana', which highlights the need to rethink the rules and regulations by which we currently govern our health care practices. Bioprinting risks further commodifying our bodies and heightens the desire for 'ideal health'. Other qualms include the devaluation of the human body and undermining the developing health paradigms of bodily self-care and disease prevention; what incentive is there to take care of the body you have if you can just print a new one?

The current uncertain and ambiguous status of the bioprinted organ, epistemologically, physically and legally, creates further issues and exacerbates some of the risks and ethical considerations mentioned above. A fundamental question that must first be asked is – what *is* a bioprinted organ? A bioprinted organ would be simultaneously

alive, not alive and capable of giving life; it would be natural *and* artificial, separate *and* embodied, human *and* thing. It is a "boundary crawler" which disrupts the "conventional boundaries and identities of biological forms and categories […] sitting ambiguously in between those entities that we tend to conceptualize as human subjects and as non-human objects" (Metzler/Webster 2011: 649). It is therefore not clear what form of categorization we are using when we talk about bioprinted organs.

A bioprinted organ could be understood through the lens of 'bio-objects' (Vermeulen et al. 2012; Tamminen/Vermeulen 2019). The common theme in the bio-objectification process involves transforming biological material to produce data or materials that are intentionally different or ideologically separated from the original thing. This lens assists epistemologically and shows how the problem of classifying bioprinted organs makes it difficult to fit them into current regulatory frameworks. Determining how a bioprinted organ is classified will determine its regulation, its legal status and, to an extent, the ethical issues it raises. This becomes particularly clear in discussions of the ownership of bioprinted organs – e.g. how to deal with testing and liability – and of data protection and counterfeiting.

Whilst from an ethical perspective our theoretical approach may be viewed as an account of justice – and much of our analysis could be understood through a justice lens – we do not write as bioethicists but as social scientists. Our methods simply aim to open up questions for debate, using hypothetical scenarios as a way to initiate discussions.

2.3 Using Hypothetical Scenarios

Many traditional science and technology studies (STS) methods and frameworks prove rather difficult to apply to future technologies that are still under development, such as bioprinting. STS often focuses on the here and now: studying laboratories, workshops, companies and publics, with scientists, engineers and users. When discussing emergent technologies, we need conceptual tools that allow us to conceptualize what is to come (Stilgoe et al. 2013). Consequently, we have chosen to combine methods from bioethics and innovation studies to create hypothetical scenarios, which we will then use as a starting point for focused discussion of the regulation of bioprinted organs in health care practices.

Foresight practices are tools that are increasingly used in business and policy-making (see Popper 2008). Two main foresight tools are horizon scanning and scenario planning, which are best used in conjunction to obtain both breadth and depth (Rowe et al. 2017). Horizon scanning presents a brief account of a broad range of issues, using creative processes designed to alert relevant parties (Amanatidou et al. 2012; Van Rij 2010). In contrast, scenario planning tends to focus on one issue and examine it in great depth (Wilkinson 2009). A related practice that is often relied on in bioethics are 'thought experiments' and 'what if' scenarios (Hedgecoe 2004; Swierstra et al. 2009). A well-known example of this was Thomson's (1971) thought experiment regarding a famous violinist being plugged into a woman's body to use her organs, as a means of illustrating and exploring notions of bodily rights. However, principlist bioethical arguments have been criticized by bioethicists and social scientists for their over-reliance on abstraction; the arguments are based on moral principles that do not necessarily reflect the social and medical realities of everyday practice (Hedgecoe 2004;

Petersen 2013; Keulartz et al. 2004; Smits 2006). However, that is not to say that these thought experiments cannot still be extremely useful, as is also shown in the STOA report presenting bioprinting to European policymakers (Boucher 2018).

