TECHNOLOGICAL MAPPING ON THE USE OF NANOTECHNOLOGY IN MEDICAL DIAGNOSES AND TREATMENTS

MAPEAMENTO TECNOLÓGICO SOBRE O USO DA NANOTECNOLOGIA EM DIAGNÓSTICOS E TRATAMENTOS MÉDICOS

Cleide Ane Barbosa da Cruz*, Universidade Federal de Sergipe (UFS) - Brasil, cleideane.barbosa@bol.com.br

Ana Eleonora Almeida Paixão, Universidade Federal de Sergipe (UFS) - Brasiil, aepaixao@gmail.com

Iracema Machado de Aragão Gomes, Universidade Federal de Sergipe (UFS) - Brasil, aragao.ufs@gmail.com

Helenice Leite Garcia, Universidade Federal de Sergipe (UFS) - Brasil, helenicelgarcia@gmail.com

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Abstract:
Nanotechnology is a science that involves the manipulation of atoms and molecules to perform processes, building things and living beings. This study aimed to map the technological innovation of studies on the use of nanotechnology in medical treatments, in order to check the growth of patent applications in this area in Brazil through deposits made by the National Institutes of Science and Technology (INCTs). Patents were analyzed deposited at the National Institute of Industrial Property (INPI) by INCTs. The results showed that five INCTs focused on nanotechnology have research related to the diagnosis and medical treatment, and by mapping could be verified which technologies on the use of nanotechnology in medical treatments are being created, contributing to its application in the market.

Keywords: Tecnologic innovation. Nanotechnology. Patent.

Resumo:
A nanotecnologia é uma ciência que envolve a manipulação de átomos e moléculas para realização de processos, construção de coisas e seres vivos. O presente trabalho teve como objetivo mapear os estudos de inovação tecnológica sobre o uso da nanotecnologia nos tratamentos medicinais, com o intuito de verificar o crescimento dos depósitos de patentes desta área no Brasil através dos depósitos realizados pelos Institutos Nacionais de Ciência e Tecnologia (INCTs). Foram analisadas as patentes depositadas no Instituto Nacional de Propriedade Industrial (INPI) pelos INCTs. Os resultados mostraram que cinco INCTs voltados à nanotecnologia possuem pesquisas relacionadas ao diagnóstico e ao tratamento médicos, e que através do mapeamento pôde-se verificar quais tecnologias sobre a utilização da nanotecnologia nos tratamentos medicinais estão sendo criadas, contribuindo para sua aplicação no mercado.

Palavras-chave: Inovação Tecnológica. Nanotecnologia. Patentes.

1 Introduction

The world has been undergoing constant changes in recent decades, and the human being may experience different reactions to it that can determine his success or failure within that environment. From there, prospecting studies appear as a tool for the decision-making process, seeking not to discover the future, but rather to draw and test possible visions so that choices can be made that will help in the construction of the future (Mayerhoff, 2008).

Therefore, technological prospecting involves the mapping of future scientific and technological progress that can influence both industry, economy and society as a whole (Caruso & Tiger, 2004), since the use of this technique can optimize the management of resources, avoiding financial, material and time wastage, as well as detecting opportunities and threats for a company or research institution (Quintella *et al.*, 2011).

In the field of science, nanotechnology emerges as a new technological revolution, which has become a promising and innovative space in the scientific area, through the control

and manipulation of atoms and molecules (Carles & Hermosilla, 2008). For this reason, scientists use it to create innovative, low-cost materials, devices and systems with unique properties (Cuadros, Méndez & Portero, 2009).

In this area of nanotechnology, nanomedicine is a relatively new field of science and technology (Boisseau & Loubaton, 2011), which can revolutionize the world medical scenario by treating diseases such as cancer and infections (Monteiro, 2015b) , aiming at revitalizing health problems, establishing tools and techniques to provide easy access to the interior of cells, and thus probing, studying and transforming the molecular processes of cells to improve therapies for diseases (Rauan, 2012).

Advances in nanomedicine research in relation to the use of nanomaterials to contribute to diagnoses and medical treatments is still a topic under discussion, as it also involves the analysis of the impacts that the use of these nanomaterials can cause both in the environment, and (nanomaterials, nanoparticles, carbon nanotubes, nanowires, etc.) can affect the environment and human health (Monteiro, 2015b).

This concern of the researchers in discovering if the materials that are being used in the nanomedicine can interfere in the human health, brings the necessity to verify the development of the technological studies on the nanotechnology, in order to identify the advances of the studies of this area applied to the health.

