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3D-ПЕЧАТЬ ТКАНЕЙ И ОРГАНОВ

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В статье представлены способы и методы применения 3D-печати органов и тканей

Ключевые слова: 3D-печать, органы, ткани, современные технологии

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3D-PRINTING OF TISSUES AND ORGANS

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The article presents methods and techniques for using 3D printing of organs and tissues

Key words: 3D printing, organs, tissues, modern technologies

In the modern world, technologies are developing at great speed, and they have penetrated into all spheres of life, so even in the medical field we cannot imagine our work without them. What was considered something fantastic 50 years ago has now become commonplace. Da Vinci robot, bionic prosthesis, 3D printing... How much has developed in just a few years? In this review we will talk about bioprinting

3D bioprinting has emerged as a promising new approach to create complex biological constructs in the fields of tissue engineering and regenerative medicine. In this article, we present the basic principles, materials, integration strategies, and applications of bioprinting. We also discuss recent developments, current challenges, and future prospects for 3D bioprinting to create complex tissues.

Material and methods

The most important characteristic for the selection of materials for the creation of human-made organs is the ability to minimize the chances of rejection of printed organs from a normally functioning organism. Materials for 3D printing of tissues and organs are: biochernils created on natural and synthetic polymers, natural-synthetic hybrid polymers, cells and tissues of the patients themselves. Biochernils are a liquid solution, similar in consistency to toothpaste, containing tissue spheroids or cellular suspensions. Natural polymers that are part of the "living ink": alginate, collagen, gelatin, fibrin, laminin. Synthetic polymers differ from natural polymers in their strength, and therefore they are more suitable for creating stable components in the human body-bone tissue, cartilage tissue, connective tissues (loose fibrous, dense fibrous). Materials based on synthetic polymers-PEG, PHEMA, PLC, PLGA. To create the biocompatibility of the human body and the organ created by the 3D printer, the cells and tissues of the patient himself are needed. Such components can be-embryonic cells, pluripotent stem cells (master cells), cell lines.

Among the 7 groups of AM technologies, the most common technology in biological production has become:

1. The laser pulse of the beam creates high pressure on the hydrogel–coated donor plate with a cellular material, which causes the hydrogel molecules to move to the working plate; A non-nozzle printing method that includes a pulsed laser source (consisting of a metal layer (gold or titanium) absorbing laser energy and a layer of biological particles). In a "biological laser", living cells are covered with the thinnest layer of metal. Under the influence of this ray, the metal begins to evaporate and droplets containing living cells are formed. A drop falls on the substrate and passes through a filter that captures the metal. Laser printers allow you to print with high resolution: they accurately repeat the shape of the printed object and the concentration of cells at each point. In addition, laser printing allows the use of very thick biological ink, which helps the finished product to keep its shape better.

2. Inkjet (InkJet, thermal, piezoelectric) - particles of a biopolymer or hydrogel with cellular substances in the form of droplets are sprayed through a nozzle, this happens due to the formation of vapor bubbles during electric heating or due to vibration of a piezoelectric unit.;

Thermal inkjet printer has an ink chamber. To create a flow of droplets, a current pulse is applied to the heating element, which heats the nozzle to 200-300℃. Short-term heating to such a temperature does not affect biological molecules (including DNA and living cells).

Piezoelectric inkjet printers use piezoelectric crystals, to which an electric current pulse is applied, and due to the vibration of the crystal, the ink exits the nozzle. The size, shape and rate of release of the droplet are determined by the applied voltage, duration and amplitude of the pulse. The disadvantages include that sound waves can damage cell membranes or vascular walls.

3. Extrusion (Extrusion, pneumatic and mechanical)

During extrusion printing, biological particles are squeezed out through the nozzle. There are pneumatic and mechanical extrusion systems. The solution for 3D bioprinting is a project of the Invitro company. Fabion prints purified collagen and living cells made up of a bead. Biological paper is a special gel containing nutrients that help the finished product maintain its shape. After printing, the organ must "mature" - it is placed in a bioreactor, where the balls merge together. Extrusion technology is very suitable for printing endocrine system devices.

