I S A

BW-Eye

Ophthalmologic Decision Support System based on Clinical Workflow and Data Mining Techniques
- Angiography Equipment Integration
- Creation of thickness maps using OCT images

Sistema de Apoio à Decisão para a especialidade de Oftalmologia baseado em técnicas de Workflow e Data Mining aplicadas em dados obtidos em ambiente clínico
- Integração do Equipamento de Angiografia
- Criação de mapas de espessura usando imagens de OCT.

Project Report
Version 1.0

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BlueWorks   BlueWorks- Medical Expert Diagnosis, Lda

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Abstract

This project was developed within the Project class of the Biomedical Engineering course of the Faculty of Sciences and Technology of the University of Coimbra.

The Project developed is a prolongation of last year's project, WIA-DM, with the aim to diminish the inherent subjectivity in medical diagnosis. Therefore, the creation of a support system for the medical ophthalmologic practice was proposed. Thus, the objective of the present project is the creation of new functionalities for the BW-Eye project.

During this Project the Angiography equipment was integrated with the BW-Eye application. The module created allows importation of examination results from medical equipments and storage on this database providing the information for a later search in the network.

In the image processing area, algorithms capable of creating thickness maps from OCT (Optic Coherence Tomography) images were developed particularly for the retinal pigmented epithelium (RPE) where the algorithm had 90% of success.

Keywords:
Decision-Support, Ophthalmology, C -Sharp, Matlab, OCT image processing

Resumo

Este trabalho foi desenvolvido no âmbito da cadeira de projecto do curso de Engenharia Biomédica, da Faculdade de Ciências e Tecnologia da Universidade de Coimbra.

O projecto desenvolvido é um projecto de continuidade em relação ao ano anterior, WIA-DM, tendo como objectivo a diminuição da subjectividade inerente ao diagnóstico médico, sendo que para tal foi proposto a criação de um sistema de apoio à decisão médica para a área de oftalmologia. Deste modo, o objectivo do presente projecto é a criação de funcionalidades para o projecto BW-Eye.

No decorrer do presente projecto procedeu-se à integração do equipamento de Angiografia, com a aplicação BW-Eye. O módulo criado permite importar os resultados dos exames médicos e armazenar estes dados na base de dados, disponibilizando a informação para uma pesquisa posterior na rede.

Na área de processamento de imagem foram desenvolvidos algoritmos capazes da criação de mapas de espessura a partir de imagens de OCT (Tomografia de Coerência Óptica). Nomeadamente, para o epitélio pigmentado da retina onde o algoritmo para a sua detecção tem um sucesso de 90%.

Palavras-chave:

Apoio à decisão, Oftalmologia, C-Sharp, Matlab, Processamento de imagens de OCT.

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Definitions and Acronyms

Acronym	Description
AM	Angiography Acquisition Module
BRB	Blood Retinal Barrier
CCC	Centro Cirúrgico Coimbra
C#	C-Sharp
DB	Database
DM	Data Mining
GUI	Graphical User Interface
ISA	Intelligent Sensing Anywhere, Lda
JPEG	Joint Photographic Experts Group
OCT	Optical Coherence Tomography
OCT-SLO	Optical Coherence Tomography - Scanning Laser Ophthalmoscope
PNG	Portable Network Graphics
RAL	Retinal Anterior Limit
RPE	Retinal Pigmented Epithelium

1. Introduction

The project developed along this year is a continuation of a previous project. This project, aims to improve and support the medical diagnosis and thus eliminating the subjectivity present in this process.

The work developed last year was based on the idea of the creation of a system to improve and support medical diagnosis and thus eliminate subjectivity. So, a series of tasks were developed:

- Software System Architecture;
- Integration of the OCT-SLO Equipment;
- Image processing for detection of features of OCT-SLO images such as: retinal pigmented epithelium (REP), retinal anterior limit (RAL), oedema, serous detachment and lamellar hole;
- Creation of a Database;
- Training neural network for detection of previously mentioned features;

1.1 Domain

BW-Eye is a project integrated in the Biomedical Engineering Course of the Faculty of Sciences and Technology of the University of Coimbra. It started on September 14th 2007 and its ending matches this document's delivery date: June 30th 2008.

The main corporate entities involved in this project are CCC (Centro Cirúrgico de Coimbra), BlueWorks (BlueWorks –Medical Expert Diagnosis) and ISA (Intelligent Sensing Anywhere).

1.2 Objectives

This project aimed to implement some new features to the project BW-Eye.

The main purpose of this project is to create an innovative system that provides helpful tools for medical diagnosis support and management resources.

The three main challenges of the BW-Eye project were:

- System integration
- Diagnostic support
- Clinical workflow support [1]

Regarding the BW-Eye project, the work done this year consisted of different tasks. In system integration, the aim was to integrate the TopCon angiography equipment with the BW-Eye application. Concerning diagnosis support, the objective was to create algorithms capable of

detecting certain features in examination images and creating the map of thickness of a series of such images, using images of OCT equipment.

1.3 Project Team

This year's continuation of the BW-Eye project was assured by the students Liliana Ferraz, Ricardo Martins and Rui Maricato, with the important support from Eng. Armanda Santos, Eng. Edgar Ferreira and Eng. Paulo Barbeiro from *BlueWorks*. Therefore a large team contributed to the development of this project as shown in table 1.

Name	Designation	Contact
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Table 1 Project Team

1.4 Planning

Table 2 shows main tasks description and duration. Detailed schedule of the develop work stages are show in Appendix 1.

Index	Task	Duration	Start	Finish
1	Research about the work done in the previous year	9 days	14-09-2007	26-09-2007
2	Study of Angiography equipment	14 days	02-10-2007	02-11-2007
3	Angiography acquisition module creation	39 days	05-11-2007	28-12-2007
4	Advanced funcionalities implementation	25 days	07-01-2008	08-02-2008
5	1st Intercalary Presentation	3 days	11-02-2008	13-02-2008
6	Angiography acquisition module test and optimization	24 days	14-02-2008	21-03-2008
7	Creation of GUI for mean regions calculus	7 days	11-03-2008	25-03-2008
8	Creation of algorithm for interpolation	13 days	26-03-2008	11-04-2008
9	Algorithm for RPE segmentation and its thickness	25 days	14-04-2008	16-05-2008
10	Creation of thickness maps.	15 days	19-05-2008	06-06-2008
11	2nd Intercalary Presentation	3 days	28-05-2008	04-06-2008
12	Project Report writing	14 days	11-06-2008	30-06-2008

Table 2 Project Main Tasks Schedule

Diagram 1 illustrates the weekly chronogram of tasks developed during the course of project.
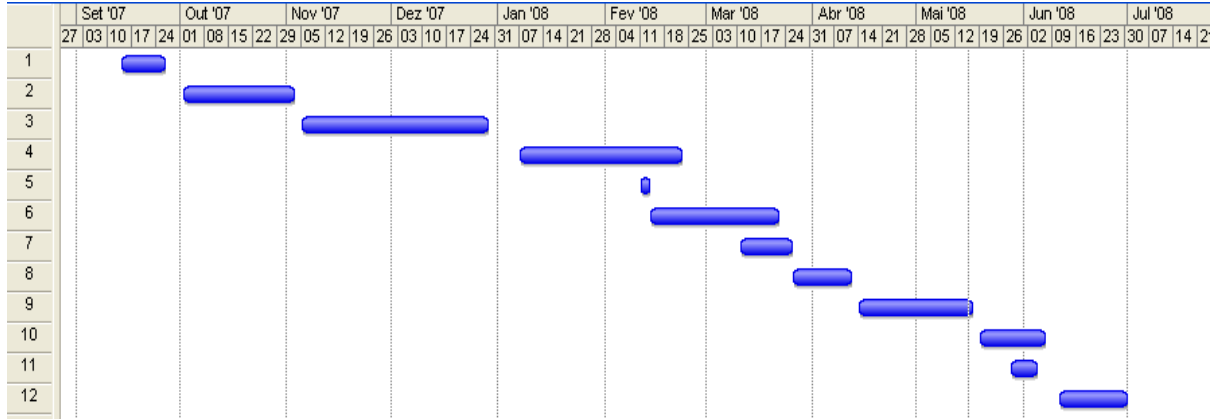
Diagram 1 Gantt Diagram of Project Tasks

1.5 Document Structure

This document is divided into five chapters. In the first chapter (Introduction) a brief thematic introduction is made, the main project objectives are pointed; project team and planning are presented.

In the second chapter (Background) there is a description of the utilities used during this project.

In the third chapter (Software Development) software requisites, implementation and tests are described.

In the fourth chapter (Image Processing) there is a description of the developed algorithms for construction of thickness maps.

Finally, in the fifth chapter (Conclusions and Future Purposes) project issues are analyzed and conclusions are described.

2. Background

This chapter is intended to give some knowledge concerning the development of this project specifically an introduction to the human eye physiology and anatomy, an elucidation on angiography and retinography and finally a summary about the OCT equipment.

2.1 The Human Eye
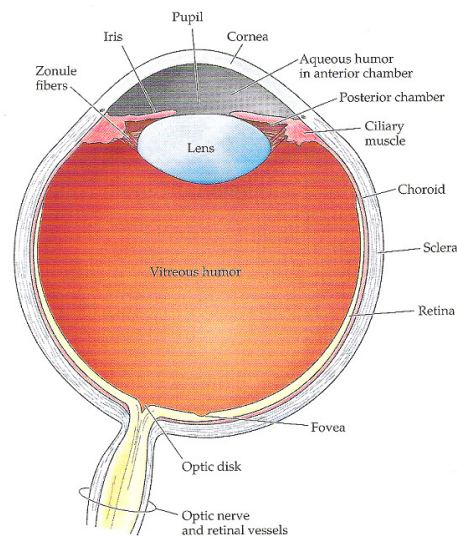
Figure 1 Anatomy of human Eye [2]

"The eye is the vision organ that detects light. It focuses light on a light-sensitive surface (the retina) using a lens and aperture or opening (the pupil), whose size can be adjusted to the amount of entering light. Its structure can be divided in several ways, but the most common is in two sections. The anterior segment is the front third of the eye that includes structures in front of vitreous humour. The posterior segment includes the vitreous humour and structures behind it." [2] The table 3 shows which structures are presented in each section.