In Brazil, nanomedicine has been promoted within the scope of the broad policies for nanosciences and nanotechnologies (N&N), since 2001, with the participation of different actors: Ministry of Health, Commission for the Improvement of Higher Education Personnel, National Scientific and Technological Development and Financing of Studies and Projects. It is these actors that induce the creation of networks for research and innovation, through the production of scientific and technological knowledge (Faria & Olivera, 2014).

However, in June 2015, scientists participated in a public hearing on national nanotechnology policy. And they consider it fundamental to deepen the scientific knowledge in the area and the environmental impacts that this can cause, who fear that the haste in formulating bills that create the national policy of nanotechnology can either halt research in nanotechnology or bring negative impacts for Brazil (Monteiro, 2015a).

It is because of this need to deepen knowledge about nanotechnology and other areas that the National Institutes of Science and Technology Program was developed with the purpose of promoting innovation and developing new technologies in Brazil, since innovation generates development to the country and enables the creation of new techniques and technologies for the benefit of the population.

The relevance of this theme is the importance of the innovation of technological knowledge in the treatment of diseases, bringing nanotechnology as an alternative to contribute to the advancement of diagnostic and therapeutic medicine, favoring that studies on this area be disseminated and can leverage research on the use of nanomedicine in the diagnosis and treatment of diseases, such as cancer.

Thus, this article aimed to identify the technologies produced on the use of nanotechnology in the medical treatments produced by the National Institutes of Science and Technology (INCTs).

2 Theoretical background

In this section, we present the concepts about nanomedicine, since it involves the application of nanotechnology to medicine.

2.1 Nanotechnology

In relation to the term nanotechnology, this one was introduced by the Japanese engineer Norio Taniguchi, aiming to designate a new technology that went beyond the control of materials and the engineering in microscale. However, the current meaning is closer to the formulation presented by Eric Drexler, which is related to the processing methodology involving atom-to-atom manipulation (Ferreira & Rangel, 2009).

Currently, many developed countries are seeking to increase their resources for the promotion of nanotechnology in order to obtain a prominent position in this area, in addition to which many companies are developing initiatives to create products based on nanotechnology (Eugénio & Fatal, 2010).

Still, nanotechnology is a new science that has been explored and applied in medicine to revolutionize both treatments and medical diagnostics. However, even with benefits, it is important to know the risks that nanoparticles can cause to the environment and our body.

It is necessary to continuously evaluate the developing technologies in the laboratories, in order to identify their potential of risk, seeking to find solutions and alternatives that eliminate or minimize possible damages to the environment or health, especially those that manipulate nanoparticles in laboratories (Quina, 2004).

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2.2 Nanomedicine

The idea of nanomedicine is not new, but exclusive of the twentieth century, since the existence of the atoms was only proven in the late nineteenth century. Nanomedicine follows two paths: that of the biological tradition involving genetic engineering to be explored by the development of biological nanomachines and that of the mechanical tradition that was certainly developed from the ideas of Feynman, who even proposed a "nanomedical" procedure for the treatment of diseases of the heart (Gomes, 2002).

One of the advances is being made with the construction of tiny mini-robots, also called nanorobots, which are smaller than a human cell and endowed with smart chips. These nanorobots will be able to recognize the minimal defects and promote repairs in the human body, having monitoring functions in the tissues and in the blood stream (Carles & Hermosilla, 2008).

These technological advances in medicine not only favor the treatment and diagnosis of diseases, but also enable the monitoring (images), tissue repair, control of disease evolution, defense and improvement of human biological systems, etc (Cuadros, Méndez & Portero, 2009).

Nanomedicine is the application of nanotechnology to medicine (Boisseau & Loubaton, 2011), and in this field important advances can lead to more effective diagnostic systems and therapeutic treatments, which would allow a better quality of life for men (Lettuce, 2011).

It is hoped that with advances in nanomedicine it will be possible to probe, study and transform molecular cellular processes to better understand the fundamental biological processes and to improve therapies for disease (Vu, Rajan, 2012), but for this we need to understand about the which comes to be nanomaterials and the effects that these can bring to biological systems.

Medicine and science have been advancing together throughout history. This advance made it possible to begin to obtain relevant results in applications of nanotechnology in medicine. These results come as a potential market, bringing revolutionary applications that can even cure cancer, treat diseases according to specific patient characteristics and achieve a substantial improvement in the population's way of life (Echevarría-Castillo, 2013) .

