

**NEW TOOL FOR THE ASSESSMENT OF THE UTERINE
CERVIX TISSUE IN PREGNANT WOMEN
BASED ON QUANTITATIVE ULTRASOUND TEXTURE
ANALYSIS**

**A Degree Thesis
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by
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Abstract

Background: Preterm delivery is the first cause of mortality in fetuses. Measuring the cervix length is used to predict the risk of a preterm delivery but it performs poorly as a predictive tool, so other methods are needed.

Results: The quantitative analysis of the cervical texture by a conventional ultrasound image of the uterine cervix has been used to quantify indirect mechanical changes of the uterine cervix (at histological and chemical level). Three different feature extractors have been used. Features obtained have been compared and a regression model has been created for each extractor. This regression model has measured the association of these detected changes with the gestational age.

Conclusions: Changes detected in the cervical ultrasound images that were associated to the cervix changes along the gestational age. This could mean that changes in the cervical ultrasound images may be quantified and, moreover, that with further research, we could probably predict the risk of preterm birth.

Resum

Antecedents: El part prematur és la primera causa de mortalitat fetal. La mesura de la longitud cervical és l'eina que s'usa per predir el risc d'un part prematur però aquesta no garanteix una bona especificitat, és per això que es necessiten altres mètodes per predir-lo.

Resultats: L'anàlisi quantitatiu de la textura cervical mitjançant imatges d'ultrason del cervix uterí ha estat utilitzat per quantificar canvis mecànics indirectes d'aquest (en un nivell histològic i químic). En el present projecte s'han utilitzat tres extractors de característiques diferents. Les característiques obtingudes s'han comparat i s'ha creat un model de regressió per cada extractor. Aquest model de regressió ha mesurat l'associació d'aquests canvis detectats amb l'edat gestacional.

Conclusions: S'han detectat canvis a les imatges cervicals d'ultrason que es poden associar a canvis del cèrvix al llarg de l'edat gestacional. Això podria voler dir que els canvis a les imatges d'ultrason del cèrvix es poden quantificar i, a més, amb més investigació, es podria predir possiblement el risc de part prematur.

Resumen

Antecedentes: El parto prematuro es la primera causa de mortalidad fetal. La medida de la longitud cervical se ha usado para predecir el riesgo de un parto prematuro, pero esta herramienta no garantiza una buena especificidad. Es por eso que se necesitan otros métodos.

Resultados: Ha sido utilizado el análisis cuantitativo de la textura cervical mediante imágenes de ultrasonido del cérvix uterino para cuantificar cambios mecánicos indirectos en el cérvix uterino (a nivel histológico y químico). En este proyecto, se han usado tres extractores de características diferentes. Las características obtenidas se han comparado y se ha creado un modelo de regresión para cada extractor. Este modelo de regresión ha medido la asociación de estos cambios detectados con la edad gestacional.

Conclusiones: Se han detectado cambios en las imágenes del cervix que se pueden asociar a cambios del cérvix durante la edad gestacional. Ésto podría llevar a confirmar que hay cambios en las imágenes ecográficas del cérvix que se pueden cuantificar y, además, que con más investigación, se podría llegar a predecir el riesgo de parto prematuro.



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1. Introduction

Preterm birth is the leading cause-of-death for children in high-income countries and the second leading cause worldwide. Preterm birth is also contributing to long-term growth impairment and significant long-term morbidity such as cognitive, visual, and learning disabilities.

The current standard method for the prediction of the preterm delivery risk is the cervix length. However, this method performs poorly as a predictive tool, so better methods are needed.

Based on this clinical need, this study focuses on the development of a new method to improve the prediction of preterm birth. This project arises from the Fetal i+D Fetal Medicine Research Center, from the Hospital Clínic de Barcelona and lead by the Prof. Eduard Gratacós, who take part in the clinical knowledge of this issue. Transmural Biotech, a spin-off of the Hospital Clínic de Barcelona and the Universitat de Barcelona whose aim is to develop innovative clinical products and services using medical technologies based on image analysis and processing, carries out the technical knowledge needed for this project.

The purpose of this project is the exploration of the capability of a new method to assess the uterine cervix in a clinical setting: the quantitative ultrasound cervical texture analysis.

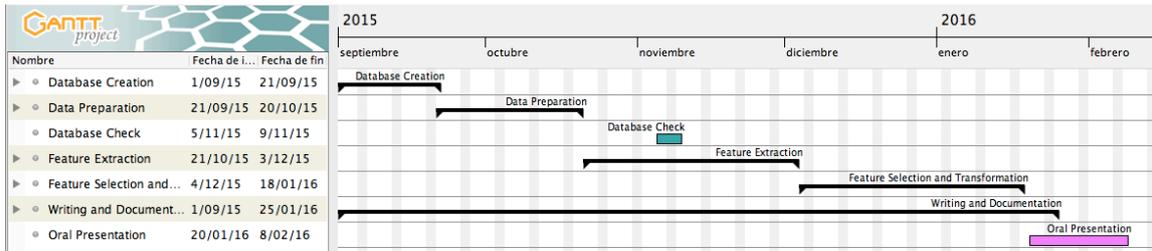
The project specific goals are:

1. Image Data Bases generation: to generate tidy Data Bases of medical images of the uterine cervix and clinical data, which will be recruited in a real clinical setting.
2. Image information extraction: to apply and develop a method based on quantitative ultrasound texture analysis in order to extract robust and reliable information from medical images of the uterine cervix.
3. Robustness evaluation: to evaluate the robustness of quantitative ultrasound texture analysis in front of ultrasound acquisition conditions of a clinical setting compared to current methods which intent to evaluate cervical remodeling.
4. Scientific proof of concept: to evaluate whether robust information obtained quantitative ultrasound texture analysis can detect changes of the uterine cervix along pregnancy.

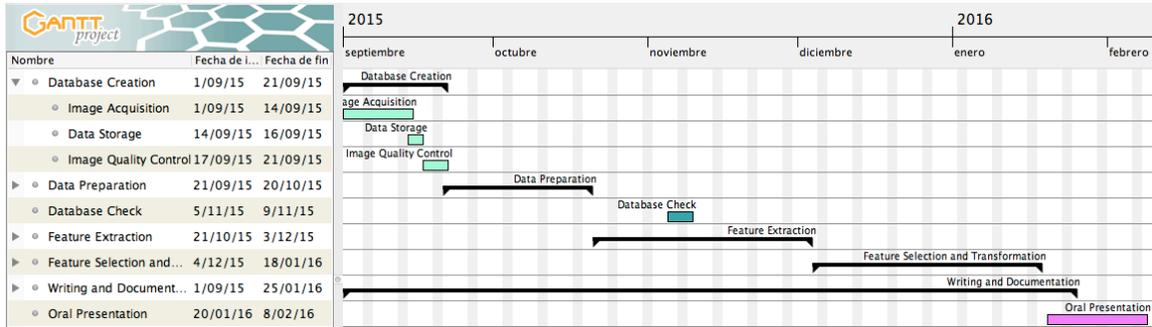
Gantt Diagrams

To be able to do all the different tasks on time, a Workplan has been planned with all the different tasks of each Work package and a Gantt Diagram. This is the calendar that has been followed:

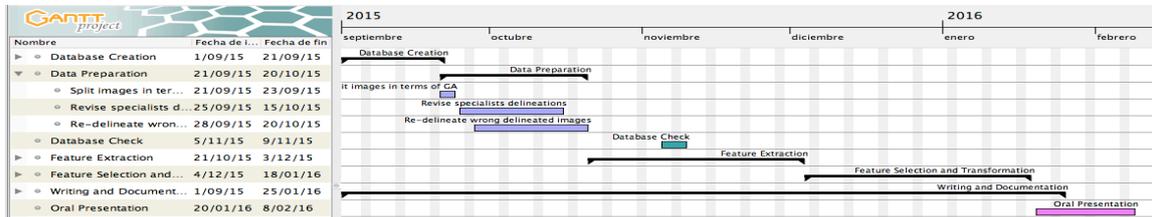
Gantt Diagram Overview



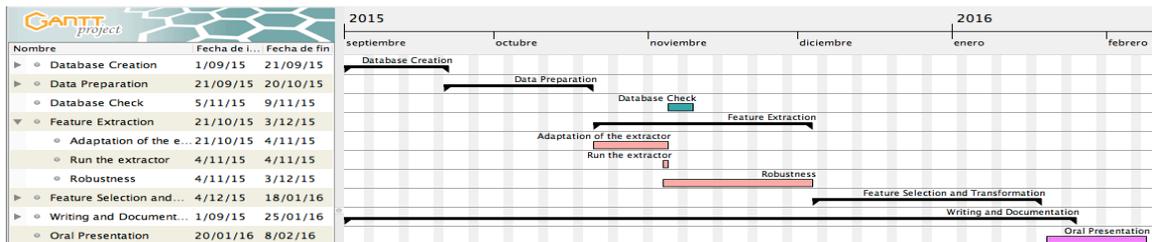
Database Creation Gantt Diagram



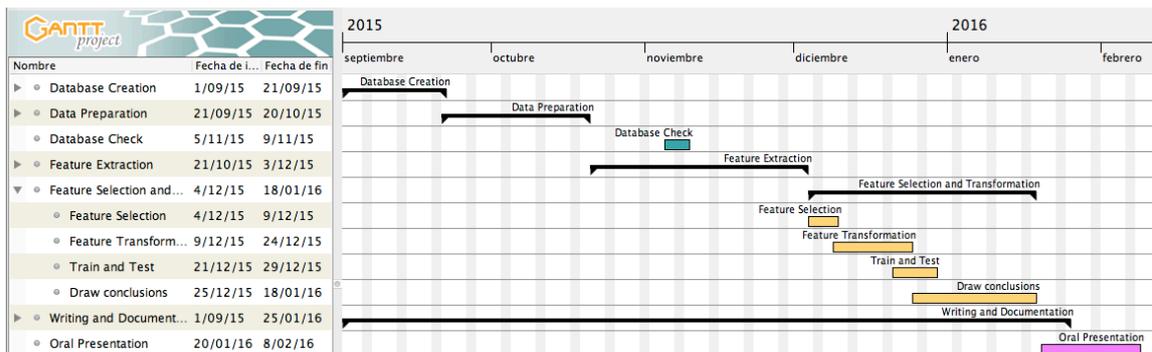
Data Preparation Gantt Diagram



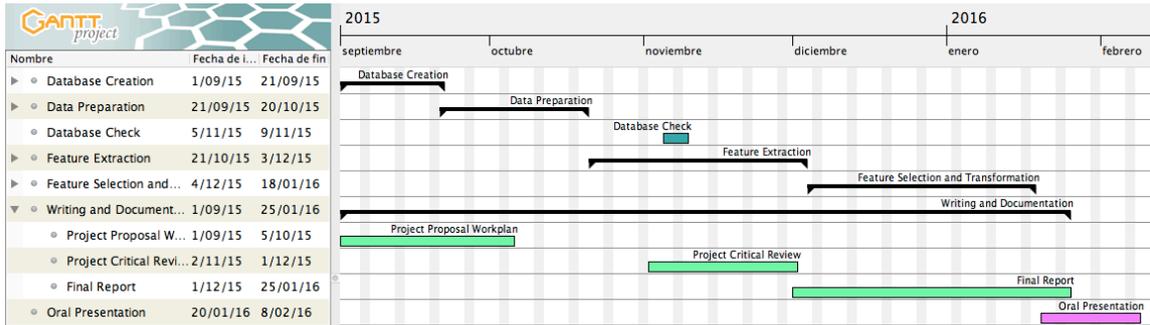
Feature Extraction Gantt Diagram



Feature Selection and Transformation Gantt Diagram



Writing and Documentation Gantt Diagram



WorkPackages

Each WorkPackage has had the following tasks:

