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Technologies and materials for bioprinting

Additive technologies [1] is one of the forms of additive manufacturing in which a three-dimensional object is created by layers of the material (printing, growing) applied successively according to the digital model. Printing is performed with the help of a special device called 3D-printer that ensures the creation of a physical object by successive applying of plastic material based on the virtual 3D-model. As a rule, 3D-printers are faster, more affordable and easier to use than the other additive manufacturing technologies. 3D printers provide product developers with the ability to print parts and mechanisms from several materials and with different mechanical and physical properties in one assembly process.

The main technologies of 3D printing [1] are extrusion printing; fusion sintering or gluing; stereolithography; lamination; printing by the method of layer melting.

The extrusion printing is based on the extrusion of the consumable material with the successive formation of the finished product. Consumables consist of thermoplastics or composite materials based on them.

Fusion sintering or gluing is based on a combination of powder material into a single whole. Similar printers apply thin coats of powder to the work platform, which are then selectively glued together with the material. The powder consists of any material that can be crushed to a state of powder - plastic, wood, metal.

Stereolithographic printers [4] use polymer resins. The resin is poured into a special container with a movable platform, which is installed in the position near the surface of the liquid. The resin layer covering the platform corresponds to one layer of the digital model. Then a thin layer of resin is treated with a laser beam, hardening at the points of contact. After the illumination, the platform, along with the finished layer, are immersed in the thickness of the next layer, and the illumination is carried out again.

In the process of lamination 3D-printers use sheet materials - paper, foil, plastic film. The layers of the material are glued on each other and trimmed along the contours of the digital model.

The layer-melt printing method creates three-dimensional objects by drawing sequential layers of material that repeat the contours of the digital model. Thermoplastics, supplied in the form of coils of threads or bars, act as materials for printing.

Medicine [2] is one of those areas where the use of three-dimensional printing has become a new impetus for large-scale changes. The rapid pace of development of modern technologies promotes the emergence of new areas of production, as well as the search for effective solutions to existing problems. Yes, 3D printing technology allows you to implement projects in the medical field. They are based on the use of 3D scanning of the destroyed parts of the body to more accurately determine the features of the problem of the victim and 3D modeling on the principles of individual approach to each individual client.

Implants, prostheses with individual characteristics of man taken into account, intervertebral discs, liver fragments and others are already printed [3] on 3-D printers. The print is actively used in surgery and dentistry, to create 3D models and build an implant contour. In the future, it is foreseen the printing of human organs and body parts .

The use of 3D printers is a promising area in medicine. Already, they are beginning to be widely used for diagnostic procedures. Every year they become [6] cheaper and more functional. It is assumed that the manufacture of prostheses and implants on the printer will be delivered to the conveyor, and this will be a promising direction of combating disability.

3D-bioprinting [8] is a technology for creating volumetric cell-based models using 3D-printing, which stores the functions and viability of cells. The first patent relating to this technology was filed in the United States in 2003 and received in 2006.

The technology of 3D-bioprinting for the manufacture of biological constructions usually involves placement of cells on a biocompatible basis, using a layer-by-layer generation method of three-dimensional structures of biological tissues. Since tissues in the body consist of different types of cells, the technologies of their production by 3D-bioprinting also differ significantly in their ability to ensure the stability and viability of cells. Some of the methods used in 3D bioprinting are photolithography, magnetic bioprinting, stereolithography, and direct extrusion of cells. The cellular material made on the bioprinters is transferred to the incubator, where it passes further cultivation.

In the sterolithography, the starting product [10] is a liquid photopolymer, which adds a special reagent-hardener, and this mixture reminds the well-known epoxy resin, only in the usual state, it remains liquid, and polymerizes and becomes solid under the influence of an ultraviolet laser.

Naturally, the laser can not immediately create the entire model in the thickness of the polymer, and it can only be said about the successive construction of thin layers. Therefore, a movable substrate with holes is used, which, with the help of the elevator lift, is immersed in the photopolymer on the thickness of one layer. Then the laser beam illuminates the areas subject to hardening, the substrate is immersed even on the thickness of one layer, the laser is again running.

The requirements for the photopolymer themselves are rather contradictory: if it is thick, it is easier to polymerize, but it is more difficult to provide an even surface after each step of immersion; it is necessary to use a special line, which at each step passes along the surface of the liquid and aligns it. A large amount of hardener at a fixed laser power will reduce the required exposure time, but inevitably the background illumination "spoils" the surrounding volume of the polymer and reduces the possible term of its use.

Full polymerization of each layer would take a lot of time, so the illumination is carried out to a level at which the layer acquires only the minimum required strength, and then the finished model, having been washed from the residual liquid polymer, has to be irradiated by a powerful source in a special chamber, so that the polymerization reaches 100%.

In photolithography, the fundamental difference from other types of lithography is that the exposure is made by visible or ultraviolet radiation, whereas in other types of lithography X-rays, electron flux, ion flow, rigid ultraviolet, etc. are used for this purpose.

