No sharp line between the natural and the synthetic: Biothetics and challenges to regulation

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ABSTRACT: The code of human life stored in our cells is being extracted and transformed into biologically functional tissues at the same time it is also spawned with different synthetic materials that support those cells to mature and grow. Such products are essential of hybrid nature as they combine autologous and synthetic components, and thus making these products (that author labels as biothetics) difficult to categorize or put under existing know legal frameworks. This paper offers a brief review of the ethical, legal and social implications that regulators should be aware of. It also reflects on the bioconstitutional tensions that arise when novel technologies challenge the understanding of relations between our bodies, life and constitutions. By doing so, the paper examines the neoliberal underpinnings in the regulation of such a relationship.

KEYWORDS: Bioprinting; biothetics; regulation; bioconstitutionalism; ELSI

SUMMARY: 1. Introduction – 2. Revolutionizing biomedical engineering: bioprinting technology – 2.1. Biothetics – 3. Preliminary considerations of some ethical, legal and social implications of biothetics – 3.1. (Bio)Ethical implications – 3.2. The legal implications – 3.3. Social implications – 4. Current legal frameworks: comparison – 5. Neoliberal underpinning, regulatory models and bioprinting – 6. Conclusion.

1. Introduction

According to the 2018 GODT (Global Observatory on Donation and Transplantation) report, 146 840 solid organs were transplanted. However, on average 20 people die daily, waiting for the donor. One of the solutions for the worldwide shortage of viable donors is bioengineering which aims at improving technologies to engineer cells, tissues and organs. One of the processes is the process of bioprinting. Using 3D printers in medicine might be one of the new technological thrilling opportunities for the humankind. The limited recourses in the matter allow us to set certain arguments that could be used for future debates and initial solutions to understand this technology and its implications on everyday life. Although printing entire organs are still not feasible at this juncture, bioprinting presents itself as a game-changing technology within the sphere of therapeutic medicine. Thus far scientist managed to print viable human tissues, such as skin grafts, cartilage and blood vessels have been used in therapeutic medicine with great success. The application of bioprinting extends beyond surgical wards, as pharmaceutical companies, cosmetics

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and personal care companies are as well interested in having this technology thrive. During COVID19 pandemic 3D printers were employed to alleviate shortages of personnel protective equipment, however, it was reported that 3D bioprinters are possible weapons against the pandemic. Bioprinting can help circumvent animal testing for covid19 vaccine as bioprinters could supply pharma with organoids that are viable for that same testing. The results in animals and humans differ and thus testing on tissues that mimic the human tissue would speed up the process.

This paper is based on my doctoral thesis research that is examining regulatory avenues for bioprinting technology. The research employs a comparative constitutional method in exploration of bioconstitutional and regulatory challenges in several jurisdictions, including the EU and the US. In the first part of the paper, I introduce the technology itself emphasizing the hybrid nature to it. As my thesis research indicates the term: "combination products" that regulators use in their narratives a bit redundant, and thus I offer a new terminology: biothetics. Further on I offer a short review of the possible ELSI read of the biothetics. The ELSI exploration consequently brings me to the proprietorship issues in bioprinting technology which comes from the fact that neoliberal "sacralization of property"[1] inevitably led to the profound desacralization of the human body on a very molecular level, as body as a commodity became a narrative with new biotechnological advancements. Taking interest in the relevance of what Jasanoff defined as bioconstitutionalism and her important work in understanding regulatory challenges in bioconstitutional legal order, I further explore how it was conditioned by the neoliberal regulatory narratives concluding that should the regulatory design remain unchanged for bioprinting, we might as well be sleepwalking into the dystopian future of Ishiguro, Orwell, or Crichton.

2. Revolutionizing biomedical engineering: bioprinting technology

Biomedical engineering is based on the processes that involve engineering principles and design concepts to medicine and biology for healthcare purposes, both diagnostic and therapeutic. In a matter of a few decades, this specific part of biotechnology emerged from experimental research programs to full flagship national public and private health institutes projects. When we are discussing bioprinting technology which is one of the biomedical engineering technologies, it is important to make a distinction between technologies such as tissue engineering, genetic engineering and neural engineering. Tissue engineering also referred to as regenerative medicine represents the creation of artificial organs from human cells using both synthetic and biological ingredients. Genetic engineering is a direct manipulation of the genes on a molecular level to transform or alter the structure of the targeted genes. And finally, neural engineering is a discipline that focuses on the repair, replacement or enhancement of the neural systems using engineering techniques. In general, the most recent developments in the bio-fabrication processes provides for manufacturing of the complex tissues constructs with a higher degree of biomimicry to native tissues.[2]

[1] T. PIKETTY, *Capital and Ideology*, Cambridge MA, 2020, 122.
[2] L. MORONI et al., *Biofabrication: A Guide to Technology and Terminology*, *Trends in Biotechnology,* 36, 4, 2018, 384-402.

