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Review Article

Technology Foresight of New Orthopedic Prostheses: Trends in Innovation and Development in Health

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Abstract

Studying technology developments is a reliable means of obtaining strategic information. New areas of knowledge are taking shape as different technologies converge to create emerging industries with great innovative potential. Technological advances in sectors like health have attracted much interest as they deal with areas at the forefront of knowledge, as is the case of nanobiotechnology. The technological development of biomaterials used in new orthopedic prostheses is a prime example of the development of nanobiotechnology. The aim of this article is to identify the technology trends in these medical devices in order to guide innovation and development in health. A technology foresight methodology was used that involved researching the Derwent Innovations Index for patent documents relating to this area. The trends encountered indicate the route technologies in the target area have taken and the paths they are likely to take in the future.

Keywords: Biotechnology; Innovation; Nanotechnology; Orthopedics; Patents; Prostheses

Introduction

Seventy years ago the World Health Organization described health as "a state of complete physical, social and mental well-being, and not merely the absence of disease or infirmity" [1]. This concept is profoundly related to development and expresses the association between people's quality of life and health. Health is therefore the result of a process of social production and is influenced by the supply of the essential goods and services for life.

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Discussions about universal access to healthcare and the production of new technologies to enhance physical, mental, and social wellbeing are increasingly overlapping, in view of the importance of assuring access to and improving the quality of the services provided to increasingly demanding users.

The demographic pattern and epidemiological profile of diseases are fundamental for comprehending health and disease processes in different countries. One example is osteoarthritis, the main disease related to the total or partial loss of joints. This progressive clinical condition 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 recommended to replace the joint with an implant [2,3]. Arthroplasty is a surgical procedure by which a joint is partially or totally replaced in order to restore mobility [4].

The technological development of the biomaterials used in orthopedic prostheses has become an important area of research, development, and innovation in health. Advances based on forward-oriented technologies like biotechnology and nanotechnology are increasingly present in scientific research and the patenting of new orthopedic prostheses.

The latest biomaterials used in the 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 [5-8].

The aim of this article is to identify technological trends in innovation and development in health by researching the Derwent Innovations Index for patent applications for orthopedic prostheses from between January 2000 and March 2014. After this introduction, section 2 discusses the convergence between nanotechnology and biotechnology and its biomedical applications in orthopedics. Section 3 discusses the strategic importance of technologies and technology foresight. Section 4 sets forth the methodology used to identify the technological trends. Section 5 presents and discusses the findings of the study, detailing the main trends and related opportunities. Section 6, the conclusion, brings together the key issues in this article and contextualizes their importance for research, development, and innovation in healthcare in the world.

Biomedical Applications and Nanobiotechnology Applied to Orthopedics

Technological convergence is defined as the blending of two or more areas of technology to form a new area of knowledge. This new transdisciplinary area is formed where the original areas interface with one another, and leads to the emergence of new industries with great innovative potential [9].

Nanobiotechnology is a case in point: the convergence of nanotechnology and biotechnology. Nanotechnology is defined as the area of technology that involves understanding and manipulating materials on a nanoscale, called nanomaterials (<100 nm). According to the National Institutes for Health (NIH) in the United States, the concept of nanotechnology is based on the understanding that at the nanoscale, the physical, chemical, and biological properties of materials differ from the properties of matter at larger scales [10]. This is the case because the phenomena that govern materials on a nanoscale are ruled by quantum mechanics. Rather than properties of mass, surface effects are what prevail. This can result in singular alterations in the properties of the materials, improving their performance or introducing new functionalities. Meanwhile, the United Nations defines biotechnology as any technological application that uses biological systems, living organisms, or derivatives thereof, to make or modify products or processes for specific use [11].

The area of nanobiotechnology is currently developing in four main areas: 1) nanostructures; 2) drug delivery and biomedical applications; 3) bio-imaging, and 4) carbon nanotubes and biosensors [12]. Nanobiotechnological applications in the field of orthopedics can be found in all of these areas. Essentially, the effectiveness of prosthesis depends on its structure, composition, interaction with the organism, and capacity to respond positively to different physiological conditions. Perfecting biomaterial is seen as a prerequisite for the success and durability of implants and their capacity to restore movement [6].

The ideal bone graft substitute would be osteogenic (producing bone tissue), osteoinducing (inducing the differentiation of stem cells into osteogenic bone cells), osteoconducting (allowing the bone tissue to migrate over the biomaterial at the tissue-material interface), biocompatible (capable of preventing inflammatory and immunogenic reactions), biodegradable/bioabsorbable (so that the material can be substituted by growing bone), capable of providing structural support, be easy to use clinically, and be cost effective [13].

