

A new paradigm in health systems, 3D technology

Un cambio en los paradigmas de los sistemas de salud, la tecnología 3D

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Abstract

Al mismo tiempo, el advenimiento de las tecnologías de impresión 3D y las perspectivas de personalización brindan importantes oportunidades de mercado, pero también presentan un serio desafío para los organismos públicos y entidades privadas que intervendrán en las distintas fases de investigación, control y uso de las nuevas tecnologías. The emergence of 3D technology and its application to biomedical models has generated a new approach to the Medicine. Biomedical devices are produced using patient-specific anatomical data. From its initial use as pre-surgical visualization models and tooling molds, the 3D printing has slowly evolved into unique tissue engineering devices, implants, scaffolds, diagnostic platforms, and drug delivery systems. There is a renewed interest in combining stem cells with custom 3D scaffolds for custom regenerative medicine and a high potential in custom tissue and organ design, or for drug detection in an appropriate anatomical structure and a patient-specific biochemical microenvironment. Achievements in the application of 3D in Medicine are described, and its revolutionary use that will allow, among others, reducing operating time, reducing input costs, as well as making more precise surgical maneuvers possible, lowering the risk of bleeding and infection. At the same time, the advent of 3D printing technologies and customization prospects provide significant market opportunities, but they also present a serious challenge for public and private entities that will intervene in the different phases of the research, control and use of new technologies.

Method: In the characterization of the research phenomenon, the descriptive study, the collection of documentary data and the correlation between the different sources were used.

Keywords: 3D printing, bioprinting, vascularized tissue, regenerative medicine.

Resumen

El advenimiento de la tecnología 3D y su aplicación a modelos biomédicos ha generado un nuevo enfoque de la medicina. Se producirán dispositivos biomédicos utilizando datos anatómicos específicos del paciente. Desde su uso inicial como modelos de visualización prequirúrgicos y moldes de herramientas, la impresión 3D ha evolucionado lentamente hasta crear dispositivos, implantes, andamios únicos para ingeniería de tejidos, plataformas de diagnóstico y sistemas de administración de medicamentos. Existe un renovado interés por combinar células madre con andamios 3D personalizados para la medicina regenerativa personalizada. Y un alto potencial en el diseño de tejidos y órganos personalizados, o para la detección de drogas en una estructura anatómica apropiada y un microambiente bioquímico específico para el paciente. Se describen logros en la aplicación de 3D en Medicina, y su uso revolucionario que permitirá entre otros, reducir tiempo de las operaciones, disminuyendo los costos de los insumos, además de posibilitar maniobras quirúrgicas más precisas, bajando el riesgo de sangrado, y de infección. Al mismo tiempo, el advenimiento de las tecnologías de impresión 3D y las perspectivas de personalización brindan importantes oportunidades de mercado, pero también presentan un serio desafío para los organismos públicos y entidades privadas que intervendrán en las distintas fases de investigación, control y uso de las nuevas tecnologías.

Método: en la caracterización del fenómeno de investigación se empleó el estudio descriptivo, de recolección de datos documental y la correlación entre las distintas fuentes.

Palabras clave: impresión 3D, bioimpresión 3D, tejido vascularizado, medicina regenerativa.

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Introduction

The 3D printing, a term introduced to the Medical Subject Headings (MeSH) terminology in 2015, promises to produce complex biomedical devices according to computer design tailored to specific patients. Since its initial use as pre-surgical visualization models and tool molds, the 3D printing has slowly evolved to create unique tissue engineering devices, implants, scaffolds, diagnostic platforms, and medications (1).

The 3D printing technology is simple, it relies on the evolution of spraying toner on paper to

smother layers of something more substantial (such as a plastic resin) until the layers are added to an object, allowing a machine can produce objects in any shape, anywhere, and as needed; the 3D printing is ushering in a new era (2).

The first attempts at 3D printing date back to 1980, thanks to the Doctor Kodama who was the inventor of the "layer by layer" approach. In 1981, Hideo Kodama, from the Nagoya Municipal Institute of Industrial Research, obtained the first patent by inventing two additive manufacturing (AM) methods of a three-dimensional plastic model with a photo-hardening polymer, in which the area of

exposure to ultraviolet rays it was controlled by a mask pattern or fiber-optic transmitter (3).