In a word, all these technologies or processes represent an ongoing evolution that is happening in the bioengineering and there is not much we can do but to wait for the revolutionary outcomes or we could anticipate the outcomes based on the few decades-long debates and prepare ourselves to keep up with science. One thing is certain: once the results of these technologies are out at the market we have to mobilize our entire experience based on the decades of dealing with technological improvements so that we can accommodate the technology that can fit the common human values without deriving us from our guaranteed rights and freedoms. The perils of some of these revolutionary technologies are already being reported to the society as biohackers managed to by using CRISPR change their DNA, and at the moment we cannot stop it.[3] On the other hand, the tissues engineering had its major success when Anthony Atala with his team managed to engineer human bladder tissues for "patients with end-stage bladder disease by isolating autologous bladder urothelial and muscle cells, expanding the cells in vitro, and attaching them to biodegradable three-dimensional matrices".[4]

The origins of the groundbreaking science behind bioprinting of human tissues are in the brilliant realization that additive manufacturing and bioengineering can be combined. Additive manufacturing, rapid prototyping, stereolithography or most commonly 3D printing is a process that turns blueprints into solid physical objects and this technology was in its nascent stage in early 1980ies. Applying such logic first two-dimensional structures made of cell adhesion proteins were developed by Robert J. Klebe in 1988. In 2002, Japanese scientist Makoto Nakamura realized that size of cells corresponds to the size of a drop of ink and his experiment showed that cells could survive the printing process.[5] But the first modification of the 3D printer into the ink-jet printer to print scaffolds was done by Thomas Boland and his team in 2003.[6] A year later Gabor Forgacs discovered that mammalian cells have physical mechanisms to form multicellular aggregates of a controlled shape and size and he managed to build the prototype of a printer that enables precise placement of cells that could form a tubular structure with a tissue as a final product.[7] The patent of Thomas Boland was published in 2006 and in 2009 the company "Organovo" created the first bioprinter based on these technologies.

So what is bioprinting? Simply put it is the use of the 3D printers to print human tissues layer by layer by fusing the living human cells into the scaffolds in a controlled environment. Most often it is described as one of the biofabrication technologies that can overcome the difficulties of producing the exact mimic of the native tissues since authors agree that by placing multiple types of cells in a

[3] F. FORMAN, [Tt] NS 3152: *Biohackers Are Using CRISPR on Their DNA and We Can't Stop It*, 25 November 2017, http://postbiota.org/pipermail/tt/2017-November/020889.html, last visited 15.12.2020; A. PEARLMAN, *Biohackers Are Using CRISPR on Their DNA and We Can't Stop It,* in *New Scientist* <https://www.newscientist.com/article/mg23631520-100-biohackers-are-using-crispr-on-their-dna-and-we-cant-stop-it/, last visited 15.12.2020.

[4] A. ATALA et al., *Tissue-Engineered Autologous Bladders for Patients Needing Cystoplasty*, in *Lancet,* 367, 1241, 2006, 1245.

[5] M. NAKAMURA et al*., Biocompatible Inkjet Printing Technique for Designed Seeding of Individual Living Cells* 11, 2005, *Tissue Engineering* 1658.

[6] T. BOLAND, W.C. WILSON, T. XU, *Ink-Jet Printing of Viable Cells*, 31.

[7] 'Scientific Origins' (*Organovo*), https://organovo.com/science-technology/bioprinted-human-tissue/scientific-origins/, last visited 15.12.2020.

designed matrix could bring us closer to producing more complex human tissues.[8] Bioprinting is a process that requires extraction of the human cells (ideally patient's cells), or reprogramming of the embryonic stem cells which are replicated to produce ink that is mixed with a hydrogel that serves as a living environment for the cells to bind and survive, a bioprinter and CAD images of the desired tissue to be printed. For cells to bind and mimic the natural processes they need a synthetic scaffold in which they communicate, exchange nutrients and multiply to form a tissue. Thus far, relatively simple tissues such as cartilage, skin grafts, vascular tissues, lung tissues and bones are being printed and applied in treatment. More complicated tissues and organs such as heart, liver or kidney, meaning those that are combined of several different cell types are more challenging to be printed, but miniature versions of them are being printed, thus making bioprinting promising technology in saving those who wait on transplant lists, living in hope that the organ they need will find its way to them.[9]

2.1. Biothetics

As it was mentioned, the scaffolds mimic the extracellular environment so that cells that are placed into them through bioink nozzles can live and form tissues. Here is what especially draws my attention, the fact that the process of printing a tissue requires synthetic materials, which essentially makes products of bioprinting non 100% human. Some authors question if because of synthetic scaffolds that are needed for the maturation of the tissue, these products might be patentable as they are non-natural occurring.[10] Here, we can observe the tension between non-organic and organic, or synthetic and natural components of bioprinting processes and products. We witness how techno-medical advances are challenging the very definition of life: while the biological definition of life focuses on biological and physical processes the legal focus on life entitlements or consequences of such advances.

The biotechnological progress that marked last few decades are groundbreaking moments of discovering possibilities of human cloning, *in vitro* productivity of human tissues, human stem cell research, genome editing, development of pluripotent stem cells, etc. Yet, these biotechnological advancements constantly challenge existing legal and ethical frameworks. For example, pluripotent stem cells have the ability to evolve into any type of cells and could play important role in bioprinting of human tissues. Research on stem cells is of great significance not only in medicine but also in physiology, medical education, biology and pharmaceutical industry. This comes from the fact that stem cells have unique abilities in proliferation and differentiation in comparison to another type of cells. Research indicates that stem cells "serve as a reliable cell source in bioprinting for tissue engineering, regenerative medicine, drug testing and cancer studies".[11] However, the production of

[8] Z. XIA et al., *Tissue and Organ 3D Bioprinting*, in *SLAS TECHNOLOGY: Translating Life Sciences Innovation*, 2018, 1.

[9] N. NOOR et al., *3D Printing of Personalized Thick and Perfusable Cardiac Patches and Hearts*, in *Advanced Science,* 6 2019.

[10] R. JACOBSON, *3-D Bioprinting: Not Allowed or NOTA Allowed?*, in *Chicago-Kent Law Review,* 91, 2016, 1129.

