What is the future of bioprinting in tissue engineering?

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Abstract

This research paper summarizes the findings of previous research about 3D bioprinting in tissue engineering. Biofabrication, particularly in the field of regenerative medicine and 3D in vitro models, shows great potential in creating intricate tissue structures that closely resemble native tissues. Preprocessing steps involve imaging the tissue using various modalities, designing the 3D model using CAD software, and considering the characteristics of the tissue for proper cell line selection. The development of suitable bioinks combining printability, cytocompatibility, and biofunctionality remains a challenge. Imaging techniques play a crucial role in characterizing tissue engineering products. Conventional tissue engineering strategies involve scaffolds, isolated cells, or a fusion of the cells with scaffolds, while 3D bioprinting enables the creation of complex tissue-like structures. These advancements have the potential to revolutionize a broad and developing sphere of tissue engineering, regenerative medicine, and biomedical research. Used methods are questionnaires and interviews help in collecting information from experienced specialists and obtaining their true opinions on the topic. As a result, bioprinting has a full potential to develop in the future.

I. Introduction

3D bioprinting is a modern ramification of a broad field of tissue engineering. 3D bioprinting is an additive manufacturing technique that employs bioinks to build structures layer by layer, mimicking the properties of natural tissues. These bioinks, used as the printing material, can be made from natural or synthetic materials mixed with living cells. Optimal bioink composition and density play a critical role in influencing both cell viability and density. Consequently, the careful selection of the most appropriate bioink is imperative for achieving specific research objectives. The suitability of bioprinters for specific bioinks can vary considerably. Therefore, it's crucial to make sure that the bioprinter and the chosen bioink are a good fit and work well together. 3D bioprinters are engineered to work with delicate materials containing living cells while minimizing damage to the final product. These bioprinters come in various types, including inkjet-based, laser-assisted, and extrusion-based systems.

Due to the development of different diseases, there are people who need organ transplants. However, not everyone can afford it, or there are simply no donors. Therefore, it makes people question whether 3D bioprinting has a future in producing artificial body parts for people who suffer from illnesses and in improving medicine. For example, according to Z. Xia, bioprinting creates tissue constructs using heterogeneous compositions with different structures. *[1]*

This research addresses the new possibilities regarding 3D bioprinting in tissue engineering. The objective of research is to find new ways in the science field in which 3D bioprinting can be used and detect already used ways from the experiments and scientific papers of scientists. It will create a summary of findings on the chosen topic.

The thesis of this research is: The future of 3D bioprinting in tissue engineering has a great future because it requires development and can contribute to artificial organ development.

II. Literature review

Biofabrication exhibits significant promise in the realms of regenerative medicine and the creation of sophisticated 3D in vitro models. It enables the production of intricate tissue structures that closely mimic native tissues to a greater extent compared to existing biomedical alternatives.

Preceding the printing process, the first step of preprocessing is to image the tomography of the tissue of interest and gain an understanding of its basic anatomical properties. This is usually achieved using conventional 2D imaging methods such as MRI, CT, or ultrasound*[2]*. Other imaging modalities used to visualize the tissue of interest include positron emission tomography (PET), single-photon emission computed tomography, or mammography*[3]*. The choice of imaging modality largely depends on the area of interest of the tissue or the characteristics of the tissue while also determining the resolution and accuracy of the 3D model to be created.

The second step of preprocessing is the designing of the 3D model using computer-aided design (CAD) software. This step is crucial in ensuring a high level of accuracy of the physical properties upon creating the 3D tissue mimic. The use of CAD software allows for increased efficiency by partially automating the design of the 3D structure in a way that follows the exact internal and external geometry while also ensuring low porosity of the structure in order to avoid future problems*[4]*.

An understanding of the basic anatomical features and functionality of the tissue of interest is critical to guide the proper choice of the cell line, which will determine the rest of the process of bioprinting as well as potential limitations. This includes considering the source of the cells, their ability to be applied in different environments, their maturation capabilities, and even the physical consistency of the bioink *[5]*.

The application of additive manufacturing in the biomedical field has become a hot topic in the last decade owing to its potential to provide personalized solutions for patients. Different bioinks have been designed trying to obtain a unique concoction that addresses all the needs for tissue engineering and drug delivery purposes, among others. Despite the remarkable progress made, the development of suitable bioinks which combine printability, cytocompatibility, and biofunctionality is still a challenge. In this sense, the well-established synthetic and functionalization routes to prepare nanoparticles with different functionalities make them excellent candidates to be combined with polymeric systems in order to generate suitable multi-functional bioinks*[6]*.

