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Article

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CONSIDERATION OF REQUIREMENTS FOR MATERIALS FOR DIFFERENT BIOPRINTING METHODS

The object of research is the characteristics of the materials used in the bioprinting process. One of the biggest problems in the field of bioprinting is the materials used for printing organs, in particular, the lack of mechanical properties of these materials, such as strength, elasticity, ductility, wear resistance, and the like. They are essential to achieve the stabilization of printed structures. During the study, the requirements for materials used in the technology of three-dimensional bioprinting, including hydrogels, were discussed. Three main methods were considered (extrusion bioprinting, drip bioprinting, laser bioprinting), for each of which separate requirements for materials are put forward. Comparative assessment of these materials for different types of printing techniques are obtained. It is also determined that the extrusion printing technique is the most used for this direction of use, however, there remains the problem of the viability of living cells through the force of the bias stress, which occurs when the substance is squeezed out from the side of the nozzle walls. It is determined that the main requirements are the ability to gel, low surface tension, wettability and viscosity of the substance. Through understanding and structured information, it is possible to provide biological connections for better cellular interactions and improve the nutrient medium for the creation of physiologically relevant, functional tissues that can be engrafted by the human body after implantation. With such initial data, it is possible to develop new materials and improve existing ones that would meet all these requirements. By identifying the key problem, new ways of solving it can be developed. The above problems are some of the main reasons why researchers are still far from the bioprinting of clinically significant functional organs. Nonetheless, thanks to the new development, bioprinting will become a key technology for future tissue engineering, regenerative medicine and pharmaceuticals.

Keywords: *bioprinting, bioink, extrusion printing, drop printing, laser printing, living cells, surface tension.*

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1. Introduction

Today 3D bioprinting is one of the main areas of development and research. In 3D bioprinting, they mean printing with living cells in order to create biological tissue. The main goal is to recreate analogs of living tissues and organs for the preservation and prolongation of human life, that is, use in transplantation, which is currently a serious unsolved problem with a tendency towards a decrease in the number of donors [1]. By using autologous human cells, the problem of rejection of transplanted organs will be significantly reduced. It is also possible to use it in the form of drug testing; it is possible to create dummies of tumors, viruses and the body environment for more accurate results of a human reaction [2, 3].

At the moment, there are different types of printers that have their own characteristics: advantages and disadvantages. The main technologies are extrusion, drop, laser printing. Most of all, the method of extrusion printing is used for research through a simple principle of operation of the mechanism, the possibility of using a wide range of materials, and affordability. Also, time is combining different types of printers to increase their efficiency at work. There are many manufacturers on the market that have already proven themselves. However, the main problem in creating artificial organs is not the lack of the required level of technical equipment, but the materials used.

It is relevant to consider the requirements for various types of materials, currently used for attempts to create living organs and tissues. *The object of the research* is the characteristics of the materials used in the bioprinting process. *The aim of research* is to identify and compare the basic material requirements for different bioprinting methodologies.

2. Methods of research

The principle of bioprinting is understood as the placement of cells inside biomaterials in a certain structural order, determined using automated systems [4]. This process requires the delivery of cells into a special environment for the possibility of their proliferation and development,

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which can be placed in special forms that are developed using CAD (computer-aided additive design) technologies. They, in turn, can be created from 3D medical images that can be obtained using computed tomography (CT)/magnetic resonance imaging (MRI). The cells loaded into the medium are called bioink or bioinks – the main building material.

There are two main types of bioinks. The first is a scaffold-based bioinks, that is, cells are loaded into hydrogels or similar materials. This type of ink allows cell proliferation and growth. In the second type, cells are printed without scaffolds, that is, cells are first formed into new tissues intended for the bioprinting process, then such formations are deposited and merged in a special way, they mature and merge to make more bulky functional tissues [5].

A descriptive-comparative method was used to analyze the basic requirements for materials that can be used to create tissue structures.

3. Research results and discussion

Each printing method has its own requirements for the materials used, which is explained by the mechanism of their work (Table 1):

1. The method of extrusion bioprinting usually uses mechanical micro-extrusion, therefore, the hydrogels that are used in it, as a rule, are defined as non-Newtonian liquids [5], in which the viscosity depends on the shear rate. In addition, bioink should have properties of low adhesion and surface tension in order to prevent it from sticking to the surface of the nozzle tip. In addition, it must have a fast gel formation to be able to maintain its shape without spreading.

