Faculdade de Engenharia da Universidade do Porto

Patents in the computer-aided diagnosis industry

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Resumo

O diagnostico ajudado por computador tem gerado interesse dentro da are de imagem médica, usando novas técnicas, algoritmos e tecnologias, esta pode ajudar os especialistas a melhorar e tornar mais rápida a sua analise, reduzindo parte do seu trabalho. As patentes são como janelas para os ativos tecnológicos das empresas, assim como para o estado de uma determinada área tecnológica. Nesta dissertação analisámos patentes relacionadas com a analise automática de retinopatias humanas. Usando motores de busca de patentes, nos exploramos a base de dados, através de palavras-chave relacionadas com esta área e a classificação internacional de patentes para refinar a procura e eliminar resultados indesejados, seguindo então a analise detalhada do nosso "dataset". Analisando o texto estruturado e não estruturado, contido nas patentes obtidas, diferentes observações foram feitas: maiores impulsionadores deste campo, linhas temporais, principais tecnologias envolvidas e a direção da evolução desta tecnologia, assim como o principal foco de proteção destas e onde é mais procurado. Tendo isto em consideração, concluímos que os Estados Unidos da América lideram no que toca ao numero de patentes atribuídas, mas a China está rapidamente a aproximar-se, a tecnologia mostra uma certa tendência para a analise remota, com sistemas portáteis e uma melhor performance, finalmente, prevemos que o desenvolvimento de sistemas de analise automática de retinopatias humanas continue e, paralelamente, que o numero de patentes também continue a aumentar.

Abstract

Computer aided diagnosis is a trending subject in the medical imaging field, through the use of new techniques algorithms and technologies, it can help technicians perform a better and faster analysis, reducing part of their workload. Patents are windows into a company's technological assets, as well as into the state of a certain technology field. In this thesis we analyze patents that are mainly related to the automated analysis of human retinopathies. Using patent search engines, we explore the patent databases, using keywords related to the area and the international patent classification to refine the search and eliminate unrelated results, proceeding then to a thorough analysis of the dataset. By analyzing the structured and unstructured text, contained in the obtained patents, different observations are made: major players in the field, patent timelines, main technologies involved and the direction of the technology evolution, as well as the main focus of protection in these fields and where it is most sought. Taking these in consideration, we concluded that the United States of America are in the lead for the number of patents attributed, but China is rapidly approaching, the technology is hinting into a remote analysis setup, with portable systems and better performance, finally, we anticipate continued development in the field of automated analysis of human retinopathies as well as a parallel increase in the number of patent applications.

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Flávio Ricardo Marques Rodrigues

“Do not take life too seriously. You will never get out of it alive.”

Elbert Hubbard

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List of Acronyms

AU	Australia
CA	Canada
CAD	Computer-Aided Diagnosis
CN	China
CSV	Comma-Separated Values
DE	Germany
DR	Diabetic Retinopathy
EP	European Patent Office
EPO	European Patent Office
ES	Spain
FEUP	Faculdade de Engenharia da Universidade do Porto
GB	United Kingdom
HK	Hong Kong (S.A.R.)
HR	Croatia
IP	Intellectual Property
JP	Japan
KR	South Korea
R&D	Research and Development
SG	Singapore
TF	Technology Forecasting
TW	Taiwan
UA	Ukraine
US	United States of America
WO	World Intellectual Property Organization
WIPO	World Intellectual Property Organization

Chapter 1

Introduction

1.1. Context and Motivation

As technology is rapidly evolving, for a technology driven business to stay competitive it must keep innovating trough investment in Research and Development(R&D). While this investment may impact positively in the company (for example, the company may maintain an advantage over possible competitor companies), companies may also lose good investment opportunities by not using technology assets strategically, mainly because their business planning diverges from their technological planning(Lee, Yoon, and Park 2009).

This is where Intellectual Property (IP) management takes the spotlight as a fundamental tool in every company. IP management provides companies with the tools to get the most out of their intellectual assets, keeping check over the key players in the market, discovering new niches and even pointing the opportunity to use their technology in new and unexplored markets. Patents are a powerful mechanism for the protection of IP also playing an important role in technological advancement, awarding the inventors for disclosing the specifications of their creation. By fulfilling a set of pre-requisites a company can claim a patent, which grants them the sole right to explore this invention, establishing a monopoly, through which only the company that holds the patent or has a license to exploit it can operate in the market and thus posing barriers to the entry of new players. By exploring patents, companies may, as well, avoid spending money in R&D for inventions that may already been made. These companies may then negotiate a license with the patent holder for rights to explore that invention without having to spend their resources developing it.

The medical imaging industry is a market that is highly dependent on technological evolution, thus investing heavily in R&D, mostly on computer-aided diagnosis (CAD). CAD is the use of software, with mathematical algorithms and image processing, to aid physicians in the diagnosis of diseases, mainly used in detection of abnormalities in medical images, like breast cancer or intracranial aneurysms (Doi 2007).

1.2. Objectives

In terms of innovation management and innovation forecasting, it is important to understand the patents that are being used by the companies in their products. As CAD is a trendy technological subject, the analysis of the current state of the art, through patent observation, can provide inputs important for the advancement of said technology, and provide insights for companies for future improvements. Innovation forecasting through unused patents can also provide clues to where the technology is evolving, and towards the kind of products we will see on the market in a few years from now.

The objective of this dissertation is to understand the use of patents in medical image industry for computer-aided diagnosis, for automated retinopathy diagnosis. As computer-aided diagnosis systems incorporate computer algorithms, which may include image processing technics, image feature analysis and data classification, these fall under computer-implemented inventions. Computer-implemented inventions have their own special difficulties, as an algorithm, on its own, is not an invention. Therefore, by evaluating the use of patents in computer-aided diagnosis, this dissertation will generate insights on the use of patenting strategies in this industry.

Through the systematic analysis of international patents and patent applications, by exploring the search engines and patent databases, like EPO's Espacenet and Google patents, we will build a relevant patent dataset. For this analysis we'll need to define specific keywords and phrases to search these databases for CAD-Retinopathy related patens or patent applications and evaluate the current innovations in the field.

We will then review the patent dataset for several attributes (e.g., filing date, country, applicant). We will also address what part of the image processing and analysis process the technology disclosed in each patent is trying to address, therefore generating insights on the areas that most patentable in the computer-aided diagnosis industry, as well as its main drivers.

1.3. Contributions

This dissertation involves the groundwork analysis for patents in the CAD for retinopathy industry, which, in the future, could be expanded into a more extensive analysis. Whit this we identify some of the patenting strategies in this technology field using diverse approaches, based on prior knowledge, as well as giving some good information into the environment involving it.

Chapter 2

State of the Art

2.1. Innovation

Throughout this thesis there will be a number of keywords that are essential to properly describe the problem and the solution encountered, one of those is innovation.

There is no specific definition that we can say is the correct one, as innovation, dependent on the context it is used, can have multiple meanings, but generally speaking, it is the process of developing and putting in practice a novel idea. In many cases, that "novel idea" can be translated as an invention. However, innovation goes beyond the invention in itself, as it is the conjugation of different aspects, for instance economic, environmental and strategic factors, that allow the invention to reach the market, be commercialized and used (WIPO 2012).

Table 2.1 presents a number of criteria that can be utilized to describe the various types of innovation, as compiled by Lee and Lee (2013), in this analysis we will focus in the single criterion, the subject, degree and activity of innovation.

Table 2.1 - Innovation types (Lee and Lee 2013).

The criterion		The type of technology innovation
Single criterion	Subject of innovation	Product or service innovation, Production-process innovation, Organizational-structure innovation, People innovation
		Administrative innovation, Technical innovation
		Technological innovation, Managerial innovation
	Degree of innovation	Incremental innovation, Radical innovation, Changes of technical systems, Changes in techno-economic paradigms
		Highly innovative products, Moderately innovative products, Low innovative products
		Sustaining innovation, Disruptive innovation
		Linear innovation, Non-linear innovation
		Competence-enhancing, Competence-destroying
	Activity of innovation	Operational effectiveness, Strategic positioning
		Explorative innovation, Exploitative innovation
Two criteria	Technological property, Change in the market	Architectural innovation, Niche creation, Regular innovation, Revolutionary innovation
	Uncertainty about technical approach, Uncertainty about market focus	Uncertainty about technical approach high and uncertainty about market focus high (Quadrant 1) Uncertainty about technical approach high and uncertainty about market focus low (Quadrant 2) Uncertainty about technical approach low and uncertainty about market focus high (Quadrant3) Uncertainty about technical approach low and uncertainty about market focus low (Quadrant4)
	Degree of value creation, Degree of technology creation	Incremental product innovation, Technical innovation, Application innovation, Radical innovation
	Technological viewpoint, Economic viewpoint	Basic I, Basic II, Diffusion-orientation, Mission-orientation

Innovation is a key element for companies in today's ever evolving markets. Technological products have very short life cycles, and, as the time goes by, it keeps getting shorter and shorter, and so, if the company stays stagnated, they will fall behind, as competitors will continue to grow in number and quality.

This stagnation not only occurs when the company does not follow the customer's needs, they may listen to all their customers' demands and still lose market share, but also when they fail to assess the market trends and do not properly set their innovation strategies.

