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Analysis of the bioprinting market in Brazil and its status in the global scenario

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Abstract: Additive manufacturing (AM) is a constantly growing manufacturing technique that can be used from the prototyping stage to the final product in several industries. 3D bioprinting is a variant of conventional AM that uses bioinks, i.e., inks with the presence of cells, to manufacture living biological structures. These structures can be used in applications in the medical field and with therapeutic potential, such as the fabrication of tissues and organ models, drug testing, among others. Considering its importance in the global scenario, this work aimed to evaluate the growth related to 3D bioprinting research in Brazil and in the world, and to analyze the Brazilian market compared to the global panorama. For this, qualitative research, literature search in research bases, and the search for patent records were used. The exponential increase of studies in the area was identified, through graphs with trend lines, exposing its enormous potential for development. It was possible to perceive the notable advance in the use of bioprinting worldwide, as well as in Brazil, a leader in research in the area in Latin America, although it is still lagging behind other countries, occupying the twentieth position worldwide in scientific contributions.

Keywords: 3D bioprinting. Biofabrication. Additive manufacturing. Biomaterials.

Introduction

The development of new technologies and solutions in the health area becomes increasingly necessary, since this area is evolving, in recent years, to a more customized approach[1]. Additive manufacturing (AM) represents a progress in this area, since this technique allows a customized production. A variation of this technique is 3D bioprinting, differentiated by the use of bioinks for 3D printing, which are materials composed of cells. Bioprinting can be used to manufacture three-dimensional living structures that mimic the human body [2,3].

Bioprinting may be used for several purposes, such as the manufacture of prostheses, assistive devices, organ models, among others. There is a recurrent shortage of tissues and organs in human tissue banks, which has a tendency to increase in the next years, highlighting the need for an alternative for the development of materials and equipment for this type of shortage. Thus, one of the main purposes regarding biomedical applications, in the long term, is the biofabrication of functional organs, which aim to be used in transplants[4,5].

Although research in the field of bioprinting advances exponentially each year, the development of structures with complex functionalities, shapes, and sizes is still a challenge[6] and therefore the evaluation of suitable techniques for biomanufacturing is essential. Currently, the main bioprinting deposition approaches include inkjet; extrusion; stereolithography; and laser-assisted. Each of these different techniques has specific properties and limitations, to be used depending on the desired characteristics of the final printed structure[4,5].

In addition to using the appropriate technique, the choice of materials is also of enormous importance. The ink used for bioprinting is called a bioink, and cellular material is an obligatory component. In addition to cells, the bioink may contain biomaterials, in order to amplify its printability properties[7]. Hydrogels are the most used type of biomaterial, because they are polymers that have a good interaction with water, providing cell viability, besides presenting a good crosslinking factor, essential for bioprinting[8].

Regarding the bioprinting scenario, it began in the mid-1980s, with the advent of 3D printing, but it was in 2004 that there was a major milestone in the area with the fabrication of the first three-dimensionally bioprinted bladder, made from autologous cells[9,10]. However, it was only around 2015 that Brazil experienced a boom in this market, with the opening of the first companies and startups in the area of bioprinting, which opened doors to the current context, in which the country is in constant development, both in relation to research and the number of companies present in the country[11]. Thus, this work proposes to assess the research advances in the area of 3D bioprinting, as well as analyze the insertion of the Brazilian market in the global context in relation to this area.

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Methods

Research Mapping

Initially, in order to analyze the general panorama of research on bioprinting, a comprehensive search on the subject was conducted. In order to obtain all the results referring to the growth of the area, the period of publication was not limited, and the term "bioprinting" was applied to all the fields of work in the databases. The searches were performed in Science Direct, Scopus, and Web of Science, through institutional access via the CAFe (*Comunidade Acadêmica Federada*) service of the CAPES Periodicals platform.