Interestingly, bone and its structures have a feature that makes them compatible with nanobiotechnology. Bone itself, the hydroxyapatite crystals present in the bone matrix, the collagen fibrils that make the collagen fibers elastic, and the Haversian system, which is responsible for carrying nutrients, vascularization, and bone innervations are all nano compounds. Thus, in the convergence of nanotechnology with biotechnology, the focus shifts more towards the interaction between the nano components of the tissue and the nanomaterials themselves, with this subject being the target of considerable research yielding countless discoveries. Characteristics like the topographic surface of implants, their physicochemical properties, their porosity, mechanical properties, and cell-recognition mechanisms, amongst other features, simulate the normal physiology of bone tissue [6,14].

In other words, this means that tissue-biomaterial interactions are being improved on the nanoscale in view of the fact that the smaller the area, the greater the contact surface. As such, the effectiveness of several biomaterials is being optimized by the application of nanotechnology. In fact, nanometals, nanopolymers, carbon nanofibers and nanotubes, and ceramic and polymer nanocomposites have all the properties of bones described above, and represent an improvement on conventional biomaterials, as can be seen from electron micrograph scans [5-8].

Similarly, biotechnology techniques can be used to produce fully customizable, highly reproducible and biocompatible recombinant proteins with a lower immunogenic potential. These proteins can interact with any biomaterial and mimic the bone cell matrix, improving the acceptance of the orthopedic implant by the organism [15].

Nanocoatings, nanofilms, and nanostructured surfaces fill fundamental gaps for tissue regeneration and bone repair. The fact that bones and bone structures are nanocomposites facilitates the function of prostheses. Prostheses depend on the interactions between surfaces to assure satisfactory results. As such, the better the tissue-material interface, the greater the chances of bone regeneration. One of the main reasons for orthopedic replacement surgery is the deficiency of some conventional biomaterials (in terms of biocompatibility, bone growth, osteoconduction, and biodegradation), especially when compared with the latest biomaterials. Through tissue engineering and nanomaterial use, tissue-material interactions can now be made that are very similar to the normal physiological reality.

The Strategic Importance of Technology

Uncertainties in decision-making processes when considering the multiple variables that affect the environment inside and outside national innovation systems in the present and the future must be addressed with care, planning, and appropriate strategic tools [16].

Of these tools, technology foresight is emerging as an effective systematic method for evaluating future conditions, whether predictable or not, with the aim of anticipating and understanding the potential directions, developments, characteristics, and effects of technological change, especially the invention, innovation, adoption, and use of new technologies [17]. Technology foresight analyzes present technological developments with the purpose of anticipating their uses in the future.

The targets of foresight studies are new technologies, and incremental changes or discontinuities in existing technologies. The causes behind the impacts of technologies and their development and adoption in the present and future can be of a social or economic origin or lie specifically in the technologies themselves [18,19].

The information and knowledge present in a technology can be inferred from scientific articles and patents. These latter documents set forth the information that is protected when the novel technology is launched on the market. They have also become traditional indicators of the results of inventive activity [18].

Methodology

This article uses a quantitative foresight technique to analyze the evidence contained in patents in order to process the technological information and extract knowledge on the area in question.

The patent documents were retrieved from the Derwent World Patents Index, maintained by Thomson Reuters. Patent mining is a strategic process designed to retrieve a representative set of patents from the target area of research from a specific period of time. For this stage, we used the International Patent Classification (IPC) of the World Intellectual Property Organization (WIPO) for prostheses, nanotechnology, and biotechnology from January 2000 to March 2014 to analyze the technological trends.

All the IPC codes related to prostheses, their materials, their different applications, and to nanomaterials and biotechnology were selected as described below:

- **For orthopedic prostheses the following groups were used:** A61F 2/02: prostheses implantable into the body; A61F 2/07: stent-grafts; A61F 2/08: muscles, tendons, ligaments; A61F 2/28: bones (joints A61F 2/30); A61F 2/30: joints; A61F 2/32: for the hip; A61F 2/34: acetabular cups; A61F 2/36: femoral heads; A61F 2/38: for elbows or knees; A61F 2/40: for shoulders; A61F 2/42: for wrists or ankles, for hands, e.g., fingers, for feet, e.g., toes; A61F 2/44: for the spine, e.g., vertebrae, spinal discs; A61F 2/46: special tools for implanting artificial joints; A61F 2/54: artificial arms or hands or parts thereof; A61F 2/56: adjustable; A61F 2/58: elbows, wrists; A61F 2/60: artificial legs or feet or parts thereof; A61F 2/62: adjustable, e.g., adjustable shank, thigh, or tubular skeletal system; A61F 2/64: knee joints; A61F 2/66: feet, ankle joints; A61F 2/68: operating or control means; A61F 2/76: means for assembling, fitting or testing prostheses, e.g., for measuring or balancing; A61F 2/78: means for protecting prostheses or for attaching them to the body, e.g., bandages, harnesses, straps, or stockings for the limb stump; A61F 2/80: sockets, e.g., of suction type.