Project: Database Creation	WP ref: 001		
Major constituent: Image Acquisition	Sheet 1 of 1		
Short description: Compilation of the images acquired by the specialists.	Planned start date:	1/09/2015	
	Planned end date:	14/09/2015	
Internal task T1: Download images	Deliverables:	Dates: 14/09/2015	
Internal task T2: Program a code that checks the image has not been downloaded before.	Image and patient information Excel.		
Internal task T3: Compile the new image information.			

Project: Database Creation	WP ref: 002		
Major constituent: Data Storage	Sheet 1 of 1		
Short description: Creation of packets to have the data in folders	Planned start date:	17/09/2015	
	Planned end date:	21/09/2015	
Internal task T1: Create folders of 10 or 20 images.	Deliverables:	Dates: 21/09/2015	
Internal task T2:	Excel folders	of	



Check the images follow the quality established in the acquisition guide.	Excel with the summary of images that have passed the control or not	
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Project: Data Preparation	WP ref: 003	
Major constituent: Image Delineation and Delineation Quality Control	Sheet 1 of 1	
Short description: Get the data ready to be able to processed.	Planned start date: 21/09/2015 Planned end date: 20/10/2015	
Internal task T1: Split data in terms of gestational age Internal task T2: Adapt a GUI in order to see the dicom images and do the quality control Internal task T3: Revise the delineations made by the specialists (Adapt a GUI in order to see the dicom images and do the quality control). Internal task T4: Make changes to the GUI in order to be able to redelineate the ROIs Internal task T5: Re-delineate the images that have been wrongly delineated.	Deliverables: Folders with images separated. Delineation control Excel	Dates: 23/09/2015 20/10/2015

Project: Database Check	WP ref: 004	
Major constituent: Remove "spontaneous preterm delivery" images	Sheet 1 of 1	
Short description: Remove the images that have been of spontaneous preterm deliveries given their identifiers.	Planned start date: 5/11/2015 Planned end date: 9/11/2015	
Internal task T1: Program a code that adds a description to the image depending if they have the identifier of a "spontaneous preterm delivery" or not.	Deliverables: Images with the new descriptor.	Dates: 27/11/2015

Project: Feature Extraction	WP ref: 005	
Major constituent: Obtain Features	Sheet 1 of 1	

Short description: Extraction of the features of the different ROIs in order to process them and draw conclusions through them	Planned start date: 21/10/2015 Planned end date: 4/11/2015
Internal task T1: Choose the extractor. Internal task T2: Adapt the extractor for the project. (Application of the extractor to the different ROIs). Internal task T3: Launch the extractor.	Deliverables: Matrix of features Dates: 4/11/2015

Project: Feature Extraction	WP ref: 006
Major constituent: Robustness Study	Sheet 1 of 1
Short description: Detect the difference of values of each feature among the gestational age or the features that have similar values in the same gestational week.	Planned start date: 9/11/2015 Planned end date: 3/12/2015
Internal task T1: Program a code that measures the Mahalanobis, Euclidean, Cityblocks, Correlation and Cosinus distance. Internal task T2: Adapt the code to the new dataset with non "spontaneous preterm deliveries". Internal task T2: Obtain matrixes of the different distance values. Internal task T3: Program a code that measures the correlation and significance among the different gestational age and between the different weeks of gestation. Internal task T4: Compute the mean and the standard deviation of the affine and ordinary distances.	Deliverables: Matrixes of distances. Graphics with the values of the correlation and significance. Dates: 3/12/2015

Project: Feature Selection and Transformation	WP ref: 007
Major constituent: Selection of Features	Sheet 1 of 1
Short description: To obtain better results, select the most important features and transform them with PCA.	Planned start date: 4/12/2015 Planned end date: 11/12/2015
Internal task T1: Program a code that measures the SNR of each feature to select them later depending on this value. Internal task T2: Select the different features	Deliverables: Selection of features Dates: 11/12/2015



depending on the Signal-to-noise ratio they provide.		
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Project: Feature Selection and Transformation	WP ref: 008	
Major constituent: Principal Component Analysis	Sheet 1 of 1	
Short description: Transform selected features with PCA.	Planned start date: 11/12/2015	Planned end date: 20/12/2015
Internal task T1: Program a code that applies the PCA to the selected Features. Internal task T2: Transform the selected features with a PCA approximation.	Deliverables: Feature transformation	Dates: 20/12/2015

Project: Feature Selection and Transformation	WP ref: 009	
Major constituent: Train and Test	Sheet 1 of 1	
Short description: Apply Random Forest to the feature transformation.	Planned start date: 21/12/2015	Planned end date: 18/01/2015
Internal task T1: Program a code that splits the data into different percentage bags of train and test samples. Internal task T2: Program a code that predicts with Random Forest methodology. Internal task T3: Save the correlation, significance and predictions. Internal task T4: Extract conclusions from task T3.	Deliverables: Correlation, significance of the different predictions.	Dates: 18/01/2015

Project: Writing	WP ref: 010	
Major constituent: Report Writing		
Short description: In order to obtain better results, select the most important features and transform them with PCA.	Planned start date: 1/9/2015	Planned end date:

	25/01/2016
Internal task T1: Project Proposal Workplan writing	Deliverables: Project Proposal Workplan
Internal task T2: Project Critical Review writing	Deliverables: Project Critical Review
Internal task T3: Final Report writing	Deliverables: Final Report
	Dates: 5/10/2015 1/12/2015 25/01/2016

Milestones

Some Milestones have been set in order to control better the time left for each task and to assure there will be enough time to finish the project on time.

WP#	Task#	Short title	Milestone / deliverable	Date (week)
002	2	Packet creation	Deliverable: Excel document with the different packets.	3
003	3	Image quality and name format control	Milestone: Have ≥ 30 correct images for each gestational age. Deliverable: Excel with the resume of all the images that have been discarded or accepted.	4
004	1	Separate the data in terms of gestational age	Deliverable: 22 folders with the proper images inside	4
004	3	Delineations of the images.	Deliverable: All the images delineated.	5-8
005	2	Adapt the extractor to the project.	Deliverable: Code launcher that extracts the features of all images and save them. Milestone: Obtain a matrix with the features of all the images.	8-10
006	3	Features Robustness	Milestone: Detect the importance of each feature by means of robustness	10-13

			through gestational age of inside the same gestational age.	
007	1	Feature Selection	Milestone: Select just features that provides the most useful information.	13
008	2	Feature Transformation	Milestone: Obtain a set of uncorrelated features	14-16
009	3	Train and Test	Deliverable: Results of the test once the train has been done.	17-18
009	4	Conclusions	Milestone: Reach conclusions about the assessment of the methodology followed in the quantitative analysis of the cervix tissue	18-20

Deviations and modifications

There have been some deviations from the first calendar but they have been solved in time and with no bigger issues.

The most important incidence has been that in the database some “spontaneous preterm delivers” had been attached. They should be removed because they cannot describe the normality this project needs to draw appropriate conclusions. So a new control of the images of the patients having spontaneous delivery has been planned.

Another modification done has been to create another task to measure the robustness of the features. Between the four different distances already computed (Mahalanobis, Euclidean, Cosine, Cityblocks and Correlation) we have computed the mean and the standard deviation of the affine and ordinary distances.

2. State of the art of the technology used or applied in this thesis:

First approaches of image processing in the medical field were to improve the quality of the images information and, with them, the diagnosis and knowledge of the human body. Biomedical engineering is the field in which these approaches have been developed, they have not stopped growing in the last years and every time is more obvious the need of binding medicine and technology to improve in diagnosis methods.^[1]

Regarding the clinical motivation of this project, new methods related to the biomedical field in order to overcome major limitations for the prediction of preterm delivery, nowadays, new methods based in the biomedical field are in research.

Taking into account that the uterine cervix changes along pregnancy, these new methods should have the potential to detect these changes of the uterine cervix towards term, as there is an association with histological, biochemical and biomechanical changes.

Based on this, research has been done in, mainly two different branches, distensibility and compression of the uterine cervix. While the former evaluates a physiologic variable, however they could never be clinically useful as they involve instrumentation of the cervical canal, the latter uses compression methods to evaluate biologically relevant figures from unphysiological variables. Of the methods evaluating the biomechanical properties, those based on ultrasound may be clinically useful as it is widely used in medicine since it is easy to perform, not expensive and portable. Those main methods are the following:^{[2][3][4][5]}

- Elastography: Evaluates the compressibility of the cervix by manual compression with the ultrasound transducer and, with it, can also be computed the quantitative elastography.
- Quantitative ultrasound tissue characterization: Computes the mean gray-level histogram of the posterior lip by ultrasound and relates it with the cervical hardness.

Even though, quantitative texture analysis based on an ultrasound image of the uterine cervix is the proposed solution to obtain indirect mechanical information. This information will have to be related to cervical remodeling to develop a new tool useful for the clinical practice.

There is evidence that quantitative analysis could extract information from subtle differences in the texture of the ultrasound images that are related to tissue microstructure and composition changes and consequently, to pathophysiological process.

