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Review Article

Human Fabrication: Ethical and Legal Aspects of 3D Bioprinting

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Abstract

3D bioprinting of human tissues and organs for the treatment or replacement of diseased body parts is widely recognized as key driver of the so-called 4th industrial revolution. Indeed, bioprinting is coming to play the role of game changer in current and future medical practices by making available unique tissues and organs for personalized regeneration or transplantation. However, this technology raises controversial issues in ethical and legal terms. From a speculative perspective, the bio-fabrication poses the question to re-think the human nature in relation to its capacity to generate new species and immortal life. From a practical viewpoint, it rises the problem to rework or establish new ethical and regulatory frameworks governing traditional informed consent, privacy protection and intellectual property rights. This article navigates these ethical and legal challenges with the aim to outline the international debate on the potential of 3D bioprinting to foster human fabrics.

Keywords: Biotechnology; Organs; 3D Bioprinting

Introduction

3D bioprinting of tissues and organs for research and therapeutic purposes is a fast developing and promising area of biotechnology [1]. The quick and successful expansion of 3D bioprinting (or bio-fabrication) in the medical field leads to consider it as game changer of tissues engineering and regenerative medicine and reasonably supports an optimistic view of the future application of this technology to provide 3D tissues and organs for the treatment of several diseases.

Now entering the stage of "evangelism" [2], after scattering doubts on its efficacy, the bio-fabrication looks at the final and challenging goal to make available in the future customized tissues and organs for personalized medicine.

In the field of transplantation, 3D bioprinting has been successfully used in specific areas. In 2006, Atala and colleagues performed the first successful transplant of a bio-fabricated bladder [3] and most recently, in 2022, the transplant of a 3D bio printed ear was efficiently conducted by using engineered autologous stem cells [4].

The application of 3D bioprinting is not limited only to regenerative surgery but it extends to the field of reproduction [5], pharmacology research for drug and toxicity testing and cosmetology [6,7].

Successes in the field of bioprinting announce the promising possibility for a future replacement of cartilage, blood vessels, internal organs like heart, liver, kidney, and they show how this

technology can vigorously promote the development of new paradigms in personalized medicine and broadly in the medical science.

However, the bio-fabrication processes raise ethical and legal issues that need to be considered now and as this technology evolves. We can presently identify, at least, two levels of discussion: on one hand, the theorical analysis of the moral and regulatory issues related to the capacity of the bioprinting to create new human species [8,9] and potential immortal life [10].

On the other, the empirical reflection on the moral and legal implications raised from the use of the 3d bioprinting in the medical practice. The main issues at stake at this level refer to the kind and provenance of cells used for fabricating 3D tissues and organs, the informed consent procedures, the privacy protection, and the regulation of intellectual property rights (IPR).

This article aims to analyze these issues and to give a modest contribution to the current ethical and legal debate on the definition of the human nature and the regulation of the body as transformed from 3D bioprinting. In particular, it seeks to highlight how the prompt advances of fabrication fosters the development of new moral and legal frameworks governing the challenging issues raised from the 3D bioprinting both at theorical and empirical level.

Bioprinting as human fabrication. Ethical Reflections

The rapid and effective expansion of 3D bioprinting for the tissues and organ regeneration and transplantation raises ethical and legal questions about the moral legitimacy of this technology and the eventual limits of its implementation in the medical practice.

Although the ultimate purpose of the bioprinting – namely, generating functional constructs for transplantation – is a desirable yet uncertain goal to be pursued, the successful pre-clinical and clinical research performed to date, including the world's first human clinical trial [11] conducted in 2022, rouse ethical concerns about this technology and its development.

On the theorical level, critical issues refer to the ethical legitimacy of the 3D bioprinting in itself and it focus on the capacity of this technology to generate new human species [8,9] with potential immortal life [10].

Three-dimensional bio-constructs derive from a mixture of engineering processes that make available customized agglomerates of stem cells and additive materials shaped according to highly sophisticated digital models. Once incorporated into the human body, these living materials develop a "new entity" [12] combining both biological and artificial elements.