Our study draws upon a more pragmatist version of scenarios, presenting short narratives that are grounded in the social realities of our existing world and within the context of a particular setting, focusing predominantly on UK and US perspectives. We have devised three narratives/scenarios which can be used as heuristics for stimulating thinking, analysis and debate about the issues associated with bioprinting. We find that the use of stories can be particularly helpful in situations like this, where real-life examples are not yet possible. The 'hypothetical' signifies this speculative character, while we use scenarios that are especially designed to raise questions, provoke discussion, and engage readers and audiences.

3. Exploring the Legal Landscape

During the preparation stages for your heart transplant, the hospital bioprints two hearts from your tissue – a contingency should there be surgical complications (damage or error to the first replacement heart). This is common practice because widespread use of 3D bioprinted hearts for transplantation is reasonably new. The operation goes smoothly; you now have a bioprinted heart in place of your old one. What happens to the spare bioprinted heart? Do you have rights over it? If the hospital were to damage or lose it, would you have recourse to get it back?

Investing property rights in human beings is one of the most contentious issues amongst bioethicists and legal scholars, because of its close alignment with commodification of the human body. This debate is inherently bound up with how 3D bioprinted organs will be treated from both regulatory and commercial perspectives – as (parts of) a human, or as something else? Understanding the nature of bioprinted organs can be both useful and necessary to figure out how to classify them. Until they are classified, it would be extremely difficult to determine how to regulate, and what rights to attach to, bioprinted organs. The above scenario provides us with a means to explore notions of ownership over human biomaterials. What must be determined here is who owns the actual organ – not the printer or the rights to the software, but the tangible, material *thing*.

Bioethicist Leon Kass points out that we can, do and should "distinguish among that which is *me*, that which is *mine*, and that which is mine as *my property*" (2002: 190). Although this distinction may seem obvious, it is in fact not so clear-cut as a result of emerging biotechnologies. My bioprinted heart is 'me' in the sense that it is literally made from my own cells; but, whilst the bioprinted heart that resides inside my body is undoubtedly "mine", can it (and the spare heart) be understood as "my property"? Quigley (2014: 692) asserts that one of the distinctive characteristics of property is that the owner has a right to exclude it from others, or in other words 'if I own a particular item, you (and everyone else) are under a *prima facie* duty not to interfere with my use of it'. This distinction is fairly self-evident for the bioprinted heart that has been transplanted, as most would agree that everyone is under a duty not to physically interfere with my use of my heart. But what about the spare?

In the UK context, the *Human Tissue Act 2004* governs the use, retrieval, storage and disposal of human biomaterials. The Act also prohibits any commercial dealings for transplant purposes; however, biomaterials such as cells and tissues that are not removed for the purposes of transplant are not governed by this prohibition (ibid.: 679). This means that third parties, usually researchers or biotechnology companies, are legally permitted to sell tissues and cells, although "the individuals who are the source of those biomaterials cannot" (ibid). This double standard has already been pointed out (Kass 2004; Rostill 2014) because it appears that we *do* allow commercial ownership and trading of human tissues by third parties, we just deny those rights to the original owner. Legal possession of body parts, even by third parties, can be understood as a type of "transient guardianship" (Lucassen/Wheeler 2010: 190) because it can only be owned and sold by medical professionals and researchers in specific ways and for specific purposes. Nevertheless, we are yet again confronted with a problem of categorization: Is the bioprinted organ to be treated as a natural organ, which therefore could not be sold? Or should it be classed as a mass of tissues and cells, and thus open to commercial dealings?

3.1 The "Landmark" Legal Cases

A useful starting point on the ownership of human biomaterials is the US Ruling of Moore vs. Regents of the University of California. The case involved a cell line, derived from the spleen of John Moore. After years of treatment for Leukemia, which involved taking his spleen and subsequent tissue samples, Moore's Doctor and hospital researchers patented and commercialized Moore's cell lines – which proved highly lucrative – without his knowledge or consent (Harbaugh 2015). Moore sued the hospital for a share in the profits, but the Court ruled against him on the basis that allowing patients to dictate future uses of their biomaterials would produce potentially "chilling" effects on medical research (ibid: 175). This ruling is often interpreted as in line with the "Lockean labor" (ibid) theory: the scientists and medics involved would have "labored" (ibid) to assemble the materials – in the case of bioprinting to make the organ – which would therefore give them ownership rights. However, Quigley (2014) notes that this US case cannot necessarily have a direct influence in the UK or elsewhere but can merely indicate how claims about commercial property rights in organs may be treated.