[11] S. DING et al., *Bioprinting of Stem Cells: Interplay of Bioprinting Process, Bioinks, and Stem Cell Properties*, *Acs Biomaterials Science & Engineering,* 4, 2018*,* 3108.

stem cells confronts the protection of unborn life and human dignity. While the EU laws prohibit patentability of inventions based on the embryonic stem cells from embryos *in vitro*[12], the UK is more flexible and under US laws Federal Government funding is not available for research that entails the destruction of the human embryo.[13]

Even with different types of bioprinting technologies, be it due to the cell types that could be used in bioprinting process or the kind of bioprinting process applied, the synthetic component plays important role in tissues production which essentially makes bioprinting a hybrid kind of technology with a dual nature to it. In some of the guidelines and analysis of the technology offered by regulators, these products are often called "combination products", and even so it can be contested that it is not clear what that means for bioprinting, as "combination products" are those that combine drug, a device and biologic product. In the EU, however, the legal framework recognizes medical devices and medicinal products. In my view, this seems misleading, and linguistically redundant. Because of this, I introduce the term "biothetics" as a term that, in social sciences, should be used to describe products that are the result of *in vivo* and *in vitro* processes. Biothetics are also products based of autologous material (materials that derive from the human body) and non-biological materials, such as synthetic materials (such as biodegradable polymers, hydrogels and dopamine-modified alginate and polydopamine hydrogels) to keep the autologous materials alive.

The word biothetics in my research refers to the processes and products of bioprinting. The word is comprised of three words which come from Indo-European language family: biology (*noun*, Greek βίος; Romanized: bíos meaning "life") and thesis (*verb*, New Testament Greek τιθημι; Romanized: tithēmi meaning "to make, to place, or to establish") and synthétique [*adjective,* late 17th century French or modern Latin syntheticus, from Greek συνθετικός (synthetikos), based on συντίθημι (suntíthēmi) "to place together"] meaning made by chemical synthesis, especially to imitate a natural product. The adjective is biothetic, the verbal noun being biothesis, and the noun that describes the products would be biothetics.

3. Preliminary considerations of some ethical, legal and social implications of biothetics

Bioprinting falls in the category of 3D printing but the laws that govern 3D printing technology are not entirely applicable to the bioprinting, as obviously the application of the technologies is very different. The 3D printing is already having an immense impact on the different aspects of modern living, but bioprinting is about to revolutionize the medicine and for a few years now, authors are examining what are some of the most pressing ethical, legal and social implications of this technology.

[12] *Oliver Brüstle v Greenpeace eV C-34/10* (Court of Justice of European Union). More on this also in: Lucchi

[13] The Dickey-Wicker Amendment is the name of an appropriation bill which prohibits the Department of Health and Human Services (HHS) from using appropriated funds for the creation of human embryos for research purposes or for research in which human embryos are destroyed. See also: *Sherley v. Sebelius* (2010).

3.1. (Bio)Ethical implications

Recent incorporations of bioethical norms in the human rights legal framework that made sure that science is "no longer regarded as the value-free domain of research".[14] This normative approach to bioethics research according to Sandor is distinguished in the two major lines of thought: the one exploring the boundaries of life (embryo research, assisted reproduction, etc.) and one exploring the frontiers of the human body (human tissue research, human DNA research, etc.).[15] In that respect, there are a few categories that caught attention when it comes to bioprinting. The first considers the ethics related to the clinical translation which again presupposes the discussion on pre-clinical and clinical testing. Technologies such as this one have irreversible impacts on biological and physiological settings of our bodies. Having hybrid object implanted in our body requires knowing exact reactions and consequences it will have on us, as presumably, we get to live with whatever comes in the post-clinical phase. For the time being, testing on animals, with all the ethical contestations this has, is the only way scientists can know what are the potential reactions to it as computer modelling or in vitro studies cannot fully answer all the concerns. This pre-clinical testing shall be followed by clinical testing where the new ethical dimension arises as the testing is done on selected individuals. The *in vivo* studies are required to show the long-term results of the implanted tissues, as well as to explore possible side effects that might emerge. The computer testing and animal testing cannot show with 100% efficacy of how the implants will behave in humans. The second category of ethical implications of biothetics is the one briefly voiced before, and it concerns the use of stem cells, especially if bioinks are composed of replicated embryonic stem cells. There are disagreements amongst regulators, ethicists and lawyers on this matter as some of them list at least ten ethical concerns in the application of embryonic stem cells.[16] Besides, the issues of using xenogeneic cells that derive from other species of animals and cells cultivated via chimera technology also rise questioning eyebrows. This especially when we take into consideration the biological risks of pathogens and similar agents being involved or the reservations that are rooted in various religious views in respect to such cells. The last argument usually comes hand in hand with the culturally and socially shaped view that such technologies imply that "humans are playing God" and that this to a certain extent reminds us of cloning. The third category is the one that is again connected to the source of the cells being used to produce bioinks, but its objective is towards the donation of cells. This category covers questions concerning the privacy of the donor, the informed consent, the invasiveness of the cell obtaining process as well as the issues around ownership of the biothetics.[17]

[14] J. SANDOR, *Bioethics and Basic Rights: Persons, Humans and Boundaries of Life*, in M. ROSENFELD, A. SAJO (eds), *The Oxford Handbook of Comparative Constitutional Law*, Oxford, 2012, 1143.
[15] *Ibidem.*
[16] R. DE VRIES et al., *Ethical Aspects of Tissue Engineering: A Review*, in *Tissue Engineering, Part B: Reviews,* 14, 2018*,* 367.
[17] P.P. VAN DEN BERG et al., *Ethical Issues Regarding the Donation and Source of Cells for Tissue Engineering: A European Focus Group Study*, in *Tissue Engineering*, 17, 2011, Part B: Reviews 229, fig 2.