All the groups from classes A61L 31/00 and A61L 33/00 that pertain to biomaterials used in the manufacture of prostheses were also searched.

- **Nanotechnology:** All the groups from IPC B82 were used. In this class, the following terms are used with the meaning indicated: "nano-size" or "nano-scale" relate to a controlled geometrical size below 100 nanometers (nm) in one or more dimensions; "nano-structure" means an entity having at least one nano-sized functional component that makes physical, chemical or biological properties or effects available, which are uniquely attributable to the nano-scale.

For nanotechnology, the classification from the database itself - the Derwent Innovations Index manual code - was also used; IPC B82 does not cover every aspect of the subject as this technology is classified in different places as a function of its application.

- **Biotechnology:** All the groups were used from IPC C12N (micro-organisms or enzymes; compositions thereof); A01N63/00 (biocides, pest repellants or attractants, or plant growth regulators containing micro-organisms, viruses, microbial fungi, animals, or substances produced by, or obtained from micro-organisms, viruses, microbial fungi or animals); A61K (preparations for medical, dental, or toilet purposes); C05F (organic fertilizers); C12Q1/00 (propagating, preserving, or maintaining micro-organisms; mutation or genetic engineering; culture media [micro-biological testing media]).

The search strategy was created using the codes for orthopedic prostheses, nanotechnology, and biotechnology, resulting in: 1) Patents for biotechnology applications (search result combines patents for prostheses and patents for biotechnology), 2) Patents for nanotechnology applications (search result combines patents for prostheses and patents for nanotechnology), and 3) Patents for nanobiotechnology applications (search result combines patents for prostheses with patents for nanotechnology and biotechnology).

In view of the fact that the patents from classes A61L31/00 and A61L33/00, relating to biomaterials, are not exclusively for making prostheses, we had to formulate some criteria to refine the search so that it only yielded prostheses with orthopedic applications. The resulting search term was: (bone* OR knee OR hip OR spine OR joint OR hand* OR foot OR feet OR acetabulum OR femoral OR spinal OR shoulder* OR elbow*) and (orthopedic* OR orthopaedic*).

Results and Discussion

The search conducted using the criteria and operators described above yielded patents in all three groups that were filed between January 2000 and March 2014 (see table 1).

Object	Results
Prostheses with biotechnology applications	1042
Prostheses with nanotechnology applications	184
Prostheses with nanobiotechnology applications	20

Table 1: Patents per type of prosthesis encountered in the Derwent Innovations Index.

Source: Own research data

The patents identified were organized into Microsoft Excel spreadsheets to prepare graphics showing the number obtained for each trend for orthopedic prostheses.

In order to identify technological trends, we created a taxonomy based on the technology focus field in the Derwent Innovations Index, putting the patents together into groups according to the innovations they describe. The following descriptions represent the general trends in orthopedic prostheses:

- Technologies related to cell and tissue biology with the purpose of improving the function or structure of bone cells in order to improve fracture repair.
- Biotechnologies designed to genetically modify characteristics or structures of bone tissue or substances from the organic component of the bone matrix with the purpose of improving, modifying, or supplying a given biochemical or physiological cellular mechanism or property.
- Technologies relating to ceramic biomaterials constituted of different bone-like composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with components of the bone matrix and bone tissue.
- Technologies relating to inorganic materials constituted of different bone-like composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with components of the bone matrix and bone tissue.
- Technologies relating to implants and devices of different sizes with diverse characteristics and functions, which may be impregnated with bioactive agents or other substances, mostly used for biomaterial testing, diagnostics, and support for cell growth (scaffolding).
- Technologies responsible for the chemical modification of substances, bioactive agents, and (bio) chemical reactions that improve biological properties and tissue-material interactions.
- Technologies related to different metal alloys constituted of different bone-like composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with components of the bone matrix and bone tissue.
- Pharmaceutical technologies applied to tissue regeneration, induction of different cell properties, and the addition of therapeutic properties to different biomaterials.