In Brazil, nanomedicine has been fostered with the participation of different development agencies, such as the Commission for the Improvement of Higher Education

Personnel, the National Council for Scientific and Technological Development, the Financier of Studies and Projects, which seek the integration of human resources with technoscientific research (Faria & Oliver, 2014).

According to Cancino, Marangoni and Zucolotto (2014) the progress in the development of nanomaterials applied to medicine has been growing over the years, due to the improvements of the protocols, combination with biomolecules, as well as concern for the toxic effects that nanomaterials can cause.

In addition, the delivery of medicines was one of the first areas to grow in this scenario and that has been developing over the years. Currently, many researchers in the field say that nanomedicine can be a refinement of molecular medicine, because it integrates innovations in genomics and proteomics for an even more personalized medicine, that is, it studies case by case, from early diagnosis to punctual treatment, making possible the minimization of the risks that can be caused to the patient's body (Cancino, Marangoni & Zucolotto, 2014).

Brazil has sought to regulate the use of nanomaterials for diagnosis, therapy and regenerative medicine and has taken a big step since 2014, through an initiative of the Ministry of Science, Technology and Innovation (MCTI), which enabled the country to start doing part of NANoREG, a nanoregulation platform organized by the European community for three years, which has 16 participating countries, with incentives from academia and industry (Liskauskas, 2015).

3 Methodology

For the research were analyzed the patent deposits made by the National Institutes of Science and Technology (INCTs) related to nanotechnology in the National Institute of Industrial Property (INPI), and the study sought only patent documents related to medical treatments and diagnoses.

In the data collection, a search was made for the INCTs related to the area of nanotechnology. We found ten institutes working with nanotechnology, as can be seen in Table 1.

Table 1: Quantitative INCTs by area

INCTs	Amount
Cheers	37
Ecology and Environment	18
Engineering and Information Technology	13
Agrarian	12
Human and Social	11
Exact and Natural	11
Nanotechnology	10
Energy	10
Total	**122**

Source: Based on data collection in the INCTs INCTs (http://inct.cnpq.br/institutos/, recuperado em 02, maio, 2016)

After the number of INCTs were surveyed, the quantities of patents deposited in nanotechnology were analyzed and analyzed according to the year of filing, inventors, patents for medical treatments per institution and by type of medical treatment.

4 Results

When analyzing the nanotechnology-related INCTs, it was verified that of the ten existing ones, only five of them have research and development of patents involving medical treatments, drug creation, as highlighted in Table 2. Therefore, the 142 patents deposited by these INCTs in INPI, in order to identify the main studies that have been carried out by these institutes.

Table 2: Number of patents per INCTs related to Nanotechnology

INCTs	Amount
INCT INAMI	46
INCT NANOCARBONO	34
INCT NanoBiofar	27
INCT Nanobiotecnologia	22
INCT NanoBioSimes	13
Total	**142**

Source: Based on data collection in the INCTs (http://inct.cnpq.br/institutos/, recuperado em 02, maio, 2016)

After analyzing the patent deposits made at the INPI, it was verified that only 47 patent deposits, or 33%, are directed to diagnostics, drug creation and medical treatments, with INCT NanoBiofar having the highest number of patents. related to the subject of this research.

