ISSN: 2047 - 0398
SPECIAL ISSUE – V|4|N|3|, December | 2014

New Orthopedic Prosthetic Devices as an Innovation Opportunity in Health in Brazil

Marcelo Kropf (*Corresponding Author*)
Doctoral student with the Chemical and Biochemical Process Technology Program, School of Chemistry, Federal University of Rio de Janeiro, and Advisor on Innovation at Instituto Nacional de Traumatologia e Ortopedia Jamil Haddad (INTO).
Instituto Nacional de Traumatologia e Ortopedia Jamil Haddad - Avenida Brasil, 500 - São Cristovão - Rio de Janeiro – RJ - Brazil | CEP: 20940-070
E-mail: marcelo.kropf@gmail.com, mkropf@into.saude.gov.br

Adelaide Maria de Souza Antunes Emeritus
Professor with the Chemical and Biochemical Process Technology Department, School of Chemistry, Federal University of Rio de Janeiro, and Senior Specialist with Instituto Nacional de Propriedade Industrial (INPI)
Instituto Nacional de Propriedade Industrial
Rua Mayrink Veiga, 9 - Centro - Rio de Janeiro-RJ- Brazil | CEP: 20090-910
E-mail: adelaide@eq.ufrj.br

ABSTRACT

Prostheses are fundamental medical devices for bone or joint replacement. According to projections for 2030, the rising costs of imports and orthopedic surgeries, and the ageing of the Brazilian population are factors of concern for the country. Modern biomaterials derived from biotechnology and nanotechnology used in the latest prosthetic devices have far superior properties than the biomaterials used today, and are proving promising in clinical applications. The fusion of biotechnology and nanotechnology could open up a market worth an estimated US$ 1 trillion. The aim of this article is to present new prosthetic devices as a socioeconomic development strategy for Brazil through its innovation system in health.

Keywords: *prosthetic, innovation, biomaterial, nanobiotechnology*

1. INTRODUCTION

Prosthetic devices, or orthopedic implants, encompass all implantable medical products with orthopedic purposes, and are used as joint replacements, artificial bones, in ligament surgery, and in maintaining spinal function in human beings (ABDI, 2010). The Brazilian Ministry of Health defines a prosthetic device as "an object that replaces a segment of a totally or partially amputated limb or a joint" (Brasil, 2008).

The main disease that leads to the total or partial loss of joints is osteoarthritis, a progressive clinical condition that results in functional incapacity or limitation due to pain, reduced range of motion, stiffness, and resulting muscular weakness. This is due to the total loss of the joint, leading to bone deformation caused by friction in bone-on-bone contact. When medical treatment designed to contain joint and bone degeneration fails, arthroplasty is indicated to replace the joint with an implant (Hirose-Pastor, Fuller & Rocha, 1994; Hochberg et al., 1996). Arthroplasty is a surgical procedure by which a joint is partially or totally replaced in order to restore mobility (Brasil, 2008).

In the general population, around 6% of adults over 30 years of age have symptomatic osteoarthritis in the knee joint, and 3% in the hip (Hochberg et al., 1996). Arthroplasty is more commonly indicated for individuals aged 65 to 79 (Insall et al., 1985). Osteoarthritis is responsible for the incapacity of approximately 15% of the world's adult population. In Brazil, osteoarthritis is the third highest cause of illness-related social security benefit payments, behind only mental illness and cardiovascular disease (Salmella et al., 2003). The situation could become even more serious, since projections published by the Brazilian Institute of Geography and Statistics (Instituto Brasileiro de Geografia e Estatística) indicate that by 2030 Brazil will have a population of about 216.4 million. The rate of ageing is set to grow in line with population growth, reaching 76.5 old people for every 100 young people. In absolute terms, there will be 40.5 million people aged 60 or over (IBGE, 2010).

The advanced materials used in the production of prosthetic devices are called biomaterials. The concept of biomaterial is quite varied. Basically, it is understood as any material designed to interface with biological systems for the purpose of evaluating, treating, augmenting or replacing any tissue, organ or function of the body. Their development is relatively recent, and they can be divided into three generations: 1) first-generation biomaterials – bone implants (the first artificial hip was developed in 1961); 2) second-generation biomaterials – bioactive devices (started in the 1970s); 3) third-generation biomaterials – tissue engineering and the engineering of regenerative materials (until the present day). This generation has created the opportunity to profoundly change medical practice, offering effective treatment at a better cost and improved quality of life for patients. The fusion of biotechnology with nanotechnology will result in an unprecedented range of applications and impacts in a huge market estimated at US$ 1 trillion (Matsui, 2007).