In 1986, Charles W. Hull invented the Stereolithography Printing (SLA). This 3D printing technique refers to a method of printing objects layer by layer using a process in which lasers selectively bind the chains of molecules together, forming polymers. The following year he will patent printing using this system, and in 1986 he will found his own company, 3D Systems.

In 1987, at the University of Texas, Carl Deckard created a patent for Selective Laser Sintering (SLS) technology, another printing technique in which dust grains are fused locally using a laser. Scott Crump, co-founder of Stratasys Inc, a world leader in 3D printing, enrolled a patent in 1988 for Fused Deposition Modeling (FDM), some of the classes of materials being ABS and SLA printing. With these as the main techniques, in less than ten years, the 3D printing was born (4).

Among the countless milestones, and when it comes to bio printing, the 2014 was a year of many announcements. The researchers at the University of Sydney were able to print small fibers that were later covered with human endothelial cells, obtaining a hollow vascular network. This would allow the organ cells to be printed around these networks, achieving adequate blood flow to keep the printed tissue alive. This research is essential for the future of printed organs (5).

This brief introduction brings us to the objective of this study, which is, firstly, to describe some of the many applications of the 3D printing in Medicine, and secondly, to determine the development and expansion perspectives of this new technology, with an analysis of detail of its use in surgical planning and pharmaceutical innovation.

Methods

In the characterization of the research phenomenon, the descriptive study of documentary data collection was used. The research was divided into two stages: first, data collection was carried out through Google Scholar; In the case of general texts, specialized notes were taken into account to assess the degree of progress in the use of constantly changing technology. In the second stage, data analysis

and interpretation were carried out.

Discussion

It has been observed that, of all the professional fields, the medicine is the sector where innovative uses are made of the 3D printing technologies. It is common for this technology to be used to create synthetic simulators, so that both students and doctors can acquire manual skills, specific pathologies of patients can also be replicated to train with real cases. The medical images are converted to 3D files, the DICOM files (Digital Imaging and Communications in Medicine) are sent directly to the Computed Tomography (CT) or Magnetic Resonance (NMR) equipment and through software, and these images go through a segmentation process, being the STL (Standard Tessellation Language) format that allows obtaining a 3D model (6).

Precisely in the medical field where this technology of addition printing has evolved to bio printing, which includes a process of cell culture in the laboratory, making it possible to form organs and / or personalized tissues. Of interest is its application in the creation of anatomical models, prototypes, personalized prostheses, among many other medical applications (7).

Another alternative is the use of stem cells that can be transformed into different cell types through the use of specific nutrients and growth factors. However, moving from 3D tissues to the entire organ is still a possibility in the future. Achieving the development of blood vessels is one of the pending challenges. It is vital for the cells that integrate the tissue to receive their nutrients and to eliminate metabolic waste. On the other hand, the degree of cell proliferation (division) has to be finely controlled (8).

In 2014, the Institute for Cardiovascular Innovation at the University of Louisville (USA) predicted that by 2023 they would be in a position to have bio printed hearts. The fundamental problem of providing organs with adequate functionality has not yet been solved, and today the scientists are working with a focus on the subject (9).

Although avascular tissue grafts can provide a measurable improvement in organ function by implanting them, the bio manufacturing of three-dimensional (3D) grafts and, ultimately,

the large-scale organs will inevitably require a perfusable vascular network. The 3D vascularized tissues have recently been manufactured through multimaterial 3D bio printing and stereolithography, although they lack the cell density and microstructural complexity necessary to achieve physiologically relevant levels of function (10).

To produce thick vascularized tissues that fully match the patient remains an unsatisfied challenge in cardiac tissue engineering (11).

The regenerative medicine (term introduced to the MeSH in 2004) is another application that is defined as the field of the medicine related to the development and use of targeted strategies that aim to repair or replace damaged, diseased organs, tissues and cells or metabolically deficient through tissue engineering, cell transplantation, or artificial or bioartificial organs and tissues (12).

Definitely, the research on the 3D printing technology for medical applications could be summarized in the following four main focus areas:

- a) The research on the fabrication of pathological organ models to assist in preoperative planning and analysis of surgical treatment;
- b) The research on custom fabrication of non-bioactive permanent implants;
- c) The research on the manufacture of local bioactive and biodegradable scaffolds;
- d) The research on the direct impression of tissues and organs with complete vital functions (13).