Quantitative texture analysis based on ultrasound has been very valuable in different medical fields such as in the investigation of breast cancer or liver diseases.^[5] In the Maternal-Fetal medicine field, quantitative ultrasound texture analysis has been also introduced with the study of the fetal brain showing a high correlation between the changes in the fetal brain tissue and the neurodevelopment. Moreover, the capability of the quantitative ultrasound texture analysis to extract robust information has been demonstrated in the analysis of the fetal lung texture to predict the risk of neonatal

respiratory morbidity. From this research, the Fetal i+D Fetal Medicine Research Center and Transmural Biotech S.L. created a new clinical product: quantusFLM.^[6]

This project aims to apply the quantitative texture analysis based on an ultrasound image of the cervix in order to solve the clinical need of predicting whether a birth is going to present risk of preterm or not. To this aim, this project will take advantage of the clinical and technology expertise of the fetal i+D Fetal Medicine Research Center and Transmural Biotech. Concretely, a scientific proof of concept will be developed in order to evaluate whether microstructural changes of the cervix in pregnant women can be detected in a robust way by cervical ultrasound images among gestation.

These results will determine the feasibility of the quantitative texture analysis to quantify the cervical changes in order to predict the preterm delivery.

3. Methodology / project development:

3.1 Data Storage

The images acquired in this project will be in DICOM format (Digital Imaging and Communication in Medicine). DICOM groups information into data sets. That means that a file can contain the patient ID within the file, so image can never be separated from this information by mistake. Furthermore, DICOM data objects consists of multiple attributes, including items such as name and also one special attribute containing the image data.

Data storage is a significant step that could bring problems to the project if it was not correctly done. It is important to have an arranged dataset in order to easily find any mistake produced before the data is processed.

3.1.1 Data size

The gestational age considered for this project is between 20-41 weeks. To have enough samples to obtain results that can represent gestation normality, a set of minimum 30 images for each gestational age has been considered. This implies a set of, at least, 1320 images (30 cases x 2 images x 22 weeks).

3.1.2 Data acquisition

Two images of the same patient in programmed visits to the doctor have been acquired. The first one, hereinafter called “basal view”, shows the normal aspect of the cervix. The other one, named “pressed view”, shows the cervix when it receives pressure from the transducer of the ultrasound scanner. An example can be observed in figure 1.

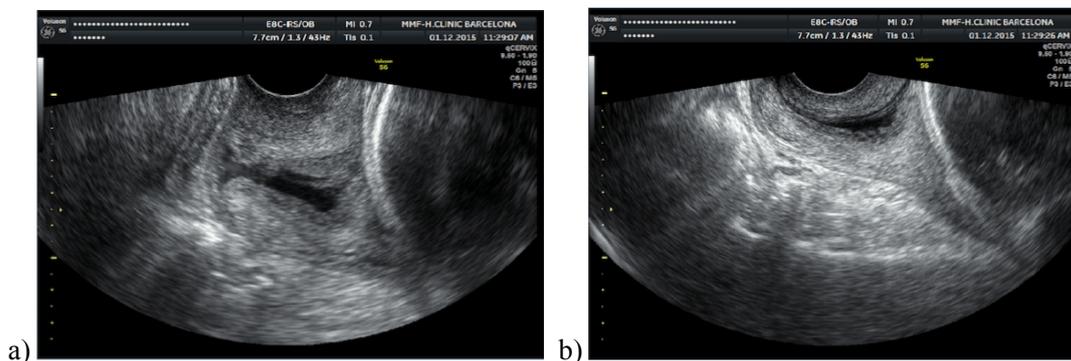


Figure 1. a) Cervix basal view b) Cervix pressed view

These two different image views are acquired in order to have different ROIs (Region of Interest) representing two different states of the cervical canal. Cervical images have been acquired according to the acquisition guide. It has been accepted for both technicians and doctors with the objective to achieve the maximum quality and relevant information of the cervical canal.

3.1.3 Quality Control

In order to look for the quality of cervical images a quality control step was considered to ensure the eligibility of the acquired images.

For that purpose, an interface based on MATLAB GUI has been developed to interact with the acquired images. The figures below show the GUI to analyze the quality of images. One of them shows an example of an accepted image and the other one, one discarded image.

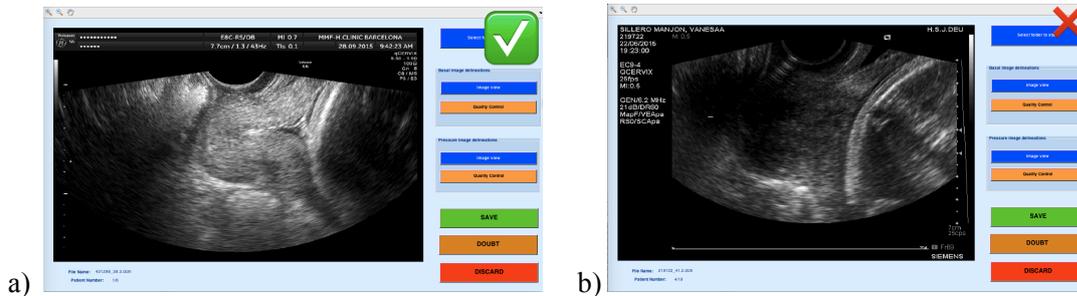


Figure 2 a) A cervical canal can be observed without any shadow, saturation or post-processing. Images as the one above will allow the specialists doing the delineation of the different ROIs and obtain relevant information. b) it has shadows that can cause lack of quality information. For example, if the information wanted were the gray-level, many of them would be lost.

The figure 3 shows the GUI with a “basal view” image ready to be reviewed. The first step has been to select the folder where the images to be checked are located (“Select Folder to Start” button). Then, the basal image is loaded and shown. To check if the image has shadows, there’s the “Quality Control” button. Same functionalities work for the “pressed view”.

Quality Control button allows the user to see if there are any shadows in the image. To do so, it converts low gray values (lower than 13) to black.

Some aspects are more compulsory than others to discard an image. For example it is necessary not to have any post-processing, as it may remove textures or information that would be hidden when extracting features.

In order to control the number of the images being discarded or accepted, a control excel table has been created. This excel will be filled with the reasons why an image has been discarded.

3.1.4 Image labeling and delineation

Once images have been included considering quality criteria, images have to be labeled and delineated.

Also another GUI used in a previous project has been modified to delineate different defined ROIs.

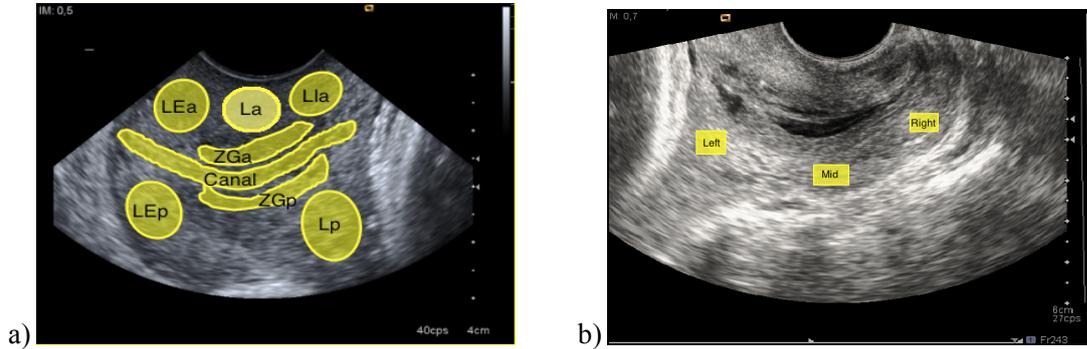


Figure 3 a,b) Show the different ROIs that have been defined in each basal view and pressed view image respectively. Many criteria have to be followed up by the delineators in order to acquire homogeneous, repetitive and feasible delineations.

Two different versions of the GUI have been made, in the following paragraphs each of them will be explained.

SPECIALISTS GUI VERSION. Delineation of an image:

To delineate each image, specialists will have to follow the following steps:



Figure 4. GUI ready to choose a folder

1. To press the “Choose folder to start” button and choose the directory where cervical images are located. After the images have been chosen, the basal and pressed view will be shown.



Figure 5. GUI view after choosing an image

2. To press the “Quality Control” button in order to check that there are no shadows that would be inside the different ROIs. After this, it will be time to start to delineate both images pressing “Start Delineations” button.

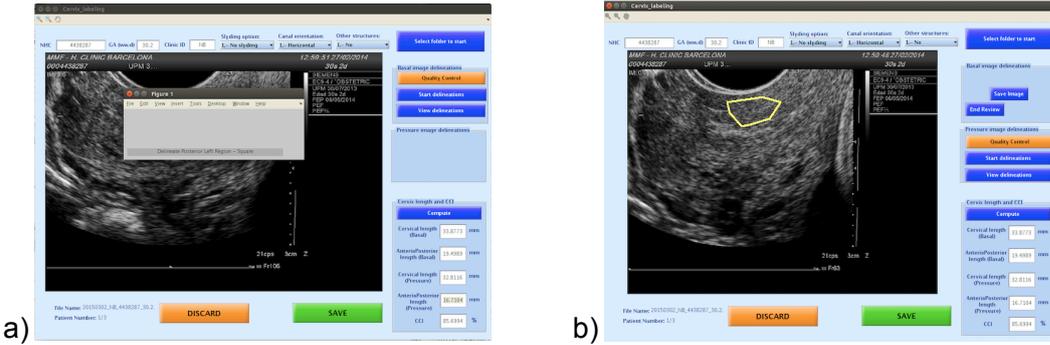


Figure 6. a) Message to delineate the ROI. b) LA ROI already delineated.

3. To delineate the ROIs. In the figures above, there is an example of a delineation procedure. First, a message to introduce the ROI that is going to be delineated appears (figure 6a). In some images there can be ROIs difficult to delineate, so there is the possibility of not delineating them. That is the reason why, after the message, a question dialog will appear asking if the following ROI is desired to be delineated or not. Then, when the user has confirmed, a free-hand marker appears, and the delineator is able to draw the ROI. In the figure 6b there is an example of a “La” ROI delineation (anterior Lip).

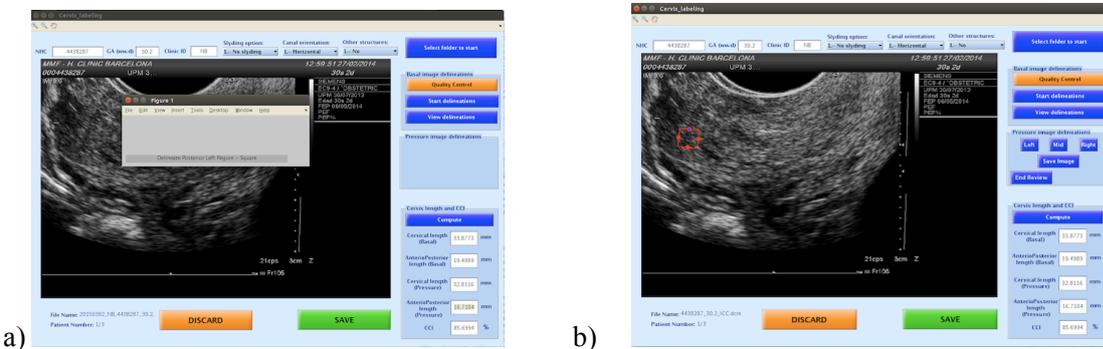


Figure 7. a) Message to delineate the ROI. b) Left ROI already delineated.