The current market is saturated with new technologies, and more and more emerge every day, so discovering new technologies becomes ever more difficult, so companies need new sources of innovative ideas.

By studying the current state of the market, the most prominent technologies or the technological innovation patterns an organization may discover new sources of innovation, with this, new ideas may come, not only from customer needs, but from suppliers or even competitors (Lee, Yoon, and Park 2009).

2.2. Intellectual Property

According to the World Intellectual Property Organization (WIPO), "the term intellectual property refers broadly to the creations of the human mind. Intellectual property rights protect the interests of creators by giving them property rights over their creations". This definition does not fully describe intellectual property, as it is a very wide concept, and may be subjective to change. It is related to items of information or knowledge, it covers anything from literature and artistic work to discoveries, inventions, and industrial designs or processes.

There are, usually, two main branches in intellectual property: copyright, related mainly to artistic creations, and industrial property, which covers inventions, industrial designs, distinguishing signs and symbols, lay-out designs, geographical indications and protection against unfair competition(WIPO 2012).

There are a number of reasons to uphold intellectual property protection, it promotes progress, by giving creators legal protection, giving them economic and ownership rights, it inspires investment in culture and technology development, originates economic growth, jobs and new industries, thus improving quality of life and the advancement of humanity.

2.2.1. Patents

Patens are part of the intellectual property protection mechanisms, they protect inventions. More accurately, patents protect the inventor's rights of authorship, rewarding creativity. They give the applicant exclusive rights, for a period of time, to economically exploit said invention, in exchange for full disclosure of its technical aspects. This right is transactional, which means that the applicant can license it, grant sublicensing rights, or even sell it. The concept of invention may vary depending on the patenting laws of each country, but there is a general consensus that describes inventions as new solutions to technical problems (WIPO 2008).

In order to obtain a patent, the applicant must first satisfy a number of conditions, as described by WIPO, in general, they are the following:

- Industrial Applicability (utility). The invention must be of practical use, or capable of some kind of industrial application.
- Novelty. It must show some new characteristic that is not known in the body of existing knowledge (referred to as prior art) in its technical field.
- Inventive step (non-obviousness). It must show an inventive step that could not be deduced by a person with average knowledge of the technical field.
- Patentable subject matter. The invention must fall within the scope of patentable subject matter as defined by national law.

There are some things that cannot be patented. According to the Portuguese institute of industrial property(Armário 2011), which represents the European thinking on this matter, those are:

- Scientific theories or mathematical methods;
- Schemes, rules or methods, such as those for doing business, performing purely mental acts or playing games;
- Inventions that go against public order;
- Human cloning and human genome modification processes;
- Methods of medical treatment or diagnostic for humans or animals.

Once the application is submitted, a committee validates it. If approved the applicant is granted the right to prevent third parties, without consent, from making or using, or gaining any kind of economic advantage from their product or process (WIPO 2008).

Patents are especially useful in the development of technology, since it is necessary for the patentee to fully disclose its invention, every inventive step and methodology used, providing others with the knowledge to further develop the technology.

2.2.2. Patents in Software

In the specific case of CADs, we are dealing with innovations and inventions that are related to software development and computer science. Specifically, the technical advances will include algorithms, mostly associated with machine learning, computer vision, and image processing.

As the definition of invention is not very clear, because an invention is something created by the human mind and so may be only a concept or an idea, the patentability of software is also very susceptible to interpretation, as it is a set of instructions or algorithms, and as is does not have a direct industrial application. However, the major patent offices, like those of Europe, the US and Japan, have been reviewing their requisites for software inventions, and as ben possible to patent some software systems, and each office, usually, has his own set of conditions and criteria for patentability.

The European Patent Office (EPO) uses the definition of computer-implemented inventions, meaning an invention “which involves the use of a computer, computer network or other programmable apparatus, where one or more features are realized wholly or partly by means of a computer program”, instead of software, so to remove the ambiguity of the term “software”. For the computer-implemented invention to be patentable it needs to solve a technical problem in a new and non-obvious way (Osterwalder 2013).

2.3. Technology Forecasting

The technology forecasting (TF) is defined as anticipating the future state of a certain technology fields using, as basis, the current and past knowledge (Choi and Jun 2014).

By monitoring technological innovation and evolution, companies and governments, can create strategies, plane accordingly and most important, be proactive and prepared in the rapidly changing technological environment(Lee and Lee 2013).

Table 2.2 contains a list of some TF methods, there are various methods, and each one of those has its pros and cons. Most of these where based on the experience and knowledge of experts in the field, thus are subjective and unstable (Jun, Park, and Jang 2012, Choi, You, and Na 2014). There are also some more quantitative methods, such as roadmaps and bibliometrics. These are more focused in the analysis of patents and scientific articles, and arrive to more objective results. However, as they tend to use only the bibliographic fields, these results may be limited (Lee, Yoon, and Park 2009, Daim et al. 2006, Lee et al. 2009).

Table 2.2 - Technological forecasting methods (Daim et al. 2006)

Category	Definition	Forecasting Methods
Direct	Direct forecast of parameter(s) that measure an aspect of this technology	Expert Opinion (Delphi, Surveys, NG), time series analysis, trend extrapolation (growth curves, substitution, life cycle)
Correlative	Correlative parameter(s) that measure the technology with parameters or other technologies	Scenarios, lead-lag indicators, cross impact, technology progress function, analogy
Structural	Explicit consideration of cause-and-effect relationships that effect growth	Causal models, regression analysis, simulation models (deterministic, stochastic, gaming), relevance trees, morphology

2.3.1. Patent Analysis Techniques

Patents have always been a source of a variety of information, being a source of technical and commercial knowledge. They give inputs in the assessment of the competitive position, help in the calculation of the firms market value, for purchase or mergers, and avoiding infringements, as they are, mostly, freely accessible and with well-structured databases (Choi, You, and Na 2014).

Its correct analysis is becoming ever more important, especially in technology driven businesses, providing valuable insights for R&D management, source of innovative ideas and technology forecasting (Lee, Yoon, and Park 2009). These analyses are also very useful to find vacant areas of technology, giving good information about upcoming industries and markets, important to organize and define an organization's R&D policies (Choi and Jun 2014). Finally, the number of patents in a certain technology gives us notions into the impact and innovation of said technology, in the respective field, and it is also possible, through the counting of patent and patent applications, to access the level of innovation of countries or entities (Choi, You, and Na 2014).

Patens are usually divided in two parts, structured text, which is normally bibliographic elements and uniform across patents, and unstructured text, that is usually more text heavy, consisting of the state of art, description, technical specifications and claims (Lee, Yoon, and Park 2009).

As the correct analysis of all this data is very time consuming and normally needs an expert's opinion, most of the patent analysis techniques use bibliographic elements, like patent citations, i.e., the count of citations of a patent in subsequent patents, to represent significant relations between patents (Lee, Yoon, and Park 2009). According to Kim, Suh, and Park (2008) this approach as four main limitations they are:

- Difficulty grasping the overall relationship among patent documents.
- The limited scope of analysis and the richness of potential information.
- Citation has no capability of considering internal relationship between patent documents.
- Finally, citation analysis is a time-consuming task because it needs an exhaustive search.

There have been great advancements in patent analyses methodologies focused on overcoming these limitations, and with the use of data mining there has been great improvement in this area (Tseng, Lin, and Lin 2007).

Data mining is the process of discovering and extracting information from big blocks of data, in our case the patent databases, applying machine learning, statistical analyses, artificial intelligence, and other methods, to discover patterns in datasets, for trend analyses, automated classification, and other useful applications. Using text data mining techniques, as text segmentation, summary extraction, feature selection, term association, cluster generation, topic identification, and information mapping, it is possible to transform unstructured text into a structured one. This kind of automated work alleviates the workload of the experts, which is expensive and subjective, obtaining as good or even better results especially in areas where accuracy is not essential (Lee, Yoon, and Park 2009).

2.3.2. Visualization Methods and Patent Maps

The visualization result is called patent graph if an analysis of patent documents is based on the structured data and patent map if it is based on the unstructured data, but the general term patent maps can refer to both cases. There are many forms to represent the obtained information through patent maps, the most popular use the information extracted from the bibliographic fields of patent document to provide simple statistical results(Jun, Park, and Jang 2012, Lee, Yoon, and Park 2009).

In their paper, Jun, Park, and Jang (2012) propose a more objective technology forecasting model for procuring vacant technology areas, using patent documents, as objective data, and a matrix map and K-medoids clustering, based on support vector clustering, as quantitative methods, this model is represented in figure 2.1.