3.2. The legal implications

Some authors such as Tran suggest that bioprinting brings more benefits that outweigh the risks in comparison to the other biotechnologies.[18] However, there are many issues to be resolved before we face the first entirely printed organ to be transplanted into a living human. Besides the blurring of boundaries between autologous material and synthetic materials, there are more predominantly regulatory aspects that need to be explored, such as ownership of data, intellectual property and privacy; issues of safety and informed consent; and standards and requirements for product development, validation and testing meaning quality assurance, preservation of genetic data. Also, biothetics are subject of many transactional interests between various actors and intermediaries thus regulators should be aware of the role of the private investors and their role in the regulation and distribution including health care organizations, patient rights organizations and insurance groups. The policymakers ought to set up regulatory panels[19] comprised of relevant authorities, scientists, bioethicists, academics, lawyers who would follow the development of the technology and be ready to answer challenges that arise. Such challenges might not be in sight at the moment, but as we have seen with other similar technologies, legal frameworks are constantly in a struggle to keep up with science. Hypothetically one of the challenges might be if bioprinting is used not only to save someone's life but also to enhance the features of the printed organ. Introducing such technology to those who would abuse the potential of it would greatly impact existing inequality in access to health care. Another potential abuse is using this technology to enhance someone's ability to compete in sports, which could happen when the line between treatment or prevention and enhancement is blurred. Can you imagine a tennis player competing in his fifties as if he was in his thirties, as he has means to support such enhancement? I surely can.

The before mentioned ownership of biothetics is the one that invites both legal and philosophical discussion: who owns our bodies and body parts? Under the principles of constitutional law, property rights protect the autonomy and privacy as fundamental rights in different ways, from country to country, but in general, in terms of liberal democratic constitutions, they give a right to any individual to make a personal decision free from state or regulation.

According to Jasanoff, the significant milestones in the life sciences and technologies constitute a bioconstitutional rather than constitutional relationship between states and citizens.[20] It brings about "far-reaching re-orderings in our imagination of the state's life-preserving and life-enhancing functions – in effect, a repositioning of human bodies and selves in relation to the state's legal, political and moral apparatus".[21] To this, I would add Sandor's observation that even though bioethics and human rights are distinctly different disciplines there is no established method to recognize when some universal norms became basic rights in the field of bioethics. Thus, what Jasanoff explores through the constitutional significance of scientific breakthroughs that have an impact over our lives, where our bodies are nexus of law and life, are what Sandor identifies as the

[18] J.L. TRAN, *To Bioprint or Not to Bioprint*, in *North Carolina Journal of Law & Technology,* 17, 2015, 178.

[19] The European Parliament has already made inquiries and has published several in-depth analysis of the technology.

[20] S. JASANOFF, *Reframing Rights: Bioconstitutionalism in the Genetic Age,* Cambridge MA, 2011, 4.

[21] *Ibidem.*

animating force behind international and supranational organizations attempt to incorporate bioethical norms into an international binding and non-binding legal framework.

The legal or better said in this context bioconstitutional and philosophical dilemma if we own our bodies is not new and it is not brought by technology subjected to this paper, but it again contests some of the existing narratives in the field. As it was mentioned earlier biothetics are hybrid products that have dual nature to it, and this fact might pose new contestations in the domain of property in body. Observed through Jasanoff's understanding of bioconstitutionalism and Sandor's perception of correlation between normative bioethics and human rights, I claim that biothetics are that major technological breakthrough that could shift the paradigm around personhood, autonomy, right to privacy, self-ownership or even ownership interests as defined in the *Moore case*. Supreme Court of California ruled that individuals do not have ownership interests in their cells once removed from their bodies, but recognized the importance of informed consent as bioethical principle *sine qua non*. Brownsword challenges such logics as he rightly wonders how is it possible that someone can have property rights over my body or me over someone else's body all the while none of us has property rights over our own bodies?[22] The paradigm of self-ownership is changed on the premise of the bioconstitutional shifts that come with new technologies and scientific advancements which changes the relation between us and the state, but also clearly our interests over our bodies and those of science.

So, the question is what is the capacity of human tissues and bodily materials once removed from the body? If we consult Locke today, he might have told us that "every man has a property in his own person".[23] However, applying his labour-desert theory, we can argue that we do not own our bodies as we did not labour to produce them but we do own the moral agency and the bodily tissues that we produce (for example, producing ova that are used in stem cells technology). Kant on the other hand would deduct that it would be morally wrong to "reduce subjects to objects in some essential sense" and thus we would not have the agency to sell our biothetics. In her comprehensive review on human body and property, Rao contests that once society permits alienation of the body part, that body part constitutes property no matter the legal status. However, she explains: "if body parts are deemed inalienable and unassailable, they should be regarded as the subjects of privacy interests rather than the objects of property law".[24]

Jasanoff draws a line between the issue of property and personhood, as the first one is within the dimension of intellectual property rights as the notion of what is property evolves once technology creates entities "between living and nonliving, human and nonhuman".[25] Which again confirms that biothetics as hybrid entities can challenge conceptions of property rights within the novel bioconstitutional capacities of state-citizens relationship.

