# Bioimpresoras 3D como herramienta de innovación en el futuro de trasplantes de órganos

## *3D bioprinters as innovation tool in the future of organ transplants*

## *Bioimpresoras 3D como uma ferramenta para a inovação no futuro de transplantes de órgãos*

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## Resumen

El presente trabajo tuvo por objetivo demostrar que la Bioimpresora 3D tendrá un impacto positivo como herramienta de innovación en el futuro de trasplante de órganos en el año 2016. La idea se basa en la investigación documental ya que es una técnica que consiste en analizar, seleccionar y recopilar información, mediante la lectura de documentos y materiales bibliográficos que contienen datos relacionados con el estudio.

Esta nueva tecnología tendrá un impacto positivo en la sociedad. Diversos estudios de diferentes autores han concluido que es una herramienta muy útil para solucionar la falta de cultura en la donación de órganos, la larga espera para ser candidato a un trasplante por donación y el riesgo de que sea rechazado por nuestro cuerpo.

Palabras clave: medicina, impresión 3D, trasplante de órganos.

## Abstract

This work was aimed at demonstrating that the 3D Bioprinter will have a positive impact as a tool for innovation in the future of organ transplantation in 2016. The idea is based on documentary research since it is a technique that is to analyze, select and collect information through the reading of documents and bibliographic materials containing data related to the study.

This new technology will have a positive impact on society. Several studies from different authors have concluded that it is a very useful tool to solve the lack of culture in organ donation, the long wait to be candidate for a transplant by donation and the risk of that is rejected by our body.

Key Words: medicine, organ transplantation, 3D printing.

## Resumo

Este estudo teve como objetivo demonstrar que o bioprinter 3D terá um impacto positivo como uma ferramenta para a inovação no futuro do transplante de órgãos em 2016. A ideia é baseado em pesquisa documental, pois é uma técnica que envolve análise, selecione e recolher informação através da leitura de documentos e materiais de biblioteca que contêm dados relacionados com o estudo.

Esta nova tecnologia terá um impacto positivo na sociedade. Vários estudos realizados por diferentes autores concluíram que é uma ferramenta muito útil para resolver a falta de cultura em doação de órgãos, a longa espera para ser um candidato para uma doação de transplantes e o risco de ser rejeitado pelo organismo.

Palavras-chave: medicina, impressão em 3D, transplante de órgãos.

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## Introduction

The European Patent Office (EPO) announced that the winner of the award the 2014 European Inventor, considered the Oscar of the inventors, it was Charles W. Hull of United States, the man who created the first 3D, a technology with a great futuristic potential printer (Know More, 2014).

This is one of the technologies of growing assimilation and impact which is currently used to indicate the emergence of new alternatives in medicine to improve the quality of people's lives: nanotechnology, biotechnology, information and communication technologies, robotics and artificial intelligence. This union has allowed to create 3D Printers of organs, which resulted in various practices in surgery of brain, development of prosthetics and replacement of organs. 3D printers are being used in the area of the medicine to improve and preserve the quality of the patient.

Worldwide, more than one billion people have a deficiency and about 200 million with any kind of functional problem, figures that are increasing alarmingly. Therefore, they require support to improve their quality of life.

Without a doubt, the 3D Bioprinter are here to stay, generating different views. Increasingly spoken more of them and their rapid evolution will make a not-too-distant day common to have one at home, as if it were a paper printer. But, what is the impact which will result in its use? This article describes the different opinions of the researchers of the area. 3D printing technologies are based on the so-called "additive processes technologies", a concept of additive manufacturing that describes the technologies in which an object is created by defining a sequence in layers. The 3D *Bioprinting* being used in regenerative medicine to combat the need for tissues and organs suitable for transplants. Compared to non-biological printing, *Bioprinting* 3D involves additional complexities, such as the choice of materials, types of cells and factors of growth and differentiation, and technical challenges related to the sensitivity of living cells and tissues building (Chimbo, 2016).