The biomaterials used in prosthetic devices have a useful life of 10 to 15 years (Rodriguéz, et al, 2004; Sato & Webster, 2004). Today, hip and knee implants account for 29% of the orthopedic biomaterials market (CGEE, 2010). These facts, combined with the high associated costs incurred with revision surgery and the replacement of implants, have heightened the need to evaluate what type of implant works best and what the cost/effectiveness of the associated surgical procedures is (Belloti, 2009).

The latest biomaterials used in new implants, resulting from biotechnological and nanotechnological advances, have properties that set them apart from today's biomaterials, and promising potential clinical applications. Basically, these biomaterials have a surprising capacity to mimic the physiological behavior of bones, interacting with the human body without causing damage or major adverse reactions (Thomas & Peppas, 2005; Laurencin, Kumbar & Nukavarapu, 2009; Sato & Webster, 2004; Mehta & Parvizi, 2009; Christenson et al., 2007).

In view of this scenario, the aim of this article is to present the market for new prosthetic devices as an opportunity for socioeconomic growth in Brazil. Innovations in the health sector are discussed as a growth strategy for Brazil in section 2. The Brazilian health sector and how it is coordinated in a "health industry complex" is presented in section 3. The growing market for prosthetic devices and the main actors involved are presented in section 4. The fusion of materials science and regenerative medicine in new prosthetic devices is discussed in section 5. Some concluding remarks about the importance of new prosthetic devices for Brazil are presented in section 6.

2. INNOVATION IN HEALTH

New technologies are being developed and applied to different areas of knowledge at an increasingly rapid pace. In health, interdisciplinarity is an important factor for technological innovation. The life sciences present classic issues that will always be on the agendas of governments, universities and research centers. The demand for scientific and technological knowledge management in the health sciences is higher than ever in a bid to produce novel technological developments to improve individual and collective health in view of the associated social and economic impacts.

Around 4.8 billion people, or 80% of the world's population, live in developing countries. Of this number, 43% live on less than two dollars a day. Recent data indicate that Latin America and the Caribbean is the region of the world with the highest levels of inequality, where 29% of the population live under the poverty line, and the 40% poorest people receive less than 15% of the total income (OPAS, 2013). Poverty is one of the factors that have a direct impact on access to health technologies, like vaccines, examinations, diagnoses, medications, and medical devices.

In response to this scenario, the World Health Organization (WHO) has published a plan of action, in effect since 2011, which aims to minimize this situation through research, development and innovation in health (WHO, 2011).

The idea of viewing health as a development strategy is now seen as a way of improving and assuring access to health services. This proposal is one of the commitments undertaken by Latin American countries in the Health Agenda for the Americas 2008-2017, and was reiterated in the Pan-American Health Organization's Strategic Plan 2014-2019 (OPAS, 2007; OPAS, 2013).

This subject is also on the political and economic agenda in Brazil. It began in 1994 with the first National Conference on Science, Technology and Innovation in Health, which confirmed the Policy for Science and Technology in Health as an integral part of the National Health Policy (Brasil, 2005).

Brazil's health sector is important to the country's economy and technology sector, accounting for over 8% of its GDP. Its importance for the country's development in the long run derives from its potential to coordinate, generate and spread future-oriented technologies that have a good chance of breaking down technology and market barriers, like biotechnology and nanotechnology (CGEE, 2010; Gadelha & Costa, 2007).

As such, this relationship between health and development can be understood as "a dynamic, virtuous process that simultaneously combines economic growth, fundamental changes to the production structure, and a better standard of life for the population" (Viana & Elias, 2007).

Health is a driver of innovation, as it is one of the key targets for R&D investments around the world, stimulating national competitive capacity in a globalized environment (Guimarães, 2006). It is responsible for a quarter of Brazilian research efforts, which makes it the sector that attracts most R&D investments for the purposes of knowledge production (Guimarães, 2005; Gadelha & Costa, 2007; Draibe, 2007).

In fact, this inherent capacity of the health sector is linked to an interdependent production system that is promoted and regulated by the state, which Gadelha (2003) calls the "health industry complex." Today, this complex is understood as encompassing health innovations in every sphere: academic, social, economic, political, scientific and technological.

3. THE HEALTH INDUSTRY COMPLEX

If the socioeconomic dimension of health is investigated from a systemic viewpoint, the government can be seen as being responsible for the health of the population as a social, democratic and universal right and a characteristic element of the welfare state, and for coordinating the production base in order to respond to societal demand (Gadelha, Costa & Maldonado, 2012). The production base for the health sector is responsible for the economic dynamism that has made health a strategic component for national development.

