Departamento Ingeniería
Eléctrica

Presentation Title

Presentation Subtile

February 22, 2019

M.Sc. Ricardo Moncayo
Advisor: Ph.D. Eduardo Romero

Pathological examination issues

- Due to the heterogeneity of the disease most of the morphological indicators of prognosis are not quantified

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- Subjective observations are susceptible to inter and intra observer variations Imagenes con kappa

The Suitability of a Quantitative Estimation

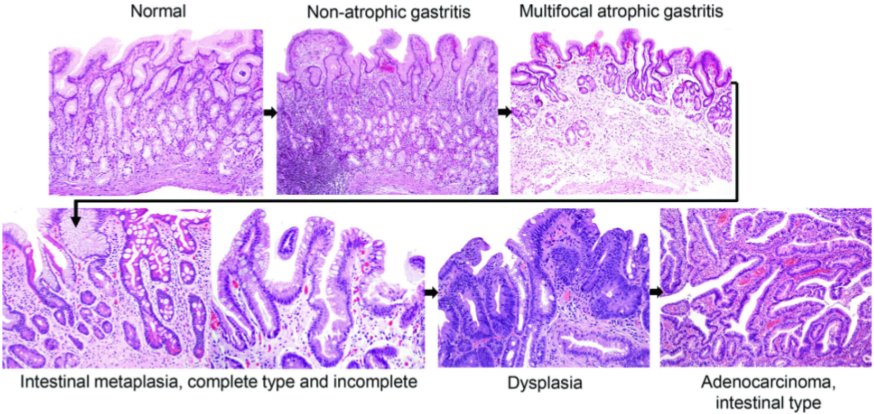
- Digital version of whole glass slide and image analysis are using to improve the diagnosis

The Suitability of a Quantitative Estimation

- Digital version of whole glass slide and image analysis are using to improve the diagnosis
- The Quantification of morphological structures to determine the predisposition of a disease and to deliver healthcareimagenes??

Quantification of Premalignant Lesions of the Gastric Mucosa - 1st case of Study

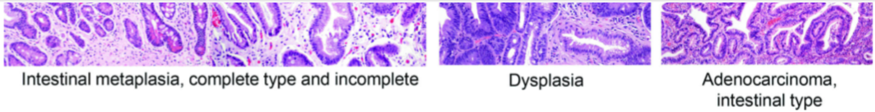
Changes of the Normal Mucosa to Adenocarcinoma



Correa's Cascade of Gastric Carcinogenesis;1976

Changes of the Normal Mucosa to Adenocarcinoma

Some studies suggest that the cancer progression could not follow this sequence!



Correa's Cascade of Gastric Carcinogenesis;1976

The Carcinogenesis Cascade Main Concerns

- Diffuse type of gastric cancer are not related with atrophy or metaplasia (Lauren classification)

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- In the non-atrophic gastritis foci of intestinal metaplasia are found[1]
- Metaplasia grade I and II have been show no risk for cancer progression[2][1]
- Dysplasia are not found in micro-early carcinomas (*Diameter* $< 5mm$)[3] [4]

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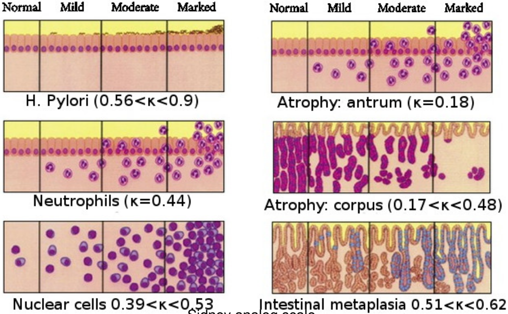
Inter-observer Variability

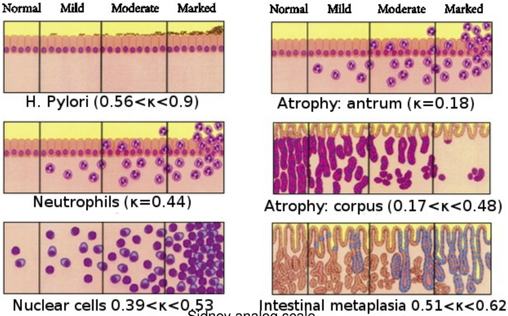
- A highly disagreement between experts reported using kappa coeficient (Aydin,2003;Offerhaus,1999)



