Bárbara Sofia Ribeiro de Amorim

A Database System to support clinical diagnosis and computer assisted feature extraction of dermoscopy images

Departamento de Ciência de Computadores
Faculdade de Ciências da Universidade do Porto
Junho de 2011

Bárbara Sofia Ribeiro de Amorim

A Database System to support clinical diagnosis and computer assisted feature extraction of dermoscopy images

Tese submetida à Faculdade de Ciências da
Universidade do Porto para obtenção do grau de Mestre
em Ciência de Computadores

Departamento de Ciência de Computadores
Faculdade de Ciências da Universidade do Porto
Junho de 2011

Acknowledgments

First of all, I would like to thank Professor Teresa Mendonça and Professor André Marçal from Faculdade de Ciências da Universidade do Porto, for the oportunity to work in a scientific project such as ADDI project with challenging tasks and ambitious goals. I want to thank them their everyday support on the development of my work.

I would also like to thank all the members of the multidisciplinary team I have been working with, for all the knowledge they shared with me, all the patience with my doubts and questions and all the time they spend teaching me.

A special thanks to professor Jorge Salvador Marques from Instituto Superior de Robótica, Instituto Superior Técnico for his precious help with the statistical model to analyze QADI.

A special thanks to clinical team from Hospital Pedro Hispano for helping me learning a lot about dermoscopy and pigmented skin lesions, Dr. Jorge Rozeira, Dra. Marta Pereira, Dra. Marta Teixeira, Dra. Ofélia Morais and Nurse Lina Santos.

I want to thank my colleagues from Galeno Project (Margarida, Juliana and Luis) for helping me with several issues during the development of this work.

I wan to thank my family and friends for being always there when I needed, smiling with me, crying with me...living with me.

Last but not least, a huge thanks to my mom and dad for their support in every step of the way, without their love and education I would not be half the person I am today.

Abstract

Dermoscopy is a non-invasive diagnosis technique for in vivo observation of pigmented skin lesions used in dermatology. There is currently a great interest in the development of computer assisted diagnosis systems, given their great potential to this area of medicine. The standard approach in automatic dermoscopic image analysis can be divided into three stages: image segmentation, feature extraction/selection and lesion classification. In order to validate the algorithms developed for each stage, a great number of reliable images and clinical diagnosis are required. This work presents a software tool to collect and organize dermoscopic data from hospital databases. It is suitable to clinical daily routine and simultaneously has a data structure to support the development and validation of algorithms created by the researchers to construct the computer assisted diagnosis system. This tool is composed by a database with three related but independent modules: Clinical Module, Processing Module and Statistical Module. It will be part of a Comupter-aided diagnosis system to diagnose pigmented skin lesions through dermoscopic images.

Contents

List of Tables

List of Figures

Chapter 1

Introduction

This report describes the work developed under Automatic computer-based Diagnosis system for Dermoscopy Images (ADDI) Project from November 2010 to June 2011. In this first chapter an introduction to dermoscopy will be made, and the potential of using this method integrated in Computer-aided Diagnosis System (CADS) in order to improve the accuracy of clinical diagnosis will be explained. The purpose of this work will be presented next, along with its objectives and the institutions that embraced it, followed by the general arrangement of the report.

1.1 Motivation

Dermoscopy is a non-invasive diagnostic technique for in vivo observation of pigmented skin lesions used in dermatology. This diagnostic tool allows the clinicians to have a better visualization of subsurface structures and permits the recognition and evaluation of important morphologic characteristics not distinguishable by the naked eye. The use of this procedure in daily clinical routine conducts to an improved accuracy and robustness of clinical diagnosis, along with an overall progress of the global health care system. For example, concerning to melanoma, the use of dermoscopy by trained observers is associated with an increase in both sensitivity (percentage of melanoma recognized over the total number of melanomas examined) and specificity (percentage of non-melanoma lesions recognized over the total number of non-melanoma lesions examined) compared with that expected by examination using the naked eye [AS01]. Several other benefits can be derived from dermoscopy, namely the earlier screening diagnosis, the restrain of selected cases for exeresis and consequently driving to the

decrease of unnecessary surgeries. All of this can be translated into human resources optimization, economical thrift and time effectiveness.

So, taking into account the advantages of dermoscopy, there is currently a crescent interest in the development of automatic decision support systems given their great potential for dermoscopy. They should provide meaningful quantitative information to assist the clinical evaluation and perform the desired diagnosis accurately. Image processing methods, classification algorithms, mathematical criteria and automatic learning algorithms, provide the necessary synergy to achieve the proposed challenge [MMV+07].

In the last few years a number of independent screening clinical tests have been proposed. These procedures are suitable for health care personal with a minimum clinical training and can reduce the number of cases that need to be analyzed be specialists. Hence the screening methods, such as the pattern analysis method [CQS+03], the ABCD Rule algorithm [MB04], the 7 point checklist algorithm [ACA+11], the Menzies' method [S.r], the Cash algorithm [HDW+07] and the 3 point checklist [JSA+04], are based on a human interpretation of dermoscopic images. The common denominator of all these diagnostic methods is particular dermoscopic criteria that represent the backbone for the morphologic diagnosis of pigmented skin lesions. Nevertheless, none of these criteria is widely accepted for fitting the mental dermatologists' model for diagnosis. Furthermore, it is widely accepted and recognized that there is still considerable work to be done in order to translate the human based criteria into methodologies and algorithms capable to be implemented on CADS.

1.2 Goals

The purpose of this work is to contribute to a CADS for automatic diagnosis of dermoscopic images. Commercial clinical software available and daily used in Dermatology Service of Hospital Pedro Hispano (HPH) and its conjunct, large database of dermoscopic images were considered as the starting point for this work. A software tools was developed to collect and organize dermoscopic data, suitable for the daily clinical routine use, but also fulfilling the need for data structures and consistency required to support the development and validation of algorithms created for CADS. The final platform will be prepared to be widely applied to other care centers and hospitals with limited modifications. The final version will be hopefully easy to use both by clinical personal and training/simulation environments.

To achieve the final goal the project was divided in six phases:

- Study of existent algorithms and methods used in daily clinical routine;
- Collection and organization of clinical data;
- Development of the conceptual model for the software platform;
- Database construction;
- Implementation of software applications to provide easy and effective access to clinical data;
- Development and implementation of a computational tool to provide statistical information, clinical individual training.

1.3 Host Institutions

1.3.1 FCUP - Faculdade de Ciências da Universidade do Porto

Figure 1.1: Faculdade de Ciências da Universidade do Porto

FCUP's mission is to generate, preserve and disseminate scientific and technological knowledge. This institution, existing since 1911, promotes education of excellence in sciences and its technological applications, providing its students a multidisciplinary learning and training in scientific areas such as Mathematics, Physics and Computer Science among others. It also gives students the opportunity to take part in scientific research projects. This college develops several scientific activities and educational programs to enhance the link between the institution and the surrounding community, instilling its students the ability to work wisely, efficiently and creatively to help turn the world into a better place [FCU].

1.3.2 ULSM - Unidade Local de Saúde de Matosinhos

Figure 1.2: Unidade Local de Saúde de Matosinhos, Hospital Pedro Hispano

ULSM mission is to meet the health needs of the population living in Matosinhos. It integrates, in a unique network, education for health, education for self care, continuing care and palliative care. It operates in Hospital Pedro Hispano and in all four health centers in Matosinhos (Leça da Palmeira, S. Mamede infesta, Matosinhos and Senhora da Hora). This institution prevent evitables diseases, to improve accessibility to health services and to garantee equity, eficiency, compassion and respect in the services they provide. The Dermatology Service, leadered by Dr. Jorge Rozeira, plays an important role in tele-dermoscopy and tele-medicine. This Hospital has won several prices on projects related with good clinical practices and integration of information systems and computational applications in daily clinical routine [HPH].

1.4 Report Structure

This report is divided in four parts.

State of the art: description of existent methodologies and algorithms developed during the last twenty years. Most of them are used nowadays as tools to help the classification of skin lesion in the daily clinical routine of dermoscopy. Brief presentation of existent software and applications.

Implementation: description of all the procedureds to develop, design and implement the presented database system. Introduction of two web applications implemented, one to access selected data from the database, Processing Module Search Tool (PMST) and the other to collect clinical opinions for statistical studies, Quantitative Assessment of Dermoscopic Images (QADI).

Results: presentation of the mathematical model developed to process data collected by QADI application and exposition of a draft resolution. Some conclusions based on the analise of data collected from HPH database.

Conclusion:presentation of the conclusions achieved and some considerations about the future work, new perspectives and new goals.

Chapter 2

State of the art

The accuracy of the clinical diagnosis of cutaneous melanoma with the unaided eye is only about 60% [KPWB02]. Dermoscopy has the potential to improve the diagnostic accuracy. This chapter presents some of the most used dermoscopy algorithms' - one purely qualitative (pattern analysis) and other three semi quantitative (ABCD Rule, Seven point checklist and CASH Algorithm). Next, a brief summary about computer-based diagnosis systems is made, with special focus in an Internet-based system.

2.1 Pattern analysis

Pattern analysis was, historically, the first diagnostic procedure suggested for dermoscopy, set forth by Pehamberger et al. in 1987 [PSW] and its basic principle is that pigemented skin lesions are characterized by global patterns and combinations of local features. This procedure takes in account all of the well-established dermoscopy features and it has the best diagnostic accuracy of all algorithms, being able to classify both melanocytic and non-melanocytic lesions. The process is divided in two major steps. First determine if the lesion is melanocytic or non-melanocytic, then analyze if it is benign or malignant. To do so specialists have to identify patterns and evaluate several dermoscopic features. The five most common patterns found in melanocytic lesions [JSA+04] are:

- **Reticular pattern:** is the most common global pattern in melanocytic lesions. It is characterized by a pigment network appearing as a grid of line segments looking like honeycomb in different shades of black, gray or brown.

- **Globular pattern:** these melanocytic lesions are filled with variously-sized, round-to-oval brown structures.
- **Homogeneous pattern:** this pattern is characterized by a diffuse, uniform, structureless color filling most of the lesion.
- **Starburst pattern:** the starburst pattern is characterized by the presence of pigmented streaks and/or dots and globules in a radial arragment at the periphery of a melanocytic lesion.
- **Non-specific pattern:** in some cases a melanocytic lesion cannot be categorized into one of the global patterns listed above and is therefore categorized as having a non-specific pattern.

In non melanocytic lesions there should be an absence of criteria for melanocytic lesions and the presence of criteria considered specific for non melanocytic lesions [JSA+04]:

- **Blue-gray blotches:** structureless areas that are round-to-oval and often irregular in shape.
- **Arborizing vessels:** discrete, thickened and branched red blood vessels that are similar in appearence to the branches of a tree.
- **Milia-like cysts:** round structures with various sizes, white or yellowish.
- **Comed-like openings:** brownish-yellow or brown-black, irregularly shaped, sharply circumscribed structures.
- **Red-blue lacunas:** sharply demarcated, round-to-oval structures. The color can vary from red, red-blue, dark-red to black.
- **Central white patch:** is usually in the center of a firm lesion and is a well-circumscribed, round-to-oval, sometimes irregularly outlined, milky-bony-white area.

However, this procedure has some lacks due to its qualitative nature. It is hard to reproduce a specific diagnosis since all the evaluation of the lesion is done based on acquired qualitative knowledge, professional experience and intuition. These factors bring some issues on reliability. So in the following years quantitative procedures and algorithms started to be developed. Today those quantitative algorithms are used

along with pattern analysis to improve performance on diagnosis accuracy and to aid dermoscopic examination also by non-experts clinical personnel. In contrast to pattern analysis those algorithms analyse only a few of the well-established dermoscopic parameters, the ones known to be closely related with malignance.