The health industry complex is organized into three dynamic, interdependent subsystems founded on public policies that support and regulate them. The "chemicals and biotechnology industry" subsystem and the "mechanics, electronics and materials industry" subsystem form the innovative, technologically specialized economic and production base. The "health service" subsystem is the driver of the industrial subsystems, in that it consumes the products that serve the current and prospective needs of society, assuring the wellbeing of the population (Gadelha, 2003; Gadelha, Costa & Maldonado, 2012).

The chemicals and biotechnology industry subsystem includes the chemical pharmaceutical, biochemical, vaccine, hemoderivative and diagnostic reagent industries. Recent developments in the Brazilian pharmaceutical industry in particular could be considered the lynchpin of this subsystem, especially for the consolidation of the production of generic medications in the last decade. The National Medication Policy (1998) and the Generics Law (1999) were key regulatory measures that were instrumental in promoting a significant upturn in the share of domestic companies in the pharmaceutical market, and marked an important turning point in the growth of national industry. The Brazilian pharmaceutical industry is particularly strategically important for this subsystem for its power to create skilled jobs and to generate income and technological capacity for the country (Gadelha et al., 2009).

In the mechanics, electronics and materials subsystem, the number of companies producing medical, hospital and dental materials and equipment rose by 37% between 1999 and 2009, resulting in a 307% leap in sales (without adjusting for inflation) in the same period, a figure which represents real sales growth of 114.3% after inflation adjustment (IEMI, 2010). According to the Brazilian Association of the Medical, Dental, Hospital and Laboratory Articles and Equipment Industry (ABIMO), this industry reported around US$ 4.28 billion in revenues in 2009, with exports worth US$ 541 million, and the creation of around 105,000 direct and indirect jobs. However, the structure of this industry is very fragmented, with 62% of the industry made up of medium-sized companies, most of which specialize in low and moderately technology-intensive segments (Fiocruz, 2012). The majority of these companies do not have the technological and managerial capacity to remain competitive, which is why the industry is not at the cutting edge of the technological frontier, despite recent progress.

The involvement of subsidiaries of large multinationals in the manufacture of products that are not produced by Brazilian companies could represent an import substitution opportunity, and concomitantly a more technology- and industry-intensive profile for national industry. If Brazilian companies were encouraged to absorb this knowledge or increase their technological capacity, they could reduce their distance from the international technological frontier.

Setting priorities to reinforce the competitive advantages of national businesses and lead them towards more technology-intensive production is now crucial. By its very nature, this industry is somewhat technologically heterogeneous, providing opportunities for companies with different specializations and sizes in different competitive niches (Gutierrez & Alexandre, 2004).

The dynamic portion of the industry in terms of growth and innovation, observance of regulatory practices, meeting domestic demand, making sustainable exports, and increased technological content is to be found in the medical and hospital equipment segment, and the dental prostheses and implants segment. These markets offer the greatest potential for national industry to develop its full competitive capacity. However, policies to promote specialization strategies must still be designed and introduced, in conjunction with coordinated state acquisitions. One of the factors that makes the mechanics, electronics and materials subsystem important is the need to stimulate development and innovation models based on new equipment for the health service subsystem. In the case of technology-intensive health technologies, the national health innovation system should forge strategic links to absorb the knowledge necessary to open up new opportunities for the country to reproduce and develop these products, such as new orthopedic prosthetic devices.

The service subsystem has the greatest economic weight in the health industry complex because of the important role it plays in the national system for innovation in health, especially in its demand for products from other subsystems, and its responsibility for creating a significant portion of the country’s direct and indirect jobs.

The health service subsystem is therefore strategic in addressing the challenges of promoting and maintaining health and the need to optimize the costs of the process. Furthermore, it is responsible for the dynamism of the health industry complex, granting it its systemic nature, as it consumes and demands health technologies.

4. THE PROSTHETICS MARKET

According to Orthoworld (2013), a provider of strategic intelligence on the global orthopedic industry, the United States, Europe and Japan account for 80% of the global market for orthopedic products. The ten biggest manufacturers of orthopedic prostheses and their respective market shares are: 1) Zymmer (23%), 2) DePuy Synthes (20%), 3) Stryker (20%), 4) Biomet (12%), 5) Smith & Nephew (11%), 6) Wright Medical (2%), 7) Tornier (2%), 8) Aescuslap (2%), 9) Exactech (1%), and 10) Mathys (1%). The other companies in this market have a combined market share of 6%.