In the realm of reproductive tissues, the legal scene appears very different. In the US case of Davis vs. Davis, which aimed at determining what should be done with cryopreserved embryos, the courts determined that "the embryos 'potential for human life' entitled the genetic parents to 'decision-making authority'" over them (Harbaugh 2015: 177). In this case, the argument for personal autonomy triumphed. In the UK, a similar case came before the courts, in which Natallie Evans requested the right to implant embryos that she had made with her previous partner (Dyer/McVeigh 2007). Both UK and EU courts sided with the rationale of personal autonomy, ruling against her and granting her partner the right to refuse the use of his materials. Many legal battles regarding the ownership rights of fertilized embryos result in the would-be parents being declared legal owners of the embryo. They therefore have the ultimate right to decide its uses (destruction, research or donation), even though clinicians have 'labored' to create them. Some legal scholars suggest that even though the cases

of Moore and Davis are apparently contradictory, they can be reconciled on the basis that embryos have a different status to spleens, due to their "potential for human life" (Harbaugh 2015: 187). This raises the question of the status of a bioprinted organ. Although the similarities between an embryo and a bioprinted organ are fairly clear – they are both new things made from patients' cells – both must be manipulated by doctors to achieve existence, both are made using advanced technologies, and both are imbued with a great deal of promissory value. The key difference is that, because it can grow into a human, the embryo has the potential for personhood rights, whereas a bioprinted organ does not. Despite difficulties in categorizing bioprinted organs, we doubt anyone would attempt to argue that it had the potential to be a 'person'. The bioprinted organ could therefore be seen as not 'life-generating' but merely *life-sustaining*, and so would be unlikely to be granted special status. That is not to say, however, that it *should* not be granted special status.

Our last foray into legal scholarship takes us to a 'landmark' UK court case with regards to ownership of human biomaterials (Rostill 2014; Quigley 2014; Hoppe 2009). The Yearworth case involved a number of men who had stored their sperm with an NHS trust prior to undergoing chemotherapy, which can cause infertility. However, the facility stored the sperm incorrectly and the sperm perished. The donors subsequently sued the NHS trust for negligence, arguing their case on the basis of property rights, and the courts ruled in their favor. This marks the first time that a tissue donor has been recognized as having property rights over their biomaterials (ibid). Hoppe (2009) argues that this ruling can be understood as the UK courts paving the way for property rights to be recognized in any tissue removed from the body. However, a number of other legal scholars refute this (Harmon 2010; Rostill 2014), arguing that the case in question is not quite the bellwether of change that it is often purported to be. The specificity of the case and its context would not necessarily extend to other biomaterials, such as bioprinted organs.

3.2 Managing Body Ownership: How Would it Work?

Having ascertained the uncertainty of the legal landscape with regards to property rights in human biomaterials that have been separated from the body, the next question is whether one *should* have such property rights. If yes, then under what circumstances? Quigley (2014: 692) suggests that philosophical conceptions of property have "use" and "control" as their key features, two features which would allow people to derive income from these uses. As we have already established, the people from whom the biomaterials originated rarely have this right, even though third parties *are* permitted to do this under the *Human Tissue Act*. Fears of commodification and undue restrictions on medical research are the key drivers of this policy, although it has been noted that granting powers of control over uses does not mean that commodification would be rife. It would not be inconceivable to devise a system in which donors would be able to own and control the uses of their biomaterials without having the right to sell them. Under the current system, property rights are not "unfettered" (ibid), even when dealing with traditional objects of property. For example, prescription drugs provided to you by your general practitioner (GP) are technically yours, but they are not yours to do with what you want as it is illegal to gift or sell them to others. Thus, just because

you own something does not mean that you are necessarily allowed to derive income from it, or use it in whichever way you please.