Segment	Structure	Description
Anterior	**Cornea**	"The transparent, anterior, dome-shaped portion of the eyeball that covers the iris and pupil, acting like a window which admits light into the eye." [3]
	Iris	"The opaque muscular contractile diaphragm that is suspended in the aqueous humour in front of the lens of the eye; perforated by the pupil and continuous peripherally with the ciliary body; possesses a deeply pigmented posterior surface, which excludes the passage of light except through the pupil, and a coloured anterior surface which determines the colour of the eye." [3]
	Ciliary body	"Annular (ring-like) structure on the inner surface of the anterior wall of the eyeball, contained within the uveal tract and composed largely of the ciliary muscle and bearing the ciliary processes".[3]
	Lens	"The biconvex transparent structure located immediately posterior to the iris of the eye which changes shape (flattens and thickens) to focus the incoming light from objects far away and at near; can develop a cloudy, even opaque cataract with age and due to a cumulative absorption of ultraviolet radiation." [3]
Posterior	**Vitreous humour**	"After being focused by the lens, light passes through the centre of the eye on its way to the retina. The eye is filled with a clear, jelly-like substance called the vitreous." [4]
	Retina	"Layer of nervous tissue, covering the back two-thirds of the eyeball, in which stimulation by light initiates an electrochemical reaction in which electrical impulses are transmitted to the brain, producing the sensation of vision; actually an extension of the brain, formed embryonically from brain tissue and connected to the brain proper by the optic nerve." [3]
	Choroid	"Behind the retina, a layer of blood vessels (choroid) supplies oxygen and nutrients to the outer layers of the retina." [4]
	Optic Nerve	Neurons from visual pathway; Cranial Nerve II. [5]

Table 3 Eye Constituents
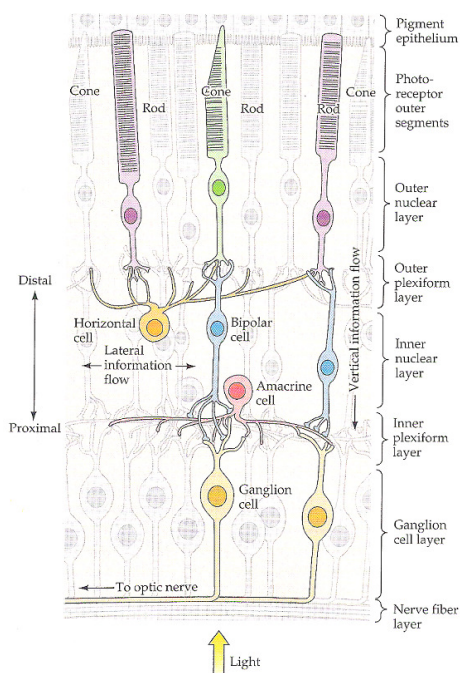
Figure 2 Retinal Layers [2]

The retina is a thin layer of neuronal cells which is itself composed by several cell layers, being that central retina is cone dominated and peripheral retina is rod dominated.

"The retina comprises only a few classes of neurons, and these are arranged in a manner that has been less difficult to unravel than the circuits in other areas of brain. There are five types of neurons in the retina: photoreceptors, bipolar cells, ganglion cells, horizontal cells, and amacrine cells. The cells bodies and processes of these neurons are stacked in five alternating layers, with the cells bodies located in the inner nuclear, outer nuclear, and ganglion cell layers, and the process and synaptic contacts located in inner plexiform and outer plexiform layers. A direct three neuron chain photoreceptor cell bipolar cell to ganglion cell is the major route of information flow from photoreceptors to the optic nerve." [2]

"Light must first pass through the thickness of the retina before reaching the rods and cones, where almost all of it is reflected by the retinal pigmented epithelium (RPE). Photoreceptors transduce light energy into electrical energy that passes along a pathway consisting of bipolar neurons, then ganglion cells. The axons of ganglion cells form the optic nerve that leaves the eye at the optic disk. Because the optic disk has no photoreceptors, images projected onto this region will not be seen, creating the so called blind spot. "[5]

"The eye has a double circulation system: the Retinal Circulation and the Choroidal Circulation.

In the retinal circulation, the central retinal artery goes through the optic disc where it divides into four large arterioles – terminal circulation.

Unlike the retinal circulation, the choroidal circulation, constituted by a blood vessels' mesh, does not go through the optic disk but crosses the sclera.

The retina is a neuronal tissue which is protected by barriers: the Blood-Aqueous Barrier and the Blood Retinal Barrier (BRB)." [6]

"BRB breakdown plays a major role in retinal vascular diseases like vase-occlusive diseases, retinopathy and intraocular inflammation.

The causes to create the BRB breakdown can be several, such as:

- Ischemia/reperfusion;

- Acute distension of retinal vessels wall;

- Biochemical Insults;

- Inflammation;

- Defective endothelial cells;

- Failure of active transport mechanisms;

The retina has a high oxidative capacity, an unusually high glycolytic activity and is extremely susceptible to hypoxia and ischemia.

More than fifteen minutes of arterial blood supply can causes permanent damages in the retina. The first effect is anoxic damage to the retinal capillary endothelium leading to oedema formation. The retinal cells destroyed by anoxia released macromolecules that increase the tissue's osmotic pressure and oedemas.

The various retinal constituents react to these alterations in different ways, causing several pathologic alterations, like cotton-wool exudates, hard exudates, oedemas, haemorrhages and others. "[6]

2.2 Angiography and Retinography

2.2.1 Retinography

Retinography is a colour photograph of the retina, where the red-free component also exists, and which excludes the red component to augment different kinds of characteristics.

Therefore, retinography shows changes in the structure and the morphology of the retina particularly lesions. Hence, it is possible to see the evolution of some retinopathies through time, such as diabetic retinopathy, arterial hypertension, thrombosis, ocular tumours, macular degeneration, etc.

Since the retinography images show some characteristics such as vasodilatation, haemorrhages, cotton-wool exudates and hard exudates situations, these diseases can be identified.
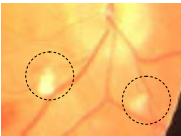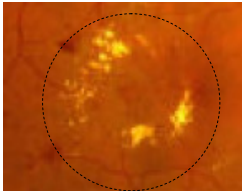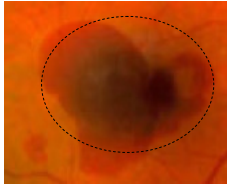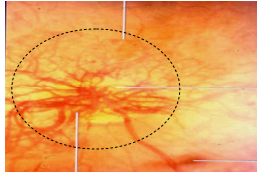
Designation	Cause	Characteristics	Image
Cotton-wool exudates	Hypoxia forces mitochondrial grouping at axons central zone.	-White blemishes with undefined boundaries; -Appear above blood vessels.	**Figure 3 Cotton wool Exudates**
Hard exudates	Ischemia-cell Necrosis-glial Cell does not have capacity of consuming all fat.	-Yellowish spot with good boundaries; - They appear around the macular zone with a radial disposition.	**Figure 4 Hard Exudates**
Haemorrhages	Tight-junctions large opening or tight-junctions traumatism with red globules escape.	-Reddish blemishes; - If haemorrhage is superficial it has a round shape.	**Figure 5 Haemorrhages**
Choroidal Neovascularization	VEGF liberation.	-Zone with strange reflectance -Sub- retinal membrane occult.	**Figure 6 Choroidal Neovascularization**

Table 4 Retinopathy Characteristics (view in retinography) [6]

2.2.2 Angiography

Retinal angiography is a diagnostic procedure that obtains images of blood vessels and other structures in the retina with the aid of an intravenous dye. After the injection of a fluorescent substance into systemic circulation, a sequence of images of the retina is acquired for a wave length equal to the fluorescent agent's emission.

This exam allows the analysis of fluorescent substance progression along the vascular tree analysis, leading to the identification of its structure and eventual problem regions. Usually, two types of fluorescent agent are used: fluorescein and indocyanine green. Fluorescein evidences the retinal circulation while the indocyanine green substance shows the retinal and choroidal circulation.

This exam allows the identification of different kinds of problems:
- Areas with new vessels (neovascularization);
- Areas with changes in the vessels (microaneurysms, vases occlusion, etc);

- Areas with other kinds of changes (serous detachment, oedemas, haemorrhages, etc) ;
- Laser Scars (resulting of cataracts operation).
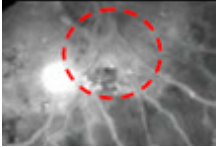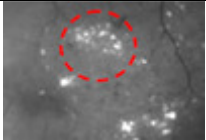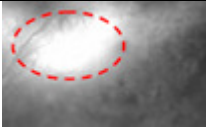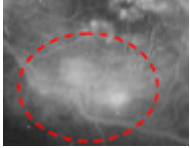
Designation	Cause	Characteristics	Image
Retinal Neovascularization	VEGF liberation.	Diffuse areas with hyper fluorescence.	**Figure 7 Retinal Neo-vascularization**
Microaneurysms	Obstruction and blood vessels swelling.	Small white spots hyper fluorescents coincident with blood vessels.	**Figure 8 Microa-neurysms**
Haemorrhages	Tight-junctions large opening or tight-junctions traumatism with red globules escape.	White blemishes hyper fluorescent dots.	**Figure 9 Hemorrhages**
Oedema	Blood vessels tight junctions opening without red globule escape.	Fluorescence diffuse area (grey blemishes).	**Figure 10 Oedema**

Table 5 Retinopathy Characteristics (view in angiography) [6]

2.2.3 Equipment

The Angiography TopCon equipment allows to do angiography and retinography exams. The proprietary software has tools that allow image enhancement, image selection, image elimination, tools for changing the image visualization scheme, etc.

This equipment's software has image processing algorithms specifically designed for optimizing image quality and providing instantaneous image capture of the base of the eye. This software includes patient database, calibrated measurement functions, and networking and connectivity options. [7] This software runs in the Microsoft Windows 2000 Operative System, using exams output printer and screenshots.