Inside the item a) the biomodels constitute exact replicas of the patient's internal anatomy that simplifies the planning of surgeries. The biomodels are employed using the patient's medical images, both magnetic resonance imaging (MRI) and computed tomography (CT).

The operator can analyze and test the available variants to decide in advance which technique to use. In this way, valuable information is obtained that allows surgery to be performed with greater certainty.

In this way it is possible to plan approaches or train the intervention by repeating with printed models the same steps that will be performed during the operation. The advances in three-dimensional reconstruction of radiological

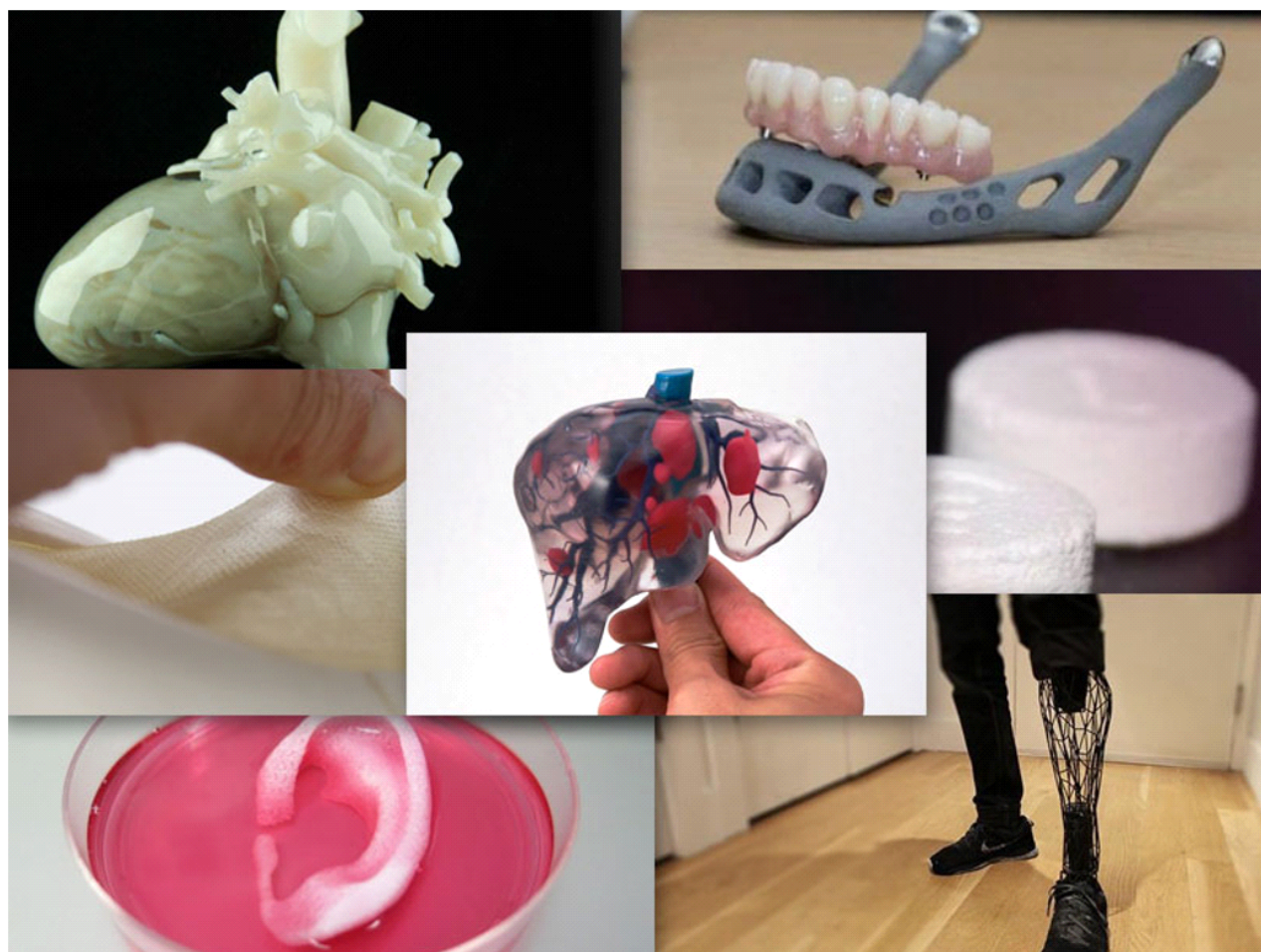
images have made virtual tools available for surgical planning (14).