[22] R. BROWNSWORD, *Rights, Regulation, and the Technological Revolution,* New York, 2011, 61–62.
[23] J. LOCKE, *Two Treatises of Government*, e-book version, 1980, 45.
[24] R. RAO, *Property, Privacy, and the Human Body*, in *Boston University Law Review,* 80, 360, 2000, 459.
[25] S. JASANOFF, *The Ethics of Invention: Technology and the Human Future*, New York, 2016, 189.

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3.3. Social implications

The previous discussion leads us to the short review of what are some of the social implications of the bioprinting technology. The last couple of years media suggested that in the future humankind will be blessed by the possibility to biofabrication personalized organs and thus the global shortage of viable organs for transplantation will be diminished.[26] Some authors argue that this technology has the same revolutionary and democratizing effect as book printing had in its time in their applicability to regenerative medicine and industry.[27] In addition, there are currently no regulations on bioprinting as well there has been no litigation on bioprinting. Some patent applications were made, but this is a topic of entirely other research.

As history teaches us, every time a new technology is introduced to the people there are two imminent outcomes. The first one is the overall social hype about the new technology and its reception in society. The second one is that as soon as the technology unveils its power and potential to the users, it could end up into the hands of people who did not have such power before. As one technology emerges something illicit happens in its early stage,[28] so it takes some time to learn how to regulate it and catch up with it. Discussing the "tinkering with humans" Jasanoff observes that "manipulations of human biology raise even more complex issues for ethics, law, and policy [...] in biomedicine, the greatest fear centres on violating human integrity and eroding the fundamental meaning of being human".[29] This inevitably leads to the question if bioprinting will become a human/genetic enhancement tool as new biotechnologies are forcing us to re-think and re-evaluate in what kind of world we want to live. Finally, it also points that biothetics have a potential to raise the inequality in access to necessary therapies, and thus instead of helping population it might help only certain categories of people, meaning those who could afford such treatments. It will be extremely difficult in the current free-market setting to safeguard the innovation which in essence should be assessable and affordable for public health. Observed in the frame of distributive justice argument, new technologies can only advance justice when it will benefit marginalised and poor. On the other hand, the instrumentalization of marginalised groups comes at play as well in the context of the black market of bioprinted organs potential. The tissue transfer follows the rules of power and wealth, meaning the most vulnerable class of society that is prone to sell their bodily products. Besides the fact that organ black markets are thriving in the war-affected zones, trading with gametes and renting out wombs for surrogacy are no exception.

In *The gift relationship* Titmuss compared the national blood donation systems in the UK and the US. The policies around blood management grew more complicated over time as in the US unlike in the UK government allowed for private supply chains. The basic premise of private blood banks was that people were more likely to sell their blood rather than volunteer to donate. He observed that for-profit blood banks exploited the regulatory gaps and were able to compensate the problems in

[26] J. GALLAGHER, *Doctors 3D-Print "living" Body Parts'*, in *BBC News*, 16 February 2016, https://www.bbc.com/news/health-35581454> last visited 10.01.2021.

[27] N. VERMEULEN et al., *3D Bioprint Me: A Socioethical View of Bioprinting Human Organs and Tissues*, in *Journal of Medical Ethics*, 2, 2017, 1–7.

[28] K.S. KRUSZELNICKI, *Mouse with Human Ear*, https://ab.co/39QpNFL, last visited 22.01.2021.

[29] S. JASANOFF, *The Ethics of Invention: Technology and the Human Future,* 120.

supply that hospitals were facing, which essentially turned blood into a commodity that was predominantly procured from indigent and homeless.[30] The gift system that was established prior to this was something that kept nations resilient and blood donation was an altruistic and valuable part of the community culture. For-profit blood banks were a mere representation of what neoliberal market rationalism can do to healthcare and thus he was a strong advocate against such a system. Not only that the blood as a commodity was devalued of its ontological quality it was indicating a deep social disparity that affected the very aim of distributive justice. Should bioprinting be left to the market regulation narratives, it can be presumed that similar occurrences as described by Titmuss would take place.

In the section where I introduced some of the ethical issues around the bioprinting, it is inescapable to make the connection with social issues and religious views that will influence the overall perception of the technology. There are alternative ways to using embryonic stem cells but studies indicate that embryonic stem cells have the greatest potential to be reprogrammed and endure printing processes.[31] The general public in different jurisdictions can show discontent towards technology that is developed around the destruction of embryos. Similarly, certain countries, even belonging to the same legal space explicitly prohibit therapeutic cell cloning (Spain, Sweden, Austria, Germany) and some do not (Denmark, the Netherlands). This perfect example is the EU, where the issues of public bioethics and ethical standards of new technologies are conferred to the competence of member states due to the constitutional principle of subsidiarity, although Charter of Fundamental Rights of the EU offers a catalogue of common bioethical principles.[32]

It is important to acknowledge that the benefits of bioprinting are many. It would potentially stop animal testing in all the relevant industries, it would undoubtedly change the future for transplantation surgery and hopefully would terminate immense financial costs. In terms of education and studying of deceases it would help science to re-evaluate the courses of treatments, it would avoid so-called “yuck” factor as it does not instigate reactions such as the ones people usually have when hearing about chimera technology or xenotransplantation.[33]

4. Current legal frameworks: comparison

To this day I did not learn of any country in the world specifically regulating this technology, and in my research, I mostly focus on the EU and US, and thus I will make a brief review of the current state of play.