Intellectual Property Search

To identify the registration of patents in the field of bioprinting, a metric related to innovation, a search was conducted both in the national database of the Brazilian National Institute of Industrial Property (INPI), as well as in the international databases World Intellectual Property Organization (WIPO), a global entity composed of 187 member states, and European Patent Office (EPO), a European institute.

Table 1 shows the terms used for the search in these databases, and the same terms used in the international databases were used for the INPI search, only translated into Portuguese, except for the term "tissue engineering", which was removed because it returned many results outside the scope. To ensure that all data involving the area of bioprinting would be identified, the Boolean operator OR was used, returning records containing any of the search terms.

Table 1 – Approach used for patent search.

Database	Search Terms	Observations
INPI	*bioimpressão 3D*; *engenharia de tecidos*; *bioimpressão de tecido*; *bioimpressão*; *biofabricação*	Due to the limitations of the platform's search tool, each term had to be searched separately. Search applied to the record title.
EPO	3D bioprinting; tissue bioprinting; bioprinting; biofabrication	Search applied to all text fields, in English, French and German.
WIPO		Search applied to all text fields.

Source: Own elaboration.

Brazilian Market Mapping

In this phase, qualitative research was used to map Brazilian companies and startups in the bioprinting industry, through the companies' own websites. This was necessary, since this is a type of data that is not unified in any database. For this, search platforms and social networks were used, since these represent the main means of dissemination of these companies, being the websites: Google, LinkedIn and Instagram. For this purpose, searches were made using the terms "company/startup + bioprinting".

Also, as a model for the representation of this data, a 2019 study conducted by Dr. Mayasari Lim[12] was used as a basis, in which she sought to map all companies in the bioprinting industry. The classification of Brazilian companies and startups was performed in a similar manner to that done by Dr. Lim, by area of activity, but adding the category of "education/training".

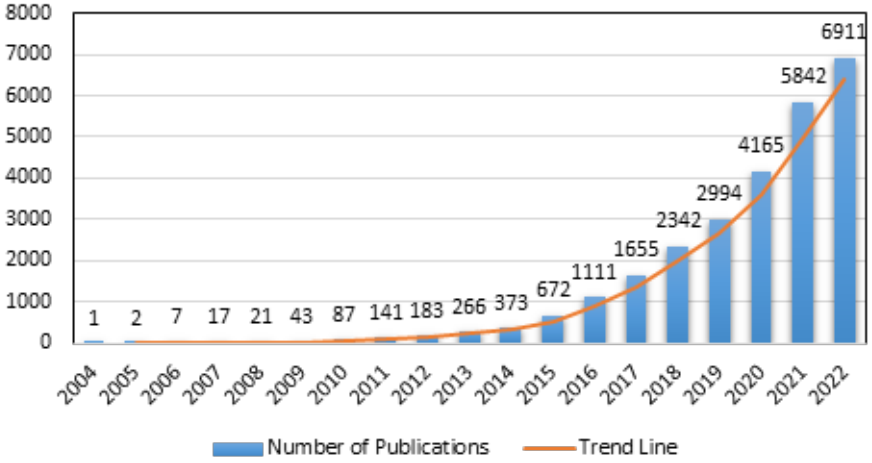
Results and Discussion

Bioprinting Publications

The Scopus database was chosen for this analysis because it returned a larger number of data, allowing for a more complete study. As it is possible to visualize through Figure 1, a total of 27,091 results were identified, with the first publication dating from the year 2004, referring to a journal article accepted for publication in 2003 and the first work to mention of the term "bioink"[7]. An exponential trend in the number of publications can also be observed, with the highest number for the current year 2022, with 6,911 publications and over 250 papers to be published in 2023. The documents that were analyzed at this stage include: full papers; review articles; book chapters; and papers published in event proceedings.