The definition and characterization of this "new entity" raises critical questions that can be summarized as following: what is the ontological foundation of the construct deriving from bioprinting [13]? Is it "a new human species" [14] or a new "creature" preserving its biological nature?

These issues feed an intense debate in the international community. However, there is presently not a clear ethical position about the ontogenetic capacity of the 3D bioprinting.

Instead, it is emerging some ethical consensus about the limits of the implementation of this technology in the medical practice. Several scholars consider ethical the fabrication of artificial tissues and organs for therapeutic uses, such as regeneration or implantation.

However, they see unethical the development of projects of human enhancement [15]. The main reason relies on the risk to fabricate immortal life, by unstopping the natural process of aging [16]. While the rejuvenation processes (e.g., the beauty regeneration) are quite accepted, interventions for improving the human life over its natural limits are widely contested.

As previously said, the ethical reflection on these issues is moving the first steps towards future straighten viewpoints. Instead, the legal analysis of these aspects remains nowadays opaque.

Several researchers recognize the need to carefully consider the rapid expansion of the 3D bioprinting and the resulting necessity to rethink or design [17,18] new conceptual categories and regulations governing the body and its parts as transformed from the engineering and digitalizing processes.

However, there is presently not a structured regulatory framework on these topics neither proposal of new legal conceptualizations of these entities.

Ethical and legal issues of the 3D bioprinting in the medical practice

The cell as building block of bioprinting

Regardless of the therapeutic or research application of 3D bioprinting in the medical practice, the central element of this process is the "cell".

The type and provenance of biomaterials used for fabricating 3D bio-constructs raises ethical issues which are known in the field of stem cells and regenerative medicine.

Stem cells are generally used as building blocks for human tissue and organ fabrication [19]. While the use of human embryonic stem cells (ESC) is intensely criticized morally [20] and legally forbidden or limited in many countries [21], human adult stem cells, in particular induced pluripotent stem cells (iPSC), are seen as good solution for their supposed ethical neutrality. As cells deriving from adult individuals, they do not raise the ethical concerns related to the use of human embryonic stem cells. Moreover, they do not pose the moral and religious problems associated with the use of xenogeneic cells.

However, adult stem cells, including reprogrammed differentiated cells, are not ethically free. A widely debated issue refer to the features of autologous stem cells and their use for transplantation. Indeed, several studies show that autologous transplant of iPSC generate tumors [22]. Therefore, genetic testing of stem cell lines suitable for clinical applications must be conducted to guarantee the safety of iPSC-based therapies.

Another group of ethical issues concerning the use of the stem cells in the 3D bioprinting relates to the origin of these biomaterials and it focuses on the distinction between autologous and allogenic stem cells.

While the use of autologous stem cells raises well known issues related to the patient safety (like the risk of tumorigenicity), allogenic stem cells processing poses further questions concerning the perception of a new identity (or personality) by the recipient of engineered cells, the development of consent procedures clarifying the complex staging of the bio-fabrication, the protection of privacy and intellectual property rights (IPR) originating from the bio-fabrication.

Informed consent, privacy protection and intellectual property rights in the medical practice of 3D bioprinting

According to the Nuremberg Code [23], the Declaration of Helsinki [23], the Convention for the protection of human rights and fundamental freedoms [23] and the most recent "Convention of Oviedo" [23], the informed consent is a legal doctrine based on the fundamental ethical principle of the autonomy of the patient to make free and informed decisions about medical treatments or research involving his/er body.

These decisions may include the consent or assent to proposed medical treatments or research projects. Otherwise, they may involve the refuse to or withdraw from therapeutic or research protocols.

While the informed consent to medical treatments is a consolidated practice worldwide and it is characterized from various processes and forms of decision making, depending on the purpose of clinical intervention or research, there is currently not a standard procedure to obtain the informed consent to the 3D bioprinting in the medical practice.

This mostly relies on the current lack of specific regulations concerning this technology and opens to several ways to develop informed consent models for bioprinting based on the respect of the autonomy of the donor and/or the patient engaged in this process.