Sidney analog scale

Inter-observer Variability

- Kappa coefficient measure the agreement between observers, $\kappa = 0$ corresponds to a bad agreement; $\kappa = 1$ corresponds to a good agreement



Sidney analog scale

Processes involved in GCa incidence are not understood, and the current grading scales are expert dependent, A Careful and reliable measurement of histological features may prevent further malignant outcomes[5][6] [7] [8]

[5]Tepes,2004

[6]Sipponen P.,1994

[7]Meining A,2001

[8]Correa P., 1992

Hypothesis

An accurate quantification of the tissue structures will allow finding a suitable characterization of the disease

Objectives

General Objective:
To formulate an automatic model to find and quantify patterns in gastric premalignant lesions in histological images of the gastric mucosa to the different degrees of atrophy and intestinal metaplasia

Contribution

- The proposal consists in highlighting the importance of an exact measurement in gastric premalignant lesions and the possibility of using this in the pathology workflow.

Expected results

- Different strategies to establishes the stage in PGC lesions
- A computer-aided system to be applied by a pathologist in the workflow

Materials and Methods

Materials

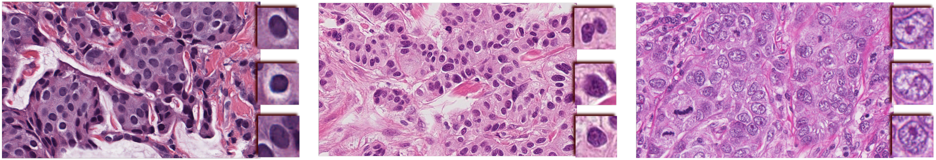
- TCGA Gastric cancer open database with 771 whole slide images and 443 of this with their histological description
- A temporal cohort of histological images with PGC from Urkunina 5000 project
- 30 GCa cases from Universidad Nacional de Colombia

Second case of Study

Nuclear Pleomorphism (NP) - The Suitability of a Quantitative Estimation

Nuclear Pleomorphism in BC

- Researching in automatic quantification strategies for nuclear pleomorphism in breast cancer(NPBca).



grade 1 grade 2 grade 3

Nuclear Pleomorphism in BC

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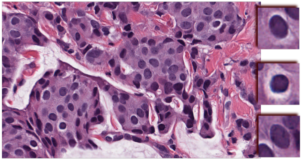
- NPBca is an indicator of the aggressiveness of the disease



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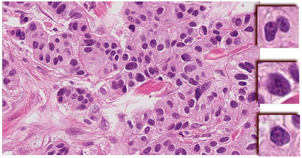
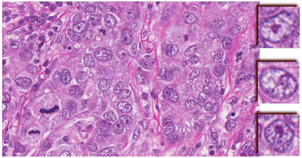


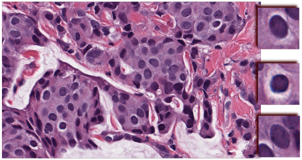
grade 2



grade 3

Nuclear Pleomorphism in BC

- Researching in automatic quantification strategies for nuclear pleomorphism in breast cancer(NPBca).
- NPBca is an indicator of the aggressiveness of the disease
- A low inter-observer agreement $(0.3 < \kappa < 0.5)$



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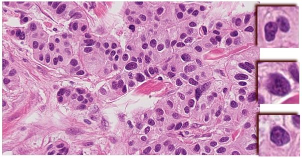
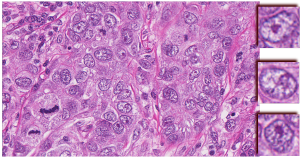
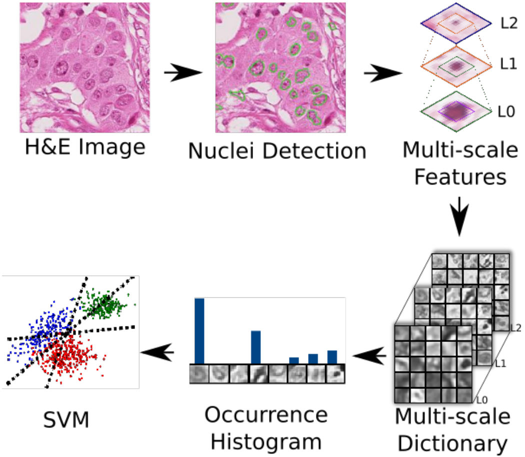