2.2 ABCD Rule

The ABCD Rule of dermoscopy is based on a semi quantitative analysis of asymmetry, border, color and some important dermoscopic structures of the given melanocytic lesion. Note that this algorithm only works on melanocytic lesions, so before this rule may be applied the given pigmented lesion must be classified as melanocytic or non-melanocytic [MB04].

- **Asymmetry:** the lesion is bisected by two axes. The first one is positioned over the larger distance between two borderers point of the lesion. The second axe makes a 90º angle with the first one. The axes intersect each other in the centroid of the lesion. Asymmetry is evaluated in terms of colors and dermoscopic structures.
- **Border:** the lesion is divided into eight parts. Every zone with an abrupt cut-off of pigmented pattern at the periphery has to be considered to TDS. In contrast, a gradual indistinct cut-off of pigmented pattern is not considered to the calculation of TDS.
- **Color:** a total of six different colors are counted to determine the total color score, namely, white, red, light brown, dark brown, greyish blue and black. White color is only considered in total score if the area is lighter than the adjacent skin tone.
- **Dermoscopic structures:** pigmented network, structureless or homogeneous areas, streaks, dots and globules are the five structural features considered here. The higher the number of these structures, the higher the probability of the lesion being a melanoma.

The calculation of Total Dermoscopic Score (TDS) is done using the following formula:

$$\text{TDS} = [(\text{A score x } 1.3) + (\text{B score x } 0.1) + (\text{C score x } 0.5) + (\text{D score x } 0.5)]$$

The values of each feature are sintetize in table 2.2

Criterion	Score
Asymmetry	0: biaxial symmetry 1: monaxial symmetry 2: biaxial asymmetry
Border	1 for each abrupt cut-off in the periphery of the lesion (value between 0 and 8)
Color	1 for each color present in the lesion (value between 1 and 6)
Differential Structures	1 for each dermoscopic structure present in the lesion (value between 1 and 5)

Table 2.1: ABCD Rule algorithm score

Total Dermoscopy Score	Interpretation
Lower than 4,75	Benign melanocytic lesion
From 4,8 to 5,45	Suspicious lesion: follow-up or excision
Higher than 5,45	Lesion highly suspicious for melanoma

Table 2.2: Final classifications for ABCD Rule

2.3 Seven Point Checklist

This procedure is based in the evaluation of seven features frequently associated to melanomas. The seven selected features are divided in two groups: major criteria and minor criteria, since not all of them have the same influence in the diagnosis of melanoma. Three features have the most important part: atypical pigment network, blue-whitish veil and irregular vascular pattern. The remaining four (irregular streaks, irregular dots/globules, regression areas and irregular pigmentation) play a secondary role in the diagnosis of melanoma [ACA+11].

Major criteria:

- **Atypical pigment network:** pigment network is a grid-like or honeycomb-like structure consisting of round pigmented lines and lighter hypo-pigmented holes. In an atypical pigment network malignant cells grow chaotically distorting the normal skin anatomy, turning the network lines irregular and causing variations

in pigmentation patterns and tones.

- **Blue-whitish veil:** blue-whitish veil is the name given to an indistinct, transparent, confluent gray-blue to whitish-blue diffuse pigmentation that may extend over almost all the area of the lesion. It is associated with pigment network alterations, dots/globules and/or streaks.

- **Atypical vascular pattern:** atypical vascular pattern is a linear-irregular red structure or dotted vessels not clearly combined with regression structures and associated with pigment network alterations, dots/globules and/or streaks.

Minor criteria:

- **Irregular streaks:** streaks are brownish-black linear structures of variable thickness. They are typically found at the periphery of a lesion and are not necessarily connected to the lines of pigmented network. Linear-irregular streaks with variable thickness are a strong indicator of malignancy.

- **Irregular dots/globules:** dots are formed when pigment or cells occur in clumps. These nests of cells appear as small uniform dark dots in benign lesions. Large groups of pigmented cells in the dermis form large dots called globules. Irregular dots/globules tend to vary in size and shape and are frequently found in the periphery of lesions in tones of grey, black or dark brown.

- **Irregular pigmentation:** pigmentation refers to structureless areas of diffuse colors. In irregular pigmentation the structureless pigmented areas have irregular shape and/or distribution; usually they are black, grey or dark brown.

- **Regression structures:** regression structures are white scar-like areas, sometimes associated with blue areas. They are also structureless areas.

To get the TDS using Seven point checklist we assign a value of 2 to the three major criteria and a value of 1 to each of the minor criteria. Then, if the feature is present in the lesion its value is summed to the final score, else zero is summed. In case the TDS of the lesion is higher than three it is classified as melanoma; otherwise it is classified as a nevi. So, in order to have a lesion classified as melanoma, it has to present at least one major and one minor criteria or three minor criteria.

2.4 CASH algorithm

The CASH algorithm for dermoscopy includes a feature not used in previous algorithms, namely, architectural organization. This feature refers to the uniformity of structures and their distribution in specific locations and it is not currently considered in any dermoscopic scoring system. However, this feature may be the most important attribute in the differentiation of pigmented lesions of the skin, particularly in separating benign from malignant melanocytic lesions. Benign lesions architecture tends to remain well organized since the moment they stop growing. In contrast, malignant melanocytes evolve with an erratic behavior, not communicating with each other and, so, they are incapable of creating an architecturally ordered structure [HDW+07].

Since colors, symmetry and homogeneity/heterogeneity have the same interpretation here that in ABCD Rule, let us focus our attention into architectural order/disorder feature.

Criterion	Score
Color	1 for each color present in the lesion (light brown, dark brown, black, white, red, grey)
Architectural order/disorder	0: none/mild 1: moderate 2: marked
Asymmetry	0: biaxial symmetry 1: monaxial symmetry 2: biaxial asymmetry
Homogeneity/heterogeneity	1 for each dermoscopic structure present in the lesion (network, dots/globules, streaks/pseudopods, blue-white veil, regression structures, blotches, polymorphous blood vessels)

Table 2.3: CASH algorithm score

2.4.1 Architectural order/disorder

Architectural disorder is divided in three classes that are described next:

- **No/mild architectural disorder:** the arrangement of the dermoscopic structures and colors in the lesion is orderly or only slightly disarranged.

- **Moderate architectural disorder:** the network often shows some variability in the colors and thickness of the lines; other structures are less uniform in size, shape color and distribution.

- **Marked architectural disorder:** the network is irregular with variable thickness lines and colors and the holes have various shapes and areas; other structures are spread in a disarranged manner, they are polymorphic in size, shape, color and distributed chaotically in the entire lesion's area.

The CASH algorithm can distinguish melanoma from nevi with sensitivity and specificity comparable with the algorithms presented previously [HDW+07].

2.5 Computer-based diagnosis systems

Several groups have developed automated analysis procedures to overcome the difficulty of diagnosis due to subjectivity, qualitative nature and low reproducibility of a specific evaluation. A pioneering study of fully automated diagnosis of melanoma was conduct by Green et al. [GMP+94]. After him, others continued working in the area of image segmentation and features extraction in order to develop improved diagnosis systems. The majority of these systems are based in the ABCD Rule criteria, such the one developed by Ganster et al. [GPR+01] in 2001, Rubegni et al. [RCB+01] in 2002 or Celebi et al. [CHU+06] in 2007. Meanwhile, diagnosis systems based in the Seven point checklist have also been in development since the first attempt of using this method, in 2006 made by Betta et al. [BDLF+06], was succefull in feature identification.

Recently an Internet-based melanoma screening System was presented by Iyatomi et al. [ICOT08]. This software is a screening system accessible from all over the world, via world wide web, and capable of diagnoses dermoscopy images within 3 to 5 seconds. It uses a neural network classifier for non-acral lesions and a linear classifier for acral volar lesions.

When an image and its associated clinical data are uploaded, the system starts with defining the tumor's area of extraction. Then, it calculates the tumor characteristics and reports a diagnosis. All the information submitted and calculated is stored in

a database which makes this system also a public repository of dermoscopic images. Dermoscopic images uploaded to the system have to respect three criteria:

- The tumor image has to fit entirely within the image frame;
- The tumor may not be part of a mucosal area;
- The tumor may not present too much hair.

This system is still in development in the University of Hosei, Japan [HU].

Chapter 3

Implementation

The standard approach for processing dermoscopic images is usually composed by three different stages: image segmentation, feature extraction and selection and injury classification. Several research groups have developed automated analysis procedures and algorithms. However in all these distinct approaches a specific problem persisted. Results of different studies are not comparable because of distinct clinical image sets used in each of them. After collected, in most cases, it is a hard task to find where the images used in the researches came from due to absence of information about them.

The proposed methodology aims to design a dedicated platform, ADDI, to support the current lack of reliable and organized information sources. A ground-truth database like the one presented next is crucial to feed the researchers' algorithms and methods for several purposes (image segmentation, classification, lesion structures evaluation,...).

This platform add a new stage (Reliable Data Sources) to the three phases standard approach and gather the all four under one software. Moreover a system like this one can provide a large amount of meaningful quantitative information to assist clinical evaluation. At a further level it may lead to a fully automatic CADS for early warning diagnosis of skin lesions.

Collecting data and construct a dedicated platform like this is a complex process, since it is not a straightforward collection of clinical cases from already existents databases. In this specific case the HPH database was used.

Databases are powerful informatics tools prepared to storage large collections of data, keep them organized and providing fast and efficient access to the available infor-

mation. They should also provide a user friendly interface. These technologies are easily implemented and adaptable to any professional area. So, implementing a tool based on a database system seemed the natural choice to develop a reliable data source component for the ADDI-Platform. The presented tool is composed by three database modules: Clinical Module (CM), Processing Module (PM) and Statistical Module (SM).

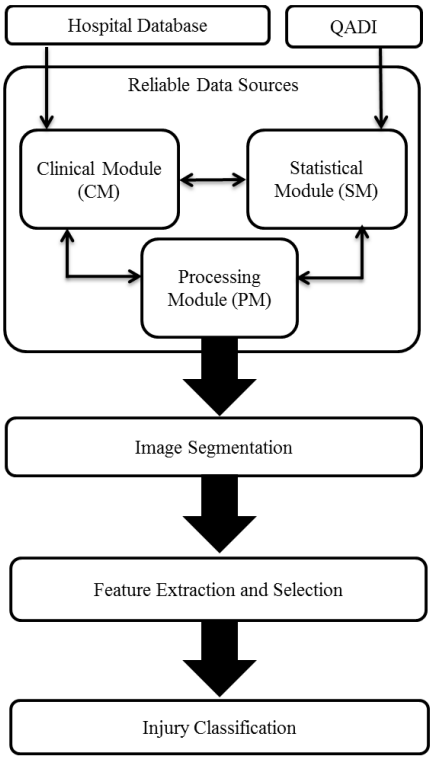

Figure 3.1: Schematic representation of ADDI Platform

The CM is to be used as clinical software where all information of patients may be stored and accessed by the authorized clinical staff only. The PM allows research team members to have access to clinical information without breaking confidentiality rules. The SM stores information of statistical studies on available data and, in the future, it will also allow clinical training on skin pigmented lesions evaluation. The construction of each of these components is divided in four stages system analysis, logical design, physical design and implementation. All stages enclose specific tasks and rules that must be followed strictly. Moreover, after the construction process, data organization, integrity and security will have to be accomplished.