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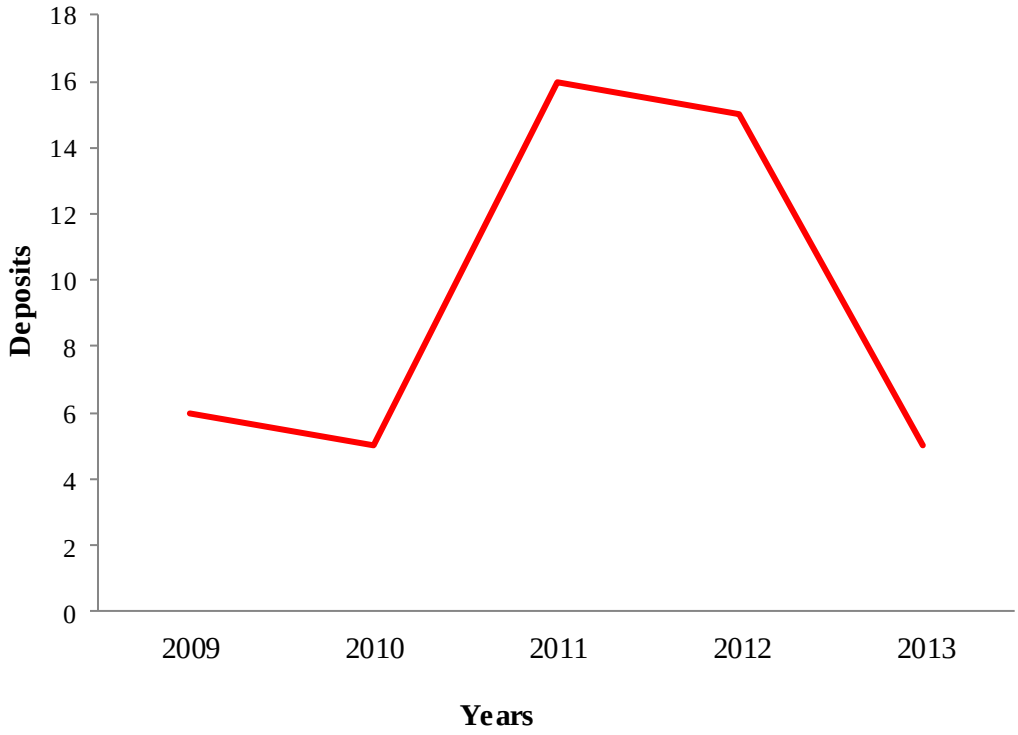
With regard to the annual evolution of the deposits found, it was observed from Figure 1 that the first deposits occurred in 2009, which can be explained by the fact that the creation of the first INCTs occurred in 2008.

In 2011 and 2012 there were more deposits, with 16 and 15 patents deposited, respectively. In this figure did not appear deposits of 2014 and 2015, since the research restricted itself to analyze only documents related to drugs, diagnoses and medical treatments. If all the patents deposited by the INCTs were analyzed, there are documents from the above years.

However, searching the database of the National Institute of Industrial Property (INPI) with the word "nano, it was noticed that the number of deposits is much larger than the production of technologies by the INCTs, since 207 deposits were identified related to nanotechnology, with deposits found between 1993 and 2015.

It is important to emphasize that the data found in the research carried out in the INCTs have a smaller number of deposits than the total that exists in the INPI, due to the fact that the research has concentrated on patent documents related to medical treatments and diagnoses.

Figure 1: Annual evolution of INCT patent deposits



Source: Based on data collection in the INCTs and INPI (2016)

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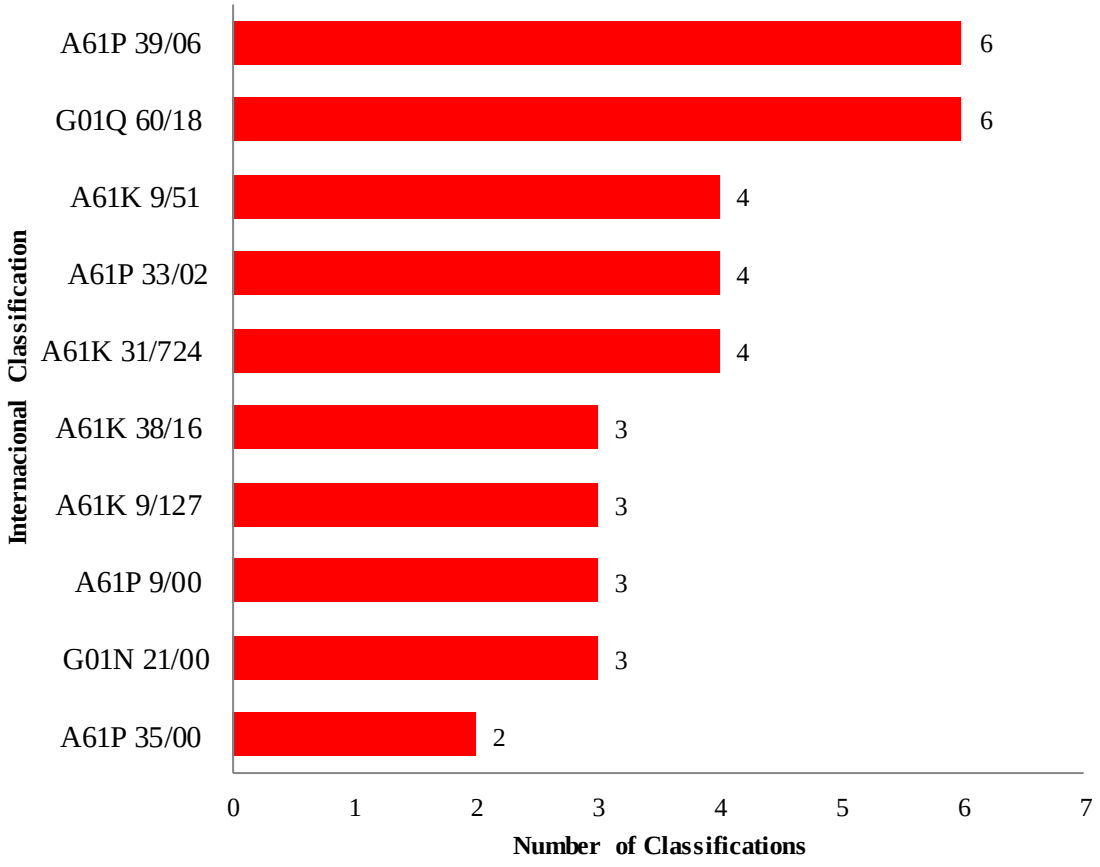
As for the IPC code, it can be seen from Figure 2 that the most present classifications in the results found were A61P 39/06 and G01Q 60/18, followed by the A61K 9/51, A61P 33/02 and A61K 31 classifications / 724.