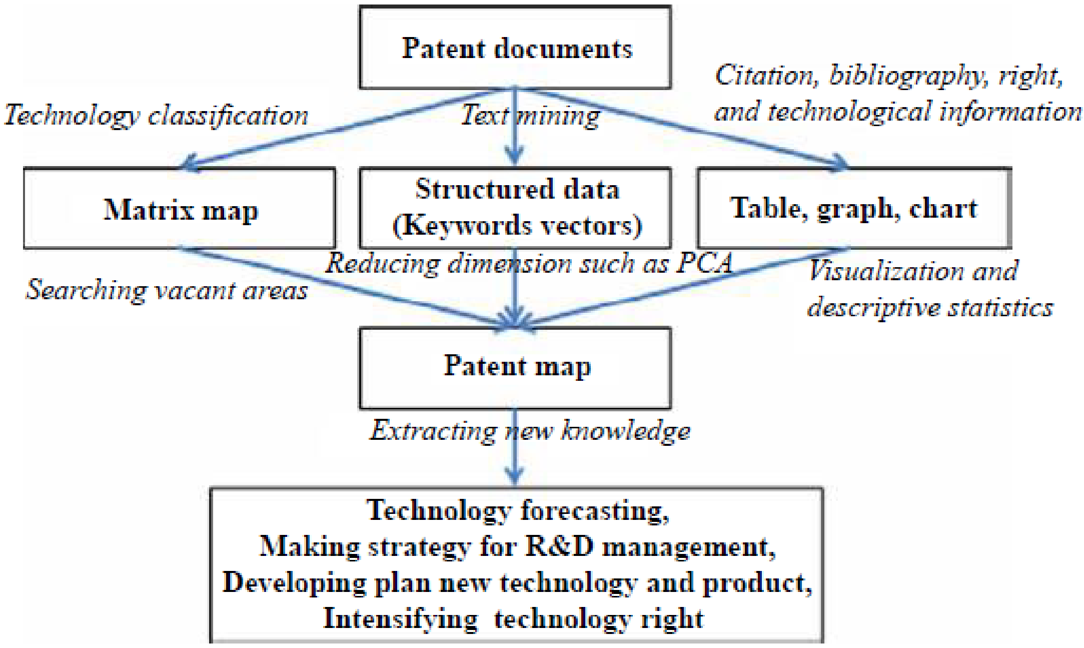


Figure 2.1 – Patent analyses based on matrix map (Jun, Park, and Jang 2012)

Another method, as described by Kim, Suh, and Park (2008), is based on keywords extraction, not involving text mining, but instead the usual method of experts opinion, creating then the map according to semantic relations between patents, an overview of their approach can be seen in figure 2.2.

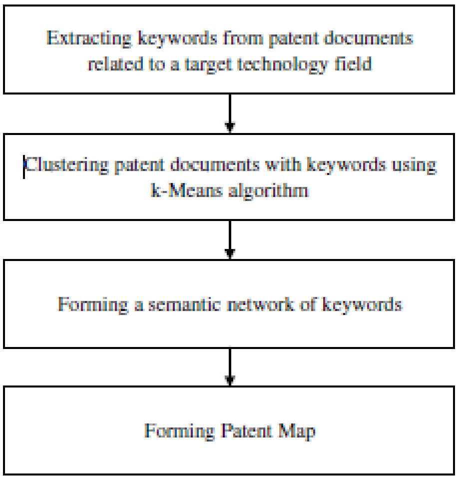


Figure 2.2 - Framework of visualization method for patent analysis (Kim, Suh, and Park 2008).

2.4. Computer Aided Diagnosis

Computer-aided diagnosis (CAD) is rapidly entering the radiology mainstream. Using computer algorithms, the output is used by radiologist as an aid to the diagnosis. This process reduces the time a technician has to spend looking through medical imagery.

CAD systems algorithms, generally, consist of a combination of several techniques, which may include: image processing, image feature analysis, and data classification by use of tools, such as artificial neural networks (Shiraishi et al. 2011).

These systems help physicians, turning the diagnosis process swift and thus expediting the process from examination to treatment. For example, in breast cancer examination, the patient is submitted to a mammography, the resulting mammogram is primarily screened for identification of suspicious areas, and then those areas of interest receive special view mammograms to determine if the patient should get a biopsy. Two CAD systems can help in the process: computer-aided detection can be used to help radiologists find the suspicious areas, and computer-aided diagnosis can be used to help radiologists decide whether a known lesion is benign or malignant on diagnostic mammograms (Nishikawa 2007).

Breast, lung and colon cancer diagnosis have a similar process, and each can consume a lot of time from a radiologist, especially in the screening examination. Therefore, most of CAD applications in clinical situations has begun in these examinations and commercial CAD systems for detection of these cancers are now available for clinical use (Shiraishi et al. 2011). As these systems prove capable of aiding physicians, it is expected that this technology expands to other medical imagery fields, one good indicator of this is the number of recent research in CAD related to other organs, for example, the brain, vascular systems and liver.

2.4.1. Computer Aided Diagnosis – Retinopathy

There are a few types of retinopathies that can be diagnosed through image analysis. Some examples are diabetic retinopathy, that may lead to blindness, retinopathy of prematurity, hypertensive retinopathy, and even cardiovascular diseases can be early detected trough the analysis of a fundus image (Mendonca and Campilho 2006).

Fundus imaging is a process where 3D structure of a retina is projected on to the 2D plane, after acquiring this image, using some kind of device (Mookiah et al. 2013).

The next step is the detection and extraction of retinal features, like the fovea, macula, optic disc and the vascular tree, and clinical features, microaneurysms, hard exudates, soft exudates or cotton wool spots, hemorrhages, neovascularization and macular edemas (Mookiah et al. 2013). This are made using one or various segmentation algorithms or some variation of, for example, thresholding techniques, histogram-based methods, region-growing and a series of other methods (Mookiah et al. 2013).

To finish up the automated diagnosis process there is then a classification step, in which each extracted feature is catalogued in classes (in this case, anatomical structures and the abnormal lesions) or, in other words, calling each feature by their name.

This is done using machine learning techniques, as artificial neural networks, support vector machines, Bayesian networks, and other algorithms. This step usually evolves two phases: in the first one, the algorithm is trained to accurately distinguish and correctly identify each feature, using for this a training dataset, composed of fundus images previously noted, usually by a physician. Most of the times, this only needs to be performed once (Mookiah et al. 2013).

The second phase consists of testing, it is the phase in which the patient's fundus images are processed by the previously trained algorithm, and from this the diagnosis is made. Figure 2.3 illustrates a CAD system for Diabetic Retinopathy(DR) screening (Mookiah et al. 2013).

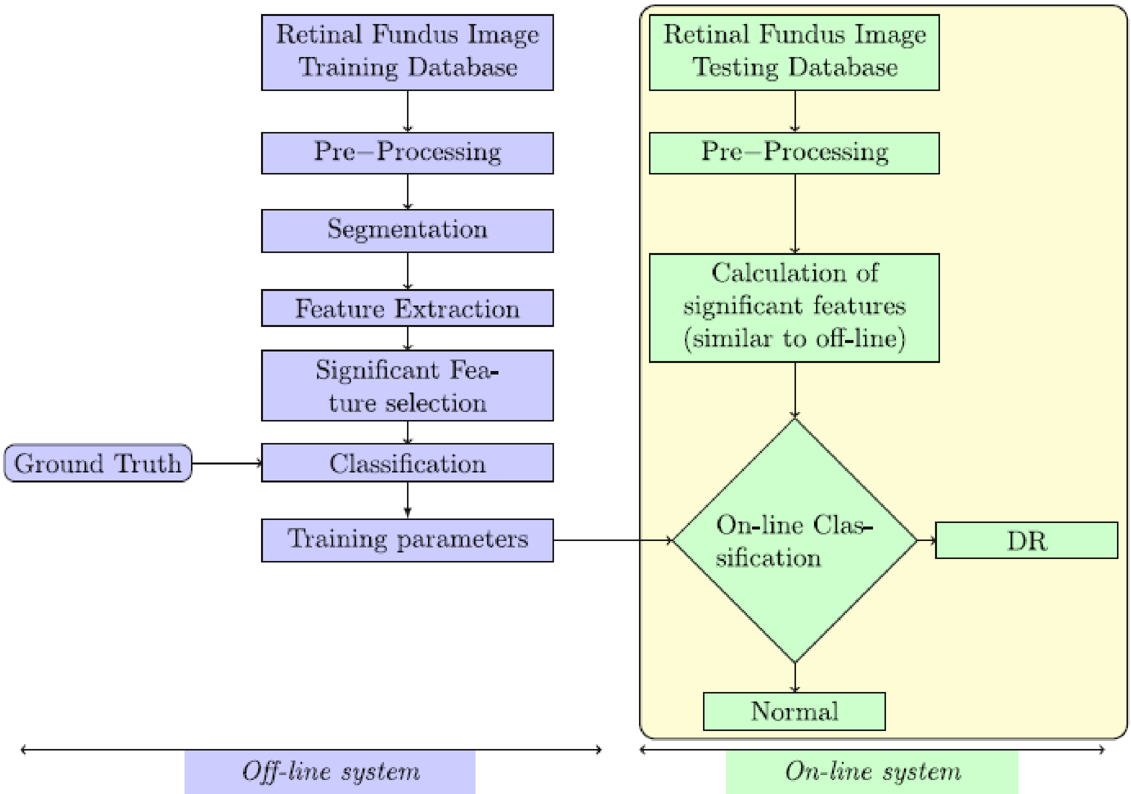


Figure 2.3 - Overview of the computational steps in automated DR diagnosis (Mookiah et al. 2013).

Chapter 3

Problem Characterizaton

The objective of this dissertation is the identification of major patenting strategies in medical image industry for computer-aided diagnosis, focused on retinal features detection and retinopathy diagnosis.