In the tissue engineering(TE) paradigm, engineering and life sciences tools are combined to develop bioartificial substitutes for organs and tissues, which can in turn be applied in regenerative medicine, pharmaceutical, diagnostic, and basic research to elucidate fundamental aspects of cell functions *in vivo* or to identify mechanisms involved in aging processes and disease onset and progression. The complex three-dimensional microenvironment in which cells are organized *in vivo* allows the interaction between different cell types and between cells and the extracellular matrix, the composition of which varies as a function of the tissue, the degree of maturation, and health conditions*[7]*.

Imaging techniques are fundamental tools for the characterization of tissue engineering products at any stage, from biomaterial/scaffold to construct/organ analysis. Indeed, tissue engineers need versatile imaging methods capable of monitoring not only morphological but also functional and molecular features, allowing three-dimensional and time-lapse in vivo analysis, in a non-destructive, quantitative, multidimensional analysis of TE constructs, to analyze their pre-implantation quality assessment and their fate after implantation*[8]*.

Conventional strategies within tissue engineering encompass (a) the utilization of scaffolds in isolation, (b) the introduction of isolated cells and bioactive compounds, or (c) a fusion of cells implanted onto or within scaffolds to emulate the body's inherent extracellular matrix (ECM) structure, thereby fostering the advancement of tissue engineering*[9]*. Within the realm of 3D bioprinting, minute elements of biomaterials, bioactive substances, and viable cells are meticulously arranged alongside operational constituents, resulting in the creation of intricate three-dimensional formations reminiscent of tissue structures.

Biomaterial inks based on cellulose nanofibers (CNFs) and photo-cross-linkable biopolymers have great potential as a high-performance ink system in light-aided, hydrogel extrusion-based 3D bioprinting. Recently, attributed to structural similarity to the extracellular matrix, low cytotoxicity, and desirable rheological properties, the gel-like cellulose nanofibrils (CNFs) have attracted increasing attention as an ingredient when formulating the bio(material) inks for hydrogel extrusion-based 3D bioprinting*[10]*. To accurately reproduce the structure of the digital model and to achieve adequate shape fidelity are challenging factors in the scenarios of extrusion-based 3D printing because of the soft nature of the CNFs-based hydrogels, which typically have a water content greater than 95%. CNFs can be either printed as a monocomponent hydrogel as a platform biomaterial*[11]* or more often in binary ink formulations with other biopolymers, such as gelatin and alginate where CNFs are more often seen as a rheological modifier to facilitate the extrudability/printability and to promote the shape fidelity performance of the formulated bioink.

Inkjet bioprinting offers distinct benefits including its relatively swift printing rate, cost-effectiveness, and straightforward accessibility. The possibility of converting a readily available printer into an inkjet bioprinter enhances its appeal. Notably, N. D. Orloff et al*[12]*. demonstrated the successful incorporation of a controller within the printing head of an adapted HP G3110 scanner, thereby creating an economical bioprinting setup. Additionally, the work of Z. Mohammadi et al*[13]*. showcased the capability of a modified HP Deskjet 1510 printer to produce biological time-temperature indicators using a bioink.

These advancements signify the promising trajectory of biofabrication, bioprinting, and additive manufacturing in revolutionizing tissue engineering, regenerative medicine, and biomedical research.

III. Methods

Different methods were chosen to be used in this research in order to obtain the most recent and reliable data on the topic regarding 3D bioprinting in tissue engineering. Both qualitative and quantitative types were chosen, so the problem can be observed more accurately.

By using a qualitative approach, it is possible to gather various opinions of renowned scientists in this field or ordinary people. For instance, the opinions of biomedical engineers, tissue engineers, and medical workers can be considered well because they are most experienced in this subject. The collection of data in this approach can be done by conducting interviews with the sample. The interview was conducted with a healthcare field worker. Before it the consent letter was provided and a positive answer was obtained. The consent letter and questions are presented in Appendix 1 and 2 respectively.

While the population is the general public aged 18-80, the scope of the interviews is people in medical, tissue engineering, or related fields.