4. To delineate the different ROIs of the pressured view images, the ROIs will be marked with a square structure, as Figures 7a and 7b show.



Figure 8. View delineations button allow to check them.

5. The delineators can check all the delineations pressing the “View Delineations” button. If the delineator wants to redo any of them, all the delineations will have to be done again. The figure aside shows the possibility of checking the three different ROIs delineated in the pressed view image.

After delineating all the ROIs of the basal and pressured view images, some computations of the cervical length will be done. These calculus, shown in the “Cervical length and CCI” GUI section, however, are part of another study carried out in this company.

When the delineation has been finished and everything has been checked, the specialist has to press the “Save” button in order to save all the information of the ROIs and delineations. Otherwise, cervical image can be discarded pressing “Discard” button if the image cannot be delineated.

The information of the different ROIs is saved in a .mat file and will be the information that will be processed to obtain the different features. In this .mat file there are different fields such as the gestational age, the different ROIs, RGB image and the DICOM image information.

The main difference between specialists and technical GUI versions is that, in the specialists one they can delineate the ROIs but not modify them. Otherwise, in the technician’s version, they are capable of modifying the wrong delineated ROIs.

GUI. TECHNICIANS VERSION.

This version of the GUI follows the same steps as the specialists one. The main differences are that, when loading the cervical image, it will also show the different already delineated ROIs. Furthermore, it will offer the possibility of modifying the ROIs if it is necessary (Figures 9a and 9b).

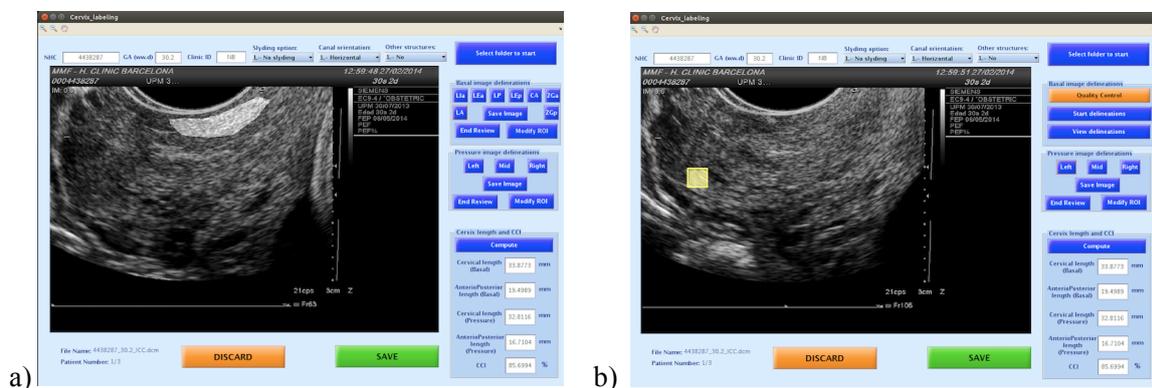


Figure 9. a) Modify button for the selected basal ROI and modified La ROI. b) Modify button for “pressed view and modified Left ROI.

Once the delineations have been checked or/and modified, they will be saved and the .mat file will be uploaded with these modifications or with the previous delineated ROIs.

With all the .mat files of the images being delineated and checked, the database will be created and ready to be able to extract image information.

3.2 Feature extraction

Once the ROIs have been delineated, some extractors will have to be applied in order to calculate the different features that could be related to changes along the gestational age.

These extracted features are expected to contain relevant information from the input data. To evaluate different kinds of features three extractors have been developed and/or adapted. Each extractor provides a concrete number of features depending on the number of measures that are being computed in each of them. Every measure is computed for each ROI. Therefore, if the first extractor computes 4 different measures, each image will provide 4 features x 11 ROIs = 44 different numbers that offer the possibility of doing comparisons between images.

In the following paragraphs each extractor is explained.

3.2.1 Local Binary Pattern

The first extractor is called Linear Binary Pattern. In the present project a variable of this extractor has been used, rotation invariant and uniform Local Binary Pattern, since the original one is not rotation invariant.^[7]

LBP recognizes that certain local binary texture patterns termed “uniform” (meaning that the appearance of the local binary pattern is uniform) are fundamental properties of local image texture. Therefore, it develops a generalized gray-scale and rotation invariant operator for detecting these “uniform” patterns. Gray-scale invariance is necessary due to uneven illumination; different images may be subjected to varying illumination conditions. Because of the complication of acquiring identic images, rotation invariance is also necessary.

How it works.

We derive the operator for a general case based on a circularly symmetric neighbor set of P members on a circle of radius R, denoting the operator $LBP_{P,R}^{riu2}$. P parameter controls the quantization of the angular space, whereas R determines the spatial resolution of the operator. Two different examples can be observed in the figures below (Figures 10a and 10b).



Figure 10 a,b) Circularly symmetric neighbor set of P members on a circle of radius R.

In these figures, each square in the grid represents a pixel position.

Computation of the LBP features:

It starts defining texture T in a local neighborhood:

$$T=t(g_c, g_0, g_1, g_2, \dots, g_{P-1}) \quad (1)$$

Where g_c corresponds to the gray value of the center pixel. g_p corresponds to the gray values of the P equally spaced pixels (if they do not fall exactly in the center of pixels, their gray value is estimated by interpolation). $t(\cdot)$ defines a texture in a local neighborhood defined by the p different pixels.

Due to obtain just the difference in terms of gray value between the center pixel and its neighbors, it computes:

$$T=t(g_c, g_0-g_c, g_1-g_c, \dots, g_{P-1}-g_c) \Rightarrow T=t(g_c)t(g_0-g_c, g_1-g_c, \dots, g_{P-1}-g_c) \quad (2)$$

The distribution $t(g_c)$ describes the overall luminance of the image, which is unrelated to local image texture, so does not provide useful information for texture analysis.

$$T=t(g_0-g_c, g_1-g_c, \dots, g_{P-1}-g_c). \quad (3)$$

For instance, for constant regions, the differences are zero in all directions. For a spot, the differences are high in all directions.

As long as it is wanted to restrict to pure gray-scale invariant texture analysis, contrast is of no interest as it depends on the gray scale. Due to achieve invariance with respect to the scaling of the gray scale; it just considers the signs of the differences instead of their exact values.

$$T=t(s(g_0-g_c), s(g_1-g_c), \dots, s(g_{P-1}-g_c)) \quad (4)$$

Where

$$s(x) = \begin{cases} 1, & x \geq 0 \\ 0, & x < 0 \end{cases} \quad (5)$$

So, taking into account just the sign of the difference, the LBP is computed following the next expression:

$$LBP_{P,R} = \sum_{p=0}^{P-1} s(g_p - g_c) 2^p \quad (6)$$

Example:

If $T = (s(g_0 - g_c) = 1, s(g_1 - g_c) = 0, s(g_2 - g_c) = 1, s(g_3 - g_c) = 1)$.

Then, $LBP_{4,1} = 1 \times 2^0 + 0 \times 2^1 + 1 \times 2^2 + 1 \times 2^3 = 1 + 4 + 8 = 13$.

Once the gray-scale invariance has been achieved, rotation invariance is the next aim.

When the image is rotated, the gray values g_p will correspondingly move along the perimeter of the circle around g_c . To remove the effect of rotation and assign a unique identifier to each rotation invariant local binary pattern it is defined:

$$LBP_{P,R}^{ri} = \min\{ROR(LBP_{P,R}, i) \mid i = 0, 1, \dots, P - 1\} \quad (7)$$

ROR performs a circular bit-wise right shift on the P-bit number, i times. Corresponds to rotating the neighbor set clockwise so many times that a maximal number of the most significant bits, starting from g_{p-1} , is 0.

For example, with a $P=8$, these are the different textures that can be found (white points are $s=1$ and black ones represent $s=0$).

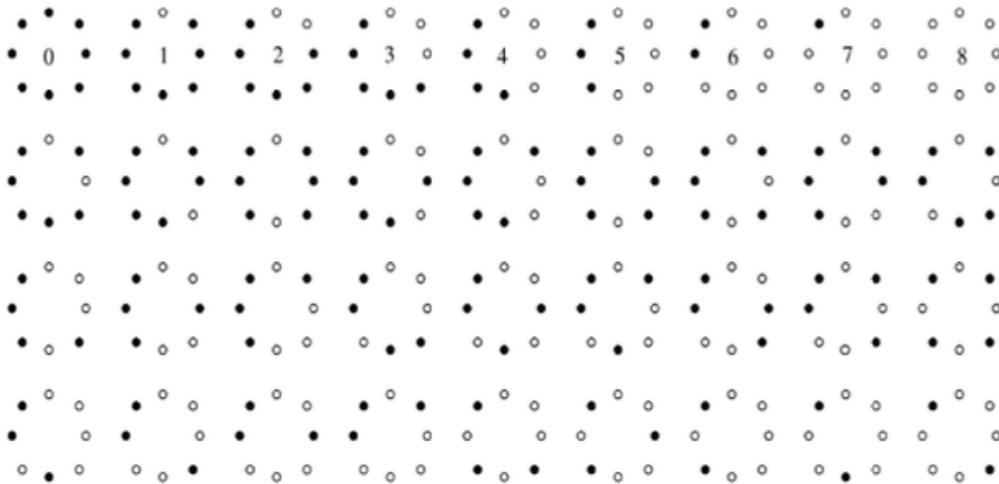


Figure 11. With a P=8, the different features that can be found.

Once rotation invariance has been achieved, it has been important to find uniform patterns in the cervical canal.

Uniform fundamental patterns have one thing in common. They have very few spatial transitions (bitwise 0/1 changes). The U is, using this methodology, the number of bitwise changes. Therefore, U is a uniformity measure and, it is considered a maximum U value of 2 to mean a uniform pattern.