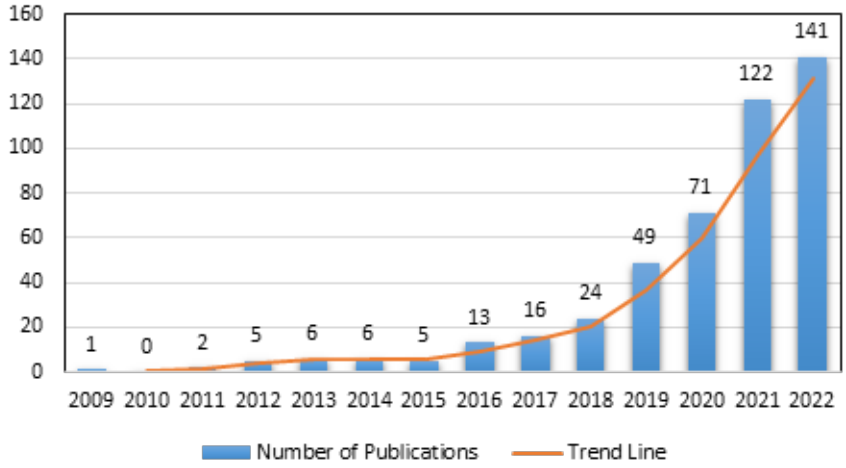
In addition, one can also analyze these documents distributed by the country or territory where the study was conducted, in order to understand the dissemination and encouragement in each region. Brazil is the twentieth country in the descending list of number of publications, and is also the first among Latin American member countries, with a total of 465 publications. The country with the greatest scientific contribution is the United States, with more than 7,000 publications, followed by China, with 6,776 publications. This may show how, still, countries that are considered more economically developed are ahead in the bioprinting research scenario. Leading the number of publications in Latin America, Brazil, when analyzed separately, also presents a behavior of exponential increase in the number of papers, as presented in Figure 2.

Figure 1 – Papers by year of publication in the area of bioprinting (2004 – current).



Source: Scopus.

Figure 2 – Papers by year of publication in Brazil in the area of bioprinting.



Source: Scopus.

Intellectual Property Registrations

Since the process of granting a patent is long and bureaucratic, the numbers regarding the requests for registrations were analyzed. When searching for patent applications related to the area of bioprinting in Brazil, the INPI platform returned 12 results, with the first requested in 2011 and granted in 2018.

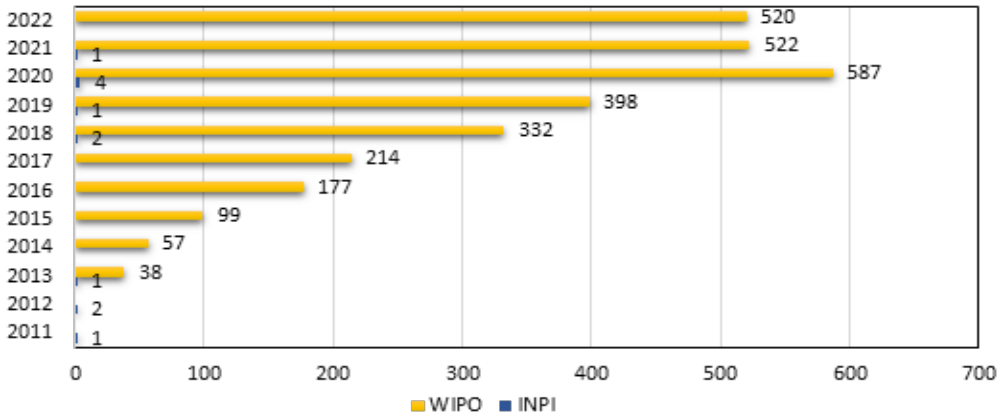
For the searches for international intellectual property records WIPO and EPO returned, respectively, 3,058 and 2,752 results, an expressive number when compared to Brazilian records. Since both platforms group records from several countries, many duplicate records of the same invention can be displayed. In both international bases, it could be observed the publication of dozens of registration requests in recent months, while, when comparing with the Brazilian base, the last patent filing at INPI dates from early 2021.