3.1 System analysis

In a first stage it is essential to fully understand the software used in the hospital as well as the daily clinical routine. Furthermore, it is necessary to aggregate all the possible information among clinical staff and specialist and gather opinions on possible improvements and development of additional features not existent in their current database system, FotoFinder.

First an analysis to the software used in HPH was made. The clinical team of Dermatology Service uses regularly this software to process dermoscopic data from hospital patients and their health care centers patients. To learn about FotoFinder we went to HPH weekly to assemble with clinical team members and discuss numerous issues about clinical process of diagnose skin pigmented lesions and to monitor their daily clinical routine. Notice that, since this service is uncharged of all patients from Matosinhos County, there are two different sources of dermoscopic images. One face to face and other operated through a Tele-medicine protocol. The work sessions in HPH provided and increased insight of the problem to be solved and allow us to found some lacks to be corrected and improvements to be implemented in a new software platform, namely:

- Improve the database structure (addiction of new fields and restructuration of others).
- Ensure data integrity (a patient may only have a clinical record, every patient is identified by the same criterion).
- Decrease the subjectivity on the diagnosis (diagnosis field can not be a text box without any restrictions).
- Compel the introduction of some important information (doctor identification, date of diagnosis).
- Restrict the permissions to change information introduced previously in the system (not allowed to make alterations to previous diagnosis or clinical notes).
- Implement a functionality that allows doing the follow-up of a specific lesion over the time.
- Automatic introduction of diagnosis date by the system;
- Optimize the search tool.

- Keep clinical confidentiality of patients' identity.

This was a time consuming challenging task and required some dedicated sensitivity, since it involves the transfer of delicate information and the collaboration between multidisciplinary areas. In these phase we face several difficulties to overcome. Promote a team work under a specific clinical environment without adding any perturbation to daily clinical routine as well as fulfilling all local requirements. Work with various sets of data with different storage places and different levels of accessibility. Last but not least, the biggest challenge was to understand the clinical mental model, almost completely qualitative, and translate it into a quantitative model. All of this turns the task of analyzing the system much more complex.

3.2 Conceptual model

The collected information was organized in different groups in such a way they still reflect the real world concepts we are involved with. This drives us to the ER-model construction [Cod90]. The ER-model for each of the three database modules we have created are apresented next.

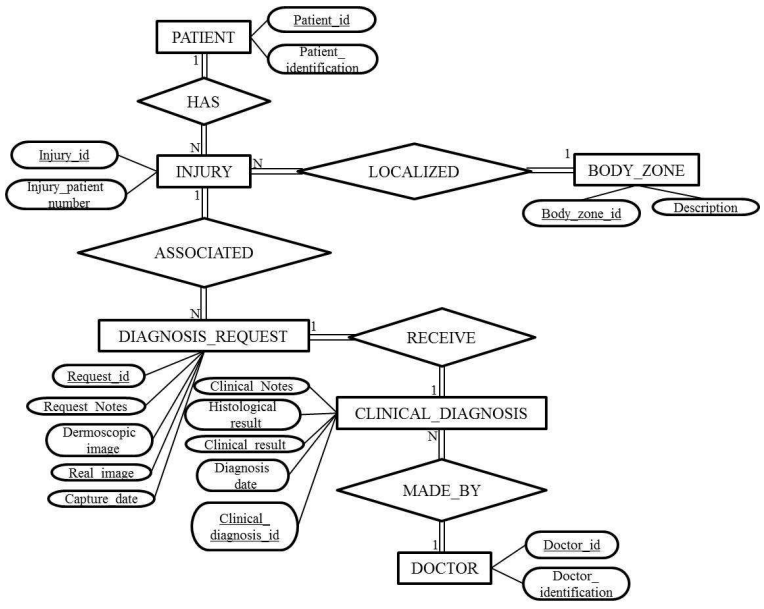

Figure 3.2: ER-model of the Clinical Module

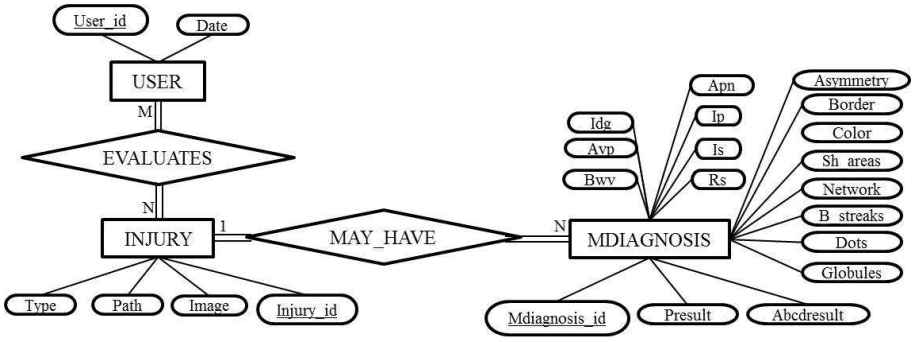

Figure 3.3: ER-model of the Processing Module

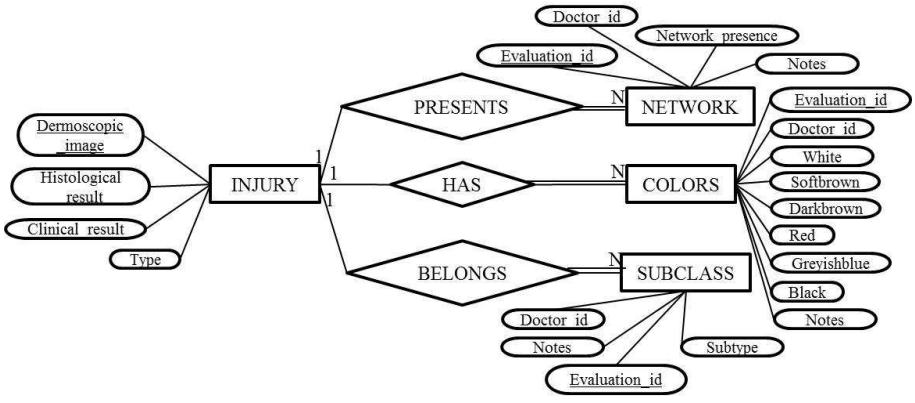

Figure 3.4: ER-model of the Statistical Module

3.3 Logical model

The next phase was to transform the ER-model into a R-model, this was done using normalization. Normalization is a systematic process that takes the ER-model built and applies him several rules [Cod90]. In This way a logical arragement that guarantees the integrity of data and minimizes its redundance is created. The R-model is completely structured from the logical view point and it is the formal representation of each of our database modules.

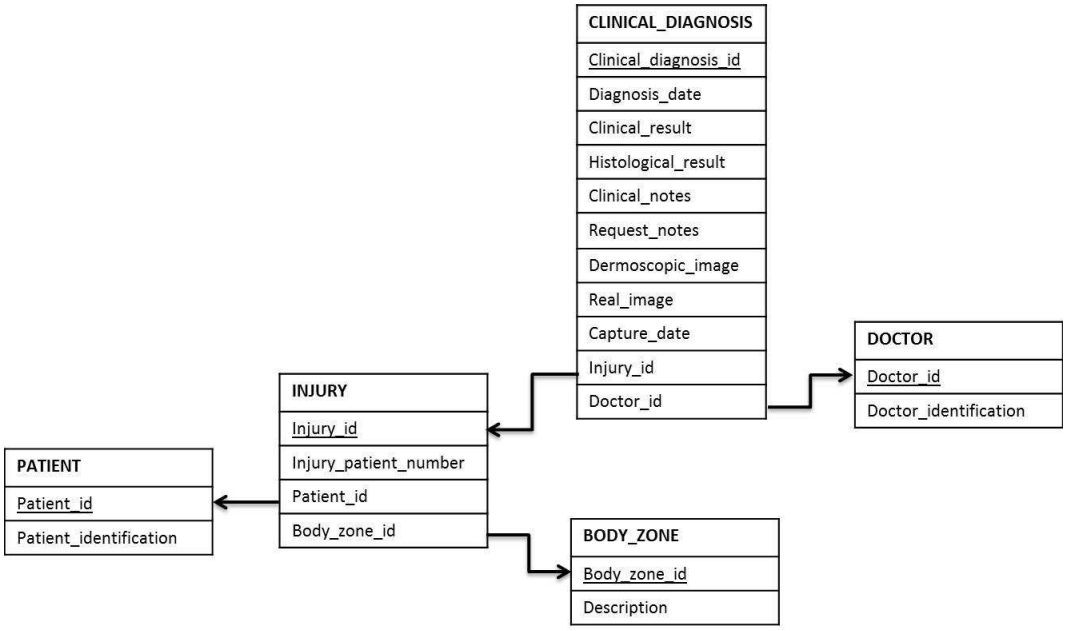

Figure 3.5: Clinical Module

3.4 Physical design and implementation

The database modules presented were implemented with SQL language using the phpMyAdmin software. The access to clinical data is made using web applications. We chose to use web applications because they are independent from the operating system and can be acessed from any place around the world. This is very usefull because the research team is spread over different laboratories in distinct places.

The tools developed were implemented using HTML and CSS to design and organize its interfaces, JS to do the information processing in the client side and PHP to do

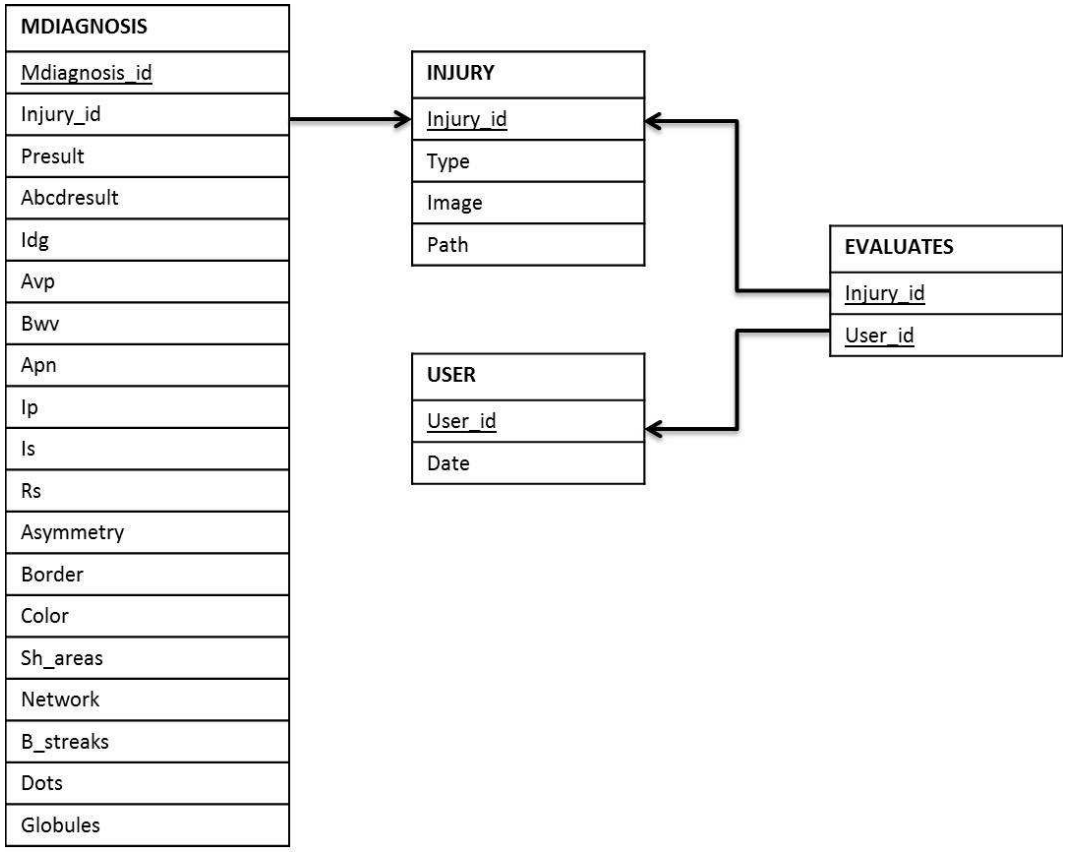

Figure 3.6: Statistical Module

information processing in the server side, including the implementation of SQL queries to the database.