**Background.**

Although it is amazing what offer us this technology in third dimension, this invention is not so new since the first took place on March 9, 1983, when printing a black plastic cup. Hulls founded 3D Systems in 1986, three years after its first printing, in Valencia (California). This technology was created to make plastic objects and test prototypes (Saber Mas, 2014).

The technique used was stereolithography, which designates a layer-by-layer manufacturing system with a UV-sensitive additive known as a 3D laser printer. In 2009, this movement began around the world with the start of the company www.sculpteo.com which develops web tools that simplify the whole 3D printer process for amateurs. At the same time, Makerbot Industry founded by Bree Pettis, launched Makerbot Cupcake CNL for individuals, so other actors became involved in the field of 3D story printers. The RepRap (Rapid Prototyping Replicator) project is a British University of Bath project to create a partially auto-replicative 3D printer (ie without patents and with plans available free of charge for everyone on the internet). The first operating model, Darwin, released in 2007, was fully open source, allowing passionate users to assemble and improve it at home.

The real take off of 3D printing occurred in 2011, when 15 000 3D printers were sold among the 40 models that are already available in the market. From 2014, 3D printing evolved from the instant manufacture of household objects to generating organic tissues from cellular bases. The reality is that we can already do things that look like science fiction. We are at the forefront of the third industrial revolution in history (Mora, 2015).

The third-dimensional (3D) printing will cause a new industrial revolution in the following years, so HP Inc. will focus on this market from 2016, and Mexico will be part of the countries that have this technology first (Hernández, 2015 ).

Overall objective: to demonstrate that the 3D Bioprinter will have a positive impact as an innovation tool in the future of organ transplants.

**Documentary methodology**

Documentary research is a technique that consists of the selection and compilation of information through the reading and critique of documents and bibliographic materials. Franklin (1997) defines documentary research as a research technique in which to select and analyze those writings that contain data of interest related to the study.

The development of a complete documentary research process gives as a product different types of documentary works, among which are compilations, essays, evaluations, comparative studies, reports, monographs, among others (Baray, 2015).

In carrying out this research process, a project was developed that communicates with clarity and coherence the results, discoveries, checks or reflections achieved throughout the documentary research process (Rivera, 2008).

**Materials and methods**

The information necessary for the development of this article is taken from the collection of theses, research from technological institutions and scientific articles dealing with the subject. The methodology to be used is documentary since the information is selected from different sites by means of the reading of documents, materials. A discussion point is presented later through a process (Martínez, 2002).

**Definition of innovation**

It is established that innovation is the introduction of a new or significantly improved product (good or service), a process, method of marketing or a new organizational method to market and society (Schumpeter, 2005).

Innovation is also defined as the process that allows to combine skills and techniques in order to give novel solutions to particular problems (Fagerber, 2005).

**What is organ transplantation?**

It is a medical treatment indicated when every other alternative to recover the patient's health has been exhausted, which is only possible thanks to the will of the people who give their consent to the donation. It is the replacement of a vital organ diseased, without possibility of recovery, for a healthy one. The organs that are transplanted in our country are: kidney, liver, heart, lung,

pancreas and intestine. Organ donation is possible only in 5 out of 1000 deaths due to the complexity of the requirements needed to carry it out; Can only be realized if death happens in an intensive care unit and immediately requires a series of coordinated steps simultaneously (Proyecto Salud, 2013).

**Definition of 3D Printer**

A 3D printer is a device capable of generating a solid three-dimensional object by (and therein lies the main difference with traditional production systems) the addition of material. Traditional production methods are subtractive, that is, they generate forms from the removal of excess material. Printers are based on 3D models to define what to print. A model is no more than the digital representation of what we are going to print using some modeling software (Chimbo, 2016).

**3D Bioprinter definition**

3D printing allows, for some years, to manufacture objects by delicately stacking resin or plastic layers. Biologists had the great idea of replacing plastic with cells to create organic structures; The function is the same 3D printing, only it prints human tissues and organs.

The printing process uses a medical polymer, inorganic materials and water gel mixed with living cells, all together under aseptic conditions resulting in a tissue with 90% of living cells that have been able to stay alive for up to four months (Gaona, 2014).