In July 2018, the European Parliament published an in-depth analysis of *Additive bio-manufacturing: 3D printing for medical recovery and human enhancement*. According to this analysis, the main challenge for the regulators will be defining and categorizing the processes and products of the technology. It recognizes the difficulty to subsume biothetics in the existing legislative framework. For example, In Vitro Diagnostic Device Regulation 2017/746, does not provide any particular

[30] R.M Titmuss, *The Gift Relationship: From Human Blood to Social Policy*, New York, 1971, 119.
[31] S. Ding et al., *op. cit.* 11.
[32] J. Sandor, *Bioethics and Basic Rights: Persons, Humans and Boundaries of Life*, 1146.
[33] N. Brown, *Xenotransplantation: Normalizing Disgust*, 8 *Science as Culture,* 1999, 327.

guidance on these distinctions and its provisions do not state clearly how substances of human origin should be judged.[34] Similarly to the observation, I offered in the previous section, this difficulty comes from the fact that this technology is of a dual nature. It remains unclear if biothetics, referred to as "combination products" are biological product or if a non-biological component to it makes it a medical device or if it falls under the advanced therapy category.

To answer that question, the so-called "Mode of Action (MoA)" determines in which way the finished product will be classified, and it depends on the achieved purpose of the product. As an example authors apply these logics on the nasal implant which "consists of substantially manipulated chondrocyte (cartilage) cells, is presented as having properties for regeneration and repair of a human tissue, and contains (as an integral part) scaffold material that fulfils its function as a medical device when deployed in the patient, the product falls within the definition of a tissue-engineered combined ATMP, as defined in article 2(1)(d) of Regulation (EC) No 1394/2007/EC [15]". This however is again contested by the very notion that biothetics represent the unclear definition of what they represent, or they can have a different intended purpose in different patients. This is well acknowledged in the Report, as it suggests that "the manufacturer may not have sufficient data and/or scientific knowledge in the early development phase to identify the principal MoA and thereby the candidate ATMP classification".[35] European Parliament analysis indicates that even recently adopted Medical Device Regulation (MDR) 2017/745 does not regulate bioprinting, and the provisions of the Regulations are not addressing the issue that products of bioprinting are custom made and not large scale industrially produced, and thus it becomes difficult to ensure the quality of the "in-house custom-made" biothetics. The entire premise of the technology is printing human organs on demand for a specific patient, the current legislative framework is challenged by it.

When it comes to the US, in 2016 the FDA issued draft guidance on the Technical Considerations for Additive Manufactured Devices which had the goal to obtain public feedback. It is organized in the two areas, the design and manufacturing considerations and device testing considerations. It recognized that bioprinting has versatile application in terms of medical devices, biologics and drugs.[36] Just like it was the case in the European Parliament report, the preliminary guidance issued by the FDA does not address the classification of the products with respect to its composition. Under 21 CFR Part 1271.3(d) provision one can argue that biothetics are covered, to a certain extent as this provision states that: "Human cells, tissues, or cellular or tissue-based products (HCT/Ps) means articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient. Products such as bone, ligament, skin, dura mater, heart valve, cornea, hematopoietic stem/progenitor cells derived from peripheral and cord blood, manipulated autologous chondrocytes, epithelial cells on a synthetic matrix, and semen or other reproductive tissue". Furthermore according to the 351(a) of the 42 USC 262: Regulation of biological products, the biological products are those that are "applicable to the prevention,

[34] A. Ferrari et al., *Additive Bio-Manufacturing: 3D Printing for Medical Recovery and Human Enhancement (European Parliament's Science and Technology Options Assessment STOA) 2018,* 89.

[35] *Ivi,* 90.

[36] Center for Devices and Radiological Health, *'FDA's Role in 3D Printing'*, 2019, https://www.fda.gov/medical-devices/3d-printing-medical-devices/fdas-role-3d-printing, last visited 10.01.2021.

treatment, or cure of a disease or condition of human beings" and under 21 CFR 3.2(e) that includes "a product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity". This short comparison indicates that both jurisdictions lack proper definitions and regulatory framework which would offer a unison and consistent protection for all the relevant stakeholders.

The EU pays great attention to the IP and data protection aspects. According to the analysis, it is not clear if the current IP framework can sufficiently protect both files and those using the technology for non-commercial purpose. As indicated before, due to the nature of biothetics is it safe to claim that they are not patentable due to the human organism exception rule. And finally, if the applicability of the morality clause will be extended to biothetics, especially when they are made of embryonic stem cells which are protected due to the understanding that human dignity extends to the embryos.[37] In the domain of the IP related discussions, it is worth realizing that bioprinting brings the question if it should be categorized as machines used for a medical purpose which would make the technology patentable or it is a medical technique that involves in vitro and in vivo processes and thus is non-patentable.[38] For other authors, it is an issue of ownership and the value of the products for different parties in the process.[39] Li warns about dangers from the monopoly that stem from the contemporary ideology to protect scientific innovations and due to the potential that this technology has to save human lives, she advocates so-called "portfolio approach" to licensing as it would be a "balanced pathway to 3D bioprinting could be built to avoid overreliance on the patent system".[40]

Further on GDPR extends to the consent, and thus any processing of patient's data must meet GDRP criteria. However, nowhere does GDPR provide clear guidance on how to treat innovation such as bioprinting. The consent to remove, store, process and use both data and tissues must be such to minimise the risk of any harm. However, there is another layer of data protection that I would like to discuss here: there is an additional value to creating data repositories for scientific research. Researchers build those repositories to improve medical practices as well as medical education, to observe and map important points in human evolution but they can also help them understand how a certain person lived, died etc. Even when the consent is obtained it is hard to make sure that data stored in the scientific community will remain protected from illegal downloads. The ethical standards behind the data protection also differ from country to country, and we should not be so naïve to think there could be no malicious attempts in examining patient's data from other countries and continents. One example, in particular, comes to mind: the so-called "race science" which aims to prove that humans can be divided into race categories based on their specific biological and physio-anatomical features. It should be noted that even in the domain of transporting and exchanging human biological materials, countries have different regulations which rarely regulate the protection of digital data on human tissues. As I previously mentioned human bioprinting

[37] *Oliver Brüstle v Greenpeace e.V C-34/10* (n 12).