With a quantitative and qualitative analyses of patent portfolios, through the systematic examination of the structured and unstructured data in international patents, by exploring search engines, like EPO's Espacenet and AULIVE's Patentinspiration, and patent database DOCDB from EPO, we can retrieve some discerning information.

This information can give us a snapshot of the current state of the technological field, like the companies with most patents, an idea of the countries with more applications in the field and the evolution of patent applications across the years, as well as some insightful views into the technology, the main components of said patents and the focus and evolution of patented innovations.

For this analysis we will adapt the methodologies sited in chapter 2, this will allow insightful view on the product pipeline, understanding the technology, its development and trends.

3.1. Methodology

As a methodology to address the issue at hand, we used patent search and analysis to answer our research questions. The search was primarily based on a keyword list and then on patent classification codes. The analysis was made through patent claims analysis, matching the said claims to the imaging processing steps described in section 2.4.

3.1.1. Search Method

The first step of our analysis is the creation of a patent dataset that contain a sufficient number of patents to make the analysis relevant, but not too many so that we get lost in the “sea of information”.

For this we defined certain keywords, which we obtained through scientific papers in the area and experts’ opinion, related to CAD and the retina, and reviewed some patents to understand their composition. Afterwards, we used the relevant codes in the International Patent Classification (IPC) for filtering our results.

3.1.1.1. Keyword Table

The papers we analyzed where selected from a set of published papers in the area, including papers from Professors Ana Maria Mendonça, Aurélio Campilho and Jaime Cardoso, experts in the field of image processing, biomedical image analysis(Mendonca and Campilho 2006, Mendonca, Campilho, and Dashtbozorg 2014, Mendonca et al. 2014, Doi 2007), machine vision and machine learning(Rocha Neto et al. 2011).

These experts, and respective papers, where chosen according to their knowledge as well as to integrate a component of interaction in this phase. As they are Professors at FEUP, it was easier to iterate with them in the retrieval of the keywords and the assessment of the usefulness of said keywords in the search for patents in CAD.

The following table contains the main keywords from the analyzed papers and that the experts validated. The keywords are divided in three categories: Automation, Imagery and Medical.

Table 3.1 - Retrieved keywords from papers examination.

Automation	Imagery	Medical
Automatic	Digital Imaging	Retinal Vessels/Vasculature
System	Segmentation	Optic Disc
Machine Learning	Labeling	Retinopathy
Support Vector Machine	Classification/Classifier	Arteriolar Narrowing
Artificial Neural Networks	Feature Selection	Diabetic Retinopathy
	Region of Interest	Retinopathy of Prematurity
	Fundus Image	Hypertension
		Retinal Fundus Image
		Retina

Through the use of a combination of these keywords we did a primary search for patents in CAD-retinopathy, this will be explained in more detail in the following chapter.

This search was used to get a broader range of results, assess the main components that are part of a patent in this technology field and retrieve the main classification symbols that represent them.

3.1.1.2. Classification Filtering

By searching for a specific keyword, normally, we get a large number of results. These results contain not only the technology we are interested in, but also a number of other patents in the most varied fields of application. Through the use of the International Patent Classification symbols, we refined our primary search, adding a filter that limits the results to a certain area or areas of interest.

The Classification represents the whole body of knowledge which may be regarded as proper to the field of patents for invention, divided into eight sections, figure 3.1 (World Intellectual Property Organization 2015).

A	HUMAN NECESSITIES
B	PERFORMING OPERATIONS; TRANSPORTING
C	CHEMISTRY; METALLURGY
D	TEXTILES; PAPER
E	FIXED CONSTRUCTIONS
F	MECHANICAL ENGINEERING; LIGHTING; HEATING; WEAPONS; BLASTING
G	PHYSICS
H	ELECTRICITY

Figure 3.1 - International Patent Classification sections (WIPO 2016).

These sections are then divided in classes, subclasses and groups, as exemplified in figure 3.2, each being more specific than their parent. After observing the various sections and the patents obtained in the primary search we evaluated that the main classifications that describe CAD are under sections **A61B** and **G06:**

A - HUMAN NECESSITIES

- **A61 MEDICAL OR VETERINARY SCIENCE; HYGIENE**
  - **A61B DIAGNOSIS; SURGERY; IDENTIFICATION**

G - PHYSICS

- **G06 COMPUTING; CALCULATING; COUNTING**

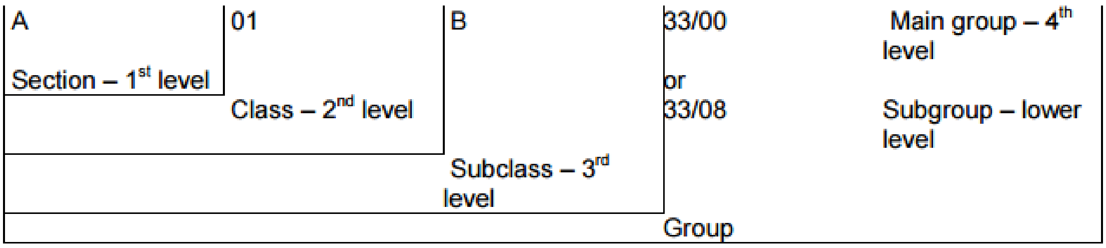


Figure 3.2 - Description of an International Patent Classification(World Intellectual Property Organization 2015).

3.1.1.3. Search Engines

For the primary search we used Espacenet(EPO 2016). This is a free online patent search engine, which has a database of patents from more than 90 countries, developed by the European Patent Office.

In the advanced search tab of the online service we are able to use keywords to search the title and abstract of patents, retrieving every patent related to a certain topic, technology or method, and screen the results according to an inventor or applicant, a time frame or their classification.

With this we were able to retrieve a significant number of patents that were used to get some of our quantitative findings, like the top companies with most patents granted, a time line with the evolution of the number of patents along the years and the local of application.

The second search was made using the Patentinspiration(AULIVE 2016) search engine. This is a more user friendly application that has a range of visualization tools. One of the major differences from the Espacenet interface is that it allows the user to look for specific keywords not only in the patent title or abstract, but also the claims or the whole patent text.

Both of these engines use the same database and have an export function that gives us the data in a spreadsheet usable format, csv or xls, which where the basis for the subsequent dataset construction and analysis.

3.1.2. Patent Analysis

After the construction of our dataset the next step was the analysis. This was made using Microsoft Office Excel™, with its data manipulation features it's a powerful tool for the quantitative analysis of our data as well as being useful for the organization of our qualitative findings.

3.1.2.1. Quantitative Analysis

The quantitative findings where obtained by reviewing the title, abstract and the structured text contained in each patent. With the review of the title and abstract we could assess which patents were about our target technology and which were not, in our dataset, constructed previously, and the structured text, which includes:

- Publication number;
- Application number;
- Priority number;
- Publication date;
- Applicant;
- Inventor.

Was useful to collect a good amount of data regarding the state of the technology, its evolution and the main players in the field, inventors and patent holders, which will be fully detailed in the next chapter.

3.1.2.2. Qualitative Analysis

The qualitative findings were made after a detailed review of the patents dataset originated from our second search. This was a smaller dataset, retrieved after a more direct search with stricter filtering.

This analysis involved the same initial steps as the primary analysis, with the correct identification of which patents where related to our target technology, then proceeding to the examination of the claims and the detailed description of each of this patents, trying to identify the components of each of these inventions, the main steps and the main claims involved in each one of these steps, this process is illustrated in figure 3.3.

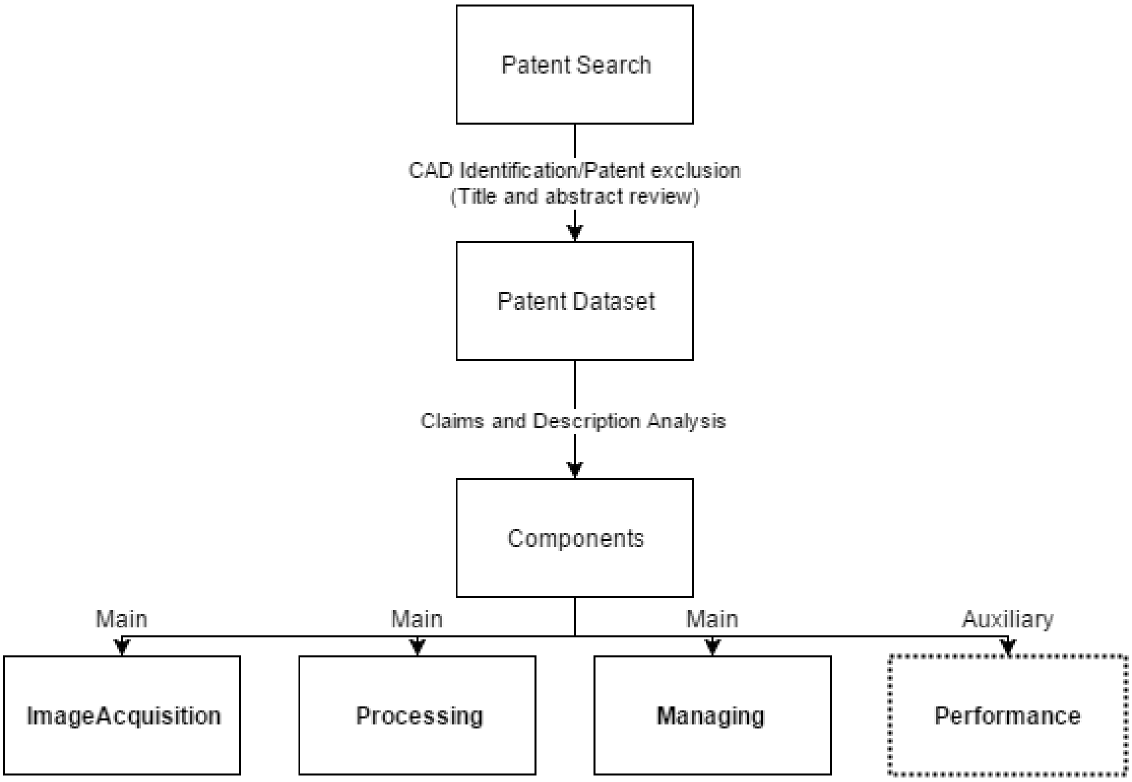


Figure 3.3 - Block diagram representing the qualitative analysis procedure.