3.4.1 Processing Module Search Tool

This application is a tool that allows all the research team members to have access to the clinical data present in PM. The PM is fed with data from HPH FotoFinder software, according to hospital specific interest. Hence, under the same database it is possible to automatically download a well-defined subset of images through the corresponding database interface. The resultant (downloaded) document is a text file including the list of image names. This procedure corresponds to the default option, assuming that each user has the complete set of images on a local folder. Therefore in a second step each user should select the images files locally. Alternatively, if the local server has a suitable capacity this tool may be easily adapted in to order to also automatically download the images files to a folder in the user personal computer.

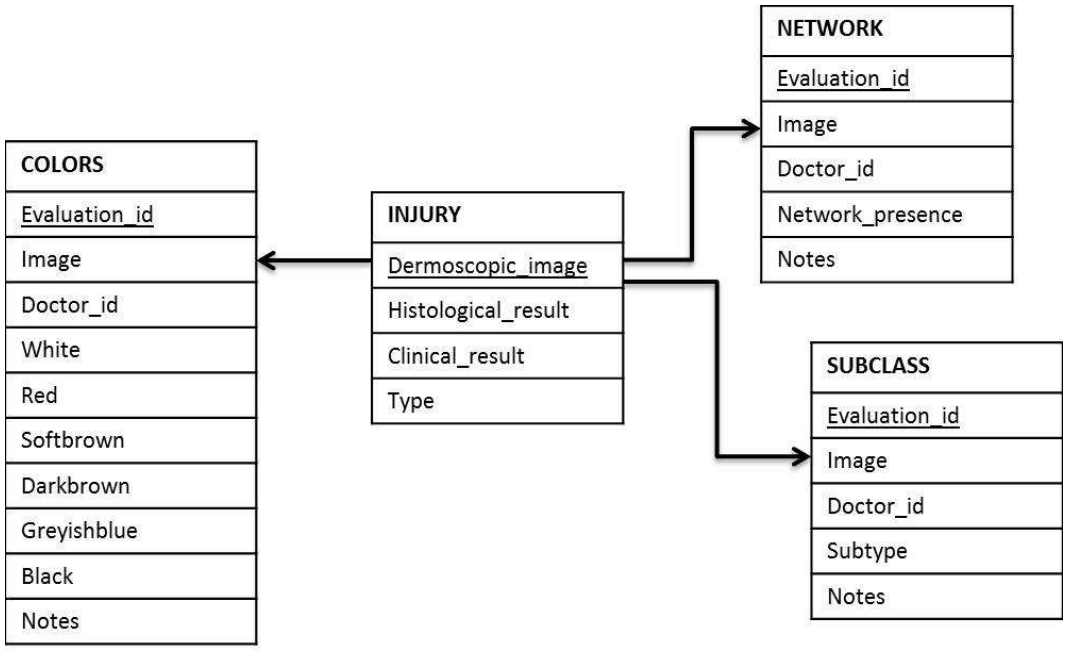

Figure 3.7: Processing Module

In both procedures the resulting information is prepared to be imported to applications developed in other platforms and programming languages. Namely, Matlab which is the software chosen by the research team members to develop the image processing algorithms. This particular application requested by the research team supplies an efficient and reliable procedure for data extraction. Furthermore it provides faster access to specific data sets, straightforward accommodation of individual requests and inhibits the presence of mismatched or duplicated images. For this sake it can be said that PMST is a robust and reliable tool for image selection from the PM.

3.4.2 Quantitative Assessment of Dermoscopic Images

In a first stage, Quantitative Assessment of Dermoscopic Images (QADI) was developed in order to collect clinical evaluations in a pre-defined set of images. Since this application is directly connected with SM, all the evaluations are automatically stored for statistical studies. This application relies on the two most used dermoscopic algorithms were used: ABCD Rule and 7 Point Checklist, both of them accepted by the International Dermoscopy Society (see pag. **??**).

Since these algorithms may only be applied in the presence of melanocytic lesions, an initial filter was introduced to check if the presented lesion is melanocytic or non-

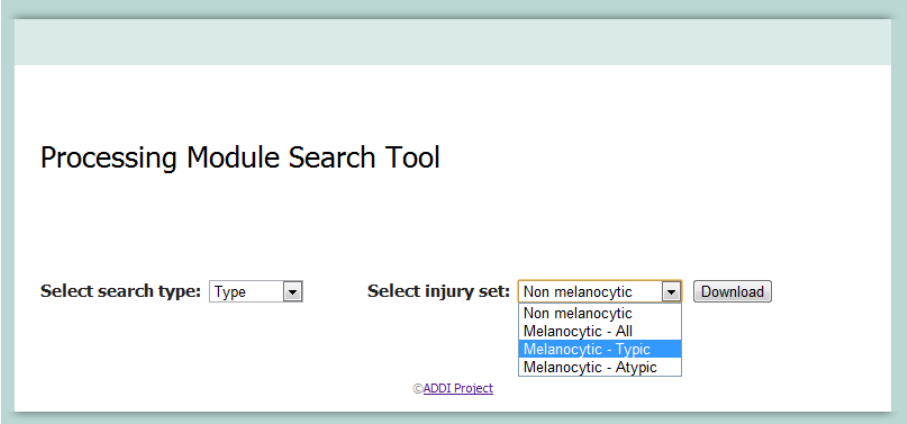

Figure 3.8: PMST: search using criterion Type

melanocytic. If the lesion is classified as non-melanocytic, the application automatically skips to the next image; otherwise the user has to evaluate the lesion. To do so the user must fulfill the form fields available for each algorithm, the necessary information for complete each label is available in the interface. Moreover, only admissible values can be introduced, since a warning pop-up shows up every time a non valid value is introduced. Furthermore at the end of each image evaluation the total score of both algorithms are displayed in the computer screen and stored together with all the parameters evaluated.

The statistical analysis of the results collected will provide the distribution function of each variable evaluated. This application is a useful tool to evaluate the sensitivity of each algorithm and in particular each one of the variables relevance in these dermoscopic algorithms and in the final clinical diagnosis. QADI can also be easily adapted to an E-training tool. If accepted by the clinical team this E-training version points to a novel procedure for guidance of non-experts in dermatoscopy allowing the user to assess for his expertise degree.

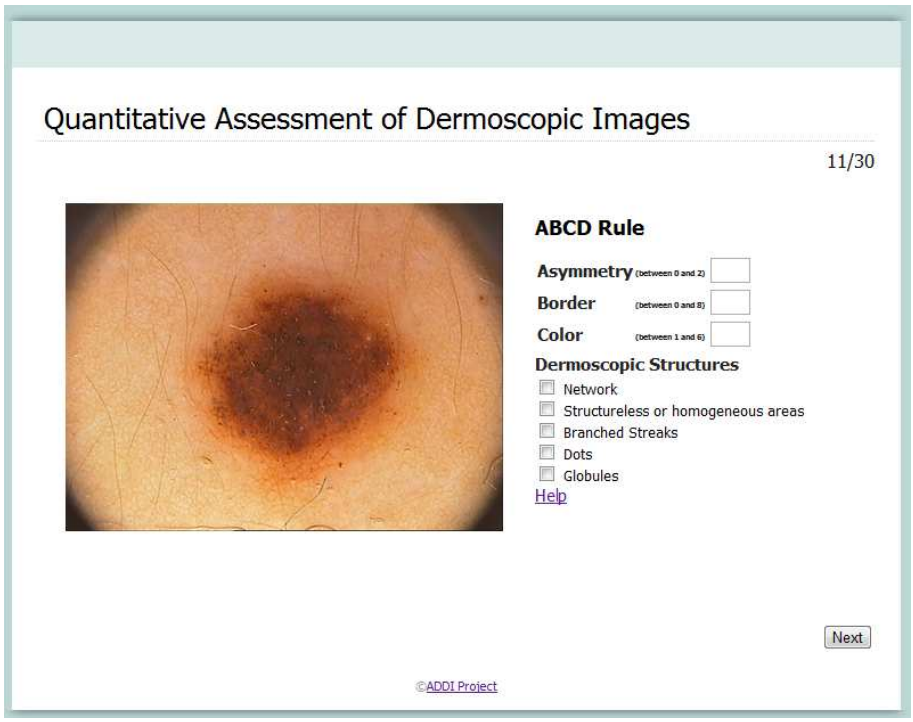

Figure 3.9: QADI: ABCD Rule form

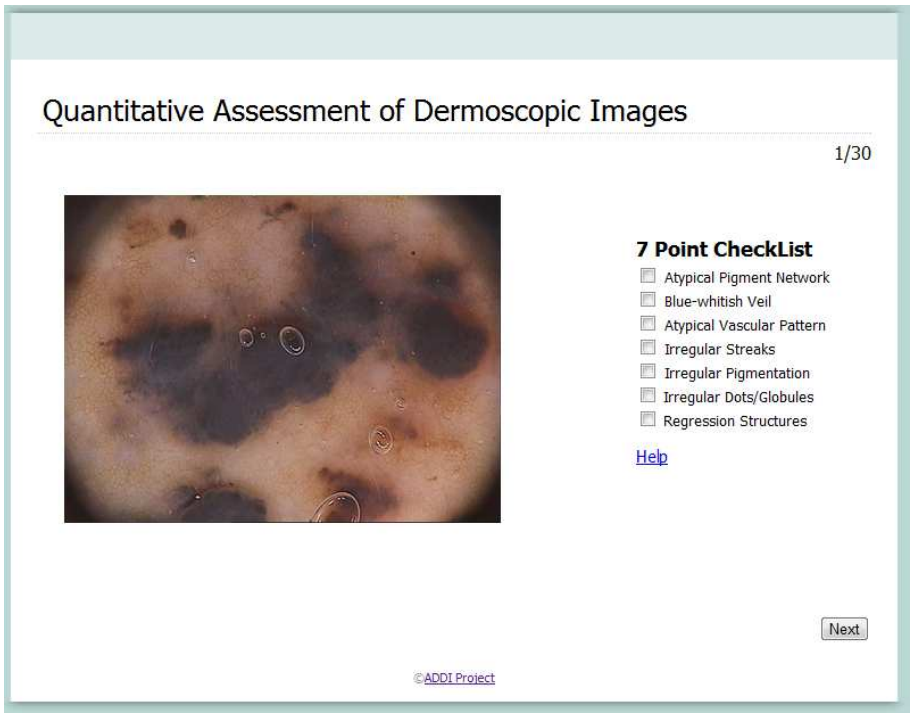

Figure 3.10: QADI: 7 Point Checklist form

Chapter 4

Results

4.1 QADI - Statistical analysis

The high degree of variability and subjectivity associated to the evaluation of specific clinical features for classification of dermoscopic images leads to the development of a dedicated software application. Moreover a first version of the mathematical model to represent Quantitative Assessment of Dermoscopic Images (QADI) is finished. aThe mathematical model already in development is contextualized and explained next.