Having delved into some of the legal arguments about where we stand with ownership of biomaterials, the purpose of this exercise is to ascertain what, if any, control one might have over a bioprinted organ. Although a bioprinted organ will have been made from *your* cells, they will have undergone a significant amount of transformation in order to be printed into a functioning organ. Would this give your doctor the right to determine uses, as with the 'Lockean labor' theory used to underpin the Moore case? Would ownership rights only extend insofar as the hospital had a duty of care over your organ, as seen in Yearworth? Or would the fact that it was made from *you* mean that you could circumscribe its uses, as with the autonomy arguments put forward in reproductive tissue cases? In the latter case, one might also pose the question, what (if any) restrictions will there be on what you can do with the organ? These questions point to significant gaps in our current understandings about what control we have over our tissues, and how these gaps might be exacerbated in a hypothetical world in which we could bioprint spare body parts from a tissue sample. The substantial grey areas and uncertainties would suggest that the rights of each party in the bioprinting process must be established a priori.

4. Regulation, Safety and Liability

Imagine you are a year along from the bioprinted heart transplant you received previously. All is well, and your bioprinted heart appears to be functioning much the same as your previous one. But then you start experiencing problems. A fault is subsequently detected that may prove fatal if not addressed; your heart specialist concludes that it must be replaced. It is currently unclear what has caused the fault, but the medical professionals believe that a replacement bioprinted heart would be the best course of treatment, and that they may be able to understand the reason for the fault post-surgery. You agree, and a new heart is bioprinted prior to the second surgery, which is implanted without issue. You have now undergone two surgeries, which both involve significant recovery time. When something goes wrong, and a bioprinted organ fails, whose fault is it? Is there someone to blame? Can it be prevented from happening again?

The legal definition and treatment of a bioprinted organ is still unclear. Should it be treated as we would currently treat a donor organ? As Gilbert et al. (2018) have pointed out, this would be inappropriate because a donor organ has already been proven to work in its previous owner's body. Under the current regulatory regime, the bioprinted organ must therefore be treated as either a product or a device. However, no scholars, as yet, have provided any serious suggestions as to how 3D bioprinted organs might be regulated. Some authors have examined the current system and raised serious questions about the ability of our existing regulations to deal with 3D bioprinting (Wolf/Fresco 2016; Li/Faulkner 2017; Gilbert et al. 2018). Similar concerns have been raised about personalized and/or regenerative medicine products (Faulkner 2016; Faulkner/Poort 2017).

Gilbert and colleagues (2018), have focused on the ethics of testing this type of technology. Pointing at an acknowledged lack of available regulatory directives, they argue that the treatment can be understood as "part medical device, part biological" (ibid.: 85). It does not fit neatly into any category because it is an inherently personal-

ized treatment that would need to be scaled up on an industrial level to meet the needs of a variety of different patients (ibid). It is also problematic because a bioprinted organ is not intended to treat any specific disease; a recipient's problems may arise from an assortment of different diseases, genetic problems, and environmental factors. Furthermore, the safety and efficacy requirements that have come to be expected in contemporary medical care would be extremely difficult to meet through our existing frameworks. As Wolf and Fresco (2016) point out, the output of a 3D bioprinter contains information and materials from multiple different sources. The bioink, the cells, the programming software, the scan/image on which the organ will be based, and the bioprinter all come from different people and places.