So, finally the expressions used to obtain the LBP feature values are the following:

$$LBP_{P,R}^{riu2} = \begin{cases} \sum_{p=0}^{P-1} s(g_p - g_c) & \text{if } U(LBP_{P,R}) \leq 2 \\ P + 1 & \end{cases} \quad (8)$$

where

$$U(LBP_{P,R}) = |s(g_{P-1} - g_c) - s(g_0 - g_c)| + \sum_{p=1}^{P-1} |s(g_p - g_c) - s(g_{p-1} - g_c)| \quad (9)$$

U (LBP P, R) = Computes the number of bitwise changes in a circularly symmetric neighbor set of P pixels.

If U (LBP P, R) is higher than 2, then it will not be considered a uniform pattern.

Each ROI feature will compute the number of the seventeen different textures with just a two bitwise changes. In the following figure, the different uniform patterns of using P=16 can be seen.

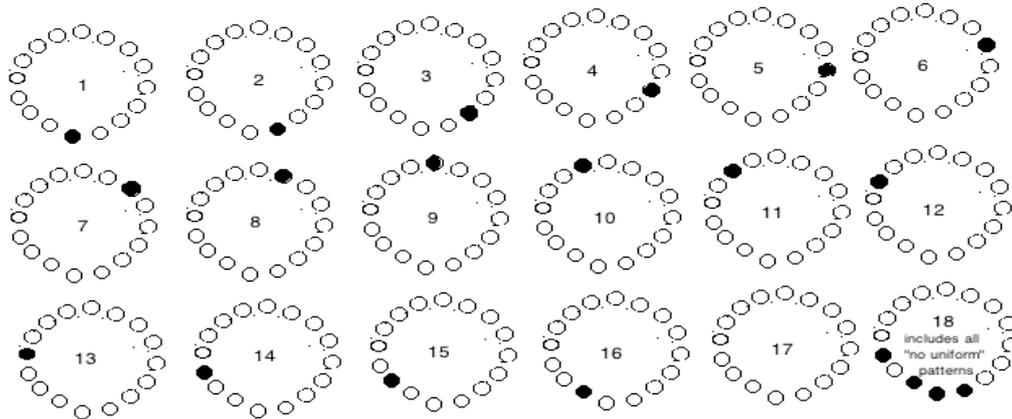


Figure 12. Different uniform patterns using P=16.

By definition, exactly P+1 “uniform” binary patterns can occur in a circularly symmetric neighbor set of P pixels. Equation 4 assigns a unique label to each of them, corresponding to the number of “1” bits in the pattern (0->P). The “nonuniform” patterns are grouped under the miscellaneous label. In practice, $LBP_{P,R}^{riu2}$ has P+2 different output values.

To apply LBP in the present project, a P=16 and R=1 has been used, so a final number of 18 features (P+2) have been obtained for each ROI, as it can be observed in the figure above.

Next two extractors have been used to compare with LBP and check results. These two extractors may be variable to grey-values and rotation in the cervical images. Hence, they are subjected to the variances of the acquisition, so they may not be feasible as the aim is to detect changes along gestational age not between acquisitions.

3.2.2 GLCM Statistics Extractor

This extractor focuses in the gray-level values of the ROI. Due to prepare the different ROIs to the computation of the features, its gray-level co-occurrence matrix (GLCM) is computed in the first place. Gray-level co-occurrence matrix calculates how often a pixel with the intensity (gray-level) value I occurs in a specific spatial relationship to a pixel with the value j.

This extractor provides four different features. These four features are: contrast, correlation, energy and homogeneity.

In the next lines an explanation of each feature is done:

1. Contrast: It returns a measure of the intensity contrast between a pixel and its neighbor over the GLCM ROI matrix. The expression used to compute it is the following:

$$contrast = \sum_{i,j} |i - j|^2 p(i,j) \quad (10)$$

2. Correlation: Returns a measure of how correlated a pixel is to its neighbor over the whole image. In this case, the image is also the GLCM matrix of each ROI, and the expression to compute it is the following:

$$corr = \sum_{i,j} \frac{(i - \mu_i)(j - \mu_j) p(i,j)}{\sigma_i \sigma_j} \quad (11)$$

Where $p(i,j)$ is the pixel value.

3. Energy: Returns the sum of the square elements in the GLCM matrix of each matrix. The expression used to compute this feature is the following:

$$energy = \sum_{i,j} p(i,j)^2 \quad (12)$$

4. Homogeneity: It returns a value that measures the closeness of the distribution of elements in the GLMC to the GLCM diagonal. The formula used to compute the homogeneity is the following:

$$homogeneity = \sum_{i,j} \frac{p(i,j)}{1 + |i - j|} \quad (13)$$

To summarize, this extractor works with the GLCM matrix, while Histogram Statistics Extractor extracts the features from the histogram of the ROI matrix. They have both been implemented with MATLAB.

3.2.3 Histogram Statistics Extractor

This extractor offers six features. Five of these features are related to the Gaussian shape of the gray-level histogram of the different ROIs. The six features are the following:

1. Mean: Is the average of the values of matrix elements. These matrixes are the gray-levels of the ROIs.

2. Variance: Provides the sample variance of a matrix. The given matrix will be the gray-level of each matrix ROI.
3. Standard Deviation: Provides the standard deviation of matrix elements. The matrix elements are each gray-level of each matrix ROI.
4. Skewness: In this case, it is the measure of the asymmetry of the probability distribution of the gray-level histogram of each ROI. This measure can be positive or negative. It computes the third standardized moment.

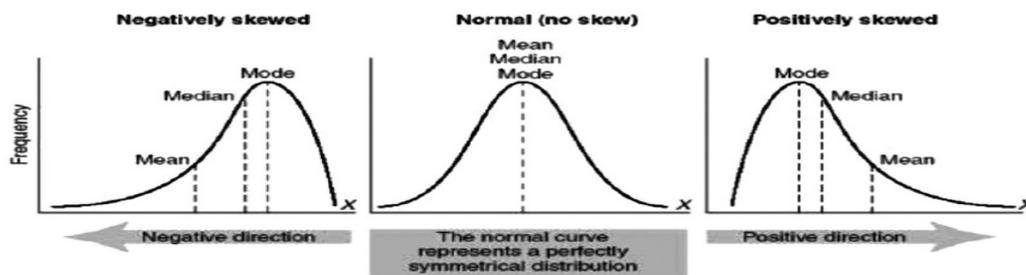


Figure 13. Skewness examples.

5. Kurtosis: Is a measure of the “tailedness” of the probability distribution of a real-valued random variable. It is a descriptor of the shape of a probability distribution function, i.e., the gray level histogram of the different matrix ROI. It is the fourth standardized moment. This measure can be positive or negative, as the figure below shows:

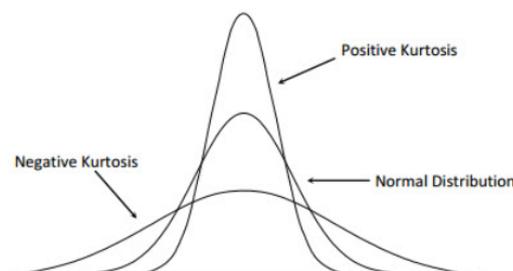


Figure 14. Kurtosis examples.

6. Entropy: With the gray-level histogram of each ROI, it computes its entropy using the information entropy formula:

$$H = - \sum_{i=1}^n p_i \log p_i \quad (15)$$

When all the features have been computed for each ROI, it has been time to start working with them. Due to interact and compare each extractor and each feature a .mat file has been created for each image.

In the following figures, an example of different features values that have been added to a .mat file can be observed.

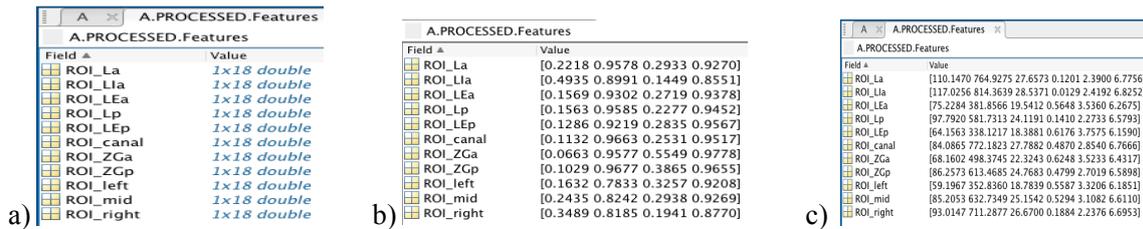


Figure 15. a) LBP, 18 features, b) GLCM, 4 features. c) Histogram, 6 features

As it can be seen, all the features of each extractor describe each ROI.

3.3 Robustness Study

A robustness study has been done in order to assure the reliability of the results of next steps. Hence, it has been also evaluated if the implementation of the extractors would be feasible in the clinical practice. A method is considered robust when extracted feature values are similar between images acquired at different conditions.

Different points of views to assess feature robustness can be assumed, however this project has been defined just one of them, which is going to be explained in 3.3.2.

In order to carry this robustness study, four different similarity measures have been done with the different extractors and features. All these measures have been programmed and computed with MATLAB.

3.3.1 Similarity measures

Five different similarity measures between image features have been measured.

3.3.1.1 Cityblocks or Taxicab distance

To compute the taxicab distance between two vectors, the following formula has been programmed and run.

$$d(p,q) = \|p - q\|_1 = \sum_{i=1}^n |p_i - q_i| \quad (16)$$

Where p and q are the two vectors with the n-dimensions.

This measure is the sum of the n differences between the n-features of both vectors.

3.3.1.2 Mahalanobis distance

This distance is based in the correlation between features that have different patterns that can be identified and analyzed. It is useful to determine the similarity between sets. It considers also the correlations of the dataset. The expression of the calculus is the following:

$$d(x_{vec}, y_{vec}) = \sqrt{(x_{vec} - y_{vec})^T \Sigma^{-1} (x_{vec} - y_{vec})} \quad (17)$$

Where E is the covariance matrix and x and y both feature vectors.

3.3.1.3 Euclidean distance

It is the ordinary distance between two points. It is computed following the expression below:

$$d(x, y) = \sqrt{\sum_{i=1}^n (x_i - y_i)^2} \quad (18)$$

Where p and q are two feature vectors. The difference between Euclidean and Mahalanobis distance is the consideration of the correlation.