Through the analysis of some of this patents and some of the papers reviewed for the keywords identification step of our work, described previously, we gathered a basis for the separation of the main elements of a CAD system, to facilitate the analysis and the visualization process, separating them in the following categories: **Image Acquisition**, **Processing**, **Managing** and **Performance,** which is kind of an auxiliary category that can be present in all the others.

Image Acquisition is the process of retrieving the image, using some kind of device for this purpose, in this case the fundus image of a retina, this was considered one of the main categories because there were some patents that had some emphasis in how they acquired or some inventive step applied in this phase, like light source or mechanism.

The **Processing** category involves all kinds of methods and algorithms, from image enhancing and analysis as well as machine learning techniques for the classification process, to detect, identify and characterize the retinal features. This is the core of a CAD system, incorporating the detection of the lesions and the diagnosis of the retinopathy, normally done through software. This involves a big number of steps so we further divided this in three sub-categories:

- **Automatic Localization and Extraction:** the processes that revolve around the segmentation of retinal and clinical features, like the optic disc, optic nerve and the vasculature.

- **Automatic Classification:** through machine learning algorithms, the previously extracted features are then classified, i.e. the pixels that represent them are tagged as something, for example veins, arteries or lesions.
- **Automatic Parameterization:** some retinopathies or other diseases can be identified by observing some characteristics of some of the features, like vessel tortuosity or caliber. Every process or method that automatically measures these parameters is put under this category.

The **Managing** component is all that include some kind of controlling or administrative step, as interfaces, database management and, sometimes, others with direct interaction with the diagnosis, like processing farms handling.

Finally, the **Performance** category, only a few patents give some information about this, or give any kind of importance to the performance aspect of their invention, but this is one of the differentiation aspects between inventions. This can range from a little reduction of costs to faster processing steps.

Chapter 4

Results

After a long, and exhausting, analysis we obtained some useful result that made us able to visualize some important aspects into the industry, the technology and its evolution.

4.1. Quantitative Findings

For our primary search, we used keywords or a combination of keywords, table 4.1, obtained previously.

Table 4.1 - Primary search: keywords used, fields of search, IPC filter used and result.

Keywords	Field	Filter	Results
"Retinal Image"	Title and Abstract	G06 and A61B	96
"Retinal Image Analysis"	Title and Abstract		58
"Retinopathy"	Title and Abstract	G06	29
"Retinal Fundus Image"	Title and Abstract		124
"Retina"	Title and Abstract	G06T7/00	86

This resulted in 411 results in total, from this we removed 151 duplicated and non-CAD related patents, after analyzing their title and abstract. The 260 patents obtained where then divided into CAD-Retinopathy and CAD-Retinopathy related, resulting in 64 related and 196 CAD systems that were used for our quantitative analysis, figure 4.1.

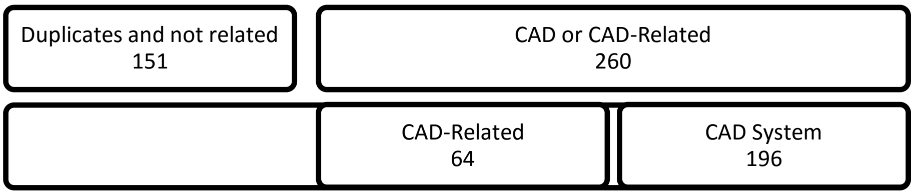


Figure 4.1 - Search results division.

4.1.1. Main Contributors

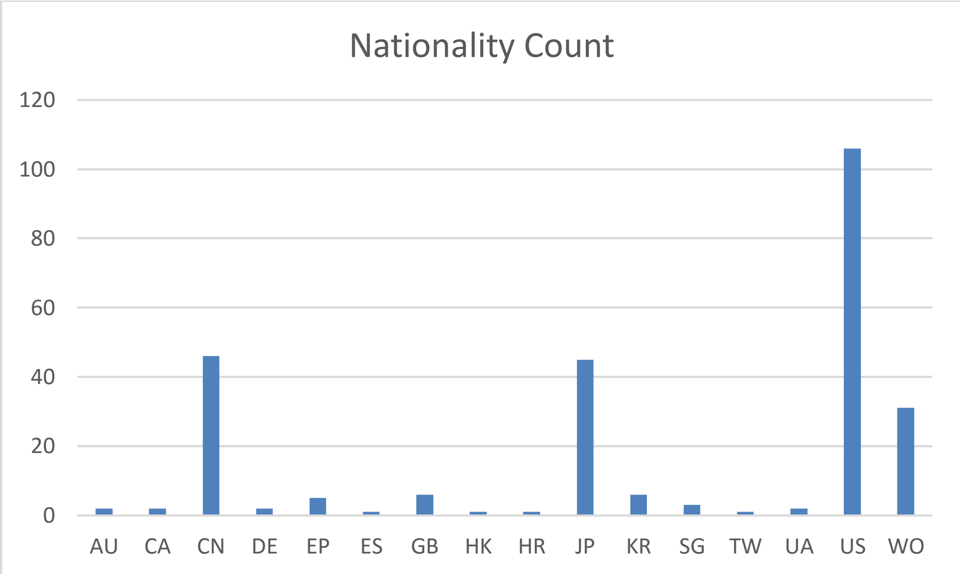
In table 4.2 are present the top 20 applicants with big multi-national companies, like Canon, specialized in imaging and optical products, Nidek and TopCon, present mainly in the medical equipment and devices industry.

Table 4.2 - Top 20 applicants.

Applicant	Occurrences
CANON KK [JP]	16
NIDEK KK	10
CANON KK	7
TOPCON CORP [JP]	7
OPTOS PLC [GB]	5
NIDEK KK [JP]	4
UNIV IOWA RES FOUND [US]	4
UNIV ZHEJIANG [CN]	3
UNIV NANJING SCIENCE & TECH	3
KOWA CO [JP]	3
UNIV SINGAPORE [SG]	3
TOPCON MEDICAL SYSTEMS INC [US]	3
UNIV GIFU TAC CO LTD	2
NIPPON KOGAKU KK	2
UNIV CENTRAL SOUTH	2
IDX LLC [US]	2
UNIV MICHIGAN [US]	2
CHINESE ACAD INST AUTOMATION	2

We can also observe in this top list that there are a considerable number of universities, this indicates a large investment by them in the development of this technologies and also that universities are one of the main incubators for its progress.

In terms of place of “birth” we could identify three regions as the main generators of this CAD systems. As we can see in the fallowing graphic the region with most published patents is the United States of America, with a fairly big margin related to the others, more than double, the other two are China and Japan with the same amount of published patents.

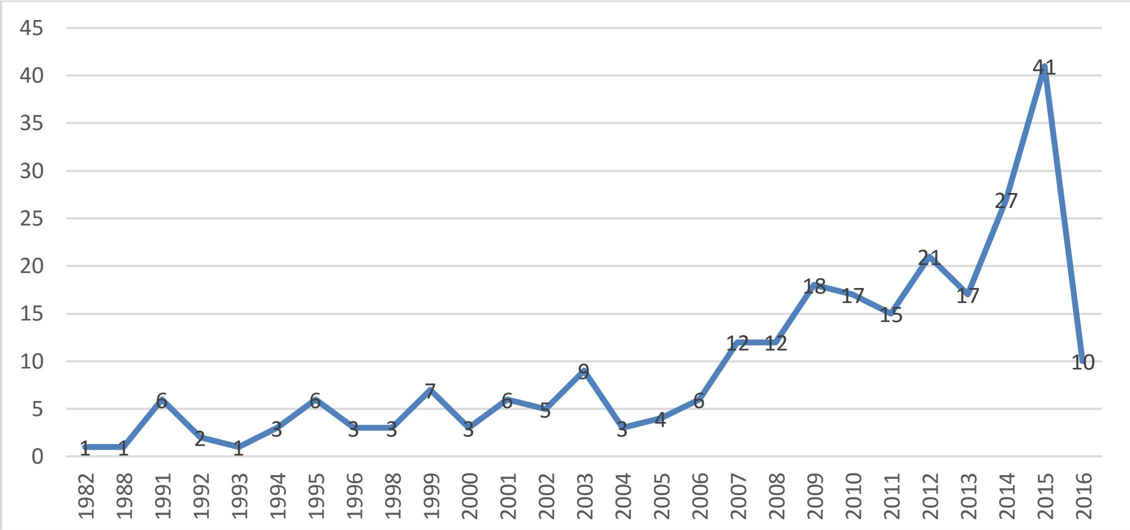


Graphic 4.1 - Dispersion of applicant nationality.