Only 20% of the world’s population lives in the countries that master these orthopedic technologies, which means that today’s opportunities lie outside these markets, especially in the biggest import markets: developing countries. It is both vital and urgent for these countries, Brazil included, to employ research, development and innovation strategies for orthopedic products.

A representative case is the Brazilian market for orthopedic products. In 2000, Brazil’s national health service (Sistema Único de Saúde, SUS) spent R$ 242.7 million on products of this kind, specifically on acquisitions of orthoses, prostheses, and materials (Belloti, 2009). In 2004, it spent R$ 60 million on 6,337 products, not counting inputs (Soares, 2005).

In 2007, the U.S.A.’s expenditure on medical products was around US$ 80 billion, and constituted one of the fastest growing components of its hospital expenses. Orthopedic implants accounted for a significant portion of this expenditure, and were forecast to grow at 9.8% a year, reaching a total of US$ 23 billion by 2012 (CGEE, 2010). In the same year, the SUS’s expenditure on orthopedic surgical procedures exceeded around R$ 575 million, of which around R$ 146 million was for orthoses and orthopedic prostheses.

Hip and knee replacements alone were responsible for around 17,000 hospitalizations in 2007, making the combined expenditure on these surgical procedures around R$ 65 million, of which around R$ 38 million was for the acquisition of implants.

In 2013, the Brazilian market for imports and exports of prosthetic devices was evaluated using the Foreign Trade Information Analysis System (known as AliceWeb2) managed by the Secretariat of Foreign Trade, under the Ministry for Development, Industry and Foreign Trade. From January to December 2013, the total amount imported was US$ 69,104,908 free-on-board (FOB), as against US$ 42,994,712 FOB total exports of artificial joints (Harmonized System code 902131). The United States alone accounted for US$ 37,728,326 FOB of Brazil’s imports of artificial joints, meaning that 54.5% of the products of this kind it imported were made by U.S. companies. Brazil’s trade deficit was US$ 26,110,196 FOB. Note that only prosthetic devices as final products were researched (MDIC, 2014). In previous years, a similar dependency on imports was also reported.

In response to this situation, the Center for Strategic Studies and Management (Centro de Gestão e Estudos Estratégicos, CGEE) began a prospective study of advanced materials for medical and dental health applications in 2007, with a time horizon until 2022. The study analyzed six technological topics, two of which, related to orthopedics, were rated as important on a scale of 1 to 5, with 5 as very important. The first topic was nanotechnology applied to the treatment of chronic degenerative diseases and surface engineering of biomaterials, rated 4.3. The second covered hip implants and resorbable plates/screws, rated 3.9.

This study sought out market strategies and research, development and innovation initiatives, both using monies from the Ministry of Science and Technology's Growth Acceleration Program (Programa de Aceleração do Crescimento, PAC). The aim was to promote technological innovation in companies, especially in strategic areas like nanotechnology and biotechnology, in view of their technological importance for health (CGEE, 2010).

Orthopedic prosthetic devices were included in the group of 100 strategic products in Ministry of Health directive 978 issued on 16 May 2008 (Brasil, 2008).

5. NEW NANOBIOTECHNOLOGY-Based Prosthetic Devices

Bones are living systems with countless functions above and beyond the structure they provide for the functioning of muscles. The skeleton protects vital organs and is where bone marrow is produced, which is essential for the production of cells from the hematopoietic and immune system (Denny & Butterworth, 2006). The primary metabolic function of bones is to store and recycle minerals, especially calcium, which is necessary for conducting nerve impulses, muscle contraction, blood clotting, and cell secretion (Castania, 2002). This is the only tissue capable of being repaired without leaving a scar, and is in a constant process of remodeling (Salgado et al., 2004). According to Nordin and Frankel (1989), the coating on the surface of bones is essential for the maintenance of the tissue, because the cells there are responsible for the resorption of bone wherever the epimysium or layer of osteoblasts has been lost, which are the cells that produce bone tissue. The lining cells easily transform into osteoblasts, and have an important role in bone growth and fracture healing. This biological process, which takes place after a bone and/or cartilage breaks, restores the tissue to its function (Johnson, 2008).

However, these physiological repair mechanisms can fail, or fractures can worsen because of different clinical conditions. For instance, cases of bone density loss caused by tumors, infections, osteoporosis and other diseases have a significant impact on the quality of life of those who live with them. In many cases, bone replacement is the last resort for the regeneration of bone tissue. Generally speaking, bone replacement can be done by three means. One is to use bone grafts from the patient themselves. This has better clinical outcomes as there is less likelihood of an immunogenic response (immune response by which the graft is seen as a foreign body, resulting in rejection). However, it has certain drawbacks: the additional cost of the surgery, pain when the bone is collected, and the limited size of the samples obtained. A second option is to use bone grafts from deceased donors, which resolves the issue of the quantity of material, but tends to increase the risk of diseases being transmitted by infection, and considerable immune response. Also, the bones may not be viable if they do not have active osteoblasts. Finally, artificial bone substitutes are the most widely used and accepted option in modern medicine (Rodriguéz et al, 2004).