3.3.1.4 Cosine distance or similarity

Measures the cosine of the angle between two feature vectors. The expression used to compute this similarity is the following:

$$similarity = \cos \theta = \frac{X \cdot Y}{\|X\| \cdot \|Y\|} \quad (19)$$

3.3.1.5 Distance correlation

Distance correlation is a measure of statistical dependence between two vectors. This measure of dependance is zero if the random variables are statistically independent. The equation to measure this distance is the following:

$$dCor(x_{vec}, y_{vec}) = \frac{dCov(x_{vec}, y_{vec})}{\sqrt{dVar(x_{vec}) dVar(y_{vec})}} \quad (20)$$

Where dCov is the Covariance distance and dVar is the Variance distance between x and y.

These previous measures of similarity have been used to compare images between them in the same gestational age.

Range of values are not the same for all these distances, cosinus distance has a range between (-1,1), Euclidean distance $(-\infty, \infty)$, Mahalanobis distance $(-\infty, \infty)$, Cityblocks distance $(-\infty, \infty)$ and distance Correlation (0,1).

The different types of distances have been normalized to be able to compare distances between ROIs and extractors. Two measures have been differentiated, affine and ordinary distances.

Affine distances will pool absolute Cosinus values and Correlation, so its range will be (0,1). Mean and standard deviation of affine distances have been computed.

On the other hand, ordinary distances will put together Mahalanobis, Cityblocks and Euclidean distances. Mean and standard deviation have been also computed for these distances.

With these measures already done, robustness study has been done. This robustness study is explained in the next section.

3.3.2 Robustness in the same week of gestational age

This study compares each image mean with all the images mean of a given gestational age.

Features of the images in the same gestational age should share about the same values. Therefore, it would mean that features do not depend just on the image but they describe the state of the cervix in that gestational week. Robustness in front of different acquisition conditions is required and different images acquired at different condition in a same week of gestational age will be assessed.

In order to make the results comprehensible they have been plot in a matrix.

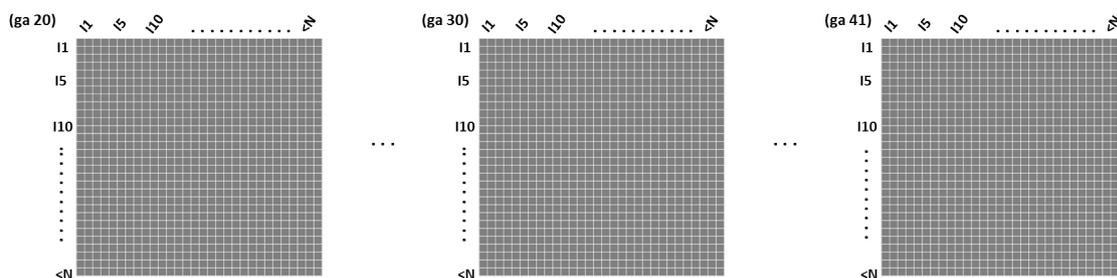


Figure 16. Schematic of robustness in the same week of gestational age matrixes.

The computed matrixes have been 22 GA x 11 ROIs x 2 distances (affinity and ordinary) x 3 Extractors = 1452.

To understand better the meaning of the values, a colorbar has been used. Hence, white values (next to 1), would mean that distances between features are big.

Furthermore, if images of the same gestational age have very different feature values we could conclude that this extractor is not useful, as feature values would depend on the image and not the gestational age.

The following figures show an example of these matrixes:

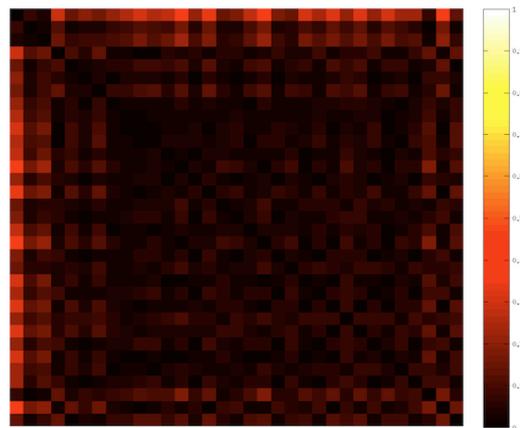


Figure 17. Affinity matrix, ga 25, LEa, LBP extractor

3.3.3 Robustness and ultrasound machines

As there could be differences between the acquired information of the images of different ultrasound machines, a robustness study to assure that there are no changes between ultrasound machines could have been made. However, almost all images have been acquired with a Siemens ultrasound machine and a too small quantity has been acquired by different brands. This substudy has not been performed due to the small set of samples of different ultrasound machines.

3.4 Associative Study

An associative study has been made in order to evaluate the features with the association of the features with the cervical changes along the gestational age. This study has been all programmed with MATLAB.

To do this association, the first step has been to apply a Random Forest regression model in order to evaluate the performance of each extractor for detecting textural changes of the cervix.

3.4.1 First step: Random Forest or regression

Random forest is a learning method for classification or regression.^[8] It operates by constructing a multitude of decision trees at training time and outputting the class that is the mode of the classes or mean prediction (regression) of the individual trees. This characteristic makes Random Forest a supervised learning method, as classes are already known.

Training algorithm for Random Forests applies the general technique of bagging to tree learners. Given a training set $X=x_1, x_2, \dots, x_n$ with responses $Y= y_1, \dots, y_n$, bagging

repeatedly it selects a random sample with replacement of the training set and fits trees to these samples.

After training, predictions for unseen samples x' can be made by averaging the predictions from all the individual regression trees on x' . The equation to find the regression is the following one:

$$\hat{f} = \frac{1}{B} \sum_{b=1}^B \hat{f}_b(x') \quad (21)$$

Where \hat{f}_b is a regression tree, B is the number of samples/trees.

In this project, gestational age is what is aimed to be associated with cervical changes. Consequently, features of each sample (image) will be used to estimate the GA. Then, association will be assessed comparing the estimated GA with the real one

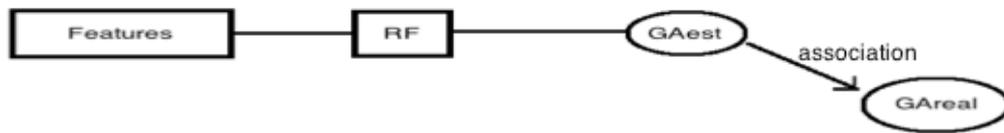


Figure 18. $Ga_{estimated}-Ga_{real}$ association schematic

One of the problems that a model can present is to have created an overfitted model. Overfitting occurs when a statistical model describes random error or noise instead of the underlying relationships. A model that has been overfit generally has poor predictive performance. In order to assure that there is no overfitting in any of the random forest models already created and that the features just contain relevant information, a feasibility and repeatability study has been performed.

3.4.2 Second step. Feasibility and repeatability study

In order to assess the feasibility and repeatability of the extracted features to detect cervical changes along gestation, data has been split into two bags.

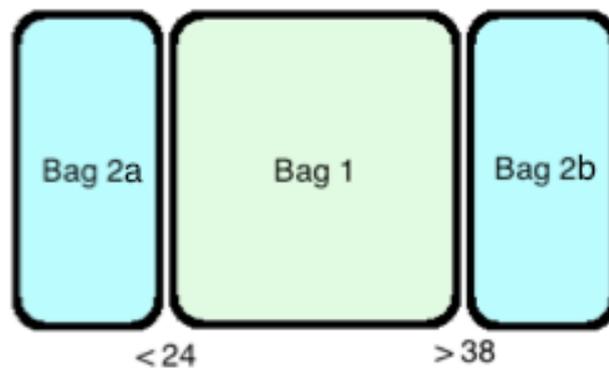


Figure 19. Is it considered that most of the cervical changes should happen between 24 and 38 weeks of gestation.

It has been considered that features between Bag2a and Bag2b should be very different, as they might represent two different states of the cervix, long before delivery and last weeks of pregnancy. So, Bag 2 has been used for feature selection and transformation and Bag 1 to compute the regression model by applying the same selection and transformation of Bag2.

3.4.2.1 Feature Selection and Feature Transformation

Feature selection and feature transformation are two different methods to obtain relevant information and avoid the noise, in the next paragraph they are going to be explained. The first method applied has been feature selection in order to select just robust features. Then, as feature transformation has been applied as it performs better with relevant information. .

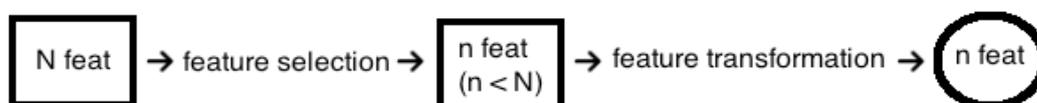


Figure 20. Schematic view of next steps. All of them have been programmed with MATLAB

3.4.2.1.1 Feature Selection, SNR.

Feature selection is the process of selecting a subset of relevant features for use in a model construction. There are four reasons why feature selection techniques are used:

1. Simplification of models to make them easier to interpret.
2. Shorter training times.
3. Reducing overfitting.
4. Data containing features that are redundant or irrelevant.

The main reason of using feature selection in this project is related to 3 and 4, as we could obtain better models than the one obtained in the first step. As reason 4 stands, there can be redundant or irrelevant data; it can be removed without losing much information.

Reason 1 has not been the one to drive this project to perform a feature selection. Due to an unknown relationship between extracted features and cervical changes, so there is no capability of interpreting them by now. As considered feature extractors provide a low number of features, training times are not really high, so reason 2 has no importance in this project neither.

In order to select the most robust features of each extractor, a feature selection based on the SNR (Signal to Noise Ratio) has been made.

SNR computes the ratio of mean to standard deviation of a measurement.

$$SNR = \frac{\mu}{\sigma} \quad (22)$$

Where μ is the signal mean and σ is the standard deviation.

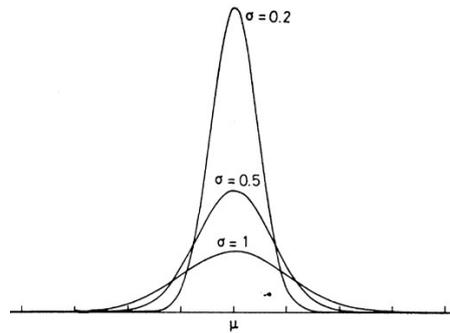


Figure 21. SNR provides a way to relate variation with irrelevant features.

Given a SNR threshold, features that provide a higher SNR will be considered as relevant while the others will be removed. Considering the different nature of each extractor, the threshold SNR value has been different for each of them.

3.4.2.1.2 Feature transformation, Principal Component Analysis

Feature transformation is a group of methods that transform new features from the previous ones. The methods are useful for dimension reduction when the transformed features have a descriptive power that is more easily ordered than the original feature. Thus, less descriptive features can be removed when building models. The feature transformation method that has been chosen in this project is PCA or Principal Component Analysis.