Table 3 shows the meanings of the IPCs highlighted in Figure 2, and it was observed that all the classifications that appeared most frequently are related to treatments, diseases or drugs, which confirms that the research sought to collect information on related patent deposits diagnosis and treatment.

Still, of the 152 classifications found, 115 are related to section A, which represents human needs and 19 classifications related to section G, which represents physical; these were the sections that were most present in the analyzed deposits, the subclasses A61K, which involves preparations for medical, dental or hygienic purposes and A61P, related to the specific therapeutic activity of chemical compounds or medicinal preparations were the most present in the deposits analyzed, reinforcing the previous mappings, showing that the patents are aimed at medical purposes.

Figure 2: Number of patents per international classification code of INCTs



Source: Based on data collection in the INCTs and INPI (2016)

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Table 3: Meaning of International Classifications of Patents deposited with INPI

Código de Classificação	Significado das classificações
A61P 39/06	Free radical scavengers or antioxidants
G01Q 60/18	SNOM [Scanning Near Field Optical Microscopy] or related apparatus, e.g. ex. SNOM probes
A61K 9/51	Nanocapsules
A61P 33/02	Antiprotozoals, e.g. ex. for leishmaniasis, trichomoniasis, toxoplasmosis
A61K 31/724	Cyclodextrins
A61K 38/16	Peptides having more than 20 amino acids; Gastrinas; Somatostatin; Melanotropins; their derivatives
A61K 9/127	Liposomes
A61P 9/00	Drugs for the treatment of disorders of the cardiovascular system
G01N 21/00	Investigation or analysis of materials by the use of optical means, i.e. using infrared, visible or ultraviolet rays
A61P 35/00	Antineoplastic agents

Source: Based on data collection in the INPI (http://www.inpi.gov.br/menu-servicos/patente/classificacao-de-patentes, recuperado em 04, março, 2016)

Regarding the profile of the depositors, of the 47 patents of the nanotechnology-related INCTs, all were deposited by universities, foundations and research centers, some of which deposited a larger number of deposits, as can be seen in Table 4.

It is important to point out that this number of patents highlighted in the table surpasses 47 found, because USP, UnB and FAPESP have formed partnerships, as well as UFMG and FAPEMING.

Table 4: Number of patents related to nanotechnology per Institution

INCTs	Amount
Federal University of Minas Gerais - UFMG	28
University of São Paulo - USP	8
University of Brasília Foundation - UnB	6
Foundation for Research Support of the State of Minas Gerais - FAPEMIG	4
Foundation for Research Support of the State of São Paulo - FAPESP	4
Federal University of Pernambuco - UFPE	4
Federal University of Ouro Preto - UFOP	2
Total	**56**

Source: Based on data collection in the INCTs and INPI (2016)

. It can be seen that UFMG is present in most of the deposits (50%) carried out by the INCTs surveyed, which can be explained due to the fact that the institution participates in the majority of nanotechnology-related INCTs.

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In turn, Figure 3 shows the inventors who are most present in the analyzed patents of the INCTs surveyed. To find this data were verified the patent deposits made by the INCTs and the search for these deposits was made through the title and order number.