4.1.2. Timeline

Using the publication date of the obtained patents, as of March of this year, we could create a timeline. As can be seen in graphic 4.2 there is a crescent number of patents published throughout the years, peaking at the year 2015. As patents are only published 18 months after their initial application date, this means that patents published in 2015 were filed from July 2013 to June 2014.

The increase in the published patent numbers can be explained by the evolution of related technologies, for instance, processing power of computers, improved image acquisition devices and new and improved image processing algorithms.

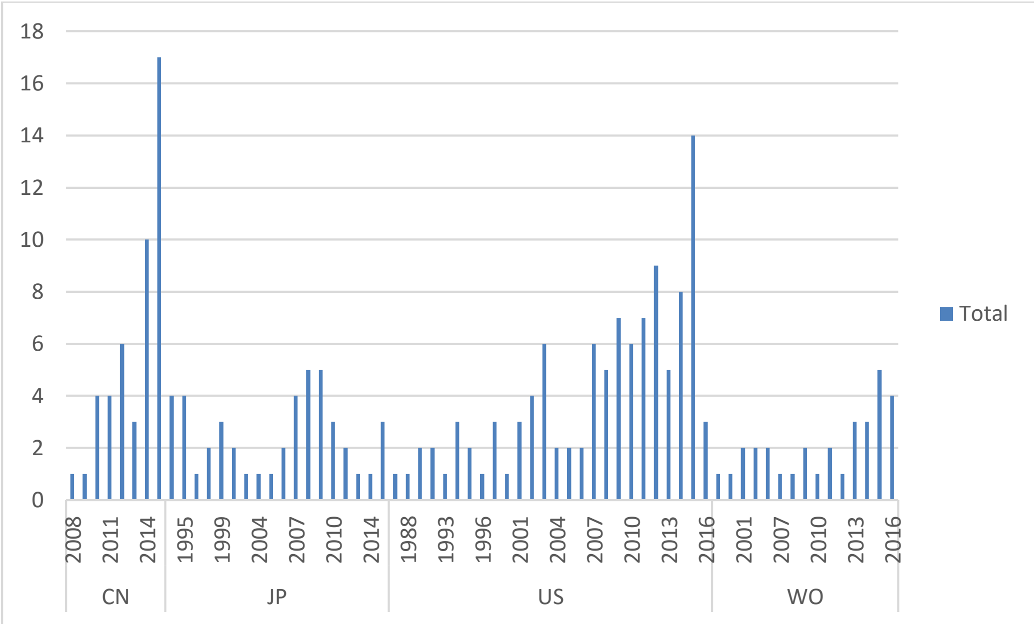


Graphic 4.2 - Timeline of publication date as of march of 2016.

This curve also shows a growing interest in the patenting of computer aided diagnosis methods, especially over the last ten years.

In graphic 4.3 we can see the distribution in the top 4 application offices. Though this graphic may not be fully representative of the evolution of the technology, it is important as it shows were the patent protection is being sought. We can see that both China and the United States of America have a crescent development of inventions in CAD-Retinopathy, Japan as been stable and the World Office applications have seen a slight increase through the years.

Doing a linear regression for each of the offices' dispersions we could verify that the Chinese has the major rate of increase, surpassing the US office by a considerable margin. This has major implications in terms of strategy, as it shows that there is a shift where the protection is sought. The emergence of China shows that this country is a new geography that may be commercially exploited by the companies in this industry in the next few years.



Graphic 4.3 - Dispersion of the patent publications through the years in the TOP 4 offices.

4.2. Qualitative Findings

To construct the dataset of this analysis we first searched for "retinopathy" in title, abstract and claims, resulting in 8322 patents (1 per family), 17346 total, we then refined this search with classification filtering using the symbol G06, which returns every patent in:

- Section G: Physics;
    - Class 06: COMPUTING; CALCULATING; COUNTING.

From this class we excluded sub-classes C, digital computers in which all the computation is effected mechanically, and Q, data processing systems or methods, specially adapted for administrative, commercial, financial, managerial, supervisory or forecasting purposes, obtaining 60 patents, but, with the analysis made in the previous section, we considered including the sub-class Q as some of the reviewed patents had a step of data processing, storage or managing, for example, incorporating patients previous history and demographics into the diagnosis or storing and managing previous analysis.

This resulted in 67 patents as the dataset of this analysis. We then proceeded to examine each patent title and abstract, as in the first analysis, resulting in 24 CAD-retinopathy patents, from this we excluded 4 patents that where not translated.

At this point, we started the analysis of the main patent claims and description. As patent claims hold validity in court, should a patent be litigated, they are written with a certain structure, and sometimes are not easy to read.

From one perspective, the claims must be descriptive enough and represent an embodiment of the invention (i.e., a way that the invention could be implemented). However, as the claims hold validity in court, they are also written very broadly, so they don't limit the scope of the patent.

The concept of dividing each one into categories was not the only in-depth analysis done. In regard to the complexity of the description of each patent, it was difficult to evaluate all the components of each invention.

We started by the abstract, which is a brief summary of the invention disclosed. However, as abstracts are always searched by the search engines, frequently they are not clear, or lack certain important or defining aspects of the invention. We then had to go deeper in the description, to try to get a visualization of what each one was about we tried to get a sense of the main features contained in them.

In table 4.3 are shown 5 of these main features summaries, by reading these we can swiftly understand the focus of the invention without the need of a deep knowledge in the technology's subject, for example we can see that the focus of patent **US2015254524A1** is a new segmentation algorithm or that patent **WO2014186838A1** comprises remote medical diagnosis with a client and server systems. The full scope of the data can be found at appendix A.

Table 4.3 - Main features of 5 of the analyzed patents.

Publication number	Main features
US2015254524A1	Main features: segmentation and extraction of the vascular tree of a subject, discovering random pathway, pattern or network through the use of an algorithm. This system constructs the vascular tree starting from a point, being then capable to automatically track various measures and parameters of said vessels.
US9089288B2	Main features: step of quality enhancement for easier extraction, being then able to classify the extracted regions between vessels, red lesions or micro aneurysms
US9008391B1	Main features: variety of technics that follows every step of a CAD system, outlining the operation of an Image Analysis System, Database and Communication System and an Application Program Interface (API)
WO2014186838A1	Main features: remote medical diagnosis, Client system that possesses: an acquisition device, interface, storage and network connection and a Server system that includes: database, management system and processing system. The operator acquires the retinal images, along with patient information, these are transferred to the main server, are analyzed, through image processing and machine learning algorithms verifying the presence or absence of retinopathies, and returning a full report to the client device.
US8896682B2	Main features: may be used separately from the acquisition unit, uses machine learning to automatically classify abnormalities present in the subject fundus image, after features and parameter extraction through image analysis techniques using patient demographics and previous data for algorithms corrections.

As explained in chapter 3, we tried to divide each patent in its main components and technologies, being separated into 4 categories: image acquisition, processing, managing and performance.

Table 4.4 is a representation of this division, for easier visualization of the main constituents of each patent we used a color scheme in this table, the criteria for the presence or absence of a field is the clear reference to something related to said category, in the embodiments or claims, like a technique, algorithm, technology or other related materials.

Table 4.4 - Patents categorization of main aspects of the invention: image acquisition, processing, managing and performance.

Publication number	Publication date	Image Acquisition	Processing	Managing	Performance
US2015254524A1	10/09/2015				
US9089288B2	28/07/2015				
US9008391B1	14/04/2015				
WO2014186838A1	27/11/2014				
US8896682B2	25/11/2014				
US2014314288A1	23/10/2014				
US8868155B2	21/10/2014				
US8831304B2	09/09/2014				
WO2012136079A1	11/10/2012				
US2012027275A1	02/02/2012				
US8098907B2	17/01/2012				
US2011129133A1	02/06/2011				
WO2010139929A2	09/12/2010				
WO2010030159A2	18/03/2010				
US7583827B2	01/09/2009				
US2009143685A1	04/06/2009				
WO2004082453A2	30/09/2004				
US2004105074A1	03/06/2004				
WO03020112A2	13/03/2003				
WO0215818A2	28/02/2002				

As we can see clearly the most prominent category is Processing, as can be expected of a CAD system, present in every patent: Therefore, in order to gain further insight into the Processing phase, it was divided in sub-categories and a further detailed analysis was made.

The other categories were less referenced, these being one of the differentiating factors between each patent, mainly in the Image Acquisition, with a novel acquisition device or process, or in terms of Performance, with faster algorithms or quality assessment methods.

Most patents have a Managing component, but it is barely mentioned, like the interface program or the storage medium and such, so this was not one of the main categories explored. One thing that was noteworthy is the observation of an increase in the investment in the managing component of the CAD systems developed, with the incorporation of online systems and databases, processing farm with remote clients, or just better software tools.

4.2.1. Processing - Sub-Categorization

We tried to evaluate, through this sub-categories, the main techniques or algorithms used or their objective, like extraction or classification of a specific feature, when it was distinguishable.