2. The method of drip bioprinting uses in its work such types of energy as electricity, heat, or sound [6]. This allows high throughput bioink to be squeezed out. Bioink must have a low viscosity and also be free of fibrous nature in order to easily pass through the nozzle without clogging. That is, the liquid must have a rheopectic property; in rheopectic fluids, the viscosity of the liquid increases when the bias voltage is applied over time [5]. Another important feature is possession of sufficient wettability for liquid to pass freely through the cartridge without flooding either the outer part of the nozzle or the printhead. In addition, the liquid has to solidify immediately after putting it into a form.

3. Laser printing method, as its name implies, uses laser energy. It is divided into two types: the first is the transfer of cells from the «donor» slide support to the «recipient» slide. The second is the use of the photopolymerization process, where the laser beam is selectively directed to certain areas, as a result, solidify [5, 7, 8]. Therefore, in the first case, the bioink must have a sufficient degree of adhesion and low surface tension in order to be evenly distributed over the intermediate layer and adhere. Also, the substance has the ability to convert thermal energy into kinetic energy and is characterized by high viscous springiness. As with other methods, it must have the ability to gel quickly so that the liquid streams can solidify without spreading. In addition, the interaction of the jet and the substrate is also important, the correct substrate must be selected so that the substance does not splatter. For the second type, hydrogels with the ability to photopolymerize should be chosen. Bioink should be additionally reinforced with non-toxic water-soluble photoinitiators and light absorbers to initiate photopolymerization and enable fabrication of tissue constructions with a uniform layer thickness [5]. In addition, the bioink must have an appropriate gelation mechanism due to chemical, physical or enzymatic crosslinking. Also important are stability and high mechanical strength, as well as the ability to retain cells, evenly distributed in the precursor solution.

Table 1

Comparative table of key material requirements

Printing method	Requirements for materials
Extrusion bioprinting: – pneumatic; – mechanical	– Low surface tension and adhesion. – Fast gelation. – Thixotropic behavior. – Ability to keep in shape. – Interaction with the substrate: wettability and surface roughness
Drip bioprinting: – electric; – acoustic; – thermal	– Low viscosity. – Fast gelation. – Low viscosity, flowability. – Rheopectic behavior. – Non-fibrous nature. – Interaction with the substrate: wettability, surface roughness and viscous forces
Laser bioprinting: – direct feeding of cells; – polymerization process	– Low surface tension. – Viscousness. – Adhesion to the intermediate layer. – Absorption of laser pulse energy. – Fast gelation. – Specific interaction with the lining: surface wettability, roughness, viscous forces
	– Ability to photopolymerize. – Addition of low toxicity water-soluble photoinitiators

Despite significant progress in the development of biomaterials for tissue engineering and regenerative medicine, a rather small amount of research is devoted to the development of biomaterials for bioprinting. Most researchers do not consider the possibility of improving biomaterials, so further efforts should be directed to the development of new materials for bioprinting [9]. To develop such materials, it is first necessary to define the existing bioprinting methods and processes, as each methodology puts forward different requirements for the materials.

The development of new bioinks for extrusion printing is critical, since most researchers use this method because of its practicality and ability to produce large-scale tissue constructs [5, 10]. Bioinks used in extrusion printing must have different properties, but the most important characteristics are shear vacuum, hardenability and fast crosslinking. Hydrogels lack the ability to harden quickly, tend to blur during extrusion and cannot maintain their original shape. Currently, there are only a few types of hydrogels that exhibit properties such as Pluronic® and sodium alginate, but these materials do not support cell growth and tissue regeneration. Therefore, new biochornil materials with all these characteristics will be the most valuable.

In drip printing, materials are used for two things: bioink, which is ejected to form droplets, and substrate materials, to deposit the droplets. New hydrogels should be developed that have lower viscosity, but have sufficient mechanical and structural properties, as well as appropriate gelation properties. In addition, such materials should not have a fibrous microarchitecture that can easily clog the nozzle or tubing line inside the cartridge head.