When artificial bone substitutes are used, the bone tissue grows over the biomaterial, covering the graft with living material. The greater the tissue-biomaterial interaction, the better the adhesion. However, the biomaterial does not cease to be a foreign body when it is implanted in the human body. Even the latest orthopedic implants can suffer wear over time, releasing debris that can trigger an immunogenic response, causing bone loss by osteolysis. Another major problem is limited bone growth around the implant, which, in association with a lack of graft adhesion, can cause new fractures. In such cases, new surgery to replace the graft is the only solution.

According to Rodriguéz et al. (2004), artificial bone substitutes should ideally be osteogenic and osteoinductive (bone production/stimulation by osteoblasts), biocompatible (capable of preventing inflammatory and immunogenic reactions), biodegradable/bioabsorbable (the material can be replaced by bone growth), capable of providing structural support, clinically easy-to-use, and cost-effective.

Creating the "perfect" bone substitute is the key target of regenerative medicine, an emerging interdisciplinary area of research with clinical applications focused on repairing, substituting or regenerating cells, tissues or organs to restore their function. When the physiological capacity of self-regeneration is deficient or non-existent and no other options are available to recover the tissue, modern biotechnology techniques are used, such as gene therapy, stem cells, cell reprogramming, and tissue engineering, to create a new tissue that is an exact copy of the damaged tissue.

A range of new biomaterials are being studied, resulting in countless discoveries. Basically, tissue-biomaterial interactions are fundamental for a graft to fulfil its function. Features like the topographic surface of implants, their physicochemical properties, their porosity, mechanical properties, and their cell recognition mechanisms, amongst other features, simulate the normal physiology of bone tissue (Thomas & Peppas, 2005; Laurencin, Kumbar & Nukavarapu, 2009; Anselme, 2011). As the main reason for the failure of treatment is inadequate interaction, perfecting biomaterials is seen as the key to the success and durability of implants and their capacity to restore movement (Laurencin, Kumbar & Nukavarapu, 2009).

In view of the fact that the smaller the area, the greater the contact surface, the enhancement of tissue-biomaterial interactions on a nanometric scale is being investigated. A bone is a nanocomposite. The hydroxyapatite crystals in the bone matrix that give it its characteristic rigidity are 1 nm thick. The collagen fibers that lend it its flexibility are 0.5 nm, not to mention the other structures that form bones (Thomas & Peppas, 2005; Laurencin, Kumbar & Nukavarapu, 2009; Sato & Webster, 2004; Mehta & Parvizi, 2009).

Mimicking the normal physiology of bones could be way to assure optimal results for new implants. Nanometals, nanopolymers, carbon nanofibers and nanotubes, and ceramic and polymer nanocomposites have all the properties of bones described earlier, and represent an improvement on conventional biomaterials, as can be seen from electron micrograph scans comparing the surfaces of new and conventional implants (Thomas & Peppas, 2005; Laurencin, Kumbar & Nukavarapu, 2009; Sato & Webster, 2004; Mehta & Parvizi, 2009; Christenson et al., 2007). By using the biotechnologies developed by regenerative medicine, customized, highly reproducible, biocompatible recombinant proteins can be produced, which are less likely to cause immunogenic responses. These proteins can interact with any biomaterial and biomimc the bone cell matrix, increasing the acceptance of these orthopedic implants by the organism (Romano et al, 2011).

6. CONCLUDING REMARKS

New prosthetic devices represent a clear opportunity for Brazil in view of the many factors mentioned in this study. Nanobiotechnology is increasingly present in new materials, and could be a differential for orthopedic medicine today and in the future. Brazil could take advantage of its main policy for socioeconomic development and innovation through health, the health industry complex, to position itself more favorably in the global market for orthopedic implants, taking advantage of the range of opportunities inherent to the different aspects of science and technology development required for these new materials.

A development agenda capable of boosting research, development and innovation by Brazilian manufacturers of orthopedic prosthetic devices must be formulated. It should be modeled on the experience of the country's pharmaceutical industry, so that it can absorb knowledge on existing technologies and create innovation mechanisms capable of galvanizing the domestic market, reducing dependency on imports of these products.

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