4.1.1 Problem description

QADI web application allows dermatologist, experts in dermoscopy, to analyze and evaluate dermoscopic images of pigmented skin lesions. The user is asked to answer several questions concerning to lesions classification and dermoscopic information about pigmented skin lesions features visible in those images.

Presently this application presents two well know clinical algorithms: the ABCD Rule and the 7 Point Checklist. In this type of algorithms there are typically a finite number of admissible answers for each evaluated parameter. One by one, all the parameters can be translated in a decision with limited values.

During the weekly work sessions it was observed that experts answers are not always the same for a given image, every clinical decision has a high degree of variability due to subjectivity. This external variable is related with the expert experience in dermoscopy. It is important to the research team to characterize the uncertainty

associated to each answer and to each expert.

The characterization of each feature uncertainty is essential to learn about which features are the most robust, and consequently the better ones to obtain realistic results, when submitted to the developed algorithms.

Moreover it may be stressed that the images present different degrees of classification difficulty. There are typical images in which all the experts probably agree in almost every parameter and there are atypical cases in which they will disagree in a great number of parameters or even in global diagnosis. Therefore it would be relevant and useful to obtain different sets of images based on their main features. These sets will be used to characterize the uncertainty associated to each image classification through a statistical analysis of the clinical classification results obtained by QADI.

Every time an expert realize an evaluation of an image, he is doing an experiment. Since the diagnosis algorithms are composed by several questions, an experiment can be defined as follow:

$$\text{z=(I,e,x)}$$

where $I \in \mathcal{I}$ is a dermoscopic image from the set of dermoscopic images $\mathcal{I}$; $e \in \mathcal{E}$ is an expert from the set of experts $\mathcal{E}$; and $x \in \mathcal{X}$ is a feature vector belonging to the set of admissible answers $\mathcal{X}$.

Then it is also necessary to define when a lesion is benign or malignant. As the ABCD Rule and the 7 Point Checklist final scores (S) are directly related with the answers given by the expert to the items of each algorithm, it can be defined as a deterministic function of the vector x.

$$\text{S} = \text{f(x)}$$

The lesion is classified as malign if S exceeds a threshold T i.e.,

$$\text{S} > \text{T}$$

The described approach is still in an initial phase of development and its main objective is to study the different uncertainties associated to the use of these algorithms and its influence in the clinical diagnosis.

4.2 Collected Data

During all weekly working sessions at HPH, under the supervision of the clinical team a set of data was collected from the FotoFinder Software and processed to be included in the database. Thereafter, individual sessions, with each one of the dermoscopy experts allowed to classify the images and evaluate the most relevant lesion features. Lesions were carried out in four groups with the following distribution: 52 non-melanocytic lesions, 154 melanocytic lesions, 7 lesions or excluded to be reviewed in group and 7 were excluded due to bad image quality. From the total bank of 358 collected cases a subset of 220 images from the total data collected was used on the analysis presented in this report.

4.2.1 Tipicity

A list with only melanocytic lesion and respective diagnosis was organized. As previously refered the clinical experts were asked to distinguish the lesions in one of two groups, group M1 or group M2.

Group M1: melanocytic lesions undoubtedly benign.

Group M2: melanocytic lesions that present atypical features and may evolve to malignant lesions or malignant melanocytic lesions.

After this clinical classification process, a statistical study was carried out comparing the experts results globally and in pairs to estimate the agreement percentage. In the two clinicians comparison the agreement percentage was around the 65% dropping, when considering the three experts, to a lower value of 51%. The results show that this is not a straightforward approach since it involves a large number of variables and a high level of individual variability between experts.

4.2.2 Color

Color is one of the most relevant feature present in the classification algorithms. Therefore experts were asked to mark another list of melanocytic lesions. Appendix C represents the classifications obtained by two experts and the analyse may be summarized as follow:

The experts were asked to mark in the list of melanocytic lesions was asked to the

experts to mark which colors were present in which of the lesions. Some conclusions were taken from the results.

- Almost every melanocytic lesion has light brown and dark brown in its area.
- The range of brown tones is much bigger than just light brown and dark brown.
- It is hard to define the border between dark brown and black.
- Malignant lesions have more colors than benign ones.
- Greyish-blue is mostly present in blue nevi or melanomas.
- Red is hard to detect because it is easily mistake with vascular vessels.

As a concluding marker it can be stressed that the

Since only two of the experts perform this evaluation it is not possible to perform any statistic analysis. Neverthless and as a concluding remark it can be stressed that the presence of color, being a relevant feature, constitutes one more challange to be added to the global problem to be solved.

Chapter 5

Conclusions and future work

The purpose of this work is to contribute to a CADS for automatic diagnosis of dermoscopic images. Commercial clinical software available and daily used in Dermatology Service of Hospital Pedro Hispano (HPH) and its conjunct, large database of dermoscopic images were considered as a starting point for this work. It was presented a database system developed to assist and support processing dermoscopic images algorithms, feature extraction and lesion classification. A first version of the database system is concluded and validation tests are already in course, both by clinicians and researchers. Moreover the database system developed proved to be adequate as an initial platform to support a computer-aided diagnosis system (CADS) for dermoscopic images.

This database is constituted by three components. The clinical module (CM) is used by the clinical team to collect, store and manage patient's information. The processing module (PM) is dedicated to research teams in order to obtain a bank of robust and reliable dermoscopic data (both images and clinical diagnosis) to test the developed algorithms. This module receives a huge and permanent flow of information, since the hospital software, FotoFinder, collects clinical cases daily. Finally, the statistical module (SM) allows the development of statistical studies over pigmented skin lesions features. The access to a database system like this is an outstanding advance in terms of accessibility to clinical information enhancing the overall efficiency and organization of the Dermatology Service. This tool is suitable both for the daily clinical routine use and also fulfills the need for data structures and consistency required to support the development and validation of algorithms created for Computer-aided diagnosis system (CADS).

During this work were developed two web applications that are being tested by the clinical and research team. The Quantitative assessment of Dermoscopic Images application allows clinical experts to analyse dermoscopic images and answers to several questions concerning to dermoscopic information contained in the image. The ProcessingModule Search Tool (PMST) application allows all the research team members have access to data collected from HPH database. It is a form where the user chooses the criteria he wants to evaluate and download automatically an image set respecting those criteria.

The component formed by the PM, CM, SM and the developed web applications will instate the reliable data sources component. This structure may be easily modified, extended and enriched with new applications. Furthermore it may also complete itself, filling some lacks of information using machine learning algorithms developed based in all the knowledge acquired with the clinical specialists. The great advantage of this component relies on the independency of each module, meaning that, although the three of them are related, each of them works as a stand-alone tool.

The database system presented will be integrated in a CADS still in development. Although all the work still in progress, we can already say that a database systems like this have positive impact in being integrated in a CADS, it has great potential for dermoscopy since this component provide meaningful quantitative information to assist clinical diagnosis and at a further level, may perform an automatic early screening of skin lesions. The final platform will be prepared to be widely applied to other care centers and hospitals with limited modifications.

The absence of a well documented robust, reliable and widespread database for research goals presents deficiency for research studies. For this reason, presently, it is very difficult, almost impossible, to compare algorithms and methods from different research group, since these studies do not rely on the same image set. Moreover tracking down the distinct image source would be a hard, longstanding and often unsuccessfully process. The database system developed will overcome these drawbacks.

In near future more functionalities should be implemented to increase the computational power of this database system. A synchronization tool will be implemented to keep PM and SM updated in real-time with CM information available at the hospital. The PM and the Processing Module Search Tool (PMST) will be extended to include additional information about lesions, namely acral, facial or other. This new information is important since acral and facial lesions have a different method of diagnosis. An user friendly interface to manage the CM will be completed according with clinical

requirements and its usability will be tested by the Hospital Pedro Hispano (HPH) team in a real clinical environment. The QADI web application will be povoated with new images, over time, in order to provide even more quantitative information about dermoscopic features. The mathematical model will also be optimized to allow a large set of statistical studies over dermoscopic lesions and the diagnosis algorithms used.

The statistical analysis for developing the mathematical model in order to quantify the uncertainty associated to the features, will be an useful process and promisses to to return interesting results.

Appendix A

Acronyms

CADS: Computer-aided Diagnosis System

TDS: Total Dermoscopy Score

SNS: Serviço Nacional de Saúde

HTML: HyperText Markup Language

PHP: Hypertext Preprocessor

JS: Javascript

CM: Clinical Module

PM: Processing Module

SM: Statistical Module

ADDI: Automatic computer-based Diagnosis system for Dermoscopy Images

QADI: Quantitative Assessment of Dermoscopic Images

PMST: Processing Module Search Tool

Appendix B

Agreement Tables

Image	Expert1	Expert2	Expert3	Agreement
IMD02	M1	M2	M2	0
IMD03	M1	M1	M2	0
IMD04	M2	M2	M2	1
IMD06	M2	M2	RG	0
IMD08	M2	M1	M1	0
IMD09	M1	M1	M1	1
IMD10	M1	M1	M1	1
IMD101	M2	M1	M1	0
IMD102	M1	M1	M1	1
IMD103	M1	M1	M1	1
IMD104	M1	M1	M1	1
IMD105	M1	M1	M1	1
IMD106	M2	M2	M1	0
IMD107	M2	M1	M1	0
IMD108	M1	M1	M1	1
IMD109	M1	M1	M1	1
IMD110	M1	M1	M1	1
IMD111	M2	M1	M1	0
IMD112	M1	M1	M1	1
IMD113	M2	M1	RG	0
IMD116	M2	M1	M1	0
IMD117	M2	M2	M1	0
IMD118	M2	M2	M2	1
IMD119	M2	M2	M2	1

Image	**Expert1**	**Expert2**	**Expert3**	**Agreement**
IMD120	M1	M2	M1	0
IMD121	M1	M2	M2	0
IMD122	M2	M1	M2	0
IMD123	M2	M2	M1	0
IMD125	M1	M1	M1	1
IMD126	M2	M2	M1	0
IMD127	M2	M2	M2	1
IMD13	M1	M1	M1	1
IMD130	M1	M2	M2	0
IMD131	M1	M1	M1	1
IMD132	M1	M1	M1	1
IMD133	M1	M1	M1	1
IMD134	M1	M1	M1	1
IMD135	M1	M1	M2	0
IMD137	M2	M1	M1	0
IMD138	M2	M2	M1	0
IMD139	M2	M2	M1	0
IMD14	M1	M2	M2	0
IMD140	M2	M2	M2	1
IMD141	M2	M1	M1	0
IMD142	M2	M1	M1	0
IMD143	M1	M1	M1	1
IMD144	M2	M1	M1	0
IMD145	M2	M1	M1	0
IMD146	M2	M1	M1	0
IMD147	M2	M1	RG	0
IMD149	M1	M1	M1	1
IMD15	M1	M1	M1	1
IMD150	M1	M1	M1	1
IMD151	M2	M2	M2	1
IMD152	M1	M1	M1	1
IMD153	M2	M2	M2	1
IMD154	M2	M2	M2	1
IMD155	M2	M1	M1	0
IMD156	M2	M1	M1	0
IMD157	M2	M2	M2	1
IMD158	M1	M1	M1	0
IMD159	M2	M1	M1	0
IMD16	M1	M1	LT	0