By using a quantitative approach, it is possible to collect statistical data and analyze them from a mathematical point of view. It will provide us with exact data that is so crucial to the research. The collection of data can be done by using questionnaires since it requires less time to complete, are understandable, and are easier to gather statistics. Moreover, a consent letter was taken before the questionnaire, so the survey can be considered as ethical. The consent letter, and questions are provided in Appendix 3 and 4 respectively. The number of questions in a survey is 6.

All of the listed methods above and their results will be in the Appendix part of the research paper.

IV. Results

Responses to the questionnaire of people in the tissue engineering sphere

The scope of the participants was small since there should be only experienced people. Therefore, there were 5 participants in the survey, and all of them were from the biology and healthcare spheres. For the first question, “What is your occupation?” 80% answered healthcare workers, whereas only 20% of all respondents reported a biology student. (Figure 1)

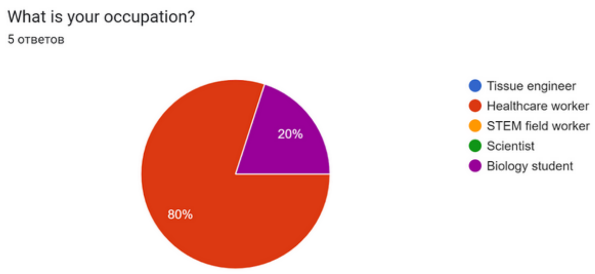


Figure 1.

For the next question, “Do you consider 3D bioprinting ethical?”, all of the participants responded positively. (Figure 2)

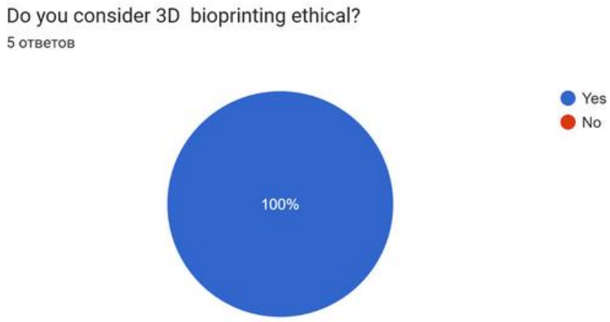


Figure 2.

The third item asked about “How old are you?”, and answers varied from 19 to 70. However, most of them are middle-aged people. The mean of the participants age is 45.8.

The third question was “Do you think there is a future of 3D bioprinting?”. As it is presented in Figure 3, all of them (100%) believe that there is definitely a future of 3D bioprinting.

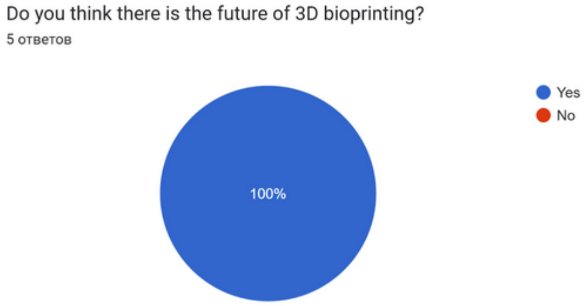


Figure 3.

The next 2 questions were more qualitative type than quantitative, so the opinions could be collected. The answers are given in the Figure 4 and Figure 5 below.

What improvements can be made into the sphere of 3D bioprinting?
5 ответов

this is a wonderful direction in medicine, as a dermatologist, many skin problems could be solved, and this is an aesthetic problem

Print more types of tissues

?

Improvements depend on the relevance to practical work

Create important artificial human body parts.

Figure 4.

What can be possibly implemented in this sphere in the future?
5 ответов

solve big problems with organ implantation, skin transplantation, cicatricial changes in the skin in various fields of medicine

Creation of artificial blood or plasm

?

A lot of new advances

More artificial organs

Figure 5.

Healthcare worker’s responses to the interview

Qualitative data obtained from a structured interview with a medical sphere worker is

presented below in Table 1. Overall, the interview contained 5 questions about tissue engineering and 3D bioprinting. The answers were written on the paper and carefully analyzed using the table. First of all, the quotes containing the main idea were written, and then the main codes were obtained by generalization. Then, those codes were translated into themes that present the answer to the main question of the research.

During the interview, it was obtained that the medical field had single research and experiments in the past. However, now this field is more advanced and will be developed in the future.