**Print in 3D.**

This is a technology owned by architects and engineers who fulfilled their dream of materializing their designs directly from the computer, with printers that layer layer by layer the desired material in the right place. Now, from model to organ, there is a long stretch, but not long enough to prevent Mironov and Dr. Gabor Forgacs from the University of Missouri in the United States adapting this technology to regenerative and transplant medicine (Carnevale, 2010).

The 3D bio-printer will be used in hospitals, laboratories, institutes and universities, and will be as essential as today is an electronic multimeter for a baker's oven (Garcia, 2015).

This is due to the possibilities offered by these machines in terms of biofabrication. Some of the immediate applications are described below.

- ✓ Manufacture of crop drops.
- ✓ Manufacture of cellular scaffolds with variable porosity and morphology.
- ✓ Manufacture of three-dimensional structures with multiple fluids.
- ✓ Direct printing of living cells embedded in biocompatible fluids (García, 2015).

**What is 3D Printing?**

Bio-printing is a technique that focuses on the identification of structures and elements that make up specific fabrics and, based on it, on the creation of a design that can generate laboratory fabrics through specialized bio-presses. Once the design is in place, the next step is to develop the bioprocess protocols required to generate several cell blocks, also known as biotins, that will be used to construct the tissue, supplanting the plastic polymers of conventional 3D printers.

The blocks of biotins are created from a bio-printer, which layer by layer will develop the final tissue in the manner of a nursery where the cellular material will grow. Components such as the hydrogel are used as a support of the tissues to vertically construct the three-dimensionality, or serve as filling material for channels or voids within the tissues. Bio-printing processes can be adapted to a wide variety of formats, from tissue to micro-scale to the cultivation of larger structures (Gaona, 2014).

**How does a 3D Bioprinter work?**

The impression of human organs has several stages. First, scientists take tissue samples or stem cells from the patient, which are grown in the laboratory expecting them to multiply. These cells are then transformed into a kind of biological ink, which is used in bioprinting. The printers are programmed to create different organs, all tailored to what the patient requires. A model of these cells, already differentiated for their use, is printed in third dimension, and then implanted in the human body, waiting for them to merge with the existing cells, replacing the organ that fails.

An organ is not printed as we know it, but it is a set of cells capable of performing processes that are not functioning by organ failure. It includes two printer heads, one to place human cells and the other to place a hydrogel, frame or support matrix. The cell print head forms the cells in drops of 100 μm- 500 μm in diameter, each with 10 000-30 000 cells (Valenzuela, 2014).

The droplets retain their shape well and pass easily through the inkjet printing process. The second injection head is used to deposit a sugar hydrogel used as a scaffold, which does not

interfere with or adhere to the cells. Once the impression is complete, the structure is left for a day or two to allow the droplets to fuse. For tubular structures such as blood vessels, the hydrogel is printed at the center and outside of the ring of each cross section before the cells are added.

A computer-controlled laser-based calibration system is used to repeatedly position the capillary tip attached to the printer head, ensuring that the cells are positioned in exactly the correct position within a tolerance micrometer. The 3D bio-printer includes a software interface that allows engineers to construct a model of tissue construction before the printer begins the physical constructions of organs, cell by cell (Valenzuela, 2014).

**The challenges of 3D Bioprint**

In theory it sounds good, but the challenges are not easy. José Becerra, Professor of Cell Biology at the University of Málaga and scientific director of the Andalusian Center for Nanomedicine and Biotechnology (BIONAND), echoes the difficulties to be solved.

- ✓ On the biological side there is technology and knowledge, based on stem cells and the science of materials. That is to say, there are the materials, the cells and the possibility of cultivating them, only remains to be combined.
- ✓ In order to do this, it is necessary to calculate precisely how the process is carried out, what is the appropriate moment to start it, how much cells to inject, or how much time is being cultured in the laboratory before being implanted. It is also essential to be very clear how the cells are fed at the time the piece is being cultivated in the laboratory. This is a basic question.
- ✓ The cells have to live every minute and therefore every minute they have to reach nutrients. The arrival of nutrients in a 3D system is complex because they have to traverse by diffusion that 3D structure. This is only possible with machines called bioreactors, which are able to include nutrients in a liquid. Bioreactors introduce oxygen, and remove carbon dioxide and other remains from cell metabolism. This is necessary from the start of the culture until it is implanted in the human body.
- ✓ Those cells that have so far fed into the bio-reactor now have to be fed into the recipient organism. This means that the blood of the organism has to reach all those cells that have

lived so far in an environment specially designed to keep them alive, explains the scientific director of the BIONAND center.