[38] P.H. Li, *3D Bioprinting Technologies: Patents, Innovation and Access*, in *Law, Innovation and Technology,* 6, 2014, 282.

[39] J.T. Harbaugh, *Do You Own Your 3D Bioprinted Body? Analyzing Property Issues at the Intersection of Digital Information and Biology*, in *American Journal of Law & Medicine*, 41, 2015, 167.

[40] P.H. Li, *op.cit.* 301.

hardware is not difficult to obtain, downloading data on human tissues is a matter of seconds, protection from both is a matter of years. This is mostly because it is a well-established notion that data and source materials (cells and tissues stored in biobanks) are not comparable and are distinct. Consequently, not only that science is constantly slipping away from regulation, but also the regulatory models need an upgrade.

5. Neoliberal underpinnings, regulatory models and bioprinting

Several international, regional and supranational documents, binding and non-binding, have been introduced to protect health, environment and society from the risks of the potential uncertainties that any scientific discovery could have. In that sense, most of the documents are centred around human dignity as an ultimate focal point which could guarantee the protection of rights. Post II WW the human rights norms in bioethics were a response to violations of basic ethical norms in all sorts of research on the human body, to the molecular level but today the focus shifted to the possibility of transformation of human nature.[41] Yet, some believe there is no need to adopt new legal norms. In my view, this is not a question if we need to adopt new legal norms but in what way can we re-imagine regulatory designs so that we can identify what rights we ascribe to biothetics. It would be premature to claim that bioprinting brings novel rights, but as this paper suggests, it is challenging many aspects of law and regulation.

What was set by Ulrich Beck as the thesis of "reflexive modernization" Jasanoff further elaborates through the thesis that although "scientific and technical advances bring unquestioned benefits they also generate new uncertainties and failures, with the result that doubt continually undermines knowledge, and unforeseen consequences confound faith in the progress".[42] Recognizing not only the advances in technology but also the uncertainties, failures and these unforeseen consequences, Brownsword points out when regulating it is the essential need to frame our inquiries as there are no doubts to why biomedical technologies should be regulated, however, the relationship between law and regulation is unclear.[43] He inquires whether a law is to be understood as a broader enterprise than regulation or narrower? Relying on work of Julia Black he posits that regulation is primarily about channelling behaviour so legislation is a species of regulation.[44] Meaning, regulation is a broader concept. But this comes with a warning because regulation is a "constant learning process" and that is especially important in the case of the emerging technologies with uncertain risks and knowing *when, what and how* to regulate is a challenge itself.[45]

Having said that, governments have developed so-called predictive methods to assess risk management, cost-benefit analysis etc. and the whole purpose is to facilitate management and

[41] J. SÁNDOR, *The Challenge of Genetics: Human Rights on the Molecular Level,* in A. VON ARNAULD, K. VON DER DECKEN, M. SUSI (eds), *The Cambridge Handbook of New Human Rights: Recognition, Novelty, Rhetoric*, Cambridge, 2020, 356.

[42] U. BECK, *Risk Society: Towards a New Modernity*, 1992; S. JASANOFF, *Technologies of Humility: Citizen Participation in Governing Science*, in *Minerva,* 42, 2003, 224.

[43] R. BROWNSWORD, *op.cit.* 6.

[44] *Ibidem.*

[45] *Ivi,* 123.

control even in areas of high uncertainty.[46] Jasanoff analyzes these tools in-depth and highlights their three major flaws or limitations. She points out that the first limitation is in the fact that in making any assessments, this tool always focuses on the known and omits to make any other predictions. Besides, when applying predictive analysis agencies involve experts and exclude political discussion so the objectivity of the analysis is blurred as it is carried out away from the general public. And lastly, these tools are unable to "internalize challenges that arise outside their framing assumptions."[47] Meaning that unknown features of the technology are left out from the analysis and are nowhere to be found in legislative processes.[48] What Jasanoff suggests is that predictive methods need "technologies of humility". She is not the only one that noted this problem. According to Wiener: "We have deployed regulation for three decades with increasing *ex-ante* analysis of its predicted impacts, but too little *ex-post* analysis of its actual impacts".[49]

"Technologies of humility" can only be achieved by observing technological disasters from the past and the risk analysis and policy-relevant science so that the four focal points such as *framing*, *vulnerability*, *distribution*, and *learning* can be developed thus providing a "framework for the questions we should ask of almost every human enterprise that intends to alter society: what is the purpose; who will be hurt; who benefits; and how can we know?"[50]

To successfully regulate any social construct it is important to acknowledge every segment of it. Viskovic warned that not all social relations are subjected to legal paradigms, as often in modern society there is more to understand before regulating it: biological, economic, political, constitutional implications of a certain phenomenon. These implications Viskovic defines as "pre-normative legal relations" and as such, they become an important source of regulation before the concrete legal norms are created.[51] So to regulate we have to understand these pre-normative circumstances so that we can mobilize creativity so that knowing when, what, and how to regulate does not become "daunting", as Brownsword puts it, but rather a learning curve.