Themes	Codes	Quotes
Bioprinting is an actual sphere, which has a great future.	Actual	“actual on the modern level”, “has its future”,, “it has a great future”, “not only medicine, but also biology and microbiology”, “it depend on the level of scientific developments and relevance to the practice”, “later development of tissue engineering”, “witness all the developments and achievements”
	Development	
	Future	
The field of bioprinting is more advanced now than in the past.	prerequisites	“it had prerequisites in the times when I worked in medicine”, “single experiments and researches”, “single practices to implement it into sphere of medicine”
	single	

Table 1.

V. Discussion

The obtained results and materials are enough and significant to the research because the answer to the main research question can be derived using them. The results can be regarded as significant, because the chosen topic is important in the modern world, and results directly answer the main question.

However, several challenges and limitations were faced. First of all, the number of participants is low. Since the scope of the participants of this study should be narrow, it was hard to find, select, and contact people. Therefore, there were only 5 participants in the questionnaire and 1 participant in the interview. Unfortunately, with this number of participants, it would be hard to generalize obtained data and conclusions to city, country, and global levels. The next limitation is the amount of time. To make research high quality and on the global scope takes a lot of time, but unfortunately in this timeline, it was hard to find people and analyze data.

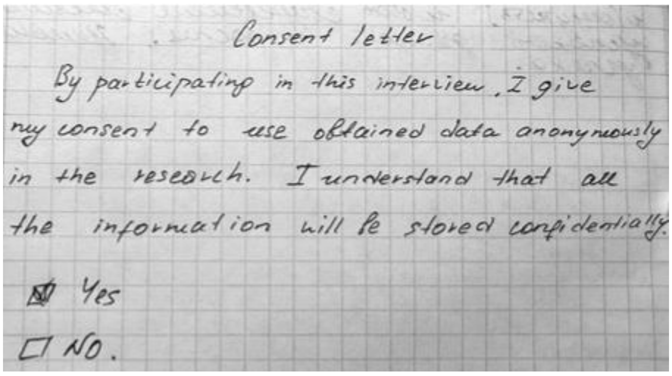
Taking the aforementioned limitations into consideration, the research’s future recommendations can be proposed. Firstly, it is important to extend the number of survey and interview participants, including people from different countries, to make it possible to generalize findings on a global level. Secondly, new methods can be implemented, so the results can be more reliable.

VI. Conclusion

This research is concentrated on the current aspect of 3D bioprinting in the field of tissue engineering. The field itself can be regarded as significant because it solves issues in biology, specifically in the medical field. Therefore, it was important to conduct such research on this topic. First of all, the question of research was "What is the future of bioprinting in tissue engineering?". In the end, our team clearly found an answer to this question after conducting primary and secondary research as well. There is definitely a future of bioprinting of artificial human body parts. The answer is formulated after a review of different sources about bioprinting, its function, advances, and principles of work. Also, the primary findings show that the majority of surveyed people in the healthcare or biology field have a positive opinion on 3D bioprinting, consider it ethical, strongly support this field, and believe that in the future there will be more artificial organs printed that are important to humans and wish to witness all the advances of this broad field of science.

VII. Appendix

Appendix 1 - consent letter to interview.

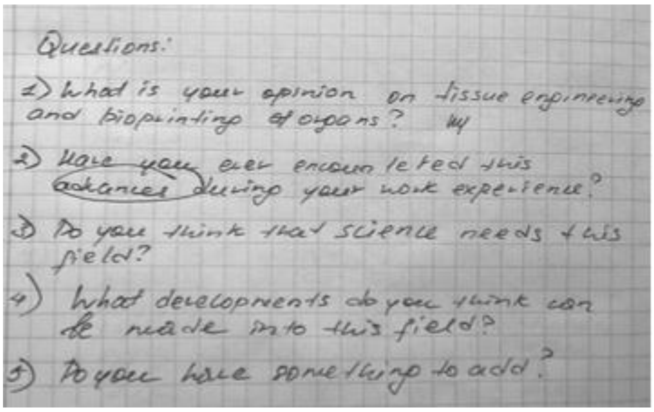

Consent letter

By participating in this interview, I give my consent to use obtained data anonymously in the research. I understand that all the information will be stored confidentially.

☒ Yes

☐ No.

Appendix 2 - interview questions.


Questions:

1) What is your opinion on tissue engineering and bioprinting of organs?