- ✓ To achieve vascularization, the creation of blood vessels that carry the nutrients to the implanted cells is the real challenge. Cells can be grown on different substrates in the laboratory, as well as promoting the creation of small blood vessels (Bejerano, 2014)**.**

**Advantages and Disadvantages of 3D Bioprinters**

**Advantage**

- ✓ Versatility. The revolution that is assumed for the manufacture of products. A single 3D printer is capable of making a myriad of different products. Much of the current manufacture is made with specific machines whose function is limited and if the product changes the machine must also be adapted or changed.
- ✓ Flexibility and rapid prototyping. The limit is the imagination and the ability to represent your ideas in 3D. It allows to realize prototypes of products with facility, which can imply an improvement in the design of these.
- ✓ Cost reduction. Both in the production process and in the transportation process. Production can be done from home.
- ✓ Customization. One of the most attractive advantages is the possibility of making your own clothes, products, objects in a personalized and exclusive way.
- ✓ New industry and industry. New industry and new sector that will create new forms of business.
- ✓ Multiple applications yet to be discovered. In the field of medicine we find surprising applications, for example, the creation of prosthesis or even the printing of organic tissues Article on tissue printing. 3D printing has a lot of field to go and will increasingly be applied in more fields.

**Disadvantages**

- ✓ Vulnerates copyright. Replication of copyrighted objects will be difficult to control as 3D scanners allow replication of any object.
- ✓ Malicious uses. Unfortunately there is the possibility of creating objects such as firearms and the danger of generalizing such objects.

- ✓ Increase of useless products. Admittedly, I myself can make a commitment to make some 3D model, I can make it prettier or uglier, but the question one has to do before getting to print anything is: will it serve me for something? (Mejía, 2016)**.**

**Ethical Concerns about 3D Printing**

- ✓ However, not everyone is comfortable with the new ability to create human parts in a laboratory.
- ✓ A research director at Gartner Inc., the research and information technology consulting firm, believes that 3D bio-printing is moving so fast that it will spark a full-scale ethical debate in 2016.
- ✓ Facilities dedicated to 3D bioimpression of human organs and tissues will advance much faster than the general understanding and acceptance of the ramifications of this technology, Pete Basiliere said in a recent report.
- ✓ These initiatives have good intentions, but they generate a number of questions that remain unanswered, Basiliere added. Who will control the ability to produce them? Who will ensure the quality of these products?
- ✓ These bioprinted organs are likely to be costly, which would make them out of reach of all but the richest patients.
- ✓ Murphy said that Organovo only uses human cells to create tissues, and sees no ethical problem with its company's activities.
- ✓ People used to worry about doing body research and that ended quickly.
- ✓ They believe the next step will be the printing of tissue strips, or patches, that could be used to repair damaged livers and other organs.
- ✓ Of course, any use of bio-printed tissues in surgical procedures would require the approval of the FDA (Food and Drug Administration of the United States). By then, the notion of a surgeon using a bioprinted kidney in a patient would no longer be something so strange. However, this technology could create new moral questions.

Ethical questions are meant to be the same concerns we have seen in the past. Many medical advances have undergone moral resistance, from organ transplants to stem cell research. Will only the rich be able to access this? Are we playing to be God? In the end, saving lives tends to triumph over any objection (Griggs, 2014).

The predictable impact of 3D printing on medicine is one of the main factors that invites us to believe that it will be possible to create organs and tissues that are compatible with the recipient from cells obtained from the patient. Proof of this are the teams capable of producing living liver tissue, which are already a reality, as shown in the catalog of the American company Organovo, one of the leaders of the sector (Prats, 2013).