By means of this data cross-checking, the names of the inventors, members of the INCTs who made deposits at the INPI for nanotechnology, were verified, and the researchers Ruben Dario Sinisterra Millián and Robson Augusto Souza dos Santos, obtained, respectively, ten and nine deposits of patents. Researcher Ruben Dario Sinisterra Millián holds a PhD in Chemistry and Robson Augusto Souza dos Santos holds a PhD in Physiology; both are permanent professors of the Federal University of Minas Gerais and members of the National Institute of Science and Technology of Nanobiopharmaceutical, which explains the amount of patents they hold in INPI.

It should also be noted that the researchers Luiz Orlando Ladeira and Ado Jório de Vasconcelos are also from UFMG and each own 5 patent deposits; justifying, once again, the reason for UFMG to emerge in this scenario. To conclude, of the ten researchers with more patents deposited, only three are not from the UFMG, which confirms what was shown in Table 3, that most of the deposits found in the analysis focused on nanotechnology are concentrated in UFMG.

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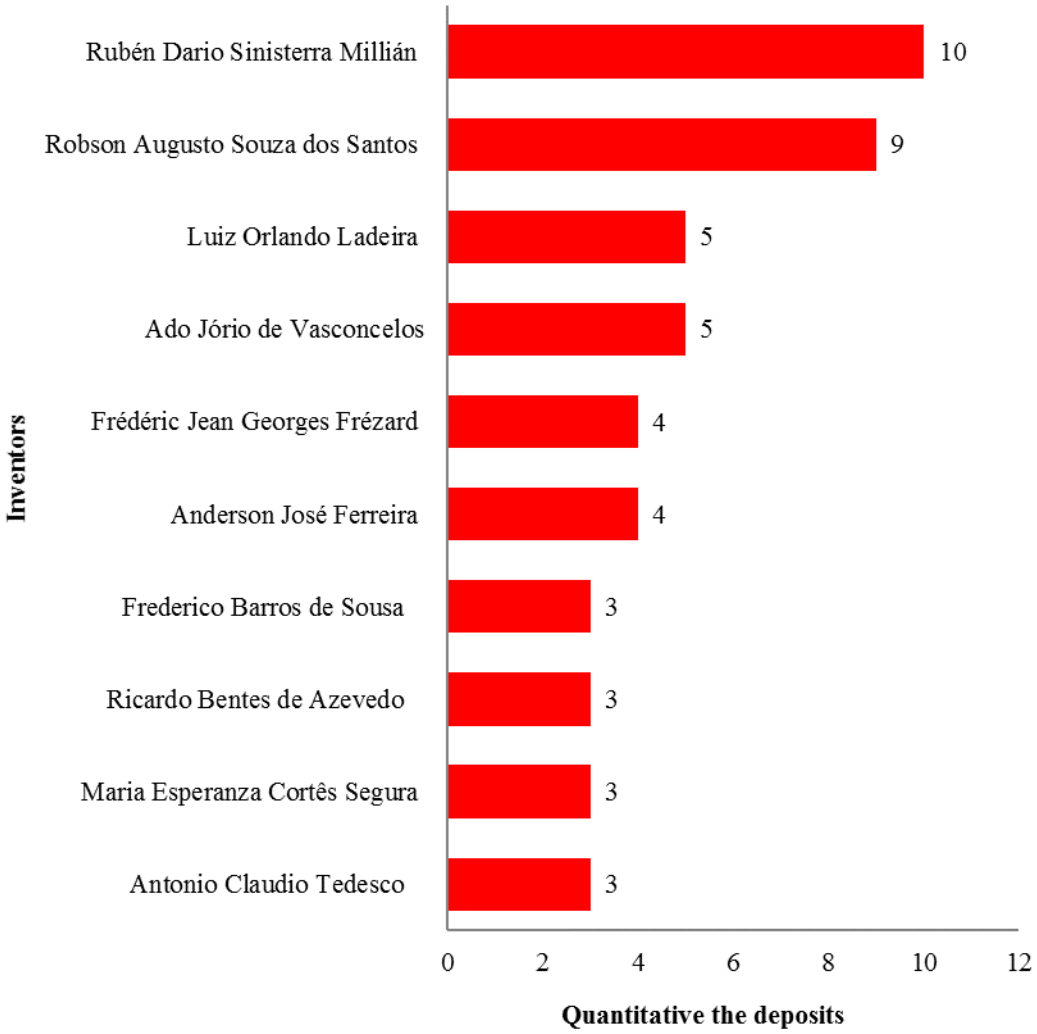
Figure 3: Patent Deposits by Inventors



Source: Based on data collection in the INCTs and INPI (2016)

In order to analyze the deposits by patent type, all the deposits made by the INCTs were searched, searching for deposits through the title and order number. Each finding was verified individually, through the search it was noticed that in Figure 4, 34 (71%) were related to medical treatments, 8 (17%) to devices used for diagnosis, and 6 (12%) to drugs. These data reveal that most of the 47 patents found deal with medical treatments developed for different types of diseases, which are highlighted in Figure 4.