I believe that globalization has contributed to differing attitudes in understanding technology. Besides the remarkable similarities, but also differences that globalization brings, countries adopt a variance of observable legal models of regulation so some models of regulation may prioritize, for instance, religion over constitutional law or fundamental rights, or globalized free trade logic which relies on the trend of relaxation of state oversight. The market is about competition, consumption, growth of private profits, production and sacralization of private property, including intellectual property monopoly.

One of the objectives of my research is to explore how bioconstitutionalism, as defined by Jasanoff, and biotechnological regulatory designs are conditioned by neoliberal ideological underpinnings. I believe that those "pre-normative legal relations" are predominantly conditioned by the ideology that is behind the currents in the production of inequality. While Foucault understood neoliberalism

[46] S. JASANOFF, *Technologies of Humility: Citizen Participation in Governing Science*, cit. 238.
[47] *Ivi,* 239.
[48] *Ivi, 240*.
[49] J.B. WIENER, *The Regulation of Technology and the Technology of Regulation*, *Technology in Society* 26, 2004, 496.
[50] S. JASANOFF, *Technologies of Humility: Citizen Participation in Governing Science*, cit. 240.
[51] N. VISKOVIC, *Pojam Prava: Prilog Integralnoj Teoriji Prava*, Split, 1981, 83-94.

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as an approach to human governance and a way of thinking and being,[52] for Harvey it is much more than that: "It has been part of the genius of neoliberal theory to provide a benevolent mask full of wonderful-sounding words like freedom, liberty, choice, and rights, to hide the grim realities of the restoration or reconstitution of naked class power, locally as well as transnationally, but most particularly in the main financial centres of global capitalism".[53] Rose observed that the projects to govern biotechnology is characterized be the alliances between political authorities and promise of capitalism as "the politics of the life sciences – the politics of life itself – has been shaped by those who controlled the human, technical and financial resources" to fund that scientific research.[54] The private corporations and foundations were involved in the capitalization of life science and thus "biopolitics becomes bioeconomics". In the section on legal implications of bioprinting technology I have mentioned the challenges, it poses to the concept of body ownership and commercialization of alienated body parts. Rose observed that new biotechnology brings novel molecular commodification. In his view the "classical distinction made in moral philosophy between that which is not human – ownable, tradeable, commodifiable – and that which is human – not legitimate material for such commodification – no longer seems so stable".[55] The health of citizens and their dependence on the biotechnological innovations is now conditioned by the very same principles that neoliberal free market thrives on: competition, the sanctity of intellectual property, competition, market discipline and circulation of commodities.

6. Conclusion

It should be noted, back in 1938 when the term neoliberalism has been coined the focus of liberal intellectual movement headed by Hayek was the redefinition of the functions of the state in market interventions opposing not only market socialism ideas developed by Oscar Lange but also Keynesian theory.[56] Cohen suggests that neoliberalism founders, in fact, did not indent to implement market ethics and principles of contract and consent on every feature of human life: "for it was the radicals of the 1960s that cleared away the very taboos surrounding the body that would have inhibited the newest possibilities of modern biotechnology".[57] And even so, this just suggests that neoliberal regulatory model did not resist biotechnological challenges as much of those advancements were a magnet for one of the creeds of the neoliberal markets: consumption. To move forward with the regulation of bioprinting we need to re-evaluate the relationship between technology and market (trade).

For Harari, we are living in an era of organisms shaped by intelligent design where *homo sapiens* is replaced by "superhumans".[58] And that is hardly a scene from the Westworld. Some scientists seem

[52] M. FOUCAULT, *The Birth of Biopolitics Lectures at the College de France*, New York, 2008, 218.
[53] D. HARVEY, *A Brief History of Neoliberalism*, epub, Oxford, 2005, 271.
[54] N. ROSE, *The Politics of Life Itself Biomedicine, Power and Subjectivity in the Twenty-First Century*, New Jersey, 2007, 31-34.
[55] *Ibidem.*
[56] D. HARVEY, *op.cit.* 59-61.
[57] E. COHEN, *Biotechnology and the Spirit of Capitalism*, in *New Atlantis,* 12, 2006, 62.
[58] Y.N. HARARI, *Sapiens: A Brief History of Humankind*, London, 2014, 8.

very well aware of this and suggest that "the only economic and reasonable way to commercialize organ-printing technology is to systematically employ scalable automated robotic technology and to build an integrated organ biofabrication line. It is not sufficient to develop just one robotic device – a bioprinter (it) will require the development of a series of integrated automated robotic devices or an organ biofabrication line".[59]

Should bioconstitutional relations between the state and our bodies be left at the mercy on neoliberal regulation creed we might as well accept that Ishiguro, Orwell and others prophesied our future.

The core values of documents such as Oviedo Convention must not be abandoned, and thus protection of our bodies via normative bioethics and principle of dignity, justice, informed consent and human rights might be uncomfortable notion for regulators who would leave bioprinting to the market. As the human body has an ontological value, we have to always remind decision-makers that the human body cannot and should be observed as a mere commodity. In doing so we should never forget that humans are embodied beings with natural limits, vulnerabilities and imperfections.

[59] V. MIRONOV et al., *Organ Printing: From Bioprinter to Organ Biofabrication Line*, in *Current Opinion in Biotechnology*, 22, 2011, 667.

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