Principal Component Analysis is a statistical procedure that uses an orthogonal transformation to convert a set of observations of possibly correlated variables into a set of values of linearly uncorrelated variables called principal components. The number of principal components is less than or equal to the number of original variables. This transformation is defined in such a way that the first principal component has the largest possible variance, and each succeeding component in turn has the highest variance possible under the constraint that is orthogonal to the preceding components.

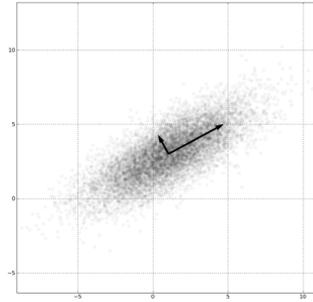


Figure 22. PCA example. In this illustration can be observed the two data projections with greatest variance

PCA is mathematically defined as an orthogonal linear transformation that transforms the data to a new coordinate system such that the greatest variance by some projection of the data comes to lie on the first coordinate, the second greatest variance on the second coordinate, and so on.

Mathematically, the transformation is defined by a set of p-dimensional vectors of weights w that map each row vector x of X to a new vector of principal component scores t , given by;

$$t_{k(i)} = x_{(i)} \cdot w_{(k)}$$

Equation 1

3.4.3 Third step. Blind validation, Random Forest

After these two steps, the applied methodology has been validated in order to check that overfitting also not occurs and assure that extracted ultrasound features are able to detect micro-structural (or textural) changes of the cervix. To do so, Random Forest has been applied to Bag 1 using the feature transformation obtained in the previous steps. The percentage of samples used for train and test has been 90% and 10% respectively.

3.4.4 Evaluation of the association

In order to evaluate association, a scanning of different variables such as SNR threshold or PCA's variance percentage has been made in the two previous steps. From the results obtained, values such as Pearson Correlation, RMSE and R^2 have been computed.

In the next section, a study of the different results and steps has been written with the conclusions.

4. Results

4.1 Robustness Study

As it has been explained in a previous chapter (3.3 Robustness Study), a robustness study has been included in this project to ensure the robustness of the features provided by each extractor in front of acquisition conditions.

To check it, different sub-studies have been made.

Robustness in the same week of gestational age

In order to assess robustness in front of acquisition conditions, matrixes implying the comparison of the different images in the same gestational week have been computed.

In the figures below, there are nine examples of the obtained matrixes using Cityblocks distance with LBP, GLCM Statistics and Histogram Statistics extractors:

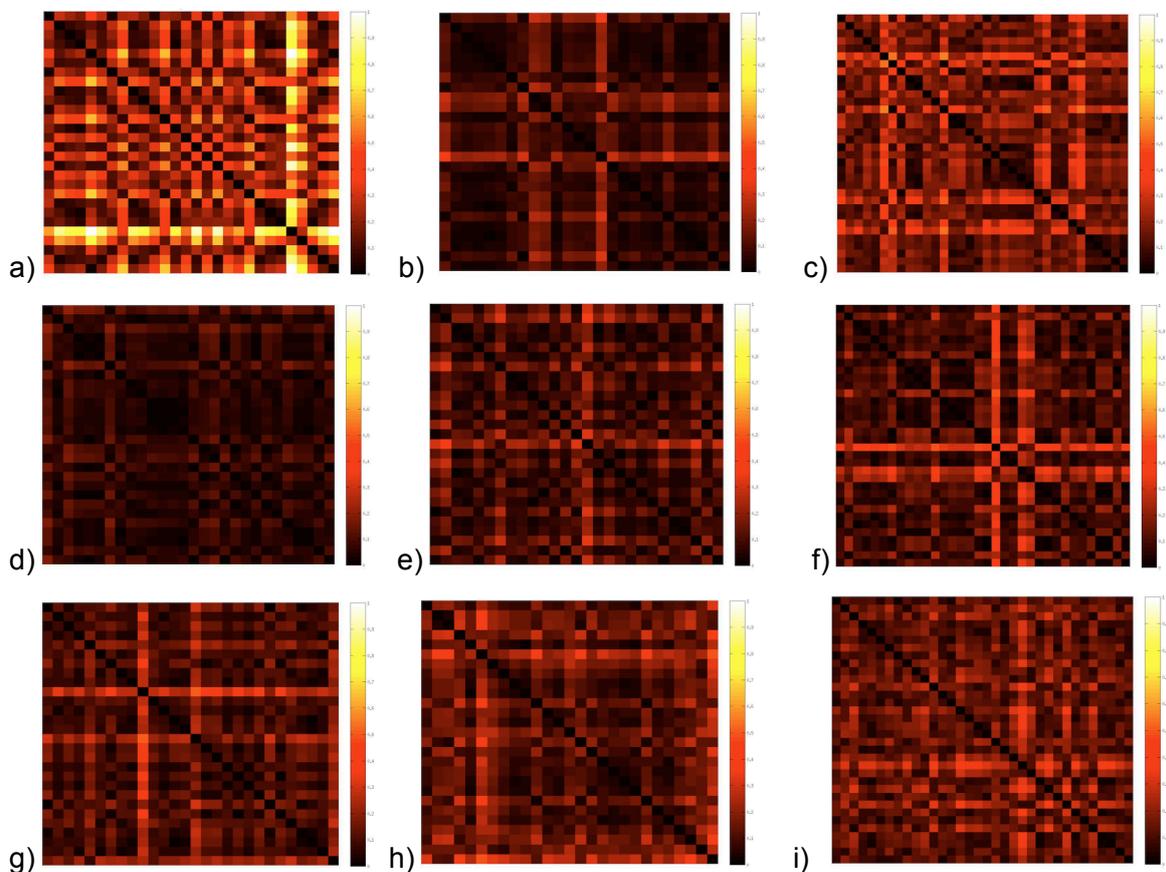


Figure 23 a) LBP, ga20, La. b) LBP, ga30,La. c) LBP, ga40, La. d) GLCM, ga20, La. e) GLCM, ga30, La. f) GLCM, ga 40, La. g) Histogr, ga 20, La. h) Histogr, ga 30, La. i) Histogr, ga 40, La

In order to compare robustness between extractors and ROIs, mean between weeks of gestational age have been computed for each extractor and ROIs according to the methodologies described in chapter 3.3

The figure below shows the robustness of each extractor and ROI. Each first column of the graphics shows the mean of the ordinary distances matrixes for each ROI and extractor, while the second column shows the mean of the affinity matrixes for each ROI.

The colorbar represents the mean value of the distances, so darker values represent no distance between images (more robust) while clearer ones represent a big difference between them. For instance, matrixes with most of its values represented in black, as for example the first matrix of LBP-LEa, purport that their mean values are similar to 0, which is that the feature values are similar in each gestational age. On the contrary, white or clearer values in a matrix, as in LBP-right, mean that the differences between feature values are big, so their value is different between different gestational weeks.

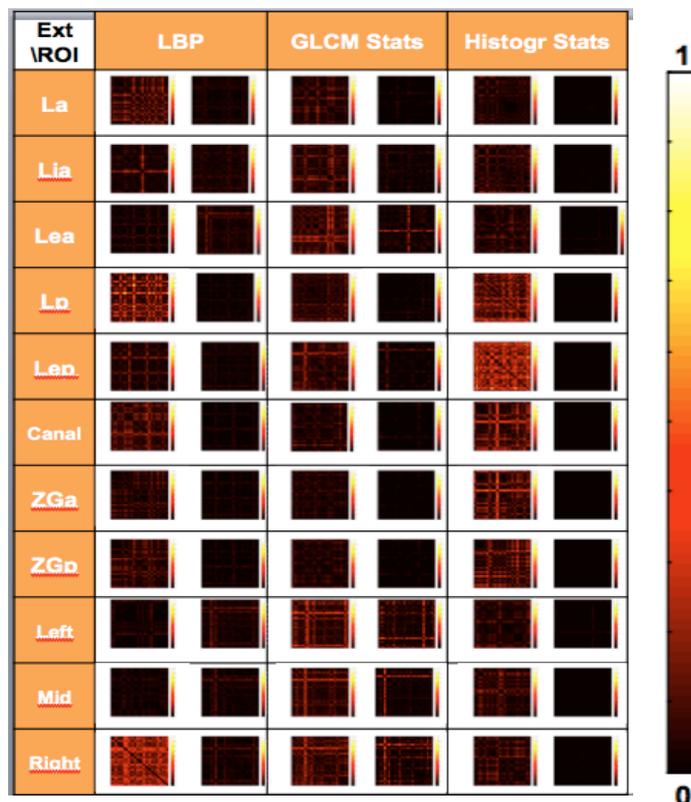


Figure 24. Ordinary mean and affinity mean matrixes represented for each ROI and extractor.

4.2 Associative study

As it has been explained in the previous chapter (3.4 Associative Study), different substudies have been done in order to find if cervical changes along the gestation can be related to changes between ultrasound images.

As it has been explained in the Associative Study chapter, three different steps have been performed. So, in this section results from them are presented.

First step. Random Forest or regression

This first step has involved doing a train with all the samples and features. These are the results that have been obtained:

	La				Lia				Lea				Lp			
	R	p	R ²	RMSE	R	p	R ²	RMSE	R	p	R ²	RMSE	R	p	R ²	RMSE
LBP	0,91	0,00	0,83	2,62	0,91	0,00	0,82	2,66	0,91	0,00	0,83	2,63	0,91	0,00	0,83	2,59
GLCM Stats	0,86	0,00	0,74	3,24	0,86	0,00	0,75	3,18	0,86	0,00	0,74	3,21	0,86	0,00	0,73	3,27
Histogr Stats	0,85	0,00	0,73	3,29	0,85	0,00	0,72	3,33	0,86	0,00	0,73	3,27	0,86	0,00	0,73	3,26
	Lep				Canal				Zga				ZGp			
	R	p	R ²	RMSE	R	p	R ²	RMSE	R	p	R ²	RMSE	R	p	R ²	RMSE
LBP	0,91	0,00	0,82	2,68	0,91	0,00	0,83	2,62	0,91	0,00	0,83	2,62	0,91	0,00	0,83	2,62
GLCM Stats	0,86	0,00	0,74	3,23	0,86	0,00	0,74	3,19	0,86	0,00	0,73	3,27	0,86	0,00	0,75	3,18
Histogr Stats	0,86	0,00	0,73	3,25	0,86	0,00	0,73	3,28	0,85	0,00	0,73	3,28	0,85	0,00	0,72	3,33
	Left				Mid				Right							
	R	p	R ²	RMSE	R	p	R ²	RMSE	R	p	R ²	RMSE				
LBP	0,90	0,00	0,82	2,70	0,91	0,00	0,83	2,62	0,91	0,00	0,83	2,62				
GLCM Stats	0,86	0,00	0,74	3,24	0,86	0,00	0,74	3,24	0,86	0,00	0,74	3,19				
Histogr Stats	0,85	0,00	0,72	3,31	0,85	0,00	0,72	3,36	0,85	0,00	0,73	3,31				

Table 1. Correlation, significance, squared correlation and Root Mean Squared Error have been computed for each training sample set , for each extractor and ROI.