Image	**Expert1**	**Expert2**	**Expert3**	**Agreement**
IMD160	M2	M2	M1	0
IMD161	M2	M1	M1	0
IMD162	M2	M1	M1	0
IMD163	M1	M1	M1	1
IMD164	M1	M1	M2	0
IMD165	M1	M1	M1	1
IMD166	M2	M2	M2	1
IMD168	NC	M2	RG	0
IMD169	M2	M2	M2	1
IMD17	M1	M1	RG	0
IMD170	M2	M2	M2	1
IMD18	M2	M1	M2	0
IMD19	M2	M1	M2	0
IMD20	M1	M1	M1	1
IMD21	M2	M2	M2	1
IMD22	M1	M1	M1	1
IMD23	M1	M1	M1	1
IMD24	M1	M1	M1	1
IMD25	M1	M1	M1	1
IMD27	M2	M1	M2	0
IMD28	M1	M1	M2	0
IMD29	M2	NC	M1	0
IMD30	M2	M2	M2	1
IMD31	M2	M2	M2	1
IMD32	M1	M1	M2	0
IMD33	M2	M1	M2	0
IMD35	M1	M1	M2	0
IMD36	M1	M1	LT	0
IMD37	M2	M2	M2	1
IMD38	M2	M2	M2	1
IMD39	M1	M1	M1	1
IMD40	M1	M2	M2	0
IMD41	M2	M2	M2	1
IMD42	M2	M2	M2	1
IMD43	M2	M2	M2	1
IMD44	M1	M1	M2	0
IMD45	M1	M1	M1	1
IMD47	M2	M2	M2	1
IMD48	M1	M2	M2	0

Image	**Expert1**	**Expert2**	**Expert3**	**Agreement**
IMD49	M2	M2	M2	1
IMD50	M1	M1	M1	1
IMD55	M2	M2	M2	1
IMD56	M1	NC	NC	0
IMD57	M2	M2	M2	1
IMD58	M2	M2	M2	1
IMD61	M2	M2	M2	1
IMD63	M2	M2	M2	1
IMD64	M2	M2	M2	1
IMD65	M2	M2	M2	1
IMD67	NC	M1	M2	0
IMD72	M2	M2	M2	1
IMD73	NC	NC	M2	0
IMD75	M2	M2	M2	1
IMD76	M2	M1	M2	0
IMD78	M1	M2	M2	0
IMD80	M2	M2	M2	1
IMD81	M1	M1	NC	0
IMD83	M1	M2	M2	0
IMD85	M2	M2	NC	0
IMD87	NC	NC	NC	1
IMD88	M2	M2	M2	1
IMD90	M2	M2	M2	1
IMD91	NC	NC	M2	0
IMD93	M1	M1	M2	0
IMD171	M2	M2	M2	1
IMD172	M2	M2	M2	1
IMD173	M2	M2	M2	1
IMD175	M2	M2	M2	1
IMD176	M1	M2	M2	0
IMD177	M1	M2	M1	0
IMD178	M1	M1	M1	1
IMD179	M1	NC	M1	0
IMD180	M2	M1	M1	0
IMD181	NC	M1	M2	0
IMD182	M2	M1	M2	0
IMD196	M1	M1	M1	1
IMD197	M1	M1	M1	1
IMD198	M1	NC	M1	0
IMD199	M1	M1	M1	1

Image	Expert1	Expert2	Expert3	Agreement
IMD200	M1	M1	M1	1
IMD201	M1	M1	M1	1
IMD202	M2	M1	M1	0
IMD203	M2	M1	M1	0
IMD204	M1	M1	M1	1
IMD205	M1	M1	M2	0
IMD206	M2	M1	M1	0
IMD207	M2	M1	M2	0
IMD208	M2	M1	M2	0
IMD210	M2	M2	M2	1
IMD211	M2	M2	M2	1
IMD221	M2	M1	M2	0

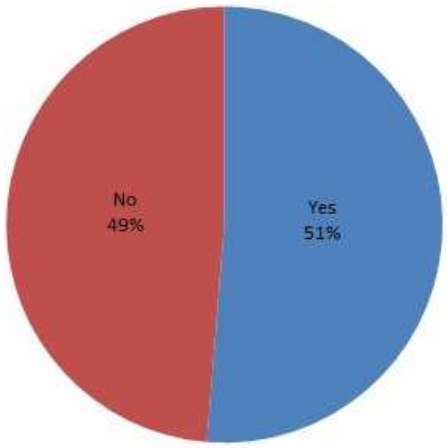

Figure B.1: Agreement percentage between three experts

M1 - melanocytic lesions undoubtedly benign.
M2 - melanocytic lesions that present atypical features and may evolve to malignant lesions or malignant melanocytic lesions.
NC - Not considered.
RG - Review in group.
LT - lesion in transformation
0 - Disagreement
1 - Agreement

Image	**Expert1**	**Expert2**	**Agreement**
IMD02	M1	M2	0
IMD03	M1	M1	1
IMD04	M2	M2	1
IMD06	M2	M2	1
IMD08	M2	M1	0
IMD09	M1	M1	1
IMD10	M1	M1	1
IMD101	M2	M1	0
IMD102	M1	M1	1
IMD103	M1	M1	1
IMD104	M1	M1	1
IMD105	M1	M1	1
IMD106	M2	M2	1
IMD107	M2	M1	0
IMD108	M1	M1	1
IMD109	M1	M1	1
IMD110	M1	M1	1
IMD111	M2	M1	0
IMD112	M1	M1	1
IMD113	M2	M1	0
IMD116	M2	M1	0
IMD117	M2	M2	1
IMD118	M2	M2	1
IMD119	M2	M2	1
IMD120	M1	M2	0
IMD121	M1	M2	0
IMD122	M2	M1	0
IMD123	M2	M2	1
IMD125	M1	M1	1
IMD126	M2	M2	1
IMD127	M2	M2	1
IMD13	M1	M1	0
IMD130	M1	M2	0

Image	**Expert1**	**Expert2**	**Agreement**
IMD131	M1	M1	1
IMD132	M1	M1	1
IMD133	M1	M1	1
IMD134	M1	M1	1
IMD135	M1	M1	1
IMD137	M2	M1	0
IMD138	M2	M2	1
IMD139	M2	M2	1
IMD14	M1	M2	0
IMD140	M2	M2	0
IMD141	M2	M1	0
IMD142	M2	M1	0
IMD143	M1	M1	1
IMD144	M2	M1	0
IMD145	M2	M1	0
IMD146	M2	M1	0
IMD147	M2	M1	0
IMD149	M1	M1	1
IMD15	M1	M1	1
IMD150	M1	M1	1
IMD151	M2	M2	1
IMD152	M1	M1	1
IMD153	M2	M2	1
IMD154	M2	M2	1
IMD155	M2	M1	0
IMD156	M2	M1	0
IMD157	M2	M2	1
IMD158	M1	M1	1
IMD159	M2	M1	0
IMD16	M1	M1	1
IMD160	M2	M2	1
IMD161	M2	M1	0
IMD162	M2	M1	0
IMD163	M1	M1	1
IMD164	M1	M1	1
IMD165	M1	M1	1
IMD166	M2	M2	1
IMD168	NC	M2	0

Image	Expert1	Expert2	Agreement
IMD169	M2	M2	1
IMD17	M1	M1	1
IMD170	M2	M2	1
IMD18	M2	M1	0
IMD19	M2	M1	0
IMD20	M1	M1	1
IMD21	M2	M2	1
IMD22	M1	M1	1
IMD23	M1	M1	1
IMD24	M1	M1	1
IMD25	M1	M1	1
IMD27	M2	M1	0
IMD28	M1	M1	1
IMD29	M2	NC	0
IMD30	M2	M2	1
IMD31	M2	M2	1
IMD32	M1	M1	1
IMD33	M2	M1	0
IMD35	M1	M1	1
IMD36	M1	M1	1
IMD37	M2	M2	1
IMD38	M2	M2	1
IMD39	M1	M1	1
IMD40	M1	M2	0
IMD41	M2	M2	1
IMD42	M2	M2	1
IMD43	M2	M2	1
IMD44	M1	M1	1
IMD45	M1	M1	1
IMD47	M2	M2	1
IMD48	M1	M2	0
IMD49	M2	M2	1
IMD50	M1	M1	1
IMD55	M2	M2	1
IMD56	M1	NC	0
IMD57	M2	M2	1
IMD58	M2	M2	1
IMD61	M2	M2	1
IMD63	M2	M2	1
IMD64	M2	M2	1

Image	Expert1	Expert2	Agreement
IMD65	M2	M2	1
IMD67	NC	M1	0
IMD72	M2	M2	1
IMD73	NC	NC	1
IMD75	M2	M2	1
IMD76	M2	M1	0
IMD78	M1	M2	0
IMD80	M2	M2	1
IMD81	M1	M1	1
IMD83	M1	M2	0
IMD85	M2	M2	1
IMD87	NC	NC	1
IMD88	M2	M2	1
IMD90	M2	M2	1
IMD91	NC	NC	1
IMD93	M1	M1	1
IMD171	M2	M2	1
IMD172	M2	M2	1
IMD173	M2	M2	1
IMD175	M2	M2	1
IMD176	M1	M2	0
IMD177	M1	M2	0
IMD178	M1	M1	1
IMD179	M1	NC	0
IMD180	M2	M1	0
IMD181	NC	M1	0
IMD182	M2	M1	0
IMD196	M1	M1	1
IMD197	M1	M1	1
IMD198	M1	NC	0
IMD199	M1	M1	1
IMD200	M1	M1	1
IMD201	M1	M1	1
IMD202	M2	M1	0
IMD203	M2	M1	0
IMD204	M1	M1	1
IMD205	M1	M1	1
IMD206	M2	M1	0
IMD207	M2	M1	0

Image	Expert1	Expert2	Agreement
IMD208	M2	M1	0
IMD210	M2	M2	0
IMD211	M2	M2	0
IMD221	M2	M1	0

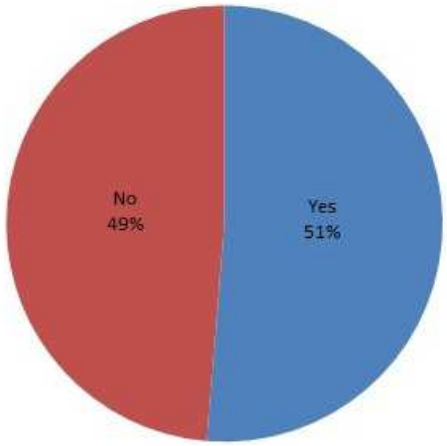

Figure B.2: Agreement percentage between two experts

M1 - melanocytic lesions undoubtedly benign.
M2 - melanocytic lesions that present atypical features and may evolve to malignant lesions or malignant melanocytic lesions.
NC - Not considered.
RG - Review in group.
LT - lesion in transformation
0 - Disagreement
1 - Agreement

Image	**Expert1**	**Expert3**	**AgreLTent**
IMD02	M1	M2	0
IMD03	M1	M2	0
IMD04	M2	M2	1
IMD06	M2	RG	0
IMD08	M2	M1	0
IMD09	M1	M1	1
IMD10	M1	M1	1
IMD101	M2	M1	0
IMD102	M1	M1	1
IMD103	M1	M1	1
IMD104	M1	M1	1
IMD105	M1	M1	1
IMD106	M2	M1	0
IMD107	M2	M1	0
IMD108	M1	M1	1
IMD109	M1	M1	1
IMD110	M1	M1	1
IMD111	M2	M1	0
IMD112	M1	M1	1
IMD113	M2	RG	0
IMD116	M2	M1	0
IMD117	M2	M1	0
IMD118	M2	M2	1
IMD119	M2	M2	1
IMD120	M1	M1	1
IMD121	M1	M2	0
IMD122	M2	M2	1
IMD123	M2	M1	0
IMD125	M1	M1	1
IMD126	M2	M1	0
IMD127	M2	M2	1
IMD13	M1	M1	1
IMD130	M1	M2	0
IMD131	M1	M1	1
IMD132	M1	M1	1
IMD133	M1	M1	1
IMD134	M1	M1	1
IMD135	M1	M2	0