Different characteristics are defined for the materials used in Laser Printing, since the requirements for processes based on cell transfer are different from those associated with photopolymerization. New biomaterials with special properties need to be developed to develop bioinks used in cell transfer technologies. These include: the ability to distribute and create a uniform film on the tape, viscousness, which facilitates blasting with controlled droplet teaching, the ability to quickly gel to provide sufficient mechanical. In addition, an appropriate biomaterial for the substrate must be installed. For hydrogels used in processes based on photopolymerization, new bioink is needed, since modern photohardening materials do not have sufficient strength to create biologically attractive and mechanically integrated tissue structures. In processes involving photopolymerization, the photohardening bioink determines the cure rate and resolution of the process.

It should be noted that the above results describe general requirements for materials and do not consider the specifics of various types of organs and structures. Therefore, they can be used as a kind of template for selecting materials to determine in which direction to go. However, one should take into account the individual needs and requirements of a particular study and its object, because each study is unique and requires the definition of a more specific, precise and narrowly focused framework.

Further research can be aimed at defining narrower and more specific requirements for the creation of specific organs, as well as targeting existing materials for each type with their characteristics.

4. Conclusions

In the course of the study, the requirements for biomaterials that are used in three-dimensional bioprinting are obtained. In particular, their main characteristics are described, depending on the chosen printing process and its technical specifics of work. It has also been determined that the development of new bioinks for extrusion printing is critical, as most researchers use this method because of its practicality and ability to produce large-scale tissue constructs.

The research results will be useful for researchers who are considering the possibility of improving biomaterials and whose further efforts will be directed to the development of new materials for bioprinting. They will also be useful for the formation of basic knowledge in the study of the sphere of 3D-bioprinting of organs and tissues.

References

1. Mironov, V. O. (2013). Vsled za sozdatelem tekhnologii bioprintinga. *Nauka iz pervykh ruk*, 15–24.
2. Matai, I., Kaur, G., Seyedsalehi, A., McClinton, A., Laurencin, C. T. (2020). Progress in 3D bioprinting technology for tissue/organ regenerative engineering. *Biomaterials, 226,* 119536. doi: http://doi.org/10.1016/j.biomaterials.2019.119536
3. Sears, N. A., Seshadri, D. R., Dhavalikar, P. S., Cosgriff-Hernandez, E. (2016). A Review of Three-Dimensional Printing in Tissue Engineering. *Tissue Engineering Part B: Reviews, 22 (4),* 298–310. doi: http://doi.org/10.1089/ten.teb.2015.0464
4. Gungor-Ozkerim, P. S., Inci, I., Zhang, Y. S., Khademhosseini, A., Dokmeci, M. R. (2018). Bioinks for 3D bioprinting: an overview. *Biomaterials Science, 6 (5),* 915–946. doi: http://doi.org/10.1039/c7bm00765e
5. Ozbolat, I. T. (2016). *3D Bioprinting: Fundamentals, Principles and Applications.* Elsevier Inc., 342.
6. Vanaei, S., Parizi, M. S., Vanaei, S., Salemizadehparizi, F., Vanaei, H. R. (2021). An Overview on Materials and Techniques in 3D Bioprinting Toward Biomedical Application. *Engineered Regeneration, 2,* 1–18. doi: http://doi.org/10.1016/j.engreg.2020.12.001
7. Shafiee, A., Atala, A. (2016). Printing Technologies for Medical Applications. *Trends in Molecular Medicine, 22 (3),* 254–265. doi: http://doi.org/10.1016/j.molmed.2016.01.003
8. Murphy, S. V., Atala, A. (2014). 3D bioprinting of tissues and organs. *Nature Biotechnology, 32 (8),* 773–785. doi: http://doi.org/10.1038/nbt.2958
9. Gopinathan, J., Noh, I. (2018). Recent trends in bioinks for 3D printing. *Biomaterials Research, 22 (1).* doi: http://doi.org/10.1186/s40824-018-0122-1
10. Mandrycky, C., Wang, Z., Kim, K., Kim, D.-H. (2016). 3D bioprinting for engineering complex tissues. *Biotechnology Advances, 34 (4),* 422–434. doi: http://doi.org/10.1016/j.biotechadv.2015.12.011

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