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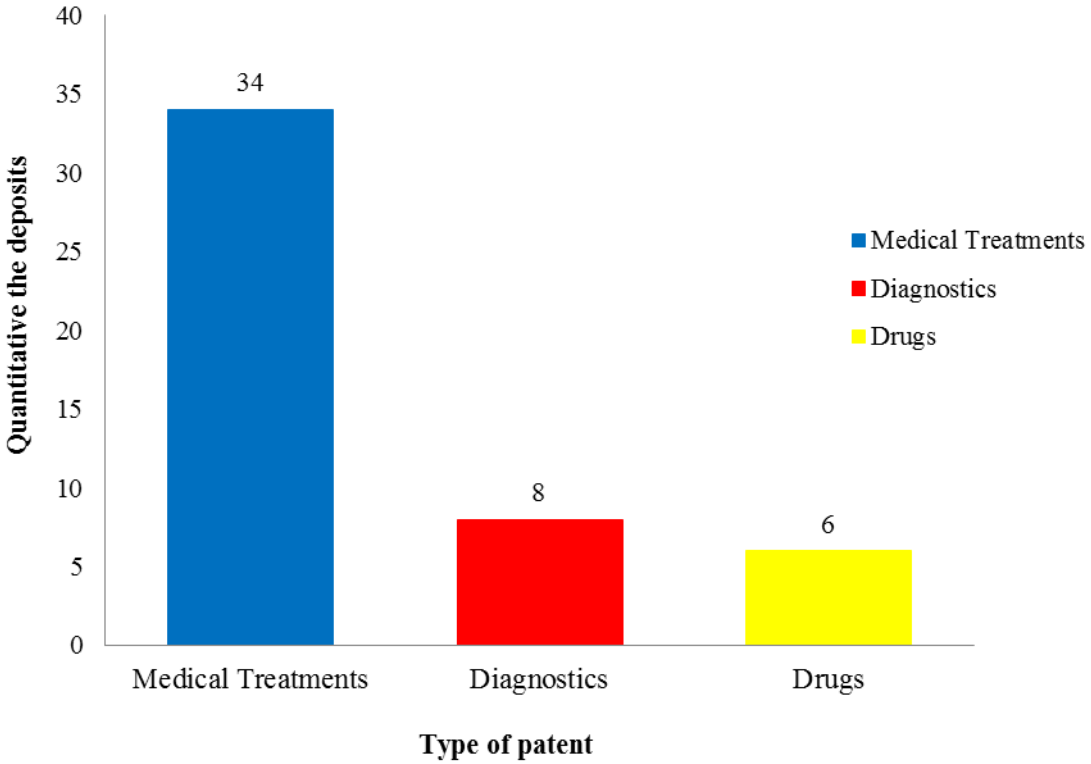
Figure 4: Deposits by type of patent



Source: Based on data collection in the INCTs and INPI (2016)

This majority of patents for medical treatments can be explained by a talk about the interview made by Monteiro (2015b) to Professor Valtencir Zucolotto, in which the researcher says that these innovations in nanotechnology are expected to be part of everyday life of medicine as quickly as possible, enabling the development of research that improves medical treatments.

In raising the types of patents in Figure 4, it was noticed that there were several types of medical treatments found in the analyzed deposits, that is why the percentage was 72% of medical treatments in relation to the percentage of diagnoses and drugs found in this analysis.

In order to analyze the types of treatment, the numbers of applications and patent titles provided on the INCTs portal were compared and a search was made at the INPI database identified through the title and summary of the deposit, which type of treatment, disease and drugs is referred to the deposit. It is observed that the majority of patents found, 19%, is related to treatment of cancer and 13% to pharmaceutical devices.

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Table 5: Patent Deposits by Type of Medical Treatment Technologies

INCTs	Amount
Cancer Treatment	9
Pharmaceutical Devices	6
Treatment of Leishmaniasis	4
Microscopy and Spectroscopy Techniques	4
Pain Treatment	4
Treatment of Neoplastic Injuries	3
Disease Detection	3
Treatment of Mycoses	2
Treatment against Dengue Virus	2
Treatment of Hypertension	2
Heart Treatment	2
Alopecia Treatment	1
Treatment of Periodontal Disease	1
Treatment of Infectious Endocarditis	1
Treatment of Ocular Pathologies	1
Antioxidant for Organ Preservation	1
Treatment of Degenerative Diseases	1
Total	**47**

Source: Based on data collection in the INCTs and INPI (2016)

This reasonable percentage of patents related to cancer treatments can be explained due to the fact that research in Brazil focuses on the diagnosis of cancer, as highlighted by the interview made by Monteiro (2015b) to Professor Valtencir Zucolotto.