Image	**Expert1**	**Expert3**	**AgreLTent**
IMD137	M2	M1	0
IMD138	M2	M1	0
IMD139	M2	M1	0
IMD14	M1	M2	0
IMD140	M2	M2	1
IMD141	M2	M1	0
IMD142	M2	M1	0
IMD143	M1	M1	1
IMD144	M2	M1	0
IMD145	M2	M1	0
IMD146	M2	M1	0
IMD147	M2	RG	0
IMD149	M1	M1	1
IMD15	M1	M1	1
IMD150	M1	M1	1
IMD151	M2	M2	1
IMD152	M1	M1	1
IMD153	M2	M2	1
IMD154	M2	M2	1
IMD155	M2	M1	0
IMD156	M2	M1	0
IMD157	M2	M2	1
IMD158	M1	M1	1
IMD159	M2	M1	0
IMD16	M1	LT	0
IMD160	M2	M1	0
IMD161	M2	M1	0
IMD162	M2	M1	0
IMD163	M1	M1	1
IMD164	M1	M2	0
IMD165	M1	M1	1
IMD166	M2	M2	1
IMD168	NC	RG	0
IMD169	M2	M2	1
IMD17	M1	RG	0
IMD170	M2	M2	1
IMD18	M2	M2	1
IMD19	M2	M2	1

Image	**Expert1**	**Expert3**	**AgreLTent**
IMD20	M1	M1	1
IMD21	M2	M2	1
IMD22	M1	M1	1
IMD23	M1	M1	1
IMD24	M1	M1	1
IMD25	M1	M1	1
IMD27	M2	M2	1
IMD28	M1	M2	0
IMD29	M2	M1	0
IMD30	M2	M2	1
IMD31	M2	M2	1
IMD32	M1	M2	0
IMD33	M2	M2	1
IMD35	M1	M2	0
IMD36	M1	LT	0
IMD37	M2	M2	1
IMD38	M2	M2	1
IMD39	M1	M1	1
IMD40	M1	M2	0
IMD41	M2	M2	1
IMD42	M2	M2	1
IMD43	M2	M2	1
IMD44	M1	M2	0
IMD45	M1	M1	1
IMD47	M2	M2	1
IMD48	M1	M2	0
IMD49	M2	M2	1
IMD50	M1	M1	1
IMD55	M2	M2	0
IMD56	M1	NC	0
IMD57	M2	M2	1
IMD58	M2	M2	1
IMD61	M2	M2	1
IMD63	M2	M2	1
IMD64	M2	M2	1
IMD65	M2	M2	1
IMD67	NC	M2	0
IMD72	M2	M2	1
IMD73	NC	M2	0

Image	**Expert1**	**Expert3**	**AgreLTent**
IMD75	M2	M2	1
IMD76	M2	M2	1
IMD78	M1	M2	0
IMD80	M2	M2	1
IMD81	M1	NC	0
IMD83	M1	M2	0
IMD85	M2	NC	0
IMD87	NC	NC	1
IMD88	M2	M2	1
IMD90	M2	M2	1
IMD91	NC	M2	0
IMD93	M1	M2	0
IMD171	M2	M2	1
IMD172	M2	M2	1
IMD173	M2	M2	1
IMD175	M2	M2	1
IMD176	M1	M2	0
IMD177	M1	M1	1
IMD178	M1	M1	1
IMD179	M1	M1	1
IMD180	M2	M1	0
IMD181	NC	M2	0
IMD182	M2	M2	1
IMD196	M1	M1	1
IMD197	M1	M1	1
IMD198	M1	M1	1
IMD199	M1	M1	1
IMD200	M1	M1	1
IMD201	M1	M1	1
IMD202	M2	M1	0
IMD203	M2	M1	0
IMD204	M1	M1	1
IMD205	M1	M2	0
IMD206	M2	M1	0
IMD207	M2	M2	1
IMD208	M2	M2	1
IMD210	M2	M2	1
IMD211	M2	M2	1
IMD221	M2	M2	1

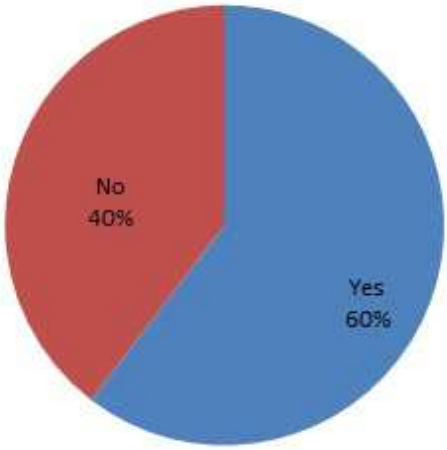

Figure B.3: Agreement percentage between two experts

M1 - melanocytic lesions undoubtedly benign.
M2 - melanocytic lesions that present atypical features and may evolve to malignant lesions or malignant melanocytic lesions.
NC - Not considered.
RG - Review in group.
LT - lesion in transformation
0 - Disagreement
1 - Agreement

Image	**Expert2**	**Expert3**	**Agreement**
IMD02	M2	M2	1
IMD03	M1	M2	0
IMD04	M2	M2	1
IMD06	M2	RG	0
IMD08	M1	M1	1
IMD09	M1	M1	1
IMD10	M1	M1	1
IMD101	M1	M1	1
IMD102	M1	M1	1
IMD103	M1	M1	1
IMD104	M1	M1	1
IMD105	M1	M1	1
IMD106	M2	M1	0
IMD107	M1	M1	1
IMD108	M1	M1	1
IMD109	M1	M1	1
IMD110	M1	M1	1
IMD111	M1	M1	1
IMD112	M1	M1	1
IMD113	M1	RG	0
IMD116	M1	M1	1
IMD117	M2	M1	0
IMD118	M2	M2	1
IMD119	M2	M2	1
IMD120	M2	M1	0
IMD121	M2	M2	1
IMD122	M1	M2	0
IMD123	M2	M1	0
IMD125	M1	M1	1
IMD126	M2	M1	0
IMD127	M2	M2	1
IMD13	M1	M1	1
IMD130	M2	M2	1
IMD131	M1	M1	1
IMD132	M1	M1	1
IMD133	M1	M1	1
IMD134	M1	M1	1
IMD135	M1	M2	0

Image	**Expert2**	**Expert3**	**Agreement**
IMD137	M1	M1	1
IMD138	M2	M1	0
IMD139	M2	M1	0
IMD14	M2	M2	1
IMD140	M2	M2	1
IMD141	M1	M1	1
IMD142	M1	M1	1
IMD143	M1	M1	1
IMD144	M1	M1	1
IMD145	M1	M1	1
IMD146	M1	M1	1
IMD147	M1	RG	0
IMD149	M1	M1	1
IMD15	M1	M1	1
IMD150	M1	M1	1
IMD151	M2	M2	1
IMD152	M1	M1	1
IMD153	M2	M2	1
IMD154	M2	M2	1
IMD155	M1	M1	1
IMD156	M1	M1	1
IMD157	M2	M2	1
IMD158	M1	M1	1
IMD159	M1	M1	1
IMD16	M1	LT	0
IMD160	M2	M1	0
IMD161	M1	M1	1
IMD162	M1	M1	1
IMD163	M1	M1	1
IMD164	M1	M2	0
IMD165	M1	M1	1
IMD166	M2	M2	1
IMD168	M2	RG	0
IMD169	M2	M2	1
IMD17	M1	RG	0
IMD170	M2	M2	1
IMD18	M1	M2	0
IMD19	M1	M2	0

Image	**Expert2**	**Expert3**	**Agreement**
IMD20	M1	M1	1
IMD21	M2	M2	1
IMD22	M1	M1	1
IMD23	M1	M1	1
IMD24	M1	M1	1
IMD25	M1	M1	1
IMD27	M1	M2	0
IMD28	M1	M2	0
IMD29	NC	M1	0
IMD30	M2	M2	1
IMD31	M2	M2	1
IMD32	M1	M2	0
IMD33	M1	M2	0
IMD35	M1	M2	0
IMD36	M1	LT	0
IMD37	M2	M2	1
IMD38	M2	M2	1
IMD39	M1	M1	1
IMD40	M2	M2	1
IMD41	M2	M2	1
IMD42	M2	M2	1
IMD43	M2	M2	1
IMD44	M1	M2	0
IMD45	M1	M1	1
IMD47	M2	M2	1
IMD48	M2	M2	1
IMD49	M2	M2	1
IMD50	M1	M1	1
IMD55	M2	M2	1
IMD56	NC	NC	1
IMD57	M2	M2	1
IMD58	M2	M2	1
IMD61	M2	M2	1
IMD63	M2	M2	1
IMD64	M2	M2	1
IMD65	M2	M2	1
IMD67	M1	M2	0
IMD72	M2	M2	1
IMD73	NC	M2	0

Image	**Expert2**	**Expert3**	**Agreement**
IMD75	M2	M2	1
IMD76	M1	M2	0
IMD78	M2	M2	1
IMD80	M2	M2	1
IMD81	M1	NC	0
IMD83	M2	M2	1
IMD85	M2	NC	0
IMD87	NC	NC	1
IMD88	M2	M2	1
IMD90	M2	M2	1
IMD91	NC	M2	0
IMD93	M1	M2	0
IMD171	M2	M2	1
IMD172	M2	M2	1
IMD173	M2	M2	1
IMD175	M2	M2	1
IMD176	M2	M2	1
IMD177	M2	M1	0
IMD178	M1	M1	1
IMD179	NC	M1	0
IMD180	M1	M1	1
IMD181	M1	M2	0
IMD182	M1	M2	0
IMD196	M1	M1	1
IMD197	M1	M1	1
IMD198	NC	M1	0
IMD199	M1	M1	1
IMD200	M1	M1	1
IMD201	M1	M1	1
IMD202	M1	M1	1
IMD203	M1	M1	1
IMD204	M1	M1	1
IMD205	M1	M2	0
IMD206	M1	M1	1
IMD207	M1	M2	0
IMD208	M1	M2	0
IMD210	M2	M2	1
IMD211	M2	M2	1
IMD221	M1	M2	0

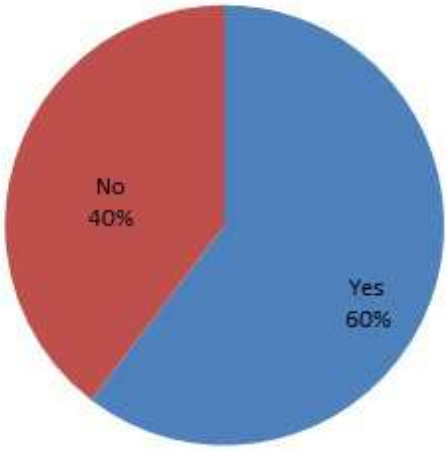

Figure B.4: Agreement percentage between two experts

M1 - melanocytic lesions undoubtedly benign.
M2 - melanocytic lesions that present atypical features and may evolve to malignant lesions or malignant melanocytic lesions.
NC - Not considered.
RG - Review in group.
LT - lesion in transformation
0 - Disagreement
1 - Agreement