2.3 Optical Coherence Tomography (OCT)

The OCT is a modern exam which allows to create cross sections of the retina and to generate high resolution tomographic images with a high degree of reproducibility. This is used in many areas of diagnosis such as ophthalmology, dermatology, gastroenterology, cardiovascular disease. This project concerns its use in applications in the ophthalmology field. [8]

The OCT uses infrared light (this means that its wave length is in the infrared region - 1mm-700nm). In this technique, light is highly reflected or absorbed by biological tissue which makes it appropriate to assess intra-ocular structures. This is a high resolution exam which makes retinal and choroidal slices allowing the detection of anatomic changes in these structures in the z-plane (retinal depth). With the OCT digital system it is possible to process the acquired images and represent them in false colours or shades of grey, increasing the contrast. The most intensely reflected signals are represented in red and white, the average in yellow and green and less intense in black and blue. [8]

Thus, with the slices of the OCT it is possible to measure quantitatively dimensions of intra-ocular structures and therefore, diagnose and assess the results of treatments and recuperation progress. Its use also extends to the study of diseases such as macular degeneration related with age, macular hole, macular edema, epiretinal membrane. [8]

The following considerations were used for the conversion of pixels into μm: each image of the B-Scan equipment, existent in the CCC, is obtained by a linear sequence of 500 T-Scans (cross scans) with a distance of 4 μm between each, composing a longitudinal B-Scan section of 2mm; and a sequence of 500 A-Scans, with 16 μm between each, composing a cross section of 8 mm. As a result, a pixel represents a real size of 7,8 μm of width and 5,8 μm of height. [9]

2.4 Data Mining

"Generally, data mining (sometimes called data or knowledge discovery) is the process of analyzing data from different perspectives and summarizing it into useful information which information that can be used to increase revenue, cuts costs, or both. Data mining software is one of a number of analytical tools for analyzing data. It allows users to analyze data from many different dimensions or angles, categorize it, and summarize the relationships identified. Technically, data mining is the process of finding correlations or patterns among dozens of fields in large relational databases." [10]

3. Software Development

Software development was one of the tasks along this project. The software integrated in the application BW-Eye was developed at BlueWorks. The main objective of equipment integration is to digitally share the data that the equipments obtain making it accessible to any terminal connected to the database.

3.1. Architecture of the BW-Eye Application

Diagram 2 illustrates the architecture of the software application.
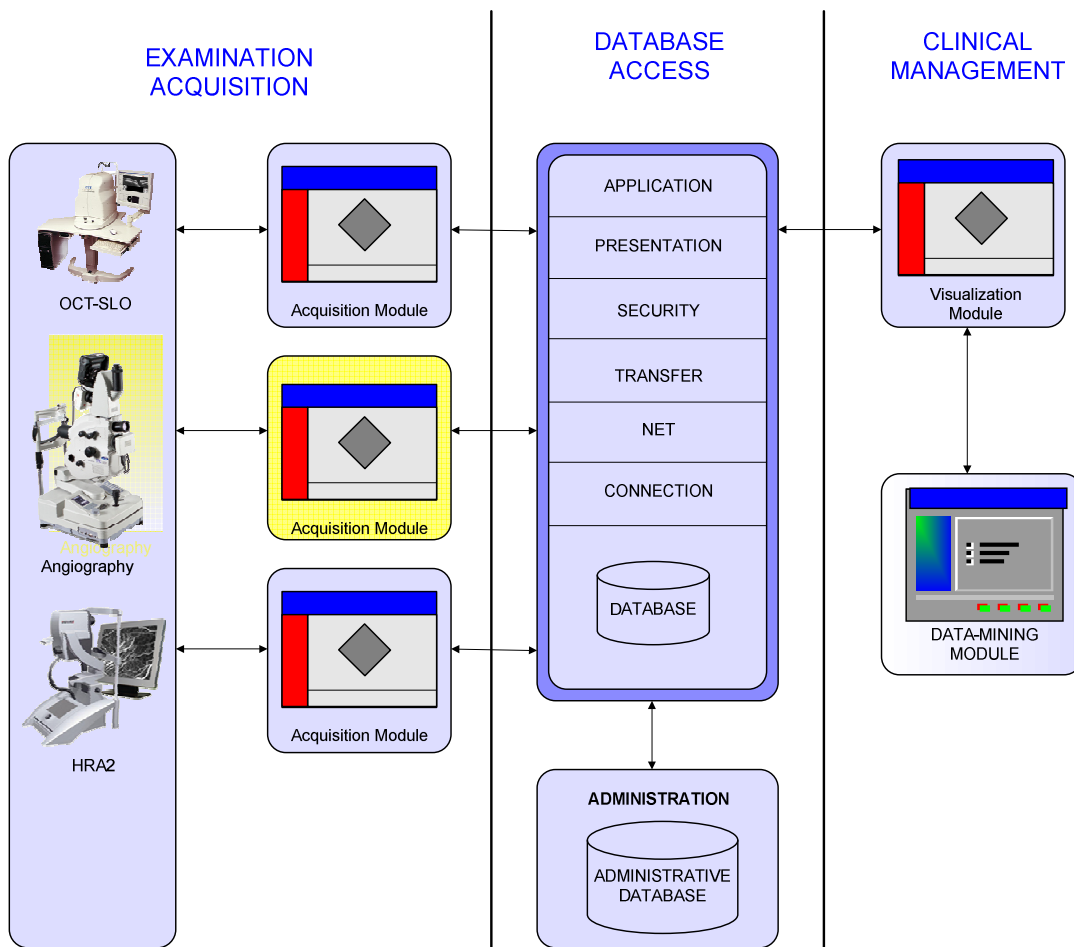
Diagram 2 Software Architecture

In diagram 2, the boxes in yellow correspond to the work that I have developed. The blue boxes represent work made or in execution by others elements.

As the previous diagram illustrates, the software's architecture is divided into three main layers:

- Examination Acquisition: set of modules that allow importing and selecting images (and other parameters) from equipment software as well as creating and saving examination reports;

- Database Access: contains the database where all doctor, patient and examination data is stored allowing clinical management and intelligent processing. This layer is accessed by a *virtual* web server (which will allow providing this service over the Internet). The health professional and patient information is imported from administrative software;

- Clinical Management: this component contains the module that allows user interaction with the database's exams. A data-mining module is also part of this component. [1]

In this chapter the element of the software architecture developed by me is explained:

- Angiography/Retinography TopCon Acquisition Module (AM): module that imports images from Angiography/Retinography TopCon software and then allows the user to select relevant images and to create an examination report.

3.2. Requisites

Being a part of a larger application, the AM shares its graphical design and functionalities in order to facilitate its use. However, this module has some special functionalities, such as brightness enhancement, that allow the user to make the same operations that could be done on the proprietary software.

We have two types of requisites: functional and user.

The functional requisites of the AM are similar to the already existent acquisition modules. Therefore we have:

- Access database;

- Check relationship between examination and request;

- Control examination saving transaction;

- Check on predefined folder the new images become;

- Parse register files;

For user requisites we have:

- Separation of the exam in series (retinography, fluorescein angiography and I.C.G. angiography);

- Visualize and navigate among images;

- Select or remove images;

- Define image importation folder;

- Define file location for interpretation of the information about the image and the patient;

- Define format to save images on Database;

- Select images to store;

- Image preview and comment;

- Enhance brightness of images;

- Save images and examination report;

3.3 Interpretation of information file

The Angiography Top-Con equipment saves the information about the patients and the images in different files. The connection between these two files is done with one manual registry (key).

The file that saves the image information (DISK0000.BTR) retrieves in this order: manual register, exam date, exam hour, exam type, instant image (only for angiography), image path and correspondent eye.

In the other hand, the file that saves information about the patients (PATIENT.BTR) retrieves in this order: manual register, last name, first name, sex, birthday date, exam date and name of doctor in charge of the exam.
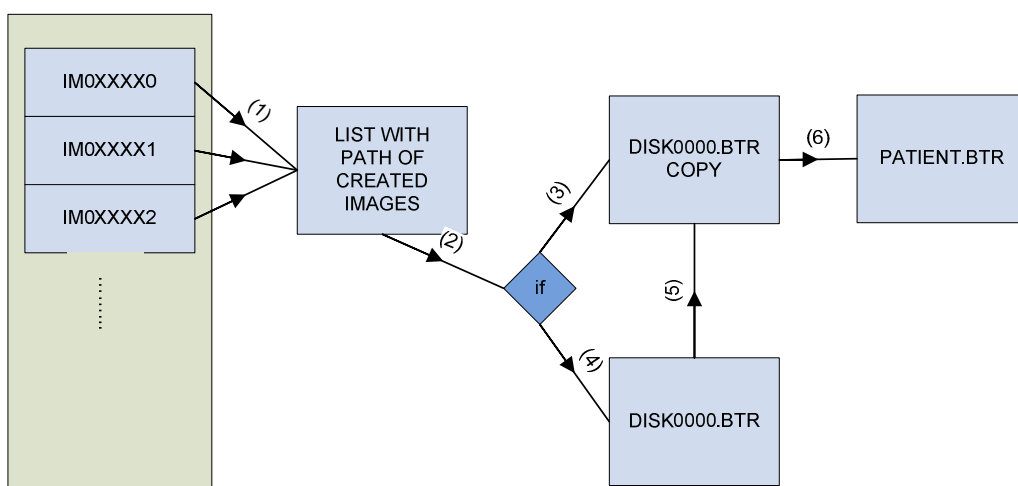
Diagram 3 Read Scheme of files

Diagram 3 illustrates the scheme of steps to analyse the information about one image. As the images arrive to the pre established folder, its path is added to a list (step 1). In step (2), it is necessary to make a decision: if the copy of DISK0000.BTR does not exist or is not updated (verified by the comparison with the previously inserted parameters), step 4, it becomes necessary to update the copy (step 5) by making a new one. However, if the copy already exists and is updated then there is a direct reading (step 3) and its search occurs through the images path.

After the image data interpretation is done, a research is done within the data file that concerns the patients (step 6) using the manual register. This search is only done when the manual register is different from the one used before.