Regardless of the variety of potential suitable models of decision making, the informed consent to 3D medical printing faces some ethical challenges.

Firstly, the unknow behavior of the materials incorporated into the recipient body, requires that the patient be informed on the potential risks to develop teratoma or other diseases unforeseeable at the time of the transplantation [24].

Furthermore, it requires that the patient or his/er legal representatives be informed about the difficulty to stop the participation to ongoing protocols by requiring the removal of the bio-constructs once they are transplanted. What makes it more difficult to withdraw from traditional trials is that, in most cases, the patient asking to be transplanted with new potentially

experimental organs is in a life-threatening situation. Therefore, according to this hypothetical scenario, he/she risks losing the opportunity to abandon the current research and the chance to access potential better treatment in the future. What is worthy, here, from an ethical viewpoint, is the duty to inform the patient about the limitations of his/er autonomy in a transparent manner.

Besides, informative processes supporting aware decisions do not engage only the materials used in the 3d bioprinting, but they also involve the data associated with the donor and/or the patient as well as their families. Specific information should be provided regarding the methods used to guarantee the privacy protection of all the subjects engaged in the bio-fabrication in relation to the phase of collection, storage, and the use of personal data gathered during the bioprinting process.

Finally, clear information should be given about the patents and the licenses developed through the bioprinting. While some scholars [25] focus on the ownership issues and the potential value of bioprinting constructs to different interested parties like physicians, researchers, biotechnology companies, others consider deeply the potential intellectual property frameworks for bioprinting [26,27].

From this perspective, Li [26] introduces two possible categorizations of the bioprinters as medical or non-medical machines by highlighting that only technologies used for medical purposes may be considered a patentable entity. Similarly, Mladenovska., *et al*. [27] emphasize the need to classify the 3D bioprinting as medical device, or not, to identify the applicable regulatory framework.

However, the debate on these aspects is still open and the lack of common visions and regulations on the intellectual property rights linked to 3D bioprinting generates uncertainty around translational research and raises the risks of breaching fundamental rights and freedoms of the subject's involved in this process, including vulnerable (e.g., donors, patients) and non-vulnerable parties (e.g., engineers, physicians, companies), thus adding urgency to adapt or rework current regulatory frameworks.

Conclusions

3D bioprinting of tissues and organs is contributing substantially to the prompt advances of medical science. Bio-fabrication has been applied to produce almost every human tissue tested for clinical application, from blood vessel to neuronal tissue. It is only a matter of time before we could print a functioning biological organ that could solve the persistent shortage of organ donation.

However, this technology raises critical ethical and legal issues that need to be considered carefully to give adequate guidance on the evolving 3d bioprinting practices in the medical context.

Although the reflection on the ethical and regulatory issues of the bioprinting is developed internationally, crucial aspects deserve to be furthermore discussed in relation to the ontogenetic capacity of this technology and its potential ability to develop immortal life.

As bioprinting advances, the implementation of human fabrics in clinical or non-clinical contexts becomes a realistic perspective and it demands the urgent development of specific regulations covering the body and its parts as transformed from engineering processes.

New or revised legislations or ethical recommendations should govern, on one hand, the problem of the classification of the "new entities" produced from the bioprinting. On the other, they should be guaranteeing the respect of fundamental rights and freedom in the performance of medical practice, focusing on the informed consent, the privacy protection, and the intellectual property rights.

Finally, legislations or ethical guidance should consider the turnover and commercialization of 3D bio-printed constructs establishing possible sanctions for illegal trafficking of artificial organs developed.

Bibliography

1. Wallace GG., *et al*. "3D bioprinting. Printing parts for bodies". Australia: ARC Centre of Excellence for Electromaterials Science (2014).

2. Kirillova A., *et al*. "Bioethical and legal issues in 3D Bioprinting". *International Journal of Bioprinting* 6.3 (2020): 272.