With the previous results, it could be possibly revealed that overfitting had happened. In order to discard this option, result of next two steps will be shown.

Second step. Feasibility and repeatability Study

After the first approximation using a Random Forest model, the different steps explained in the previous chapter have been followed. The results obtained after the feasibility and repeatability study are the following:

	LBP			GCLM Stats			Histogram Stats		
	R	R ²	RMSE	R	R ²	RMSE	R	R ²	RMSE
La	0,88	0,7744	2,25	0,77	0,5929	2,94	0,83	0,6889	2,6
Lia	0,86	0,7396	2,36	0,77	0,5929	2,96	0,79	0,6241	2,86
Lea	0,88	0,7744	2,24	0,76	0,5776	3,01	0,79	0,6241	2,88
Lp	0,89	0,7921	2,15	0,77	0,5929	2,95	0,77	0,5929	0,94
Lep	0,87	0,7569	2,26	0,77	0,5929	2,98	0,63	0,3969	3,63
Canal	0,87	0,7569	2,31	0,8	0,64	2,81	0,79	0,6241	2,84
Zga	0,86	0,7396	2,34	0,78	0,6084	2,92	0,79	0,6241	2,84
ZGp	0,86	0,7396	2,34	0,79	0,6241	2,86	0,77	0,5929	2,96

Left	0,91	0,8281	1,89	0,76	0,5776	3	0,83	0,6889	2,56
Mid	0,92	0,8464	1,8	0,79	0,6241	2,87	0,82	0,6724	2,66
Right	0,9	0,81	1,89	0,76	0,5776	3,04	0,83	0,6889	2,56

Table 2. Correlation values are still high but lower than in the previous table.

After these last results, a ROI that has provided high correlation values has been chosen to do a validation.

Third step. Blind Validation. Random Forest

This chosen ROI has been LEp (Lip Exterior Posterior), and a “train and test” test has been made obtaining the next values.

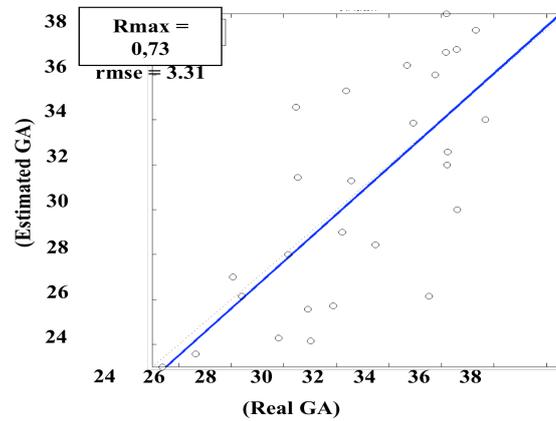


Figure 25

5. Budget

The object of this thesis has not been a prototype. It has been the study of the capability of extracting information from acquired cervix images. This is the reason why the costs of this project are just related to license software and personal.

Personal

Object	Hours	Price per hour	Total
Junior Engineer	960	8€	7680€
Senior Engineer (supervisor)	200	15€	3000€
Specialists acquiring images (2)	300	15€	4500€
Specialists delineating images	200	15€	3000€
			18180€

Table 3

Software

Object	Price	Units	Total
Matlab License	2000€	3	6000€
			6000€

Table 4

Total

Personal	18180 €
Software	6000 €
24180€	

Table 5

The results of this project have been positive in terms of having found evidences to continue this project. After this first step, several other studies can be made to finally obtain an alternative method able to predict whether a delivery is going to be preterm or not. It means that the feasibility of this thesis depends on the following steps. As it is an investigation study, it needs investors that trust its feasibility since the whole project is concluded and can bring the new tool to the market.

6. Conclusions and future development:

From the previous results presented in chapter 3.5 these are the conclusions that can be drawn.

Robustness Study

With this study there has been concluded that there are robust features in the three extractors.

The figure below (Illustration 17), shows the robustness of all the extractors in the Anterior ROIs (La, Lia, LEa; pointer 1), this fact can be related to the proximity of the transducer which provides better image quality.

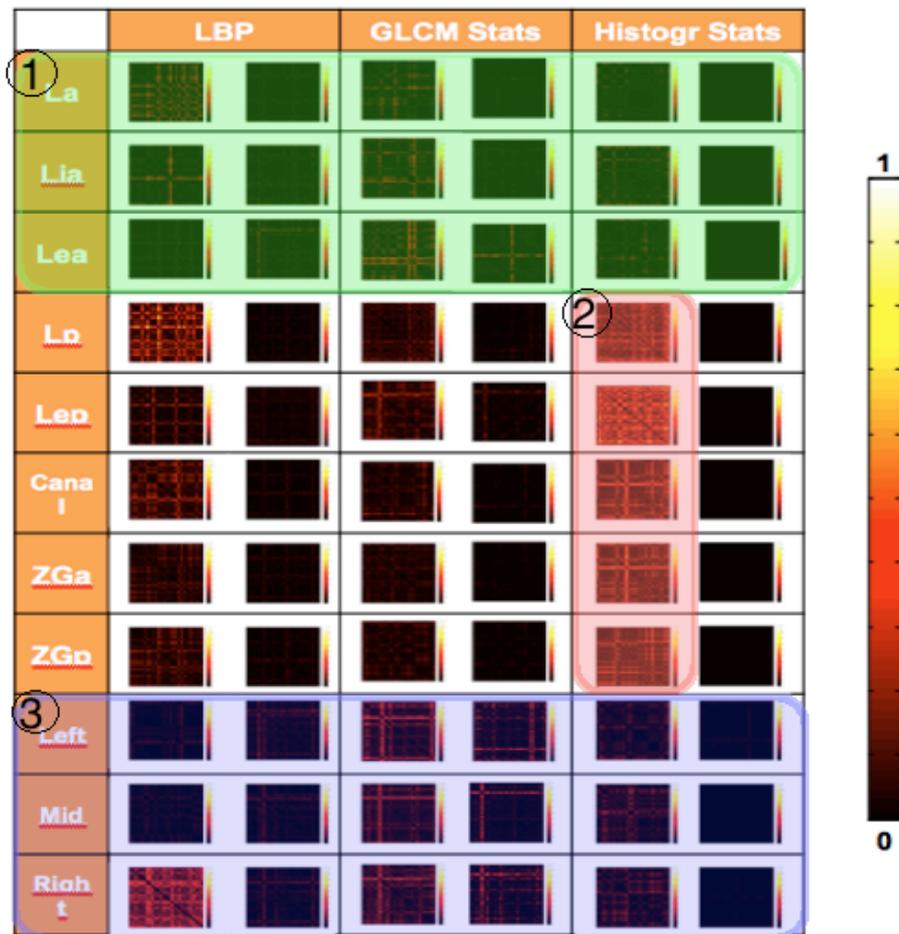


Figure 26. Extractor/ROI conclusions

In pointer 2, can be observed that Histogram Statistics Extractor is not very robust focusing on the mean ordinary matrix of the Posterior Lip nor the ROIs next to the canal and the cervical canal itself. However, features offered by this extractor seem to be more robust in the other ROIs than the other extractors.

All three extractors seem to be robust in the ROIs considered in the “pressed view” (3rd pointer).

Robustness was the subject studied in this part, however this thesis focuses on the cervical changes that can be detected, so an Association Study had been made.

Association Study

First step. Random Forest or Regression

Results showed an association for all extractors and ROIs. However, overfitting may have happened as correlation $R^2 > 0.9$ for all the ROIs and all extractors.

Second step. Feasibility and repeatability Study

After following all the steps, the main conclusion that can be drawn is that, using LBP extractor and selecting robust features and transforming them, there is an association between features and changes in the cervical canal along the gestational age.

With the premise that two of the three extractors do not perform with grey-scale or rotation invariance, it would seem plausible to conclude that Histogram Statistics Extractor and GLCM Statistics Extractor would not provide as good results as Local Binary Pattern Extractor.

From the results of **table 2** of the previous chapter, there can be concluded that LBP showed a higher association than the other two extractors for all the ROIs. Meanwhile Histogram and GLCM have similar values. From this experiment Histogram and GLCM extractor may be excluded for future work.

Feature selection and transformation have been useful to select robust features and transform them. In this project, they could have been applied alone. The main difference between them is that, while feature selection does not consider relationships between features, feature transformation does. In this project they have been both applied in order to remove the possible correlation between relevant features and to be more robust against noise.

In Basal images and anterior regions, the La region (generally) presents more feasibility. It seems that manual delineation in this region is more reproducible than in the interior and exterior regions.

As LBP seems to be more feasible and reproducible in different ROIs, the third step has been performed using LBP and the LEp ROI.

Third step. Blind Validation. Random Forest

Results obtained in this last step, suggest that a statistical learning model could be performed to determine changes in micro-structural changes. To strongly support this concept another training and test experiment should be performed.

This training and test experiment should be done with a bigger database, as just with 30 images in each gestational age, using a 90% of training it leaves just an image to do the test. So, in order to obtain better results, this database should include more images for each gestational age.



Nevertheless, having a 73% correlation it is enough to corroborate that there is an association between the selected and transformed features and the micro-estructural changes occurred in the cervical canal along the gestational age. Therefore, it is possible to develop a new tool to quantify micro-structural changes in the cervix by ultrasound images that could be associated with the risk of preterm delivery. To this purposes, further research will be done.

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Glossary

A list of all acronyms and the meaning they stand for.

DICOM: Digital Image and Communication in Medicine

GLCM: Gray Level Co-occurrence Matrix

La: Anterior Lip of the Cervix.

LBP: Local Binary Pattern

Lla: Interior Anterior Lip

LEa: Exterior Anterior Lip

LEp: Exterior Posterior Lip

LP: Posterior Lip

PCA: Principal Component Analysis.

SNR: Signal To Noise Ratio

RMSE: Root Mean Square Error

ROI: Region of Interest.

Stats: Statistics

ZGa: Glandular anterior zone

ZGp: Glandular posterior zone