Table 6: Quantity of patent deposits by Type of Medical Treatment Technologies

INCTs	Medical Treatment	Diagnostics	Drugs
Cancer Treatment	x		
Pharmaceutical Devices			x
Treatment of Leishmaniasis	x		
Microscopy and Spectroscopy Techniques		x	
Pain Treatment	x		
Treatment of Neoplastic Injuries	x		
Disease Detection		x	
Treatment of Mycoses	x		
Treatment against Dengue Virus	x		
Treatment of Hypertension	x		
Heart Treatment	x		
Alopecia Treatment	x		
Treatment of Periodontal Disease	x		
Treatment of Infectious Endocarditis	x		
Treatment of Ocular Pathologies	x		
Antioxidant for Organ Preservation		x	
Treatment of Degenerative Diseases	x		
Total			

Source: Based on data collection in the INCTs and INPI (2016)

The Table 6 shows that most of the types of treatment cited, thirteen are related to medical treatments, three are related to diagnoses, and only one is related to drugs. Comparing with the data with Table 5, it can be seen that all pharmaceutical devices are linked to drugs. Also, it has been noted that there are various types of medical treatments, ranging from Treatment against Dengue Virus to Treatment of Leishmaniasis.

5 Conclusion

The use of technological mapping studies is essential to guide companies and researchers in the development of the technologies that are constantly being created, besides being an instrument that assists in the decision making process, since these studies are aimed at analyzing the technological changes, and as these have been leveraging well over the years, it is necessary to use tools such as prospecting to guide future decisions so that companies and institutions plan to improve and encourage technological development.

However, in the case of this research to explore the studies of technological innovations on the use of nanotechnology in the medical treatments, an analysis was made through the deposits made by the INCTs, allowing that the study becomes reduced, only covering institutions that are researching the development of new technologies for the improvement of medical treatments and other purposes.

When analyzing the patents deposited by the INCTs, it is understood that even these institutions were formed from 2008, there are a significant number of patents produced by them, and in the case of INCTS related to nanotechnology that are only 10, production has arrived to 147 deposits.

In order to investigate only patent deposits involving medical treatments, the five INCTs that have studies focused on the development of drugs and treatments for different types of diseases were analyzed. What was found were 47 that began to be deposited as of 2009, and no deposits were found for medical treatments performed in 2014 and 2015, showing the need to deepen these studies for the expansion of technologies to improve human health.

Regarding the institutions, it was noticed that the participants of these INCTs, the Federal University of Minas Gerais, the University of São Paulo and the Foundation University of Brasilia were the ones that deposited the most patents related to medical treatments, and the inventors who obtained the largest number of deposits were Professors Rubén Dario Sinisterra Millián and Robson Augusto Souza dos Santos, both of UFMG.

Still, the survey showed that of the analyzed deposits, 19% is related to cancer treatments, and this study has been deepened in Brazil in recent years, due to the growth of the disease in the country. Regarding patents, it was observed that 72% is related to medical treatments.

In view of all the information found, there were some shortcomings in Brazil in this area, since patent production is still developing differently from other countries, such as the United States, which have been leveraging their studies on nanotechnology and its applicability. In addition, the little exploration of nano in medical treatments can be explained by the fact that scientists still do not know about all the risks that the use of this science brings to human health. Also, the INCTs related to the area have several Brazilian educational institutions participating, but little integration of these in the production of patents, since it was found, when analyzing individual patents, that institutions are depositing separately and not together.

Thus, the analysis of the technological production, through the deposits made by the INCTs, made it possible to verify that studies on nanotechnology have been increasing; however, there is a need to explore this area in other fields of knowledge, such as expanding the incentive for research institutions to explore the development of technologies using nanotechnology to improve medical treatments.

As suggestions for new work, it would be interesting to analyze the patent production of all nanotechnology-related INCTs to see which technologies are being produced most by each institute and what research they are doing further.

In addition, it would be important to verify through the patent bases, the companies that are investing more in nanotechnology in Brazil, and what technologies are developing for the market.

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