3. Atala A. "Tissue engineering of human bladder". *British Medical Bulletin* 97 (2011): 81-104.

4. Ricci G., *et al*. "Three-dimensional bioprinting of human organs and tissues: bioethical and medico-legal implications examined through a Scoping Review". *Bioengineering* 10.9 (2023): 1052.

5. Laronda MM., *et al*. "A bioprosthetic ovary created using 3D printed microporous scaffolds restores ovarian function in sterilized mice". *Nature Communication* 8 (2017): 15261.

6. Arslan-Yildiz A., *et al*. "Towards artificial tissue models: past, present and future of 3D bioprinting". *Biofabrication* 8 (2016): 014103.

7. Murphy SV and A Atala. "3D bioprinting of tissues and organs". *Nature Biotechnology* 32 (2014): 773-785.

8. Thacker Eugene. "The thickness of tissue engineering: Biopolitics, biotech, and the regenerative body". *Theory and Event* 3: muse.jhu.edu/article/32555 (1999).

9. Lapworth Andrew. "Habit, art, and the plasticity of the subject: The ontogenetic shock of the bioart encounter". *Cultural Geographies* 22 (2015): 85-102.

10. Yudin BG. "Institutionalization of Bioethics and Human Enhancement". *Workbooks Bioeth* 23 (2016): 5-11.

11. Pullen LC. "Non-transplantable organs and tissues: a golden opportunity". *American Journal of Transplantation* 22.9 (2022): 2127-2128.

12. Lapworth Andrew. "Theorizing bioart encounters after Gilbert Simondon". *Theory, Culture and Society* 33 (2016): 123-150.

13. Vermeulen N., *et al*. "3D Bioprint Me: A Socioethical View of Bioprinting Human Organs and Tissues". *Journal of Medical Ethics* 43 (2017): 618-624.

14. Tishchenko PD. "Designing of the person: ideas and technologies". *Workbooks Bioeth* 23 (2015): 5-11.

15. Yudin B. "Technoscience and "human enhancement". *Epistemology and Philosophy of Science* 48.2 (2016): 18-27.

16. Bushev S. "The philosophical and natural-science aspects of the study of the problem of aging and technological immortality". *Soc Poli Nauki* 3 (2018): 198-200.

17. Nissan AM. "Regulating the three-dimensional future: how the Fda should structure a regulatory mechanism for additive manufacturing (3D Printing)". *Boston University Journal of Science and Technology Law* 22 (2016): 267-297.

18. Mason J., *et al*. "An overview of clinical applications of 3-D printing and bioprinting". CADTH Issues in Emerging Health Technologies. Canadian Agency for Drugs and Technologies in Health (2019).

19. Lo B and L Parham. "Ethical Issues in Stem Cell Research". *Endocrine Review* 30 (2009): 204-213.

20. Volarevic V., *et al*. "Ethical and safety issues of stem cell based therapy". *International Journal of Medical Sciences* 15 (2018): 36-43.

21. "Directive 2004/23/EC of the European parliament and of the council of 31 March 2004 on setting standards of quality and safety for donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells". *Official Journal of the European Union* 102 (2004): 48-58.

22. Blum B and N Benvenisty. "The tumorigenicity of diploid and aneuploid human pluripotent stem cells". *Cell Cycle* 8 (2009): 3822-3830.

23. Nijhaman LP., *et al*. "Informed consent: issues and challenges". *Journal of Advanced Pharmaceutical Technology and Research* 4.3 (2013): 134-140.

24. Razak SSA., *et al*. "Incorporating informed consent in 3D bioprinting medical treatment". *Journal of Academic Res in Business and Social Sciences* 12 (2022): 751-756.

25. Arbaugh JT. "Do you own your 3D bioprinted body? Analyzing property issues at the intersection of digital information and biology". *American Journal of Law and Medicine* 41 (2015): 167-189.

26. Li Ph. "3D bioprinting technologies: patents, innovation and access". *Law, Innovation and Technology* 6 (2014): 282-304.

27. Mladenovska T., *et al*. "The regulatory challenge of 3d bioprinting". *Real-world Evidence* 18.8 (2023): 659-674.