Traditionally, the evaluation of patients with maxillofacial fractures, deformities and tumors in which the resection and / or reconstruction may involve bone tissue, includes imaging studies such as conventional X-rays (Rx), computed axial tomography (CT)), nuclear magnetic resonance (NMR), among others. Not so long ago, it was only possible to obtain low resolution images with Rx in a two-dimensional plane. Currently, the resolution achieved and the possibilities of obtaining three-dimensional images have made these methods an almost indispensable tool in the diagnostic evaluation, in the planning and in the execution of the treatment of these patients (15).

The previous simulation of all complicated surgical steps using prototype models can help to predict intra and postoperative complications. This can result in a reduction in the time during the surgery that allows a more profitable use of the operating rooms not only in terms of occupation but also in the consumption of supplies and hours of medical and paramedical equipment during the surgical act. In the figure 1 we can observe some structures printed with 3D technology, these devices are currently available.

It is important to mention another important development that is the pharmacological innovation. The development of high-performance 3D bio printed tissue models is already applied in the research, drug discovery, and toxicology (16). The process of the 3D printing can be applied with good expectations to create drugs since it involves the use of robotically controlled syringes, so that drugs can be constructed using a bio tint with a gel texture, where the chemicals and catalysts are mixed. In the future, a doctor could formulate a tablet containing the exact combination of medications to treat a unique condition, and print it using a 3D printer that contains multiple nozzles with a different ingredient in them and the printer precisely sets each material by tiny drops (17). An attractive, but unexplored, application is to use a 3D printer to initiate chemical reactions by printing the reagents directly on a 3D reaction software matrix, and thus put the design, construction and operation of the reaction equipment under digital control (18).

Figure 1: Example of printing 3D structures



Source: <https://impresiontresde.com/cosas-impresion-3d-medica-puede-hacer-ya/>

Discussion

The examples we have mentioned show that we are in an expanding market, with a horizon not yet defined in its medical applications, one of the great pending aspects being to achieve a perfusable vascular network. On the other hand, high profitability is expected, either due to savings and the best use of available resources. It has been possible to verify through different companies that offer this type of products, the Gross Margin that is applied on the cost of materials ranges between 90 and 95%, even reaching some 97% for some objects.

According to the new market research report developed by 3D Bioprinting Market by Component based on a Global Projection to 2024 and published by Markets and Markets TM, the 3D Bioprinting Market is projected to reach \$ 1,647 million in 2024 from \$ 651 million in 2019, at a CAGR (Compound annual growth

rate) of 20.4% from 2019 to 2024.

This technology is aimed at a wide audience definitely linked to the new technologies; the scientists, businessmen, engineers and doctors, legislators, public and private organizations, and potential users with the intention of reporting on the advancement of the 3D applications in medicine, identifying open and ongoing issues, and open new and great economic perspectives for the Health sector affected actually by the sustainability factor.

Conclusions

The study and debate on the importance of incorporating 3D technology into immediate medical care is currently open, as well as evaluating the associated ethical challenges, legal measures that include patents and effective controls to prevent inappropriate use, as well as the social aspects that they derive from the cultural, religious and economic

differences that will ultimately determine the success of this technology (19).

The public and private social security systems of each country must also carry out a risk-cost-benefit analysis, which today is not yet fully defined but the results are expected to be very good. We are facing a technology with great potential and high growth, although it has the limitation of being a new market, unknown to part of potential investors, and in need of capital for research and development (R&D).

Conflicts of interests

The author declares that he has no conflicts of interest.