Methods and techniques that give favorable results to this innovative technology, called Bioimpresora 3D

We show the few transplants of this type that have been performed to date, when there is no alternative and technology is used as a last option.

The case of Hannah Warren, a two-year-old girl who suffered from a rare disease (congenital tracheal agnesia), was very upset that prevented her from feeding on her mouth, speaking or breathing normally because her trachea had not developed. She was the youngest person in the world to receive a bioartificial tracheal transplant, from plastic fibers to which were added the girl's own cells extracted from her bone marrow. This happened on April 9, 2013 (the person responsible for the intervention: Paolo Macchiarini (Tardón, 2016).

In the words of Julio Acero, head of the Oral and Maxillofacial Surgery Service of the Ramón y Cajal University Hospital in Madrid, the progress of Atala and his colleagues consists of a combination of three-dimensional printing with tissue engineering. At present, three-dimensional printing is routinely used in our anaplastology workshop, to make cranial implants, reconstruction of guides to repair the jaw, plaques to fix the flaps. The aim of combining cell growth with 3D printing, adds this specialist, is to give a more lively structure to the organ, in this case the ear, with its skin, its cartilage (Tardón, 2016).

Atala himself emphasizes that the new technology would allow the production of living tissues and organs for surgical implantation. The ear is not the only artificial organ with which you are working in the laboratory, other prototypes of kidneys, bladders, skin, bones, heart are being created. Although we are in an initial phase, Becerra argues, bioprinting is a very promising way. Without a doubt, regenerative medicine for the creation of organs is a very hopeful option, which in the future could benefit the patients who are waiting for a transplant (Tardón, 2016).

This promising method is not the only one that is being worked on in the laboratory to reduce transplant waiting lists and avoid rejection. Among other utilities, there are two other formulas that could also be successful in the future, the decellularization of organs and the use of animal organs, the first technique there is an experience in Stockholm, which consists of the washing of organs to remove the cells of the Donor and thereby avoid an immune response of the recipient patient upon receipt of the implant. As for the use of animal organs, the name of the Spanish Juan Carlos Izpisúa is key, this scientist conducts an investigation that aims to develop human organs inside pigs. The project is being carried out on a farm in Murcia (Tardón, 2016).

A group of surgeons at a New York hospital has highlighted the relevancy of having the ability to print a 3D heart to save the life of a small two-week-old baby who needed to undergo a complicated surgical operation. This group of doctors printed a 3D heart from the data obtained on an MRI of the baby's heart. This organ was badly damaged and that organ reproduction in 3D allowed the doctors to study it and develop a detailed strategy before operating. This is a remarkable advance for congenital heart disease and again demonstrates the ability of 3D printing to be an important element in all types of medical procedures and procedures (Pastor, 2014).

Contribution of the knowledge and understanding acquired during the research on the 3D Bioprinter in the future of organ transplantation

As we could observe in previous research on the methods and techniques of 3D printing in the field of medicine, all the publications that exist on transplants are of positive impact, gave favorable results to the people who submitted to them as a last resort and Knowing that they were created by means of a Bioimpreora 3D.

The real cases are still few, but work is being done to improve them and show society that they can supply an organ donated by another person in an effective and safe way, with the advantage

that it is not likely to be rejected by The receptor body was created with its own cells, giving an almost null percentage of rejection by the body.

The specialists in charge of this new technology show that it is advancing by leaps and bounds every day, and that it comes to change the method of obtaining some organ or part of the body to be transplanted and leave behind the difficult process of enlisting and being accepted as Candidate for some type of organ donation.

**Conclusions**

3D printing is present in almost every area and has proven to have an incalculable future. It makes us visualize the present and ask ourselves about the great importance of this innovative technological tool in our lives.

The conclusion is that the technology of Bioimpresoras 3D will have a positive impact on society, because thanks to its use can save millions of lives with the creation of organs, Some parts of the body may be replaced with living cells of the patient.

There is still a long way to go as there are obstacles in cellular technologies, bioproduction and integration, which play an important role for the separation of stem cells in transplants. Technological advances are proof that everything is possible and imagination is the only limit.

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