The WIPO platform also allows an analysis of various components of patent registrations, such as by country and applying institution. When analyzing the registrations by territory, the United States leads with 1,127 applications, while the United Kingdom is the territory with the lowest number of registrations on the platform, with 17 applications. When filtering these results by the applying institutions, one can see that the registrations are divided between companies and research institutions, with the company Organovo Inc. leading the ranking, with more than 100 applications.

It is important to note that when analyzing the records further, one realizes that some records relate to traditional 3D additive manufacturing, rather than 3D bioprinting, but it was not possible to eliminate these results without losing data relating to bioprinting. The same limitation is observed in the EPO platform.

Figure 3 shows a comparison in patent publication between Brazil and the rest of the world, using data from INPI and WIPO. Most patent filings in Brazil occurred in the last 5 years, representing 8 applications, 5 of which are related to the registration of bioprinting machines or bioprinting systems, and methods for bioprinting. Although the Brazilian intellectual property registration database does not contain many patent applications, it is possible to note a change and growth in the number of these, demonstrating the development and increased interest in the area of bioprinting in Brazil.

Figure 3 – Patent registrations published in the area of bioprinting in Brazil and worldwide.



Source: Adapted from INPI and WIPO.

Map of Bioprinting in Brazil

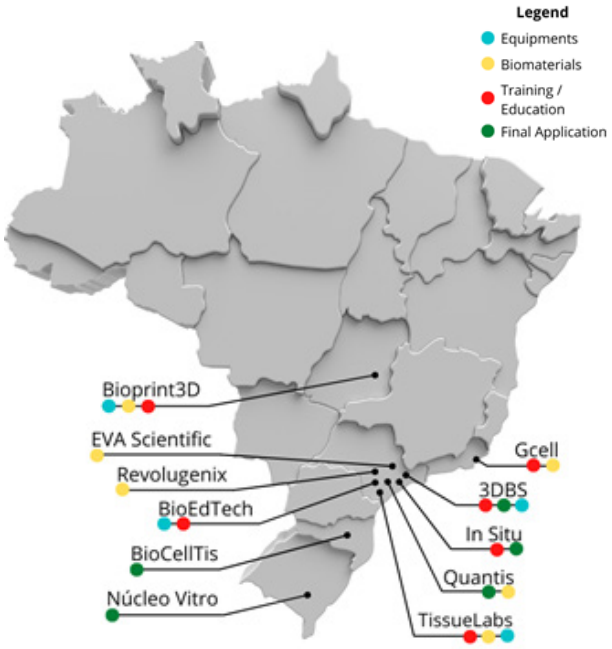
The bioprinting scenario in Brazil is constantly developing, with companies active in the commercialization of equipment and materials, in the development of bioprinted products, as well as training and consulting[11]. With this in mind, we sought to conduct a mapping of companies and startups active in this sector in the country using as a basis the study of Dr. Mayasari Lim, which proposed to map, in 2019, all companies in the field of bioprinting, subdivided by their performance, being them: supplier of tools or hardware; supplier of bioink or materials; and distributor focused on applications[12].

Later, in 2020, the same researcher published an update with new companies that emerged, or that she had left out in the first version. As far as Brazil is concerned, the first version of the map presented only one company, 3D Biotechnology Solutions. In the 2020 version, the scheme has the presence of 6 Brazilian companies[13]. However, as presented through the study by Massaguer and Millás in 2019[11], it is known that Brazil has a larger number of companies and startups active in the area of bioprinting. Therefore, the more in-depth mapping was elaborated for Brazil alone and Figure 4 presents the result of collecting this data. Similarly to Dr. Lim, it was possible to characterize the Brazilian companies in the following categories: suppliers of equipment, such as bioprinters; suppliers of materials, such as hydrogels; suppliers of training; and suppliers of products for final applications, such as biocuratives.