4.1 Current Regulatory Landscape

Under the EU regulatory system, the European Medicines Agency (EMA) controls and provides directives on the regulation of various types of product. At present, the regulation of Advanced Therapy Medicinal Products (ATMP) would likely be the most relevant to bioprinting. The ATMP regulation was originally introduced as a result of the increasingly diverse forms of product that do not fall into the drug or device category. Brevignon-Dodin (2010: 121) highlights that it was designed to be "tailored yet flexible enough to keep pace with scientific progress", although some have questioned whether this has been successful (see also Faulkner/Poort 2016). The EU provides the overarching regulation and individual countries may have their own authorities which have further requirements. In the UK context for instance, the two relevant authorities are the Human Tissue Authority (HTA) and the Medicines and Healthcare Regulatory Agency (MHRA). Thus, in order to get market approval in the UK, a bioprinted organ would need to comply with requirements of EU regulation for ATMPs, along with those set out by the HTA and MHRA.

Examining the existing regulatory regime, a number of scholars highlight its complexity and variability. According to Faulkner and Poort (2017), the ATMP regulations were supposed to be radically different from existing directives, namely in its flexibility for including a variety of different products. However, as a result of a combination of factors and the instrumental role of "pharmaceutical industry lobbying" (ibid.: 215), the resulting ATMP regulation is remarkably commensurate with the existing requirements for pharmaceuticals, such as the requirements for placebo-controlled clinical trials. The imposition of a pharmaceutical frame on ATMP regulation effectively encourages the regenerative medicine industry to produce products that fit a "'medicines' rather than a 'devices' paradigm" (ibid.: 226). Faulkner's analysis of the marketing of regenerative medicine in the UK shows that there is a tendency for developers to choose "non-mainstream gateways to market in preference to central pathways" (2016: 322). These include the 'hospital exemption' and the 'specials' routes, which are two separate but similar pathways for bypassing EU regulation, so that unlicensed products may still be delivered in a clinical setting, provided they are 'non-routine' (Mittra et al. 2014). Significantly, the fact that several ATMPs must go through 'exemption' routes would suggest that the ATMP regulation is not quite as flexible as it is purported to be.

Li et al. (2017: 4) assert that a bioprinted product has "the characteristics of an ATMP and some similarity to an ATMP-device combination". However, according to

the flowchart provided by the UK government (2015) to help developers understand if their product would fall under ATMP regulation, a 3D bioprinted organ would be considered 'outside the scope'. But what about regulating bioprinted organs as devices? Faulkner (2016) suggests that an increasing number of tissue-engineered products are being designated as medical devices by developers, because the regulatory pathway is seen as less stringent than the ATMP/pharmaceutical route. However, the medical device route would not be without complications either, as Morrison et al. (2015) note that the customized nature presents further challenges. Still others, such as Gilbert et al., suggest that because 3D bioprinted organs are "individualized, custom-made devices" (2018: 85) (because each organ would be personalized for each patient), under current rules they would technically be exempt from regulation. Therefore, we are in a position where all commentators on 3D bioprinting disagree on how it would be regulated, and whilst most point to the inadequacy of our current system for dealing with these technologies, it appears that few alternative ideas are forthcoming.

4.2 Problems of Testing and Standardization

Whilst some scholars have speculated about how 3D bioprinting will be regulated under the current system, one of the key concerns remains how it would be possible to meet our existing requirements for clinical testing. The existing gold standard for testing safety and efficacy is the randomized controlled trial (RCT), in which one group is provided with a placebo treatment (or the current best treatment) in order to comparatively determine a treatment's efficacy. Because this is the existing practice for regulatory approval, it raises questions as to how appropriate this paradigm is for testing emerging biotechnologies (Gilbert et al. 2018). One of the reasons 3D bioprinting seems so promising is the fact that it can be personalized, which means that this testing model would be highly inappropriate. Furthermore, as Gilbert et al. point out, "how could it be morally acceptable, given the severe risk of major harms, to test the safety of an organ which has been specifically made for me with my own stem cells on someone else?" (ibid.: 82). This question certainly merits further attention from bioethicists, policymakers, and clinicians alike. The unique nature of each bioprinted organ, and its function in different individuals, is not necessarily something that can be standardized to the extent that we currently demand.