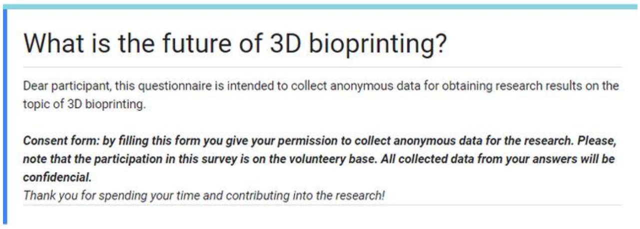
2) Have you ever encountered this advances during your work experience?

3) Do you think that science needs this field?

4) What developments do you think can be made into this field?

5) Do you have something to add?

Appendix 3 - consent letter for the questionnaire.

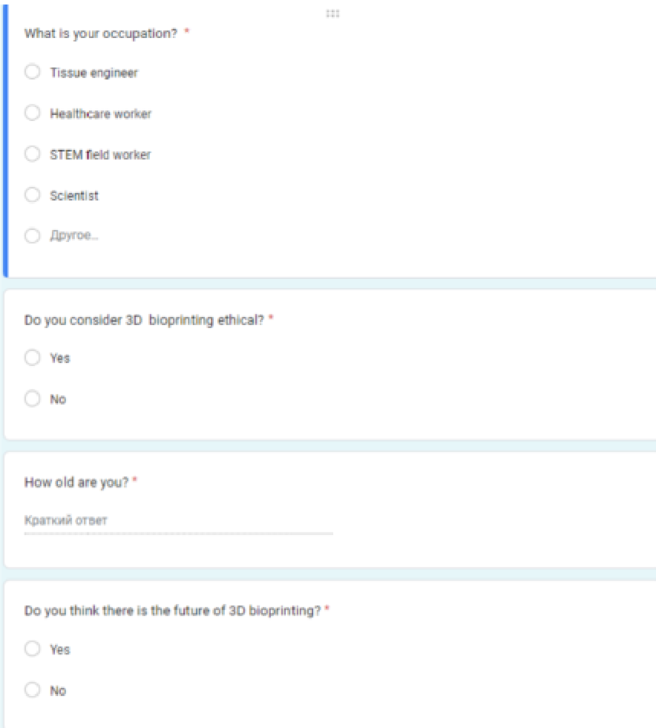

What is the future of 3D bioprinting?

Dear participant, this questionnaire is intended to collect anonymous data for obtaining research results on the topic of 3D bioprinting.

Consent form: by filling this form you give your permission to collect anonymous data for the research. Please, note that the participation in this survey is on the volunteery base. All collected data from your answers will be confidencial.

Thank you for spending your time and contributing into the research!

Appendix 4 - questions of the questionnaire.


What is your occupation? *

- Tissue engineer
- Healthcare worker
- STEM field worker
- Scientist
- Другое...

Do you consider 3D bioprinting ethical? *

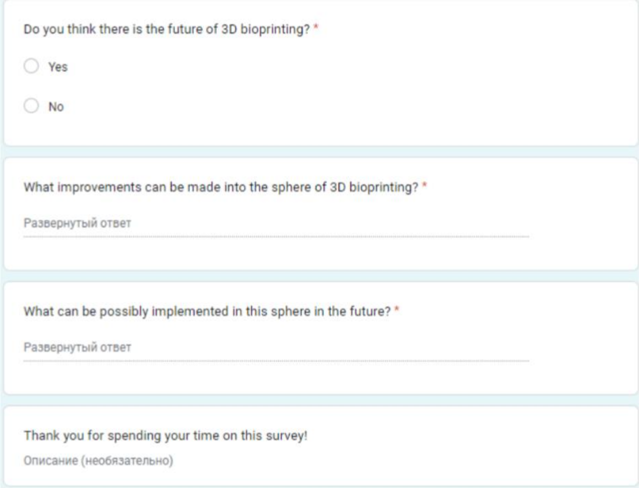
- Yes
- No

How old are you? *

Краткий ответ

Do you think there is the future of 3D bioprinting? *

- Yes
- No


Do you think there is the future of 3D bioprinting? *

Yes

No

What improvements can be made into the sphere of 3D bioprinting? *

Развернутый ответ

What can be possibly implemented in this sphere in the future? *

Развернутый ответ

Thank you for spending your time on this survey!

Описание (необязательно)

VIII. References

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