3.4 Implementation

AM is the module that allows the connection between the angiography Top-Con's proprietary software and the BW-Eye application, therefore allowing its integration. The essential step in this module is the interpretation of the files that save the information about the exported images. When the images are in the module it is possible to manipulate, save and create the exam report.

The following topics explain the stages the module goes through and the specification methods used by the AM.

3.4.1 Module Initialization
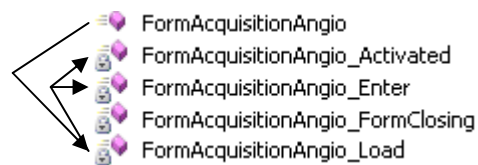
Diagram 4 Order of events initialization

AM initialization occurs in two distinct phases:

- Plugin file read (*FormAquisitionAngio* constructor is called and its *UserControl* is initialized);

- Module Load (*FormAquisitionAngio_Load* the AM is made visible in the Main Interface tab control);

In the diagram 4 the arrows show the sequence of methods used AM initialization:

- The class constructor initializes the graphic objects and creates a personalized menu to add to the quick launch bar;

- Next, the *FormAcquisitionAngio_Activated* and the *FormAquisitionAngio_Enter* are activated and the specific menu for this module is added to the menu application toolbar;

- *FormAquisitionAngio_Load* activates the *fileSystemWatcherImagePath*. This object is activated when one image is created in a pre-established folder by the user. This method also loads the doctor list from the DB and checks the location of the files and settings necessary for the module to work. If the settings are not defined, the *FormOptions* GUI is charged.

3.4.2 Module Menu

The Menu Module allows to check for incomplete sendouts to the database by showing pending requests and related information. It also has an option which shows information about the module and the aplication.

This menu opens the *FormOptions* facilitating the predefinitions and personalizations required by the user, as shown in figures 11 and 12.
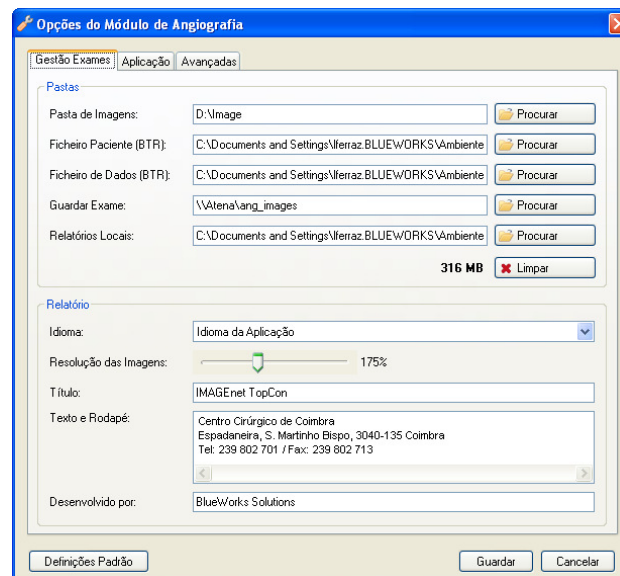
Figure 11 Options Window
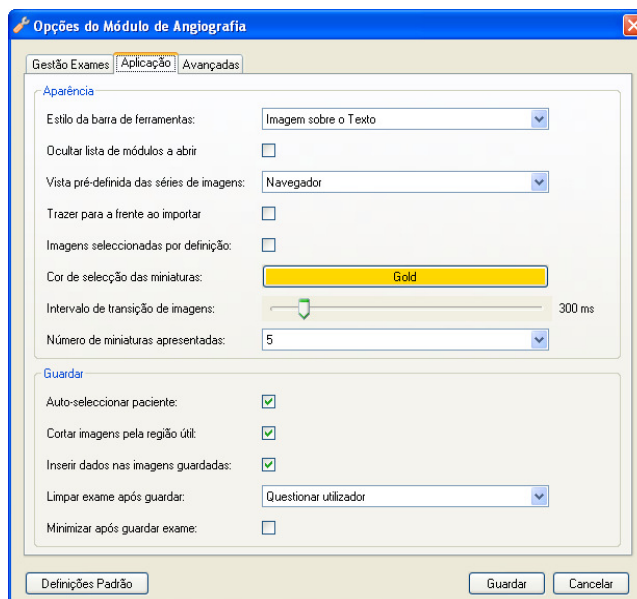
Figure 12 Options Window

3.4.3 Selection of Images

The AM module is already initialized and the pre-established folder awaits for the arrival of the exam images.

Features	Description	Methods
Image/File Reading	With the creation of images in the pre-established folder, the timerFile is activated and therefore starts the interpretation process concerning each image. During the interpretation of the DISK0000.BTR file the PATIENT.BTR file is read returning the information regarding the patient associated to the image/exam.	*fileSytemWatcherImagePath_Created()* *ParseFilePac()* *ParseFileDisk()*
Partition into Series	After the creation of an AngioImage object, it is added to its corresponding series. The miniature images from different series are presented in different tabs. If an image is inserted in an incorrect series the user may move it to its corresponding series.	*AddExam()* ExaminationSeriesTab: *InsertImage()*

Patient and Doctor Validation	The patient and doctor's name are acquired automatically from the reading of the PATIENT.BTR file. This validation by the database is necessary. The patient validation is done automatically from the database using the patient name and date of birth avoiding user validation.	*GetAllPatientsFromDatabase()* *GetAllDoctorsFromDatabase()* *SetPatientContext()* *buttonFindPatient_Click()* *buttonFindDoctor_Click()* *toolButtonDoctor()* *toolButtonDoctor()* *comboBoxAllDoctors_SelectedIndexChanged()* *AutoSearchPatient()*
Image Selection	All the miniature images created are already selected. The user can select or unselect by clicking on the corresponding miniature. It is also possible to select or unselect all the miniatures at the same time by clicking on the checkbox of the corresponding tabs in each series.	ExaminationSeriesTab: *checkBoxSelect_Click()* Thumbnail: *SelectionThumbnail_Click()* *ChangeSelectionStatus()* *pictureBox1_Click()*
Image Removal	It is possible to permenantly remove selected images from each series. It is possible for the user to recover deleted images by using a specif button.	*toolStripButtonRemoveUndo()* ExaminationSeriesTab: *buttonRemove_Click* *RemoveSelectedImages()* *RecoverDeletedImages()*
Image enhancement tools	It is possible to apply simultaneous adjustments to the selected images within the series: increment or decrement of a pre established factor by using brightness, gamma factor and contrast. User may cancel the changes and return to the initial image. These tools are also available for the preview image.	ExaminationSeriesTab: *buttonBrightMore_Click()* *buttonBrightLess_Click()* *buttonGammaMore_Click()* *buttonLessMore_Click()* *buttonContrastMore_Click()* *buttonContrastLess_Click()* *ChangeFilter()* *buttonReset_Click()* *OriginalImage()* BWEye.Shared *ApplyContrast()* *ApplyBrightness()* *ApplyGamma()*

Table 6 AM Image Selection Features

Figure 13, illustrates the Image Selection tab page, where user can see the images that are selected (the golden frame) and all other features.

At the top of AM window we have the fields to select/show the doctor and patient's names and buttons for quick access to save the exam.

On the right sidebar we have tools not only to adjust the images, select the outline of the report and insert comments to the series, but also buttons to move the images to another series (if the images are in the wrong series). Finally, there is also the possibility to eliminate the images desired by the user.

In the central region, the thumbnails of the images imported are presented. The selected images have a golden frame.
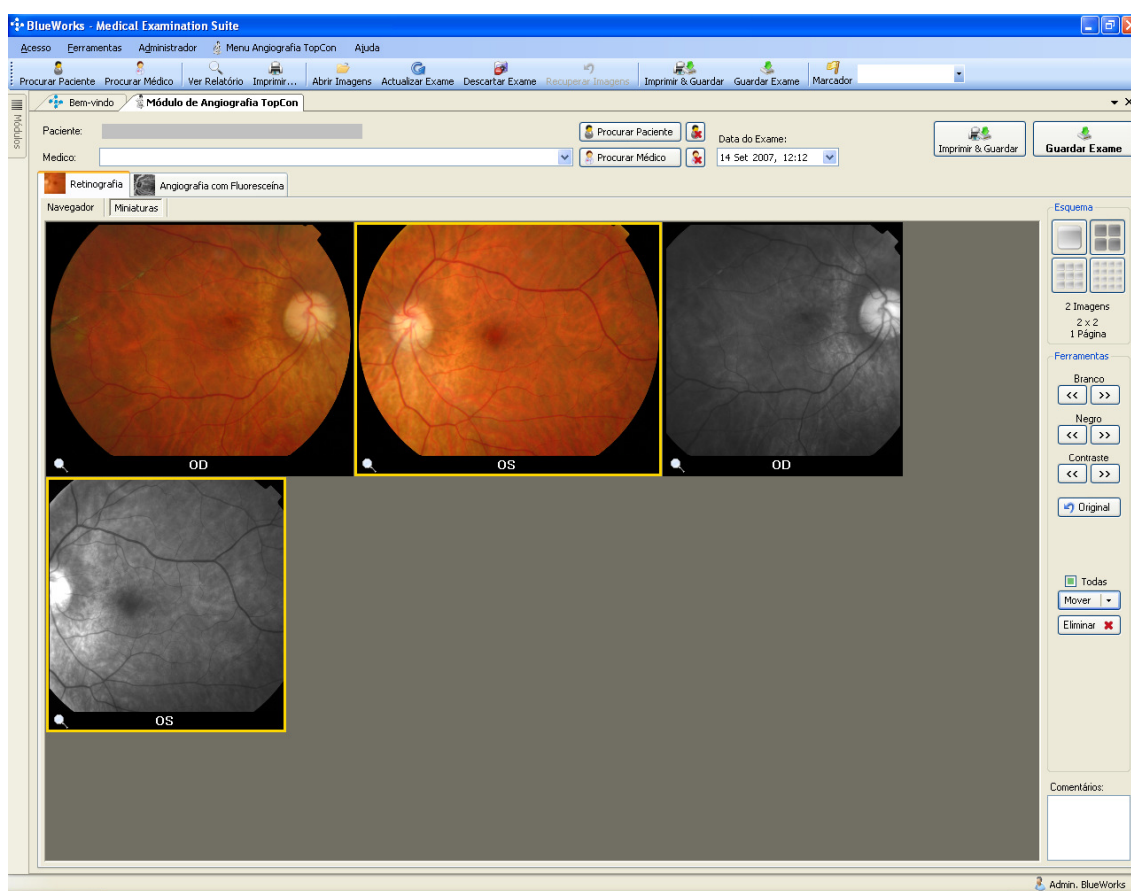
Figure 13 AM Image Selection Window