The requirement for animal testing in the preclinical phase of any trials would need to be met before any further testing could be carried out. In their analysis of the regulation of cultured red blood cells, Mittra et al. (2014: 186) have noted that there were significant issues with the animal testing phase. Similarly, the use of animal cells combined with bioink in animal models would not constitute the same product as using human cells. Whilst it would theoretically be similar, there may be doubts as to the extent that we can compare them effectively for safety and efficacy purposes. Alternatively, testing human cells that have been bioprinted into organs in animals would trigger an immune response in the receiving animals which would likely not occur in humans, so the findings would be flawed in those circumstances too. As Mittra et al. (2014) assert, this problem has been noted with other regenerative medicine products and is one that the European regulatory system has yet to resolve. Whilst the bioinks and the composite materials that are combined with the cells to make the organ could be tested and likely standardized, the personalized nature of the individual organ and

the physical characteristics would make any type of product standardization very difficult. This means that the safety of the product/organ cannot be assured because there can be no standard by which it is measured.

However, it has been noted that even if the actual product faces standardization issues, the *process* in which a 3D bioprinted organ is produced may adhere to a standard process – in terms of the software, the use of the bioprinters, and the creation of the bioinks and their infusion with cells (Gilbert et al. 2018). Nevertheless, when and if researchers reach the point of human testing, the ethical considerations of testing the transplantation of bioprinted organs on healthy volunteers seem positively absurd. How could one possibly justify replacing a healthy organ with a bioprinted one to ascertain the safety of the process in other individuals? Should the first 3D bioprinted organs then be tested on those who are already sick? And how could we use a placebo group or next best treatment? Gilbert et al. (2018) point out that existing gene therapies, where biologically engineered cells are injected into the body, have similar issues of efficacy and safety that have been described above. However, unlike gene therapies, 3D bioprinted tissues would have to replace an existing organ, which could not be adequately preserved, thus making the process irreversible. Therefore, Gilbert and colleagues note that participation in an experimental trial of a 3D bioprinted organ, if unsuccessful, may preclude patients from accessing further existing treatments, thus further disadvantaging them. In addition, it may also prove difficult to undertake longitudinal studies of the safety and efficacy of bioprinted organs. The likely use of IPSCs as the building blocks for the bioprinted organ may mean that we cannot truly understand its safety until longitudinal studies are completed. Take, for example, the case of a woman who had stem cells injected into her face as a cosmetic treatment, and, some time later discovered fragments of bone growing in her eyelids (Jabr 2012). Or another case, which involved a quadriplegic woman who underwent stem cell therapy in her back, as part of an approved clinical trial, and 8 years later discovered a 'nose' (which was in fact a growth of nasal tissue secreting mucus) growing on her spine (Wilson 2014). The issue with IPSCs is that they have the ability to grow into numerous different types of tissue. It is worth noting that in the same clinical trial mentioned above, the majority of other participants saw improvements, and recovered some movement and sensation, thus highlighting the individual variability of stem cell therapies and our limited understanding of them. We also acknowledge that there is a significant ethical difference between stem cell therapies for cosmetic reasons and those carried out for life-saving treatment, but the examples above are merely intended to demonstrate the current lack of knowledge about the long-term effects in this area.

The consequences of a nose growing on one's back, or a bone at the surface of one's skin, whilst not ideal, have not yet proven fatal. However, what if a fragment of bone was to grow inside a vital organ? This scenario raises the need to address our current problems with emerging biotechnologies and how we test and manage them. We need to develop new regulatory regimes for the testing of bioprinted organs, which pays attention not only to the actual thing at the moment of creation/medical intervention, but also to sustainability.