References

1. Chia HN, Wu BM. Recent advances in 3D printing of biomaterials. *Journal of Biological Engineering*. 2015; 9:4.
2. D'Aveni RA. The 3D printing revolution. *Harvard business review*. 2013; 91(3): 34-35.
3. Kodama H. Automatic method for fabricating a three-dimensional plastic model with photo-hardening polymer. *Review of Scientific Instruments*. 1981; 52(11): 1770-3.
4. García Villegas C., Vidarte Pastrana M. Estado del arte de la bioimpresión 3D. Colombia: Fundación M3D, 2011..
5. Ministerio de Ciencia, Tecnología e Innovación Productiva. Estudio de vigilancia tecnológica e inteligencia competitiva en tecnologías de impresión 3D para alimentos. Buenos Aires; 2015. Recuperado de: <http://www.mincyt.gob.ar/estudios/estudio-de-vigilancia-tecnologica-e-inteligencia-competitiva-en-tecnologias-de-impresion-3d-para-alimentos-11655>.
6. Gerke BA, Yamashita AL, Sigua-Rodriguez EA, Olate S, Iwaki LC, Vessoni, I, Filho L. Análisis Descriptivo y Cualitativo de Tres Software Gratuitos Usados para la Conversión de Formato DICOM para STL. *Int. J. Odontostomat*. [Internet]. 2019 Mar [citado 2020 Abr 28]; 13 (1): 103-111. Disponible: https://scielo.conicyt.cl/scielo.php?script=sci_arttext&pid=S0718-381X2019000100103&lng=en&nrm=iso&tlng=en.
7. César Juárez AAC, Olivos Mezad A, Landa Solíse C, Cárdenas Soria VH, Silva Bermúdeze PS, Suárez Ahedog C, Olivos Díaz B, Ibarra Ponce de Leóni JC. Uso y Aplicación de la tecnología de impresión y bioimpresión 3D en Medicina. *Revista de la Facultad de Medicina de la UNAM*. 2018; 61 (6): 43-51.
8. Bazan, S. Impresión 3D de órganos, la próxima frontera. [Internet]. Bitácora digital. 2(6); [2015]. Disponible en: <https://revistas.unc.edu.ar/index.php/Bitacora/article/view/12805>
9. Ozbolata I, Gudapatia H. A review on design for bioprinting. *Bioprinting*. 2016; 3: 1-14.
10. Skylar Scott MA, Uzel1 SGM, Nam LL, Ahrens JH, Truby RL, Sarita Damaraju S, Lewis JA, et al., Biomanufacturing of organ-specific tissues with high cellular density and embedded vascular channels *Sci. Adv*. 2019; 5 (9).
11. Noor N, Shapira A, Edri R, Gal I, Wertheim L, Dvir T. 3D Printing of Personalized Thick and Perfusable Cardiac Patches and Hearts, *Adv. Sci*. 2019; 6 (11).
12. Pub Med-MeSH Major Topic. "Regenerative Medicine". [Consultado: 25-agosto-2017]. Disponible en: <https://www.ncbi.nlm.nih.gov/mesh/?term=Regenerative+Medicine>
13. Yan Q, Dong H, Su J, Han J, Song B, Wei Q, Shi Y, A Review of 3D Printing Technology for Medical Applications. *Engineering*. 2018; 4(5): 729-742.
14. Perez Mañanes R, Calvo-Haro J, Arnal Burro J, Chana Rodríguez F, Sanz Ruiz P, Vaquero Martina J. Nuestra experiencia con impresión 3D doméstica en Cirugía Ortopédica y Traumatología. *Rev. Latinoam. Cir. Ortop*. 2016; 1 (2): 47-53.
15. Mantrana G, Jacobo O, Hartwing D, Giachiero V. Three-Dimensional printing models in the preoperative planning and academic education of mandible fractures. *Cir. plást. Ibero-latinoam*. 2018; 44 (2): 193-201.
16. Murphy S, Atala A. 3D bioprinting of tissues and organs. *Nature Biotechnology*. 2014; 32 (8): 773-85.
17. Bucco, M. La impresión 3D y su aplicación en los servicios médicos (prótesis, fármacos, órganos). Buenos Aires: Repositorio Digital San Andrés: 2016.
18. Symes M, Kitson P, Yan J et al. Integrated 3D-printed reaction ware for chemical synthesis and analysis. *Nature Chem*. 2012;

- 4: 349-354.
19. Vijayavenkataraman S, Lu WF, Fuh JYH.
3D bioprinting – An Ethical, Legal and Social

Aspects (ELSA) Framework. 2016; 1–2: 11-21.