- Technologies linked to bone-like (bio) polymeric composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with the components of the bone matrix and bone tissue.
- Technologies related to chemical processes and treatment of biomaterials based on engineering of different components.
- Other technologies applied to tissue engineering, biomaterials, or the tissue-material interface that do not fit into the above categories, or which fit into more than one category, indicating interdisciplinary convergence of different technological areas to obtain the same goal.

The following trends were found in the patents for prostheses with biotechnological applications (see figure1):

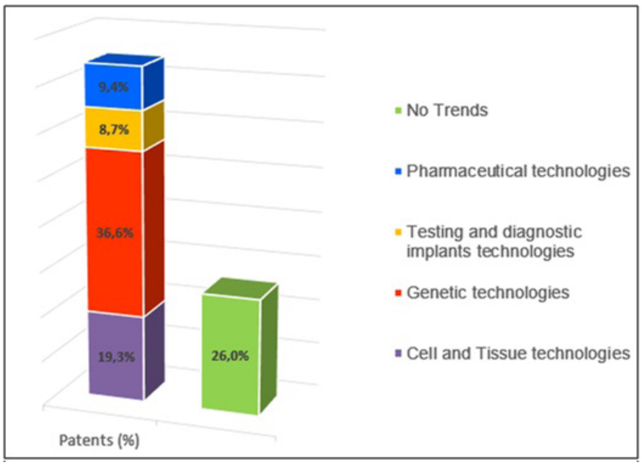

Figure 1: General trends in orthopedic prostheses with biotechnology applications (2000-2014).

- 36.6% of the patents are for technologies that genetically modify the characteristics and structure of bone tissue or substances from the organic component of the bone matrix, in order to improve, modify, or supply a given biochemical or physiological cellular mechanism or property.
- 19.3% of the patents are for technologies related to cell and tissue biology with the purpose of improving bone cell structure or function in order to improve fracture repair.
- 9.4% of the patents are for pharmaceutical technologies applied to tissue regeneration, induction of different cell properties, and the addition of therapeutic properties to diverse biomaterials.
- 8.7% of the patents are for technologies associated with implants and devices of different sizes with different characteristics and functions, which may be impregnated with bioactive agents or other substances, mostly used for biomaterial testing, diagnostics, and support for cell growth (scaffolding).
- 26% of the patents are for technologies without general trends.

The technological trends in prostheses with biotechnological applications indicate that tissue engineering has developed the capacity to genetically modify cells, proteins, adhesins, and other components of the bone matrix to improve bone repair. Properties like osteoinduction, osteogenesis, and biocompatibility are optimized *in loco* in the fracture itself. The use of drugs like antibiotics and anticoagulants in biomaterials or directly in the tissue is designed to reduce or completely eliminate the risk of infection or bleeding. Tests with scaffolds (alloplastic grafts or micro-prostheses designed to provide temporary support) for *in vitro* and *in vivo* cell growth are examples of important steps towards improved fracture repair.

The following trends were found in the patents for prostheses with nanotechnology applications (see figure 2):

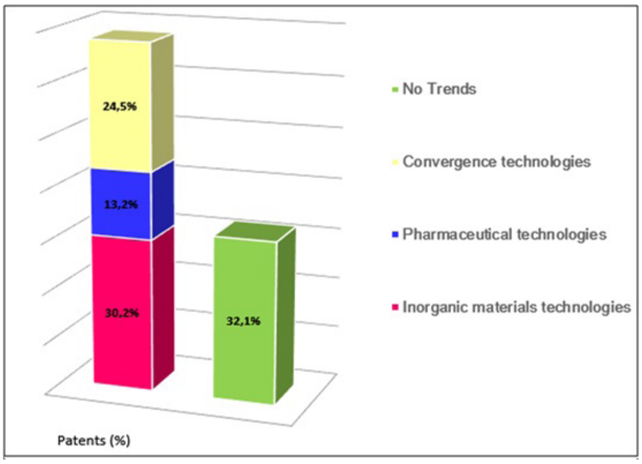

Figure 2: General trends in orthopedic prostheses with nanotechnology applications (2000-2014).

- 30.2% of the patents are for technologies for inorganic materials constituted of different bone-like composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with components of the bone matrix and bone tissue.
- 24.5% of the patents are for technologies for biomaterials or the tissue-material interface that involve the convergence of different technological areas for a common purpose.
- 13.2% are patents for pharmaceutical technologies applied to tissue regeneration, induction of different cell properties and the addition of therapeutic properties to diverse biomaterials.
- 32.1% of the patents are for technologies without general trends.