3.4.4. Preview Image

When an image is double clicked or when the preview button is activated a FormPreview window opens. This form allows zoom ajustment as well as the use of the

previously mentioned tools. It also shows details and information regarding the image. The user may save the image by using the Form Preview menu.
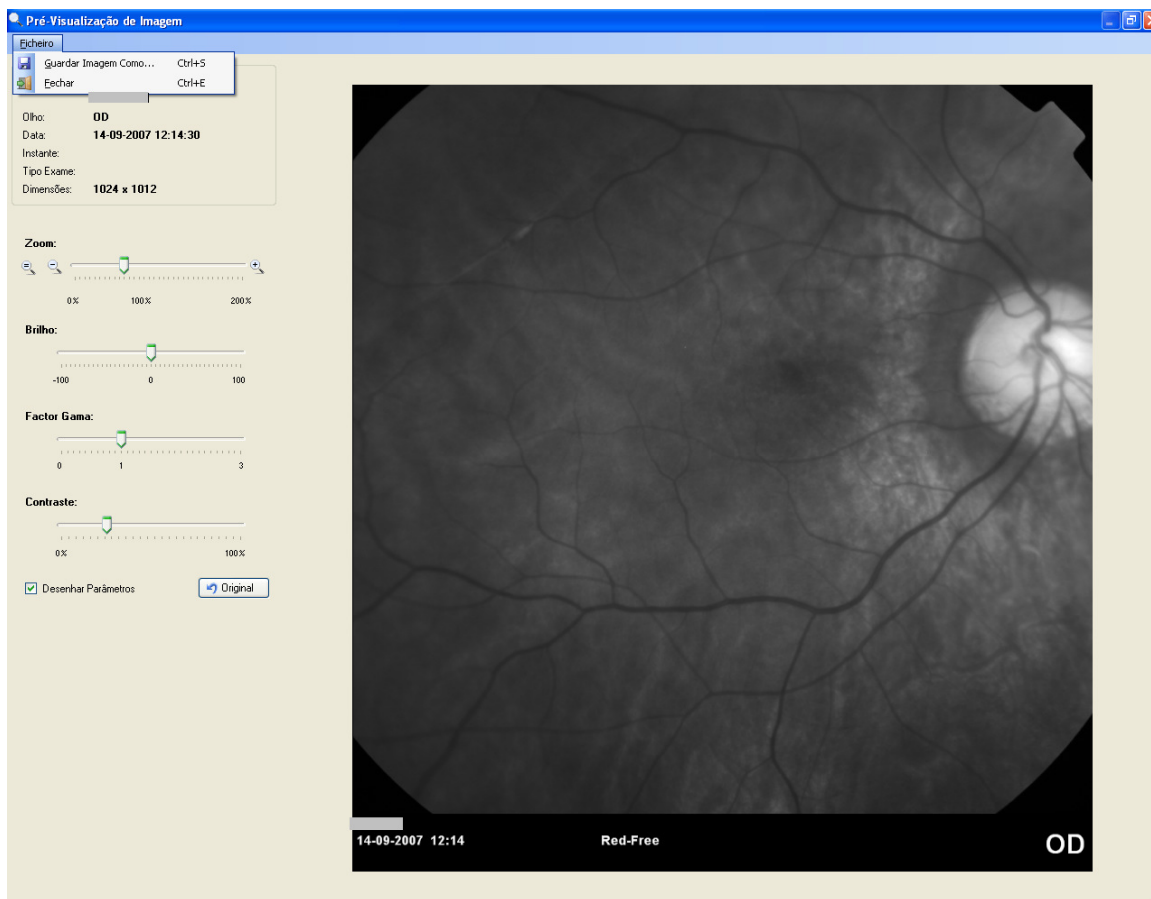
Figure 14 AM Preview Image Window

3.4.5. Examination Report

Table 7 describes examination report defining and saving features.

Features	Description	Methods
Inserting Comments	To insert comments about the exam series, the user must digite the text in the respective area fore each series. By selecting a textbox its corresponding group is automatically enlarged in order to facilitate usage.	ExaminationSeriesTab: *textBoxComments_TextChanged()* *textBoxComments_Enter()* *textBoxComments_Leave()*

	The images selected in its series are automatically put in the *.pdf report.	
Saving Images and seeing the report	The report allows the user to select the number of images per page (1,4,9 or 16). This selection is possible for each series independently. Another option is the preview of the report. On each of the images of the report the eye and its instant are presented (for the angiography). Each report is composed by small reports (one per series). The exam report and the images used are saved in the database.	*SaveExamination(()* *CreateRepor()* *InsertImagesInDocument()* *toolStripSaveExam_Click()* *toolStripButtonPreview_Click()* *toolStripButtonPrint_Click()* *webBrowser_DocumentCompleted()* *RunPrintProcess()* *toolStripButtonPritnSave_Click()* ExaminationSeriesTab: *rbThumbs_CheckedChanged()*

Table 7 AM Examination Report Features

3.5 Challenges

As the integration of the AM module progressed, I came across some difficulties. These were overcome with the vital help from the BlueWorks team who was always available to explain and help in developing this module.

One of the difficulties was the ambiance of programming in C#. The former experience in other programming languages was very helpful in learning this new language as was the previously mentioned help.

Another obstacle was file interpretation and the attempt to understand how they were written. Overcoming this situation took a high dose of persistence allowing us to, at the end, achieve the objective / do the task.

Finally, adapting the OCT module for the AM was a task that required great help from BlueWorks team thus helping in the understanding of some of the methods implemented in the OCT module.

3.6 Software Tests

A set of tests were performed on the AM module to check the ability to execute required tasks as well as to verify application behaviour. Table 8 describes tests conditions and results.

Feature	Functionality	Condition	Result	Approval
Module Loading	Paste an image on watcher folder	Module not loaded	Nothing	**OK**
Module Loading	Left click on module icon	Module not loaded	Opens AM	**OK**
Module Loading	Right click on module icon	Module not loaded	Nothing	**OK**
Import Image	Paste an image on watcher folder		Imports images and sets requests parameters	**OK**
Import Image	Paste an image on watcher folder	Different Patient	Opens warning window when previous exams were not saved and new exam import is detected. Asks if user wants to save, substitute or cancel.	**OK**
Import Image	Load images	Same Patient	Imports images and sets requests parameters	**OK**
Import Image	Load images	Different Patient	Opens warning window when previous exams were not saved and new exam import is detected. Asks if user wants to save, substitute or cancel.	**OK**
Image Selection	Click on selection thumbnail		Selects/ unselects the current thumbnail	**OK**
Image Selection	Click on all requests check box		Selects/ unselects all thumbnails	**OK**
Image Selection	Double click on selection thumbnail		Opens Preview Window	**OK**
Image Selection	Click on Preview button		Opens Preview Window	**OK**
Move Image	Click to move images from another series	Images unselect	Nothing	**OK**
Move Image	Click to move images from another series	Image selected	Moves image to selected series	**OK**
Enhance Images	Click on buttons to apply different types of enhancement	Images unselected	Nothing	**OK**
Enhance Images	Click on buttons to apply different types of enhancement	Images selected	Images Enhance	**OK**
Enhance Images	Click on button to return to original Image	Images unselect	Nothing	**OK**
Enhance Images	Click on button to return to original Image	Images selected	Returns to the original image	**OK**
Remove Images	Click on button to remove images	Images selected	Images are removed	**OK**
Remove Images	Click on button to remove images	Images unselected	Nothing	**OK**
Remove Images	Click on button to restart images		Restarts images previously removed	**OK**
Create Report	Click on button to view report	Images selected	Opens pdf report to be save	**OK**

Create Report	Click on button to view report	Change schema of report	New pdf report with the new schema	**OK**
Save Examination	Click on save examination button		Shows progress bar. Examination is saved	**OK**
Exit	Click on exit button of module		Opens window to confirm and application continues open.	**OK**

Table 8 Software Tests

4. Image Processing

Image processing is an important part of this project.

The image processing developed through this project was based the OCT images. The purpose of this processing was the creation of thickness maps using extraction structures specifically from the RPE. It is possible to create these maps for other kinds of structures.

Ultimately, the thickness maps are loaded in a GUI where the average for each region is calculated.

4.1 Requisites

The first step in developing this algorithm was the segmentation of the RPE. In an OCT image, the RPE is presented as a red region. This colour is the result of the high reflectance of this area.

Last year's developments of this project created a feature which superiorly limited the RPE, taking into consideration that the inner surface is represented by a red line in OCT images. [1] The main goal of RPE segmentation is to improve the existent algorithm (for shadows due to the presence of vessels) and create the segmentation from the inferior limit taking into account the red region in the OCT image.

The algorithm for the creation of thickness maps is based on interpolation point by point.

The map to be interpolated is created from the information in each of the OCT slices and the orientation of this slice. With a significant number of OCT images (more than nine) we get the map that is to be interpolated.

As this Project serves as a continuation of a previous Project and because Matlab is part of the Biomedical Engineering program these algorithms were developed in this high level language. Additionally, this language can adapt to applications developed in C#.

4.2 Implementation

4.2.1 Retinal Pigmented Epithelium Segmentation

The algorithms developed last year were based on images in PNG (Portable Network Graphics) format. Because now the images exported by the OCT equipment are in JPEG (Joint Photographic Experts Group) format some adaptive measures were required such as the segmentation filter and the way to obtain the angle of the slice.