Here are two examples of this sub-categorization, the first, US9008391B1, revolving around the examination of the detailed description of the patent and the second, WO2014186838A1, obtained through the claims section.

US9008391B1 (numbers between [] refer to items in the patent description)

- **Automated localization and extraction:**
  - **Pre-processing:**
    - [0142] 1. Image-Level Fundus Mask Generation;
    - [0151] 3. Image Size Standardization;
    - [0153] 4. Noise Removal;
    - [0145] 2. Optic Nerve Head Detection;
  - [0176]-[0197] Interest Region Detection: User specified parameters according to lesion of interest;
  - [0198]-[0201] Local Region Descriptors: number or vector used to describe the extracted features;
  - [0297]-[0308] Vasculature extraction: Using a plurality of technics;
  - [0309]-[0366] Lesion Localization: using the interest regions and descriptors.
- **Automatic classification:**
  - [0413] Multi-Level Descriptors for Screening;
  - [0415] Hybrid Classifiers;
  - [0419] Ensemble Classifiers;
  - [0421] Deep Learning.
- **Automatic Parameterization:**
  - [0367]-[0381] Lesion-Based Biomarkers.

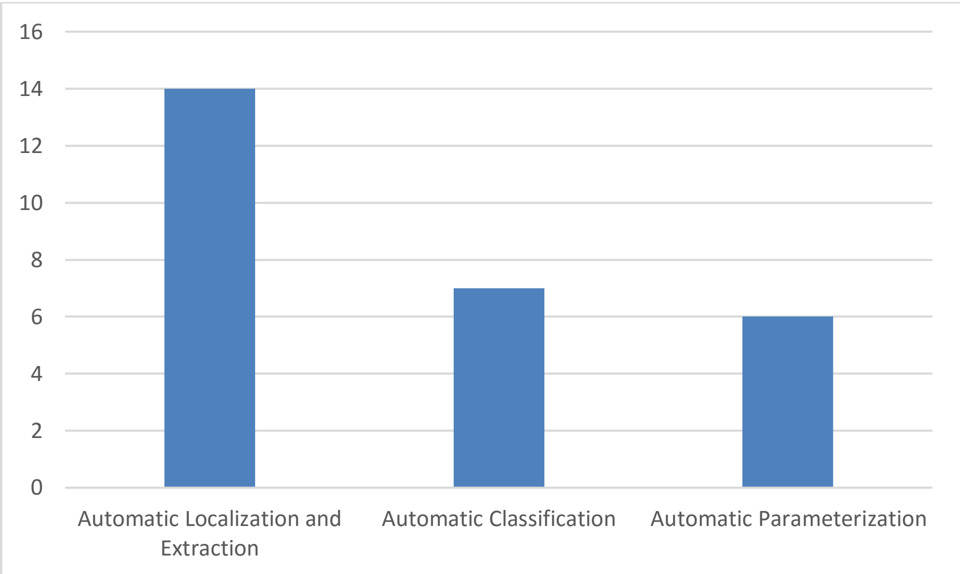
WO2014186838A1 (numbers between () refer to claim number in the patent)

- **Automatic localization and extraction:** Claim: 16-27; 30-31; 33
  - (16) image analysis is performed at least in part using a machine learning algorithm;
  - (18) identify blood vessels;
  - (19-24) microaneurysm detection;
  - (26-27) hemorrhage detection;
  - (30-31) optic disc and cup, optic disc atrophy region detection;
  - (33) Bright lesion detection.
- **Automatic classification:** Claims: 28-29.
  - (28) processing devices aggregate candidate features with candidate features from a microaneurysm detection process;
  - (29) a) a rule based selection of candidate features; and b) a machine learning algorithm.
- **Automatic parameterization:** Claims: 32-34
  - (32) cup-to-disk ratio, peripapillary atrophy;

- (34) Blood vessel abnormality analysis.

These where two of the better examples, as there were cases in which it was very difficult to assess specific techniques or algorithms used, or in which the patent only described loosely the subfield of the technique, for example “plurality of machine learning techniques” as in patent [US8896682B2]. This was another reason for doing the main features analysis.

The following graphic illustrates the number of clear references to algorithms related to one of the sub-categories that we identified. This does not imply that the invention does not use algorithms associated to this processes, as most of them have at least one step of each, it mainly indicates that the allusion to them is very light or too broad.



Graphic 4.4 - Graphical representation of the Processing sub-categorization.

Nonetheless we can infer some indicators from this, we can see that most of the patents have some greater focus in the automatic localization and extraction process, generally the inventions have some new approach in using the image processing algorithms or do some changes to them to make them most suitable for their system.

The automatic classification process is less specified, most of the patents use classification algorithms in a lot of stages, but rarely fully indicating the changes made to them. Most of the references are in parameters modification and in the training step of the classifier.

Lastly, the automatic parameterization, this is contained in almost all patents, but the small number indicates that this is mainly a supporting process in most of them. On these 6 patents, from which we identified this process, the automatic parameterization is used for diagnosis purposes, using the parameters obtained, for example, vascular tortuosity, cup-to-disc ratio, vessel caliber and others, as another indicator of presence or absence of retinopathies.

Chapter 5

Conclusions and Future Work

Through patent observation we can retrieve a numerous amount of good information related to the state of a certain technology, as patent holders have to fully disclose the details for the invention they want to protect, as well as giving insights into the industry it belongs through the structured data contained in the patent.

The analysis present in this work gathered some good insights into the CAD-retinopathy industry, allowed us to gather information about prior technological advancements in the field, and determine, possible, future trends.

We identified major players in this area, most of them multinational companies that have a long history behind them, some related to medical imagery products, like the Japanese Nidek and TopCon Corp, others more in the image acquisition sector, for example the well-known Canon, but we also identified that there are a great number of universities who are very active in this field.

This increase in university investment can be an indicator to the state and the future of technology. As one of the main centers for innovation, the substantial number of published patents and the increase of publications across the years by universities is an indicator for the "healthiness" of this technology, and that its future prospects are very good.

Across patent offices the most prominent is the US office, with the most patents published and a steady increase every year, but China's office is catching up with the biggest rate of increase of all the offices and the most number of patents published in 2015 in this field, showing that this country is a new geography that may be commercially exploited by the companies in this industry in the next few years.

The review of the patents in the second search, with the smallest dataset, may not demonstrate the full scope of the technologies involved, but can be representative of the main components, and some of the directions that these systems are tacking.

By analyzing their claims, we could identify the most important components, the ones they wanted to protect, and then the description gave us the technological aspects of said components.

We could see that the processing step of a CAD system is one of the most important, as it involves the core of the system, image analysis.

This is done through algorithms and mathematical methods, not patentable, most of the techniques are only referenced sometimes not even specified, so the main focus of these patents is in how they use these techniques, and, in conjunction with the other components, they produce an innovative system that satisfy all the conditions for patentability, subject matter eligibility, novelty, and non-obviousness. This lack of specificity throughout the patents was one of the principal insights we obtained from this analysis, leading us to approach the analysis in a different way.

In this dataset we could identify a slight trend in the latest patents, the increase of the managing component, mainly in remote diagnosis with processing farms or in databases for patient demographics integration in the diagnosis, follow up, and comparison analysis.

Other trends can be detected, but these are more general and extend across all patents, one is the increase in the quality of the image acquisition process, reducing wasted time in image enhancement and false positives, this leads to the second trend, optimization of the system performance.

Based on these observations, technological advances in the field of computer-aided diagnosis, are expected to increase. Therefore, we anticipate continued development in the field of automated analysis of human retinopathies as well as a parallel increase in the number of patent applications.

5.1. Future Work

One future work improvement is the extension of the second analysis to involve a broader dataset, doing this “by hand” wold consume a lot of time, so using datamining techniques, mining for regular expressions, we could gather sufficient data for a thorough analysis, mapping the technology and finding vacant areas of technology.

An interesting future development wold also be the expansion of these researches into other CAD fields, especially other angiopathies, and by assessing technology relations we could, perhaps, find new uses for already know inventions, finding new niches or unexplored markets.

Appendix

A. Full scope of main features analysis.

Publication number	Main features
US2015254524A1	**Main features:** segmentation and extraction of the vascular tree of a subject, discovering random pathway, pattern or network trough the use of an algorithm. This system constructs the vascular tree starting from a point, being then capable to automatically track various measures and parameters of said vessels.
US9089288B2	**Main features:** step of quality enhancement for easier extraction, being then able to classify the extracted regions between vessels, red lesions or microaneurysms
US9008391B1	**Main features:** variety of technics that follows every step of a CAD system, outlining the operation of an Image Analysis System, Database and Communication System and an Application Program Interface (API)
WO2014186838A1	**Main features:** remote medical diagnosis, Client system that possesses: an acquisition device, interface, storage and network connection and a Server system that includes: database, management system and processing system. The operator acquires the retinal images, along with patient information, these are transferred to the main server, are analysed, through image processing and machine learning algorithms verifying the presence or absence of retinopathies, and returning a full report to the client device.
US8896682B2	**Main features:** may be used separately from the acquisition unit, uses machine learning to automatically classify abnormalities present in the subject fundus image, after features and parameter extraction through image analysis techniques using patient demographics and previous data for algorithms corrections.