The trends in the technologies identified in the patents for prostheses using nanotechnology applications are for the specific characteristics of biomaterials and the interactions between inorganic matter from the tissue matrix and the inorganic components of different biomaterials, like hydroxyapatite crystals and carbon nanotubes. The convergence of different technological areas can be explained by the interdisciplinarity and transdisciplinarity often seen in nanotechnology. Pharmaceutical technologies are also very important, since drug delivery mechanisms applied directly to the biomaterials of these prostheses eliminate the risk of infection, improve biocompatibility, and reduce the risk of immunogenicity arising from tissue-material interactions. The adequate bioabsorption of these biomaterials tends to reduce the risks inherent to the loss of prostheses by osteolysis.

The following trends were found in the patents for prostheses with nanobiotechnology applications (see figure 3):

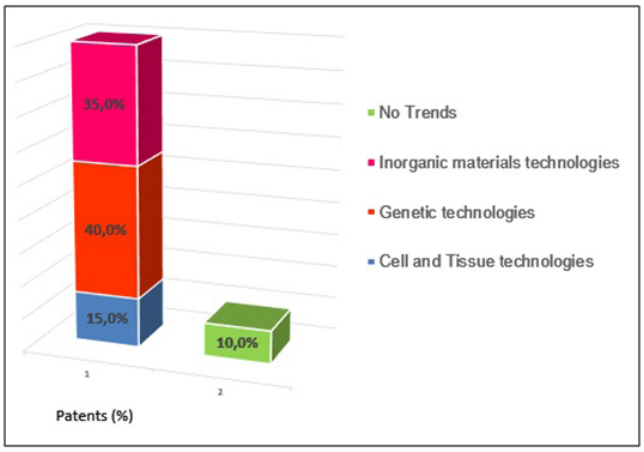

Figure 3: General trends in orthopedic prostheses with nanobiotechnology applications (2000-2014).

- 40% of the patents are for technologies for inorganic materials constituted of different bone-like composites in different forms, sizes, and rearrangements, and associated with the most varied of agents capable of improving their functions and their applications as biomaterials, including interaction with components of the bone matrix and bone tissue.
- 35% of the patents are for biotechnologies with the purpose of genetically modifying the characteristics and structure of bone tissue or substances from the organic component of the bone matrix, in order to improve, modify, or supply a given biochemical or physiological cellular mechanism or property.
- 15% of the patents were for technologies related to cell and tissue biology with the purpose of improving bone cell structure or function in order to improve fracture repair.
- 10% of the patents are for technologies without general trends.

Although only 20 patents fell into this category, the convergence of nanotechnology and biotechnology indicates the main specific trend for the production of prostheses in the future, since it allies technologies for tissues and materials designed to make the perfect prosthesis.

Another trend that deserves mention is the use of (bio) polymers as (nano) materials in prostheses. Not only are they biodegradable and biocompatible, but they are also elastic, capable of mimicking the elastic properties of the bone tissue conferred by collagen fibers.

Although the other technological areas were only covered in a few of the patents (< 7%), these technologies are also fundamental for the purposes of studying trends. The trajectory of the developments made thus far and the direction of new technologies that the latest orthopedic prostheses represent could guide future innovation and development trends in orthopedic medicine and tissue engineering.

Concluding Remarks

The scientific literature and patent descriptions indicate that current technological developments have progressed in areas of research responsible for the optimization of tissue-material interactions. From the tissue perspective, efforts are geared towards regenerative medicine, genetic modification, and chemical or pharmacological mediation to assure cell growth and stimulation of bone matrix formation. Meanwhile, the research geared towards materials focuses on improving biocompatibility and bioabsorption, and reducing immunogenicity. It is therefore clear that it is far more interesting to focus developments on the huge field of tissue engineering and nanomaterial production than to worry about specific alternatives for certain subareas of orthopedics.

The technology foresight approach adopted here, investigating patents for prostheses in the Derwent Innovations Index, was effective in identifying technological trends for innovation and development in health, especially in the field of orthopedic medicine. By organizing the technologies according to a taxonomy that represents the innovations described in the area under study, general and specific trends were identified, which indicate that technological convergence is the way forward to develop devices that can effectively and safely substitute parts of the human body. Nanobiotechnology is a promising area for the development of means to improve tissue-material interactions. The limited number of prostheses encountered is indicative that this area of knowledge has great growth potential and offers many opportunities for innovation and development in health.

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