It was possible to identify, currently, 11 companies active in the bioprinting business in Brazil, an expressive number for a relatively new area, but one that points to a notorious room for growth. As illustrated separately through Figure 5, it is possible to observe that most companies work with the offer of training and education and with the supply of biomaterials. There is an overlap of activities, since a company may have more than one area of activity.

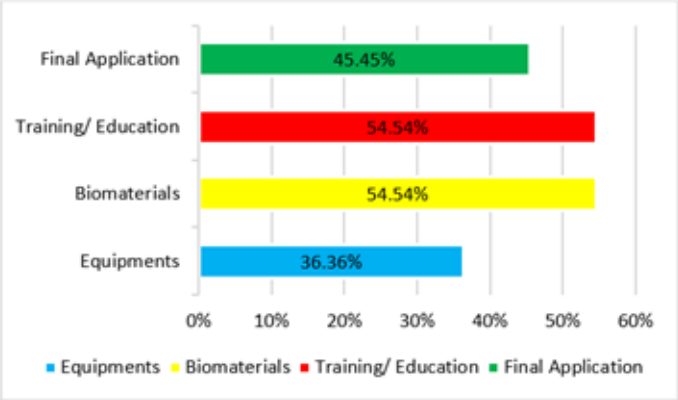
Furthermore, one can notice a tendency for these establishments to be distributed in the southeastern region of the country, a technological hub and a region of high investments in research, with almost 60% of all bioprinting-related companies. Among the 11 companies and startups mapped, only In Situ is not established in a capital, being located in the countryside of the state of São Paulo. It is worth noting that Revolugenix, despite having been created in 2011, has only recently started to operate in the field of bioprinting.

Figure 4 – Map showing the geographical distribution and areas of activity of bioprinting companies in Brazil.



Source: Own elaboration.

Figure 5 – Graphical representation of bioprinting companies' areas of activity in Brazil (%).



Source: Own elaboration.

Conclusion

With the advent of 3D bioprinting, a range of new possibilities have emerged in the area of biotechnology and regenerative medicine. Likewise, the number of researches on the subject has been growing exponentially, and the investments made in the area are increasing every day.

By analyzing the publications and intellectual property registrations, it is possible to notice the remarkable advance in the use of bioprinting worldwide, as well as in Brazil, the leader in research in the area in Latin America, being the twentieth country with the largest number of publications on the subject. The countries that lead this ranking of published works are, respectively, the United States and China, with more than 7 and 6 thousand articles, which can be justified since they are economic powers and invest massively in research.

Regarding patent applications, the international research platforms, WIPO and EPO, returned around 3 thousand results each, while the INPI platform, of Brazilian national search, returned only 12 results. This can be justified by the difficulty found in the international platforms to filter the records related to conventional 3D printing, besides showing several duplicate requests, because they were made in more than one country, while INPI allows a more individualized search, filtering the records more easily. Of this total of 12 requests, 8 were made in the last 5 years.

Through these comparisons, one can see how Brazil is behind the main countries contributing to research and development in 3D bioprinting nowadays. Despite this, the country is in an exponential growth of development, observed through its scientific contributions, which have jumped from 24 to 141 productions per year in the last 5 years.

Furthermore, with the elaboration of the bioprinting map in Brazil, it was possible to visualize the growth of this market, as well as understand in more depth the distribution of companies in this industry and their area of activity. The country currently has 11 companies and startups operating in the area, mostly providing training, with a distribution of almost 60% of these establishments in the southeast region of the country, justified by being a tech hub and research investments center.

Therefore, it was possible to analyze the data concerning the scientific contribution and development in the area of 3D bioprinting today, as well as to observe the context of the Brazilian market in the global panorama. Thus, it is concluded that this is a branch with a significant potential for expansion and great impact on the biomedical sector for the coming years, and it is essential to emphasize the attention and encouragement that research institutions need, especially analyzing the Brazilian scenario.

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