US2014314288A1	**Main features:** algorithms for the image processing part of an CAD system, evolving the analysis of a fundus image and the grading of the severity of the retinopathy.
US8868155B2	**Main features:** software tool, this tool evolves the various steps for a computer aided diagnosis system. This invention, as well as the tool, revolves around image processing with the objective of retrieving various measures that when used with the predictor, an algorithm that given some parameters is capable of differentiating a normal eye and an eye with abnormalities, is able to detect the signs of diabetic retinopathy.
US8831304B2	**Main features:** automatic identification blood vessels trough use of 3D SD-OCT scans information to help in the classification and segmentation of the vessel network, that can be further improved by the application, as needed, of a post processing algorithm for false positives removal and smoothing.
WO2012136079A1	**Main features:** system designed to detect lesions and/or other signs of retinopathies, through image possessing and analysis, and also a prediction for early signs of retinopathy, according to statistical algorithms that involve measurements, from the preceding image analysis.
US2012027275A1	**Main features:** through the use of various image enhancing techniques, like filters and morphological operators, mathematical algorithms and classification methods, this invention detects the presence of lesions, or disease indicators, mainly: microaneurysms, blot hemorrhages and exudates. This culminates in the assessment, according to the number of lesions detected, of the presence of a disease or not.
US8098907B2	**Main features:** method for microaneurysm detection, with a new approach: parallel processing of an retinal image for localization and extracting undesired features, that, according to prior knowledge, don't contain mycroaneurisms, reducing then false positives detection.
US2011129133A1	**Main features:** combination of an automated microaneurysm detection and management system. There are two analyses possible: microaneurysm analyses and differences analyses, one detects MAs and the other detects changes across a baseline or reference image and another image, providing an overview of the evolution of the retinopathy. The results are then stored and can be further reviewed or analysed, using the systems software, by a professional giving access to each patient records and results.

WO2010139929A2	**Main features:** detection of lesions in the retina, mainly microaneurysms. Trough the use of mask data, this invention imitates the number of false positives by excluding areas such as those derived of incorrect acquisition, dust in the sensors, damage to the sensor, etc... The detected regions are then classified using a classification method, such k-nearest Neighbour classifier.
WO2010030159A2	**Main features:** acquisition step of a fundus image, using a fundus camera, a pre-processing step, an image enhancing step, a vessel extracting step, an foveal avascular zone(FAZ) area determining step and an analyzing step, this involves a grading step to determine the severity of the Diabetic Retinopathy: non-proliferative diabetic retinopathy(NPDR) and proliferative diabetic retinopathy(PDR); Diabetic Macular Edema: mild moderate and severe.
US7583827B2	**Main features:** this invention has two preferred methods for the detection of lesions: one involving background estimation, in a sub-set of the original image, identifying candidate and classifying, as lesion or not, according to a threshold, obtained from a previously used algorithm; the other method uses region growing, from a starting point a candidate is obtained, then classifying said candidate using again an thresholding technique and algorithm.
US2009143685A1	**Main features:** process for the enhancement of flavoprotein autofluorescence (FA), involving a novel capture apparatus, for image acquisition and further processing and analysis. This invention provides methods for early diagnosis of various systemic diseases such as diabetes based on metabolic dysfunction that are discernable in the eyes.
WO2004082453A2	**Main features:** extraction of the main features of the eye for easier detection of lesions, microaneurysms and exudates, using for this a thresholding technique that is corrected according to patient information, clinical and structural, like previous lesions that may lower the threshold for easier detection, and then using the obtained threshold to classify each detected lesion.
US2004105074A1	**Main features:** obtaining 2 stereo fundus images at different angles, detection of optic disc, derive 3D surface from the 2D images, extraction of optic nerve head, measuring and disparity mapping of features (cup-to-disc ratio and deformities). Used mainly for early diagnosis of glaucoma, patient follow-up and therapy evaluation.
WO03020112A2	**Main features:** image acquisition evaluation and report, features extraction, grading of the retinopathy and database interaction for

	change evaluation and risk prediction. Used for detection of: hemorrhages, exudates, optic nerve head and vessels
WO0215818A2	**Main features:** central database of all patient images, reports, demographic data and other identifying information, off-site retinal grading algorithms which permits measuring the rate of progression or regression of the identified lesions with the use of previous patient data.

References

Armário, Susana. 2011. "Introdução à Propriedade Industrial."

AULIVE. 2016. "PatentInspiration - Free online patent search and analysis." Accessed 15.04.2016.

Choi, S., and S. Jun. 2014. "Vacant technology forecasting using new Bayesian patent clustering." *Technology Analysis & Strategic Management* 26 (3):12. doi: 10.1080/09537325.2013.850477.

Choi, S. W., Y. Y. You, and K. S. Na. 2014. "Forecasting promising technology using analysis of patent information: Focused on next generation mobile communications." *Journal of Central South University* 21 (11):4303-4310. doi: 10.1007/s11771-014-2429-y.

Daim, Tugrul U., Guillermo Rueda, Hilary Martin, and Pisek Gerdsri. 2006. "Forecasting emerging technologies: Use of bibliometrics and patent analysis." *Technological Forecasting and Social Change* 73 (8):981-1012. doi: 10.1016/j.techfore.2006.04.004.

Doi, Kunio. 2007. "Computer-aided diagnosis in medical imaging: Historical review, current status and future potential." *Computerized Medical Imaging and Graphics* 31 (4-5):198-211. doi: 10.1016/j.compmedimag.2007.02.002.

EPO, European Patent Office. 2016. "Espacenet - Advanced search." Last Modified 09.03.2016 Accessed 30.03.2016. https://worldwide.espacenet.com/advancedSearch?locale=en_EP.

Jun, S., S. S. Park, and D. S. Jang. 2012. "Technology forecasting using matrix map and patent clustering." *Industrial Management & Data Systems* 112 (5-6):786-807. doi: 10.1108/02635571211232352.

Kim, Young Gil, Jong Hwan Suh, and Sang Chan Park. 2008. "Visualization of patent analysis for emerging technology." *Expert Systems with Applications* 34 (3):1804-1812. doi: 10.1016/j.eswa.2007.01.033.

Lee, Kyungpyo, and Sungjoo Lee. 2013. "Patterns of technological innovation and evolution in the energy sector: A patent-based approach." *Energy Policy* 59:415-432. doi: 10.1016/j.enpol.2013.03.054.

Lee, Sungjoo, Byungun Yoon, Changyong Lee, and Jinwoo Park. 2009. "Business planning based on technological capabilities: Patent analysis for technology-driven roadmapping." *Technological Forecasting and Social Change* 76 (6):769-786. doi: 10.1016/j.techfore.2009.01.003.

Lee, Sungjoo, Byungun Yoon, and Yongtae Park. 2009. "An approach to discovering new technology opportunities: Keyword-based patent map approach." *Technovation* 29 (6-7):481-497. doi: 10.1016/j.technovation.2008.10.006.

Mendonca, A. M., and A. Campilho. 2006. "Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction." *IEEE Transactions on Medical Imaging* 25 (9):1200-1213. doi: 10.1109/tmi.2006.879955.

Mendonca, A. M., A. Campilho, and B. Dashtbozorg. 2014. "An Automatic Graph-Based Approach for

Artery/Vein Classification in Retinal Images."

Mendonca, A. M., A. Campilho, B. Dashtbozorg, and S. Penas. 2014. "RetinaCAD, a System for the Assessment of Retinal Vascular Changes."

Mookiah, M. R., U. R. Acharya, C. K. Chua, C. M. Lim, E. Y. Ng, and A. Laude. 2013. "Computer-aided diagnosis of diabetic retinopathy: a review." *Comput Biol Med* 43 (12):2136-55. doi: 10.1016/j.compbiomed.2013.10.007.
Nishikawa, R. M. 2007. "Current status and future directions of computer-aided diagnosis in mammography." *Comput Med Imaging Graph* 31 (4-5):224-35. doi: 10.1016/j.compmedimag.2007.02.009.
Osterwalder, Rainer. 2013. Patents for software? : European Patent Office.
Rocha Neto, A., R. Sousa, G. Barreto, and J. Cardoso. 2011. "Diagnostic of Pathology on the Vertebral
Column with Embedded Reject Option."
Shiraishi, J., Q. Li, D. Appelbaum, and K. Doi. 2011. "Computer-aided diagnosis and artificial intelligence in clinical imaging." *Semin Nucl Med* 41 (6):449-62. doi: 10.1053/j.semnuclmed.2011.06.004.
Tseng, Yuen-Hsien, Chi-Jen Lin, and Yu- I. Lin. 2007. "Text mining techniques for patent analysis." *Information Processing & Management* 43 (5):1216-1247. doi: 10.1016/j.ipm.2006.11.011.
WIPO, World Intellectual Property Organization. 2008. "Understanding Industrial Property." In: WIPO, World Intellectual Property Organization.
WIPO, World Intellectual Property Organization. 2012. "DL 450 Intellectual Property Management."
WIPO, World Intellectual Property Organization. 2016. "CLASSIFICATIONS/IPC/IPCPUB v6.3." Accessed 26/06/2016. http://web2.wipo.int/classifications/ipc/ipcpub/#refresh=page.
World Intellectual Property Organization, WIPO. 2015. Guide to the IPC.