4.3 A Look at Liability

Alongside issues of regulation and testing, is necessary to determine responsibility and liability when things go wrong. As Wolf and Fresco (2016) highlight, prior to implanting a bioprinted organ into a patient, who would have the final say as to its viability? And should anything go wrong post-implantation, will it be possible to establish what or who is at fault? If you receive a heart transplant from a donor and the heart malfunctions (i.e. you get an infection or there is physiological damage), you do not have recourse for litigation against the donor. However, if you have a pacemaker or another similar medical device in the UK and a malfunction is proven to be the result of manufacturer error, under the Consumer Protection Act 1987 you would have the right to take the manufacturers to court with a product liability claim. Furthermore, in the US, an increasing number of medical device manufacturers are beginning to provide guarantees on their heart devices in order to entice hospitals to use their products (Kelly 2015). If this trend continues, warranties for medical devices and products might become more commonplace. This further increases the regulatory complexities of bioprinted organs because their classification may have ramifications for any liability claims. Because they are artificially made, the reason for any malfunction may exist independently of the patient; nevertheless, it is unclear whether a bioprinted organ would be considered a 'product' for the purposes of law. Li and Faulkner (2017) highlight the difficulties of fitting bioprinting into existing regulatory regimes, and our analysis of bioprinted organs underlines those difficulties.

Faulkner and Poort have asserted that there are two types of regulatory adaptation; "commensuration"; which involves "the stretching and maintenance of a pre-existing legal framework"; and "replacement", which requires the "breaking of existing classifications and establishment of a novel regime" (2017: 209). In their analysis of the ATMP regulation, they conclude that although the stretching and flexibility of existing regulation may seem the most pragmatic, it may produce further confusion and complications. Having a flexible regulatory framework risks a lack of clarity of the rules and standards. However, as Faulkner and Poort state, considering the rate at which new developments are made, we must certainly doubt whether "old rules" are capable of addressing the "new risks" (ibid.) that come with new forms of biotechnology. Bearing in mind that the usual starting point for legislators is to investigate whether new technologies can fit into the existing regulatory framework, our discussion suggests that it is likely 3D bioprinted organs will not.

5. The Dark Side: From Black Markets to Counterfeits?

Imagine a world where bioprinters are available to purchase at a reasonable sum and can be used in a do-it-yourself (DIY) context to print organs on demand. Although in some countries, organ bioprinting would perhaps be available through national health services, there are many countries worldwide where the cost of treatment is not provided by the state. With the right skills, expertise and equipment, the less lawfully inclined can open up an illicit organ bioprinting workshop, where the uninsured, undocumented and vulnerable are able to purchase custom bioprinted organs much cheaper than from legitimate sources. In these workshops, there are no regulatory requirements, tests, guarantees or responsibility regarding the safety

or build quality of these organs. Just as some doctors and hospitals worldwide still implant stolen organs, will this also be the case for 'counterfeit' bioprinted ones? Will the black market in organs ever really disappear, or will it simply transform, reshape and adapt to exploit the vulnerable in new ways?

One of the problematic, but widely cited, benefits of 3D bioprinting technology is that it promises to solve the problem of illegal trade in human organs (Li 2014; Li/Faulkner 2017; Gilbert et al. 2018). The logic behind this is that if we can bioprint new organs, the current issues of supply and demand will disappear, eliminating organ trafficking altogether. However, whilst aspects of the current market may become less prevalent, the assertion that the black market or illegal trade of organs will disappear may be somewhat premature. We suggest that it is more likely that the advent of 3D bioprinting may simply contribute to changing this trade's format, altering its processes, but nevertheless still hurting those amongst us with least access to resources.

Beyond notions of *supply and demand*, common themes amongst scholars regarding the black market in human organs (Cohen 2013; Scheper-Hughes 2000) are *inequality* and *exploitation*. Just because we may have the power to solve one specific problem does not mean that inequality and exploitation will disappear. As suggested above, there are other ways that this inequality might manifest in a world where we can bioprint body parts. The cost of equipment may turn out to be cheap, but the product may be very expensive – because the cost of production and the cost of sale do not always have a direct correlation, and also vary per country. For example, according to Cohen (2013: 282) the average yearly cost of an immunosuppressant regimen for someone who has received a kidney transplant in the US is approximately $20,000 per year. However, according to an NHS England (2013) report, the cost of providing the same service in the UK is £5,000 per year. Considering the disparity in health care costs of drugs, and the complexity of bioprinting and variety of expertise required, it would not be inconceivable that the cost of a bioprinted organ may be so high in some countries that it would lead to medical tourism. This also depends on whether a bioprinted organ is available from national health care services, private insurance companies, neither, or both.