These changes are necessary, since the JPEG format is a commonly used method of compression for images. In most cases it uses a lossy compression algorithm; these algorithms take advantage of the inherent limitation of the human eye and discard information that cannot be seen. The PNG format supports true colour (16 million colours) and doesn't do image compression. [11]

After that it is necessary to do some changes on the filter used. The new filter used is based on the usage of a different colour map. The function responsible for this filter receives a RGB image and provides a grey scale image. This conversion is made for each point and each point is considered the biggest value in the RGB component therefore presenting a grey scale image. Figure 15 (c) and (b) shows the image with different filters.

(a) Original Image, Angle=30   (b) Cut Image

(c) Red Component   (d) RGB Biggest Value Component
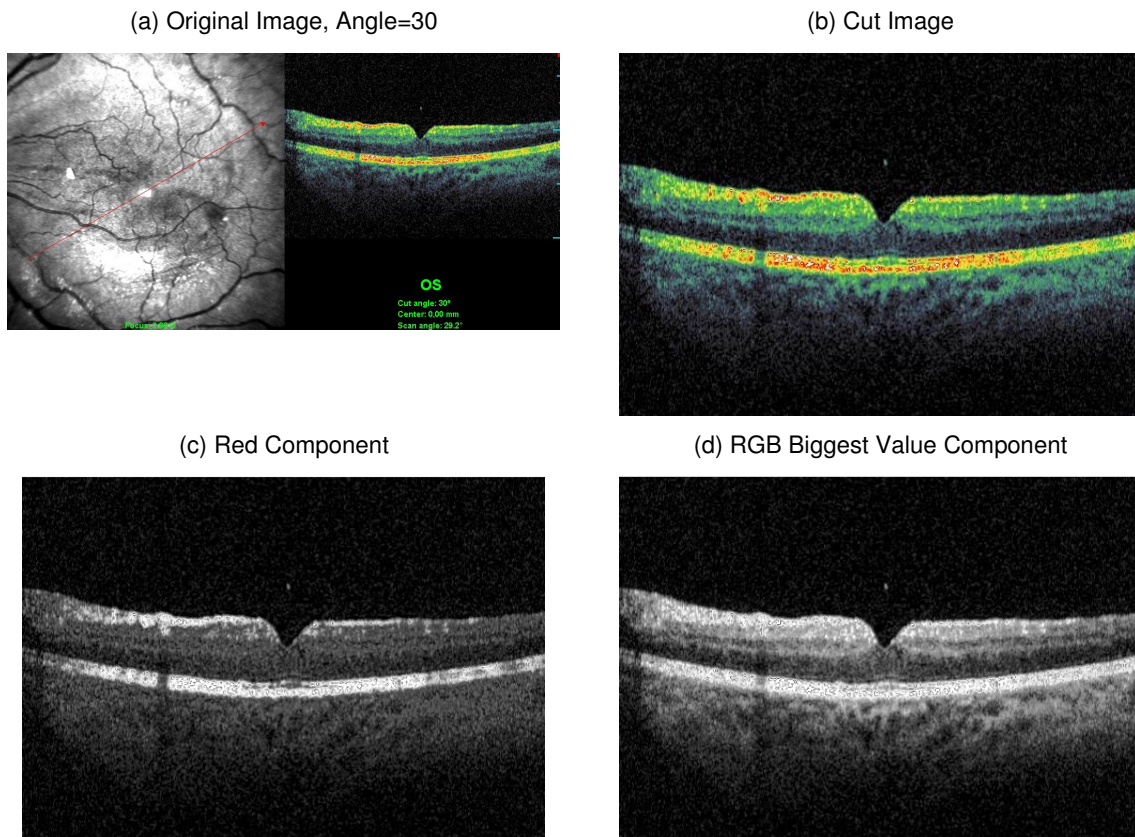
Figure 15 Original OCT Image with different kind of filters

Using the developed function from last year, *GetEpithelium*, as a starting point we started by making a study of this algorithm based on snakes. [1]

After this phase, changes in the algorithm were made in order to make an external surface segmentation of the RPE. Figure 16 shows the first image segmented.
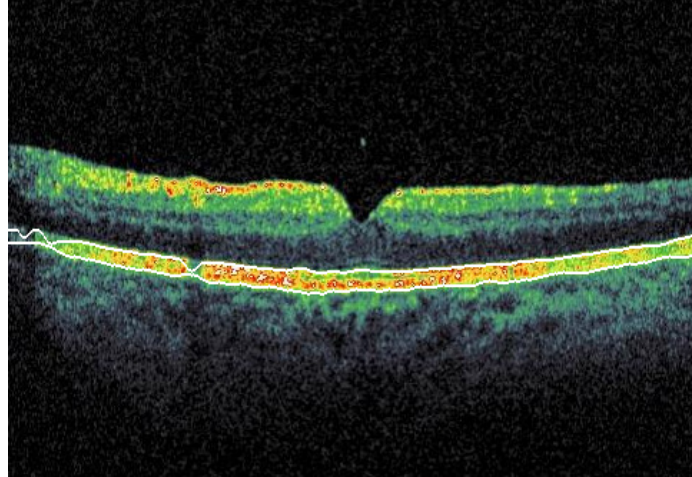
Figure 16 Segmented Image with first process

Thus, the functions *GetEpitheliumIN* and *GetEpitheliumOUT* are very similar to the original function, *GetEpithelium*,

```
[epitheliumIN img_display] = GetEpitheliumIN(display, display_final,
    img, file, kernel, threshold, neig, meanR, blur, borderRange)


        [epitheliumOUT img_filtered img_displayOUT min max]
= GetEpitheliumOUT(display, display_final, img, file, kernel, thresh-
                old, neig, meanR, blur, borderRange)
```

The steps to create the RPE segmentation, from the original image, are very similar to the steps initially proposed having changed only one step. This change is due to the different types of image formats, as previously described.

Stage	Filtering Purposes
Image cut	- Use of function *CutImage* - Isolate useful image area
Strong Component Isolation	- Remove components with less weight - Normalize resulting 2D matrix in order to maximize contrast range
Blurring	- Apply a circular averaging filter of radius blur - Smooth rough noise on empty areas
Binary conversion	- Annul pixels lower then threshold - Differentiate interest region
Noise removal	- Apply a 2D median filter of size kernel - Remove salt & pepper like noise

Table 9 Spatial Filtering Stages on RPE segmentation [1]

The first segmentation obtained, as illustrated in figure 16, shows some limitations. If we have a vessel intersection, the OCT image shows a shadow in this region, resulting in a sudden peak in the segmentation line. These peaks express an error in the algorithm.

To correct this error the *BezierCurve* function is used. [12]

```
[X,Y] = BezierCurve(img,Px,Py,show)
```

This function receives a group of points in relation to x and y and returns the points to construct a curve, without abrupt changes, based on the original points.

The *GetEpitheliumIN* and *GetEpitheliumOUT* functions return, respectively, the points responsible for the inner and outer surface of the RPE. For each of these limits some points are obtained to be used in the *BezierCurve* function. Figure 17 shows the results obtained after the application of this function.
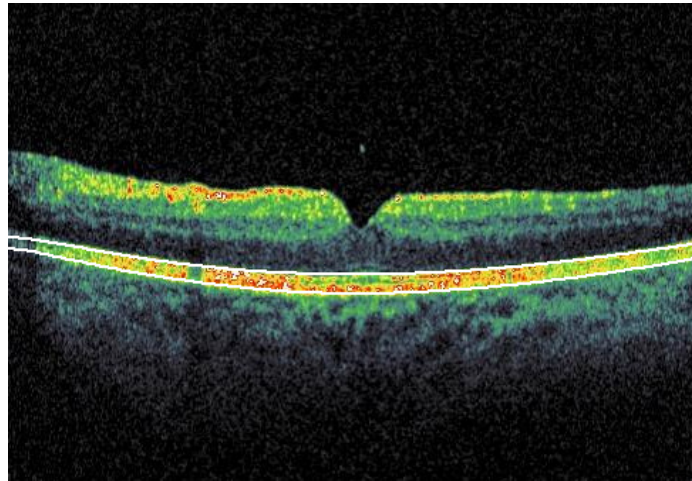
Figure 17 Segmented Image using *BezierCurve* function

```
[thickness ymin ymax epitheliumIN epitheliumOUT]
= GetEPThickness(display, display_final, img, file, kernel, threshold,
        neig, meanR, blur, borderRange, imgRetina)
```

After the RPE segmentation, the calculation of the structure's thickness is the last step for creating the thickness map.

The function responsible for calling the segmentation functions and thickness calculus of the RPE is *GetEPThickness*.

This function calculates the RPE thickness in pixels making the difference between the *epitheliumIN* and the *epitheliumOUT*.

4.2.1.1 Situations where RPE segmentation fails

Sometimes RPE segmentation fails, Figure 18 shows images examples where segmentation fails.