Appendix C

Color Tables

Image	White	Red	Soft Brown	Dark Brown	Greyish-Blue	Black
IMD02			1	1		
IMD03				1		
IMD04	1		1	1		
IMD08			1	1		
IMD09			1	1		
IMD10			1	1		
IMD101			1	1		
IMD102			1	1		
IMD103			1	1		
IMD104			1	1		
IMD105			1	1		
IMD106	1		1			
IMD107			1	1		
IMD108			1	1		
IMD109			1	1		
IMD110			1	1		
IMD111			1	1		
IMD112			1	1		
IMD113		1	1			
IMD116			1	1		
IMD117		1	1	1		
IMD118			1	1		
IMD119			1	1		

Image	White	Red	Soft Brown	Dark Brown	Greyish-Blue	Black
IMD12			1	1		
IMD120			1	1		
IMD121			1	1		
IMD122			1	1		
IMD123			1	1		
IMD125			1	1		
IMD126	1		1	1		
IMD127	1			1		
IMD13			1	1		
IMD130	1	1	1			
IMD131	1		1	1		
IMD132			1	1		
IMD133			1	1		
IMD134			1	1		
IMD135			1	1		
IMD137			1	1		
IMD138			1	1		
IMD139			1	1		
IMD14	1		1	1		
IMD140			1	1		
IMD141			1	1		
IMD142			1	1		
IMD143			1	1		
IMD144			1	1		
IMD145			1	1		
IMD146			1	1		
IMD147			1	1		
IMD149	1		1	1		
IMD15					1	
IMD150			1	1		
IMD151			1	1		
IMD152			1	1		
IMD153	1		1	1		
IMD154	1		1	1		
IMD155			1	1		
IMD156			1	1		

Image	White	Red	Soft Brown	Dark Brown	Greyish-Blue	Black
IMD157			1	1		
IMD158					1	
IMD159			1	1		
IMD16			1	1		
IMD160			1	1		
IMD161			1	1		
IMD162			1	1		
IMD163			1	1		
IMD164			1	1		
IMD165			1	1		
IMD166	1		1	1		
IMD167			1	1		
IMD169	1			1	1	
IMD17			1	1		
IMD170			1	1		1
IMD18			1	1		
IMD19			1	1		
IMD20			1	1		
IMD21			1	1		
IMD22			1	1		
IMD23			1	1		
IMD24			1	1		
IMD25			1	1		
IMD27			1	1		
IMD28			1	1		
IMD30	1		1	1		
IMD31	1		1	1		
IMD32	1		1	1		
IMD33	1		1	1		
IMD35			1	1		
IMD36			1	1		
IMD37	1		1	1		
IMD38			1	1		
IMD39			1	1		
IMD40			1	1		
IMD41			1	1		
IMD42			1	1		
IMD43	1		1	1		
IMD44			1	1		

Image	**White**	**Red**	**Soft Brown**	**Dark Brown**	**Greyish-Blue**	**Black**
IMD45			1	1		
IMD47	1		1	1		
IMD48	1		1	1		
IMD49			1	1		
IMD50			1			
IMD55	1		1	1		1
IMD56			1	1		
IMD57	1		1	1		
IMD58	1		1	1		1
IMD59	1	1	1	1		1
IMD61	1		1	1		1
IMD63			1	1		1
IMD64	1		1	1		1
IMD65	1		1	1		1
IMD72	1		1	1		
IMD75			1	1		1
IMD76					1	
IMD78			1	1		
IMD80	1		1	1		1
IMD81		1	1			
IMD82		1	1			
IMD83	1		1	1		
IMD85		1			1	
IMD87					1	1
IMD88	1		1	1		
IMD90	1		1	1		
IMD91				1	1	
IMD93			1	1		
IMD171				1	1	
IMD172			1	1		
IMD173			1	1		
IMD175			1	1		
IMD176			1	1		
IMD177			1	1		
IMD178			1	1		
IMD179			1	1		
IMD180			1	1		
IMD181			1	1		

Image	**White**	**Red**	**Soft Brown**	**Dark Brown**	**Greyish-Blue**	**Black**
IMD182			1	1		
IMD196			1	1		
IMD197			1	1		
IMD198			1	1		
IMD199			1	1		
IMD200			1	1		
IMD201			1	1		
IMD202			1	1		
IMD203			1	1		
IMD204			1	1		
IMD205			1	1		
IMD206			1	1		
IMD207			1	1		
IMD208			1	1		
IMD210	1		1	1		1
IMD211			1	1	1	
IMD221			1	1		

Image	White	Red	Soft Brown	Dark Brown	Greyish-Blue	Black
IMD02			1	1		
IMD03				1		
IMD04			1	1		
IMD08			1			
IMD09			1			
IMD10			1			
IMD101			1			
IMD102			1			
IMD103			1	1		
IMD104			1	1		
IMD105			1	1		
IMD106	1		1			
IMD107			1	1		
IMD108			1	1		
IMD109			1			
IMD110		1	1	1		
IMD111			1	1		
IMD112			1	1		
IMD113		1	1			
IMD116			1	1		
IMD117		1	1	1		
IMD118			1	1		
IMD119				1		1
IMD12	1		1			
IMD120			1	1		
IMD121			1	1		
IMD122			1	1		
IMD123			1			
IMD125			1	1		
IMD126			1			1
IMD127				1		1
IMD13			1			
IMD130	1		1	1		
IMD131		1	1	1		
IMD132			1	1		
IMD133			1			
IMD134			1	1		
IMD135		1	1	1		

Image	White	Red	Soft Brown	Dark Brown	Greyish-Blue	Black
IMD137			1	1		
IMD138			1	1		
IMD139				1		1
IMD14	1		1	1		
IMD140				1		1
IMD141			1	1		
IMD142			1	1		
IMD143			1	1		
IMD144			1	1		
IMD145			1	1		
IMD146			1	1		
IMD147		1	1			
IMD149	1	1		1	1	
IMD15					1	
IMD150	1	1			1	
IMD151			1	1		
IMD152			1	1		
IMD153	1		1			
IMD154	1		1			
IMD155			1	1		
IMD156			1			
IMD157			1		1	
IMD158					1	
IMD159			1			
IMD16			1	1		
IMD160			1	1		
IMD161			1	1		
IMD162			1	1		
IMD163	1		1			
IMD164		1	1	1		
IMD165			1	1		
IMD166			1	1		
IMD167			1	1		
IMD169				1	1	1
IMD17			1	1		
IMD170			1	1		
IMD18				1		
IMD19				1		
IMD20				1		1

Image	**White**	**Red**	**Soft Brown**	**Dark Brown**	**Greyish-Blue**	**Black**
IMD21				1		1
IMD22			1			
IMD23			1			
IMD24			1	1		
IMD25			1			
IMD27			1	1		
IMD28			1			
IMD30			1	1		
IMD31				1	1	
IMD32			1	1		
IMD33			1			1
IMD35			1			
IMD36		1	1			
IMD37			1	1		
IMD38				1		1
IMD39				1		
IMD40			1	1		
IMD41				1		1
IMD42			1	1		
IMD43				1		1
IMD44				1	1	
IMD45			1			
IMD47			1	1		
IMD48			1			
IMD49				1	1	
IMD50			1			
IMD55		1		1	1	
IMD56			1			1
IMD57				1		1
IMD58	1			1	1	
IMD59	1	1		1	1	
IMD61		1	1		1	
IMD63			1	1		
IMD64	1		1		1	
IMD65				1		1
IMD72			1	1		
IMD75				1		1
IMD76						

Image	**White**	**Red**	**Soft Brown**	**Dark Brown**	**Greyish-Blue**	**Black**
IMD78						1
IMD80				1		1
IMD81		1	1	1		
IMD82		1	1			
IMD83				1		
IMD85						
IMD87					1	1
IMD88	1				1	1
IMD90				1	1	1
IMD91					1	1
IMD93			1			1
IMD171				1		1
IMD172		1	1			
IMD173			1			
IMD175			1	1		
IMD176			1	1		
IMD177			1	1		
IMD178			1	1		
IMD179			1	1		
IMD180			1	1		
IMD181			1	1		
IMD182			1	1		
IMD196			1			
IMD197				1		1
IMD198			1			
IMD199			1			
IMD200			1			
IMD201			1			
IMD202			1	1		
IMD203			1	1		
IMD204			1	1		
IMD205				1		1
IMD206			1	1		
IMD207			1	1		
IMD208			1	1		
IMD210				1	1	1
IMD211					1	1
IMD221			1	1		

References

[ACA+11] G. Argenziano, C. Catricala, A. Ardigo, P. Buccini, P. De Simone, L. Eibenschutz, A. Ferrari, G. Mariani, V. Silip, I. Sperduti, and I. Zalaudek. Seven-point checklist of dermoscopy revisited. 2011.

[AS01] G. Argenziano and P. Soyer. Dermoscopy of pigmented skin lesions - a valuable tool for early. 2001.

[BDLF+06] G. Betta, G. Di Leo, G. Fabbrocini, A. Paolillo, and P. Sommella. Dermoscopic image-analysis system: estimation of atypical pigment network and atypical vascular pattern. 2006.

[CHU+06] M. Celebi, A. Hassan, B. Uddin, H. Iyatomi, W. Stoecker, and R. Moss. A methodological approach to the classification of dermoscopy images. 2006.

[Cod90] E. F. Codd. *The relational model for database management: version 2.* Boston: Addison-Wesley Longman Publishing Co., Inc, 1990.

[CQS+03] P. Carli, E. Quercioli, S. Sestini, M. Stante, L. Ricci, G. Brunasso, and V. De Giorgi. Pattern analysis, not simplified algorithms, is the most reliable method for teaching. 2003.

[FCU] FCUP. Misson of FCUP in society.

[GMP+94] A. Green, N. Martin, J. Pfitzner, M. O'Rourke, and N. Knight. Computer image analysis in the diagnosis of melanoma. 1994.

[GPR+01] H. Ganster, A. Pinz, R. Rohrer, E. Wildling, M. Binder, and H. Kittler. Automated Melanoma Recognition. 2001.

[HDW+07] J. Henning, S. Dusza, S. Wang, A. Marghoob, H. Rabinovitz, D. Polsky, and A. Kopf. The CASH (color, architecture, symmetry, and homogeneity) algorithm for dermoscopy. 2007.

[HPH] HPH. Mission of HPH in society.

[HU] HU. Hosei University.

[ICOT08] H. Iyatomi, M. Celebi, H. Oka, and M. Tanaka. An Internet-based Melanoma Screening System with Acral Volar Lesion Support. 2008.

[JSA+04] R. Johr, H. Soyer, G. Argenziano, R. Hofmann-Wellenhof, and M. Scalvenzi. *Dermoscopy : The essentials*. Elsevier - Health Sciences Division, 2004.

[KPWB02] H. Kittler, H. Pehamberger, K. Wolff, and M. Binder. Diagnostic accuracy of dermoscopy, 2002.

[MB04] A. Marghoob and R. Braun. *Atlas of dermoscopy*. Taylor and Francis Taylor and Francis Group, 2004.

[MMV+07] T. Mendonca, A. R. S. Marcal, A. Vieira, J. Nascimento, M. Silveira, J. S. Marques, and J. Rozeira. Automatic analysis of dermoscopy images - a review. 2007.

[PSW] H. Pehamberger, A. Steiner, and K. Wolff.

[RCB+01] P. Rubegni, G. Cevenini, M. Burroni, R. Perotti, G. Dell'Eva, C. Sbano, P. Luzi, P. Tosi, P. Barbini, and L. Andreassi. Automated Diagnosis of Skin lesions. 2001.

[S.r] DS Medica S.r.l. Menzies' Method.