This scenario also raises questions about who should receive a bioprinted organ, and with what priority. For example, what about patients who have already received donated organs? Should they be entitled to have their 'second-hand' organs replaced with 'self-grown' organs? And existing living donors? For people who have altruistically donated a kidney, should they be entitled to have a new spare bioprinted one in the space where their donated one was? Whilst we are not suggesting that the answer should be 'no' to any of the above questions, these factors would nevertheless pose extra strain on an already strained health care system, and the advent of a new technology will not magically make these issues disappear. 'Transplant tourism' (Cohen 2013; Scheper-Hughes 2005) may well still persist, but in a different format – perhaps more aptly transformed into 'implant tourism' where people in need of new organs shop around and travel to where the wait time for implanting a bioprinted organ is lower and the price is cheaper.

Linked to this problem is a fundamental question: should bioprinted organs be considered a profitable technology or part of standard medical care? As appears to be the common theme, how a bioprinted organ is classified will have a significant impact on its use, and the associated issues. If it goes the 'pharmaceutical route' and is con-

sidered patentable and profitable (Li 2014; Harbaugh 2015), then counterfeiting may become a genuine issue. There is already a booming trade in 'knock-off' prescription drugs, and these pharmaceutical counterfeits are one of the most lucrative areas in the global economy of counterfeit goods (Behner et al. 2017). It has even been suggested that "more than half the counterfeit pharmaceuticals sold today are fraudulent versions of treatments for such life-threatening conditions as malaria, tuberculosis, HIV/AIDS, and even cancer" (ibid: 5). Considering the prevalence of this problem, it may seem somewhat surprising that the majority of reflections on the ethics or social consequences of 3D bioprinting appear to dismiss the possibility of counterfeiting as a problem. In fact, Li and colleagues (2017) appear to be the only scholars thus far that have taken counterfeiting seriously. We would contend that the risk of counterfeiting would be linked to bioprinting's treatment with regards to intellectual property, including whether the technology can (or indeed should) be patented.

6. Conclusion

The uncertainty surrounding the classification of bioprinted organs that has been outlined here becomes inherently entangled with problems of regulation and intellectual property, which are in turn bound up with the legal definition of bioprinted organs. New ways of thinking about bioprinted organs, either as bio-objects, or using another theoretical lens, may be required to determine what new regulations or legal rights, if any, need to be introduced. Being not fully human, nor fully artificial, but biological material inherently connected to a person, the bioprinted organ and its treatment fall outside our current categorization boundaries.

By means of a legal scenario, we have highlighted that the ownership of a bioprinted organ is not clear-cut due to its ambiguous status, and legal scholars have yet to determine how it should be treated or if changes must be made. Looking at regulation, we have suggested that rather than follow a 'commensuration' model, new purpose-made regulation may be required to govern bioprinted organs. Just as new laws and regulations were introduced with the advent of organ transplantation, the same may be needed for bioprinted organs. Looking at testing, the RCT model of clinical trial appears inappropriate for the testing of bioprinted organs because both the ethical and practical considerations would make it extremely difficult. And considering the vast potential for harm caused by errors, the software (i.e. the modelling programs used by bioprinters) should meet stringent standards to prevent any glitches or security concerns. How this technology is controlled and made available also creates further risks; if it is only made available at a high cost, it may not solve the organ shortage as easily as it is claimed. The way that this technology is treated for legal, regulatory and economic purposes will have important social and ethical implications and must be dealt with as part of the technology's further development and potential use in health care.

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