(a)   (b)

(c)   (d)
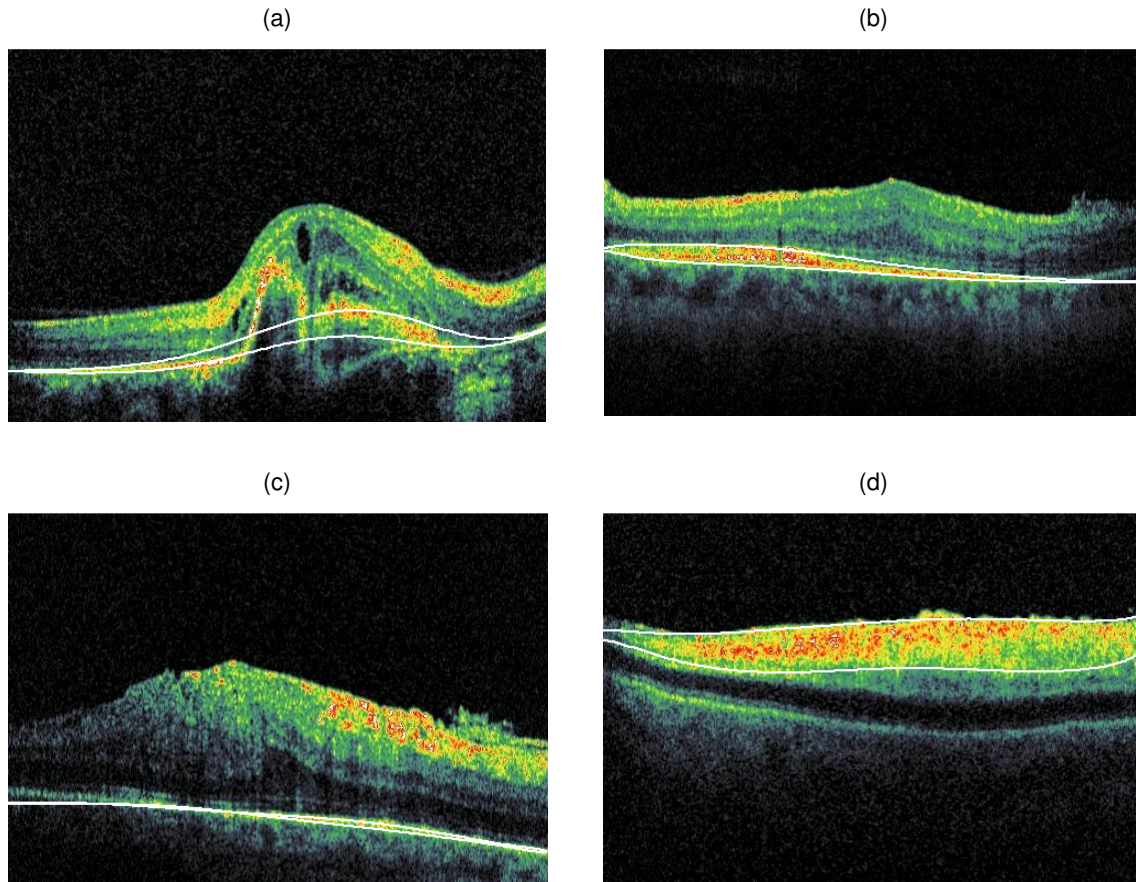
Figure 18 Images where RPE segmentation fails

These fails were due to the fact that:
- The borders of the OCT images are darker than the rest of the image (Figure 18 (b) and (c));
- The RPE is very thin without representative pixels (Figure 18 (d));
- In cases of RPE detachment (Figure 18 (a));

4.2.2 Thickness Map

For the construction of the thickness map, the segmentation of the RPE and the orientation of the angle of the OCT slice are necessary in order to create the map that is to be interpolated.

From images as those shown in figure 15(a) and after the application of the *CropImage* function we get the angle of the OCT slice and its location.

```
[imageOut angleOut endPoint startPoint imageAngle]
                = CropImage(imageIn)
```

The method to obtain the thickness of the RPE has been explained in the previous topic.

In order to obtain the line which indicates the orientation of the OCT slice angle, an approximation of the intervals of the RGB components is made which correspond to the red arrow. Once the images are in jpg format this approximation does not form a perfect arrow. Thus, we get a binary image where only the orientation of the slice arrow is segmented as shown in figure 18. [1] This way we get useful information.
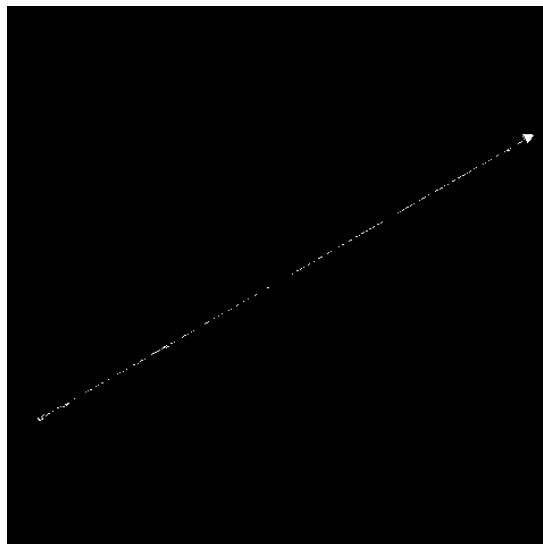
Figure 19 Arrow Segmented

```
Map=ThicknessMapEP(display, display_final,file, kernel, threshold,
          neig, meanR, blur, borderRange, varargin)
```

With the map to be interpolated already constructed (figure 19), it is only necessary to make the interpolation of the rest of the points that do not contain information.
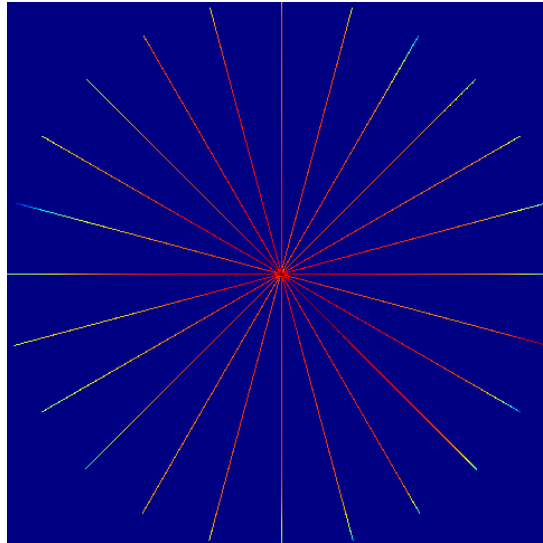
Figure 20 Map to be interpolated

This function receives the values to be applied in the processing of the image and an undefined number of OCT images. For each image that enters the function, the orientation of the slice's angle is calculated as well as the segmentation and thickness calculus of the RPE. Therefore, for each image a line is drawn where each pixel corresponds to the thickness of the RPE at that point. This line is oriented according to the slice's angle. The factions of these lines create Figure 19.

From the image in figure 19 and with the help of the function, which belongs to the Matlab image processing toolbox, we can obtain the values of the two closest points and its distance to the point which is to be interpolated. With this information it is possible to interpolate point by point based on rectangular coordinates taking into consideration the values of the two closest points with the relative distance to the point to be interpolated. This way, we get the thickness map as represented in Figure 20.
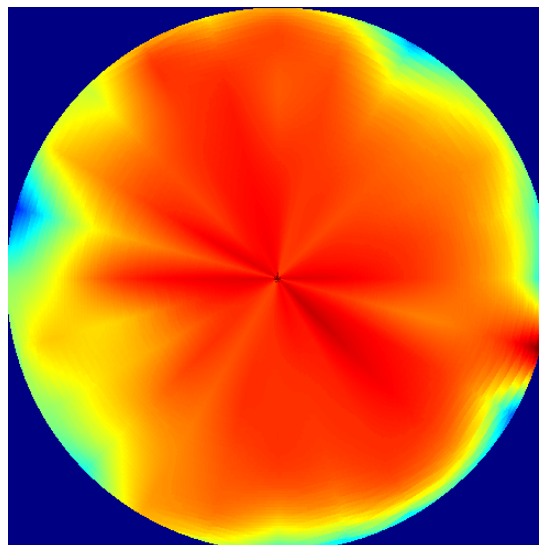
Figure 21 Thickness Map of RPE

4.2.3 GUI for calculate mean regions

Figure 21 shows the calculation of the mean of the represented regions using GUI with a thickness map.
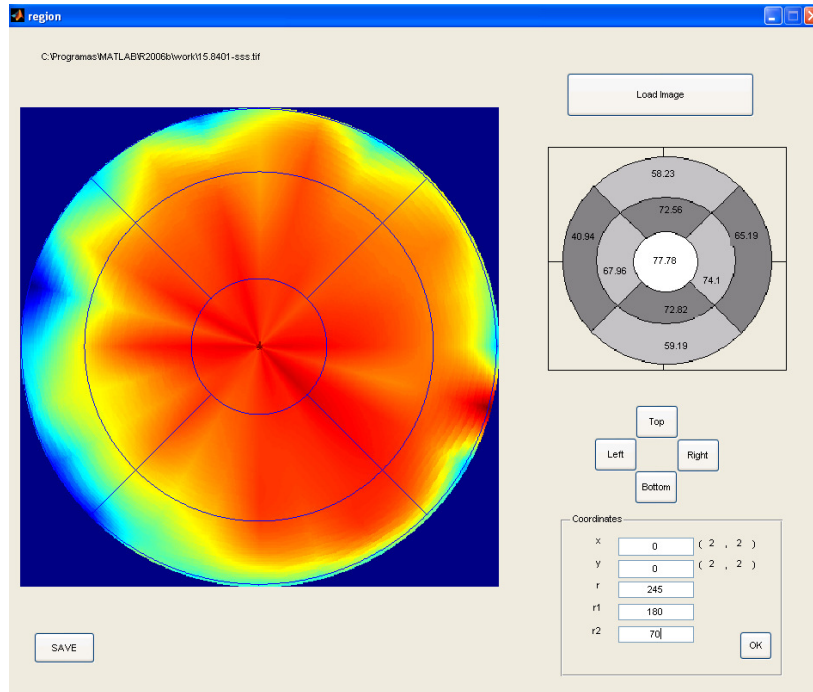
Figure 22 GUI for calculate mean regions

For the calculus of these regions we use a mask, demonstrated in figure 22. Each region of this mask has different index values, so it is only necessary to use the function *find* from Matlab to distinct the different regions.
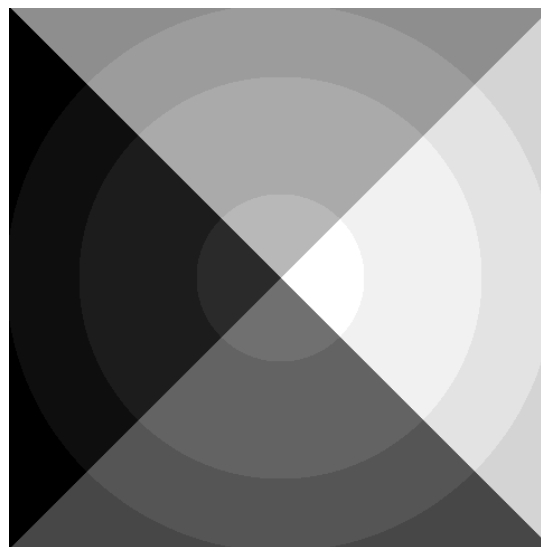
Figure 23 Mask use for calculate indices position

Once we have the location of the absolute values of each region we use Matlab's mean function which gives us the *mean* of the index of each pixel per region.