Developers are working to get the first body fully functioning in the human body.

At the first stage, scientists tried to get the human body through the formation of an artificial structure in the form of an organ, and then filled this structure with living cells. However, over the last decade, scientists have invented a 3D printer that can create a body structure and fill it with living cells.

Some scientists believe that the creation of an organ can be without the formation of its pre-frame, while using the possibility of self-organization of living cells. Scientists have been conducting experiments to create liver bits. Initially, the necessary cell blocks were formed, and then they were layered with a 3D printer to give them the opportunity to grow together.

When creating bodies [5] based on three-dimensional print, scientists distinguish several levels of complexity of print.

The easiest way is to print flat structures that consist of just one type of cell, such as the skin. The following are complicated by tubular structures, from two types of cells - blood vessels. The third level is hollow bodies, such as a stomach or bladder. The most complex organs are the kidneys, the heart, the liver.

Implantation of the first three types of human organs has already been carried out in practice. Above the creation of the bodies of the fourth level - kidneys, liver and heart, scientists continue to work diligently [6]. The first successful experiment to build organs on a 3D printer was held in 2006. A group of bioengineers from the

Wake Forest Institute for Regenerative Medicine has developed and published bladder bladder for seven patients.

Doctors used stem cells of patients to create an artificial organ. Samples of donor tissue in a special sealed chamber with an extruder were applied over a bladder mucosa, heated to the natural temperature of the human body.

6-8 weeks in the course of intensive growth and subsequent division cells recreated the human body.

The printing of organs on a 3D printer is fully covered by just a few companies. The greatest successes were achieved by engineers from the American company Organovo [5] who were able to print hepatic tissue.

Today, 3D printers in medicine have already been used for many purposes. One of them is the creation of fragments of the skull. In the United States, a successful operation was performed, resulting in a patient receiving a printed implant of the skull. With the help of 3D - printers are already printing many prostheses, and taking into account the individual characteristics of the person. To increase their strength, special microcavities leave in prostheses for the migration of their own cells of the patient's bone tissue.

Martin Myers [9] was one of the first patients in the United States who had been made with 3D-printed knee. Conformis has printed 3D-knee, which was more accurate and more natural compared to conventional. Using a patented technology called iFit ConforMIS converts CT data into implants that have exactly the same size and shape to match the unique 3D structure of the joint. His Jig toolkit uses the same data to create the cutting process and placement of the joint itself, which in turn helps the surgeon determine the exact location of the patient's implant. This reduces the operation time and minimizes the number of required bone cuts.

In dentistry, 3D printers allow surgeons to quickly make inexpensive three-dimensional models for information that shortens the time of surgery, improves communication between the patient and the physician and speeds up the recovery of the patient. With a three dimensional bulky model, surgeons are much easier to navigate inside the living person during surgery.

3D-modeling [7] of human connective tissue consists of several stages.

The first stage of creating a model is the receipt of initial morphometric information. For this purpose, clinical and instrumental research methods (X-ray, ultrasound, computer and magnetic resonance imaging, etc.) are used. The quantitative data obtained as a result of the research carried out are used in the second and third stages for the creation of computer models with parameters that are installed in morphometry and located in the virtual space.

The second stage - the creation of a computer model is to construct a plane two-dimensional model of a human body in three projections.

The third stage is a three-dimensional reconstruction and creation of a three-dimensional computer model. The second and third stages can be performed using the specially developed software and 3D system of 3ds max modeling.

The process of 3D printing of the joints begins with the x-ray of the damaged part of the patient's body. The resulting data is converted into a three-dimensional computer model, which is immediately sent to print. A 3D printer produces an exact copy of the joint from a special porous material. This material contributes to the growth of cells and easily overgrown with cartilage tissue. Gradually, the bone gets the right shape, and the material breaks down. As a result, there remains only a bone that is no different from the original.

One of the most important aspects in the manufacture of surgical implants is the selection of materials that will not cause unwanted reactions from neighboring cells and tissues. The properties of the material affect the behavior of cells, functional and morphological changes, reproduction. The reaction of the patient's body to the implant depends on the topography, chemical and energy characteristics of the material used.

The advantage of producing implants is pure titanium and its Ti6Al4V alloy. Pure titanium is more resistant to corrosion and is considered the most biocompatible material. It has the ability to spontaneously form a stable and inert oxide layer, being placed in an oxidizing medium. In cases where a stronger implant is required, doctors usually choose a Ti6Al4V alloy that is also resistant to corrosion and is well tolerated with a low density.

Other biocompatible metals, also available in powder form, are stainless steel 316L and alloys of chromium and cobalt. The 3D printing with metals is carried out under controlled conditions (neutral gases, limited access to oxygen). Thus, the purity of the objects obtained and the properties of the materials are preserved.

Bioprinting is a revolution in medicine nowadays. This involves the co-development of several technologies, in particular: the development of 3-D models, the production of artificial organs, the implementation of compatibility of artificial materials and human tissues.

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