4. Electrospinning

A method of interweaving polymer fibers with cells to create collagen-based scaffolds in tissue cultivation. This technology is much cheaper and provides good accuracy and control over the frames under construction. Another example is the preparation of long cell chains in tubes made of a hydrogel framework, the framework is then removed, and the prepared cellular material is used for bioprinting using an extrusion printer. The main task of this method is to use cells prepared in a special way: in the form of blocks, spheroids, cell sheets or cylinders assembled in an extracellular matrix.

5. The Kenzan method

It is designed for the spatial organization of spheroids using microneedles. The method is based on the art of ikebana. The spheroids placed by the robot on the microneedles create an extracellular matrix where the spheroids can interact with each other. The needles are made of stainless steel with a thickness of 160 microns and are placed in the form of a matrix at a distance of 500 microns.

6. Electrohydrodynamic method

Liquid ink in an electrostatic field is capable of forming droplets or a jet whose dimensions are smaller than the diameter of the nozzle. The maximum height is limited by the distance between the nozzle section and the substrate, since it is necessary to maintain a uniform electrostatic field.

7. Bioprinters with hybrid technology

With the help of laser technology, it is difficult to print a so-called scaffold, a frame. Therefore, a laser printer is often combined with an extrusion printer: an extrusion printer prints a supporting layer of collagen, and a laser printer imprints living cells into it. Other combinations of technologies are also possible. For example, there is a problem: if a large enough organ is printed, it does not hold its shape well, collagen does not have time to harden. Acoustic or magnetic waves are used to support the organ during solidification, so that the printer becomes extrusion-acoustic or extrusion-magnetic.

Usage: The 3D bioprinter allows you to create tissue-engineered structures that can be used in various fields of medicine and tissue engineering — for example, for the regeneration and transplantation of bones, skin, blood vessels and other tissues and organs. In the future, such technologies can help solve the problem of a shortage of organs and tissues for transplantation — it is assumed that in the future it will be possible to print even a heart, kidneys and liver on a bioprinter.

Medical applications

Although the ability to create vascular features in bioprinted tissues is often limited, new bioprinting methods can solve this problem, for example, a coaxial nozzle system was used to print vascular channels longer than a meter. These channels supported the growth of human coronary artery smooth muscle cells inside the matrix. Using the 3D printing technique, the authors were able to produce pipelines with a diameter of less than a millimeter, but, unfortunately, they could not demonstrate bioprinting close to the diameter of the capillary.

Currently, 3D bioprinting is a promising approach to bone and cartilage regeneration. In bone engineering, the printed skeleton has been designed as a bone substitute providing mechanical support and facilitating cellular activity (migration, proliferation and differentiation). In an experiment conducted on rats, in vivo implantation was performed. After 6 weeks, new bone nodules and blood vessels were observed in the shins. This shows that the degradation of PLA did not cause rejection and cytotoxic response.

If we talk about the cardiac system, many attempts have been made to regenerate the heart using cardiac stem cell therapy. Frames for implantation were printed in the studies. But, unfortunately, this has led to problems related to degradation, immunogenicity and mechanical properties. Therefore, a new method was proposed related to bioprinting without a frame. Due to this, the heart tissue showed spontaneous beating and electrophysiological properties that are inherent in ventricular myocytes

Neurons and glial cells are fragile and therefore difficult to 3D print. Previous studies first printed undifferentiated hiPSCs, and then allowed the cells to differentiate and assemble themselves into brain organoids. It has been reported that biomaterials for joint printing and human neural stem cells (HNSCS) can encapsulate stem cells, followed by their in situ expansion and differentiation into functional neurons and neuroglia.

Attempts have also been made to print neurons directly. Printing of neurons of the cerebral cortex and neuroglia using matrigel and alginate showed long-term survival of neurons after printing (up to 70 days). However, their analysis showed early and immature network activity. Other researchers have developed printing technology using fibrin-based bio-ink.

Due to the limited number of nephron structures, there was a problem with kidney tissue transplantation. The presence of 100 neurons was reported in the organoid of a kidney cultured through a well of which 5x105 cells were initiated. However, the kidney contains approximately 1x106 nephrons. Therefore, although 3D printing technology is developing rapidly, there are many structures in our body that we still cannot reproduce with modern technologies

Conclusion

3D bioprinting is an advanced new and developing technology with incredible potential. She has demonstrated great potential in the field of tissue engineering. Due to high efficiency and micro-scaling, the areas of bioprinting are rapidly expanding. It has become a powerful tool for creating complex systems

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