4.3 Algorithm Tests

The RPE segmentation algorithm was tested on 598 OCT valid images obtained in clinical environment. This number of images is the result of 24 different exams. The RPE segmentation failed sometimes essentially because of a lack of information on images borders (dark regions).

	OCT
Correct Detection	543
Incorrect Detection	56
Detection Success (%)	90,80

Table 10 RPE Segmentation Tests

We got RPE thickness values in the 60-90 µm range.

Algorithm processing time of the RPE segmentation takes 4s to run. On the other hand, the algorithm for creation of the thickness map, for 12 OCT images, where this number is the usual number of slices per exam by B-Scan exams, takes 55s to run.

5. Conclusions and Future Proposals

5.1 Conclusions

It has already been mentioned this project is integrated in a larger project, BW-Eye. Our goal this year was to contribute to this ambitious project which intends to unite areas such Medicine and Informatics.

Initially, it was necessary to study the previously developed project not only regarding the software but also retinopathies and its characteristics.

One of the main goals of the BW-Eye project is the integration of equipments so the information that was previously saved locally could be available in the network. In this project, we studied the angiography equipment in order to proceed to its integration. For the construction of this module, an exhaustive study of the files responsible for saving the files for each exam was necessary.

In the next phase we proceeded to process the image which was also an important goal in this project.

The type of image processing developed aimed to create RPE thickness maps from OCT images and calculate the mean for each region of the map.

The first step was the RPE segmentation. This segmentation revelled 90,8% successful results. The unsuccessful cases were due to the fact that sometimes the borders of the OCT images are darker than the rest of the image hence causing the segmentation to fail. Other regions where sometimes the algorithm fails is in the optic disk and in images with RPE detachment.

After image segmentation thickness maps are created. This algorithm is constrained by the quality of the segmentation and also by the number of images in its origin. Ideally, 12 images with different slice angles produce thickness maps without regions with abrupt transitions. As that number decreases there is an increase of noticeable transitions. At the end, this map is charged in the GUI which automatically gives the mean values for each region.

During the project's development there were several challenges that needed to be overcome.

The first difficulty was the C# training and understanding the way the angiography equipment files were written.

After that, during the image processing it was necessary to test different approaches to see which was most efficient in the interpolation algorithm.

The final challenge was writing the project report in English.

5.2 Futures Proposals

The BW-Eye project still has much to be done in order to achieve the main objective: the creation of a system that supports medical diagnosis.

To reach these objectives it is needed to:

- Continue the integration of equipments;
- Improve the image processing algorithms. In case the thickness maps are needed it necessary to make a selection of images to use, ideally this choice should be automatic.
- Continue the image processing extraction features, to apply in the data mining module;
- Development of the Data Mining module;

In the future, this system can transform the way in which ocular diseases are diagnosed basing them on more objective aspects.

Reference

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[10] – *UCLA Anderson School of Management.* http://www.anderson.ucla.edu/ (accessed June 2008).

[11] - Wikipedia. *Image file formats.* http://en.wikipedia.org/wiki/ (accessed June 2008).

[12] – *The MathWorks.* http://www.mathworks.com/, (accessed June 2008).

Appendices

Appendice 1 – Project Timetable

Tasks	14-Sep	15-Sep	16-Sep	17-Sep	18-Sep	19-Sep	20-Sep	21-Sep	22-Sep	23-Sep	24-Sep	25-Sep	26-Sep	27-Sep	28-Sep	29-Sep	30-Sep
Research about the work done in the previous year																	

Table 11 September Time Table

Tasks	1-Oct	2-Oct	3-Oct	4-Oct	5-Oct	6-Oct	7-Oct	8-Oct	9-Oct	10-Oct	11-Oct	12-Oct	13-Oct	14-Oct	15-Oct	16-Oct	17-Oct	18-Oct	19-Oct	20-Oct	21-Oct	22-Oct	23-Oct	24-Oct	25-Oct	26-Oct	27-Oct	28-Oct	29-Oct	30-Oct	31-Oct
Interpretation of angiography equipment files																															
C# initiation																															

Table 12 October Time Table

Tasks	1-Nov	2-Nov	3-Nov	4-Nov	5-Nov	6-Nov	7-Nov	8-Nov	9-Nov	10-Nov	11-Nov	12-Nov	13-Nov	14-Nov	15-Nov	16-Nov	17-Nov	18-Nov	19-Nov	20-Nov	21-Nov	22-Nov	23-Nov	24-Nov	25-Nov	26-Nov	27-Nov	28-Nov	29-Nov	30-Nov
Interpretation of angiography equipment files																														
Creation of Select Images Tab Page																														
Creation of AngioImage object																														
Study of OCT algorithms to apply																														
Separation of images series																														
Implementation of images zoom																														
Implementation of select/unselect images																														
Search about tools of enhancement																														
Creation of Report																														
Implementation to save results on DB																														

Tasks	1-Dec	2-Dec	3-Dec	4-Dec	5-Dec	6-Dec	7-Dec	8-Dec	9-Dec	10-Dec	11-Dec	12-Dec	13-Dec	14-Dec	15-Dec	16-Dec	17-Dec	18-Dec	19-Dec	20-Dec	21-Dec	22-Dec	23-Dec	24-Dec	25-Dec	26-Dec	27-Dec	28-Dec	29-Dec	30-Dec	31-Dec
Implementation to save results on DB																															
Search about tools of enhancement																															
Connection to DB to select doctor and patient																															
Implementation of enhancement tools																															
Creation of algorithm to remove images																															
Interpretation of angiography equipment files																															
Changes in the report creation																															

Table 14 December Time Table

Tasks	1-Jan	2-Jan	3-Jan	4-Jan	5-Jan	6-Jan	7-Jan	8-Jan	9-Jan	10-Jan	11-Jan	12-Jan	13-Jan	14-Jan	15-Jan	16-Jan	17-Jan	18-Jan	19-Jan	20-Jan	21-Jan	22-Jan	23-Jan	24-Jan	25-Jan	26-Jan	27-Jan	28-Jan	29-Jan	30-Jan	31-Jan

Table 13 November Time Table

Tasks																															
Changes in the report creation																															
Save image on Preview window																															
Implementation to save results on DB																															
Algorithms organization																															
Creation of AM document																															
Creation of Options GUI																															
Implementation of menu options algorithms																															
Creation of English language version																															

Table 15 January Time Table

Tasks	1-Feb	2-Feb	3-Feb	4-Feb	5-Feb	6-Feb	7-Feb	8-Feb	9-Feb	10-Feb	11-Feb	12-Feb	13-Feb	14-Feb	15-Feb	16-Feb	17-Feb	18-Feb	19-Feb	20-Feb	21-Feb	22-Feb	23-Feb	24-Feb	25-Feb	26-Feb	27-Feb	28-Feb	29-Feb
Interpretation of angiography equipment files																													
1st Intercalary Presentation																													
Resolution of AM bugs																													
Creation of slideshow images																													
Optimization of AM																													

Table 16 February Time Table

Tasks	1-Mar	2-Mar	3-Mar	4-Mar	5-Mar	6-JMar	7-Mar	8-Mar	9-Mar	10-Mar	11-Mar	12-Mar	13-Mar	14-Mar	15-Mar	16-Mar	17-Mar	18-Mar	19-Mar	20-Mar	21-Mar	22-Mar	23-Mar	24-Mar	25-Mar	26-Mar	27-Mar	28-Mar	29-Mar	30-Mar	31-Mar
Tests of AM																															
Resolution of AM bugs																															
Optimization of AM																															
Creation of GUI to calculate mean regions																															
Study for creation of thickness maps																															
Creation thickness map algorithm																															

Table 17 March Time Table

Tasks	1-Apr	2-Apr	3-Apr	4-Apr	5-Apr	6-Apr	7-Apr	8-Apr	9-Apr	10-Apr	11-Apr	12-Apr	13-Apr	14-Apr	15-Apr	16-Apr	17-Apr	18-Apr	19-Apr	20-Apr	21-Apr	22-Apr	23-Apr	24-Apr	25-Apr	26-Apr	27-Apr	28-Apr	29-Apr	30-Apr
Creation thickness map algorithm	X	X	X	X			X	X	X																					
Tests of thickness map algorithm									X																					
Study for RPE segmentation										X				X	X															
Changes of AM document											X																			
Optimization of RPE algorithm detection																	X	X			X	X								
Creation of RPE algorithm segmentation																							X	X						
Tests of RPE algorithm segmentation																							X	X					X	
Creation of algorithm to calculate thickness																												X		
Optimization of RPE algorithm segmentation																													X	X
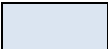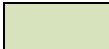
Table 18 April Time Table

Tasks	1-May	2-May	3-May	4-May	5-May	6-May	7-May	8-May	9-May	10-May	11-May	12-May	13-May	14-May	15-May	16-May	17-May	18-May	19-May	20-May	21-May	22-May	23-May	24-May	25-May	26-May	27-May	28-May	29-May	30-May	31-May
Optimization of RPE algorithm segmentation																															
Tests of RPE algorithm segmentation																															
2st Intercalary Presentation																															
Creation of thickness map algorithm																															
Tests of thickness map algorithm																															
Export/Select images to membranes project																															
Creation of maps to membranes project																															

Table 19 May Time Table

Tasks	1-Jun	2-Jun	3-Jun	4-Jun	5-Jun	6-Jun	7-Jun	8-Jun	9-Jun	10-Jun	11-Jun	12-Jun	13-Jun	14-Jun	15-Jun	16-Jun	17-Jun	18-Jun	19-Jun	20-Jun	21-Jun	22-Jun	23-Jun	24-Jun	25-Jun	26-Jun	27-Jun	28-Jun	29-Jun	30-Jun
Creation of maps to membranes project																														
2st Intercalary Presentation																														
Organization of algorithms																														
Project Report writing																														
Image processing documentation																														

Table 20 June Time Table

BW-Eye Project		
Weekend/Holiday		
Classes		
Personal laptop in store for repair		