grade 2

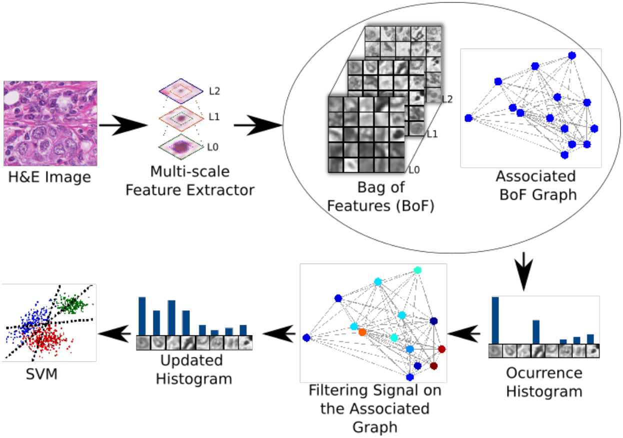


grade 3

Previous: A Bag of Features Based Strategy



Previous: A Bag of Features onto a Graph Strategy



Research Products

- Moncayo, R., Romo-Bucheli, D., Romero, E. **A Grading Strategy for Nuclear Pleomorphism in Histopathological Breast Cancer Images Using a Bag of Features (BOF)**. In Progress in Pattern Recognition, Image Analasys, Computer Vision and Applications, Pages 75-82, november 2015. ISBN 978-3-319-25751-8
- Romo-Bucheli, D., Moncayo, R., Cruz, A., Romero, E., **Identifying histological concepts on basal cell carcinoma images using nuclei based sampling and multi-scale descriptors**. In 2015 IEEE 12th International Symposium on Biomedical Imaging (ISBI), April 2015, pages 1008-1011, ISSN 1945-7928
- Moncayo, R., Romo-Bucheli, D., Arias, V., Romero, E., **Scoring Nuclear pleomorphism using a visual BoF modulated by a graph structure**, In the 13th International Symposium on Medical Information Processing and Analysis, October 2017

The Next Step

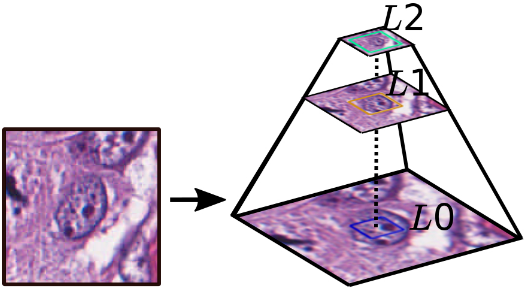
The use of nuclear pleomorphism grade would be correlated with the patient outcome resulting in a reliable measure for the patient

Materials

Coming soon...

Multi-scale Features

- Each nucleus candidate is represented by multiple scales characterized by the discrete cosine transform (DCT) using enough coefficients to reconstructing the original image
- The coefficients from different scales are concatenated into a single feature



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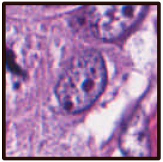

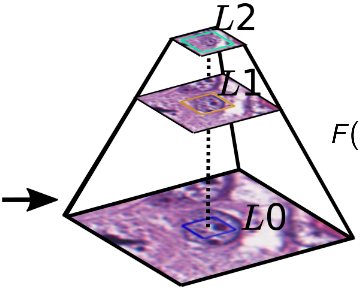

$F(X_i) = \{DCT(L0), DCT(L1), DCT($

Probabilistic Latent Semantic Analysis(PLSA)

- Each multiscale representation is used as a **document** for build a PLSA model to find some topics

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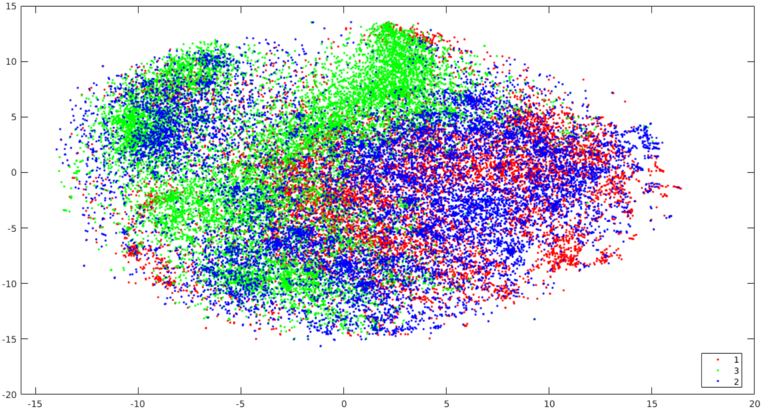
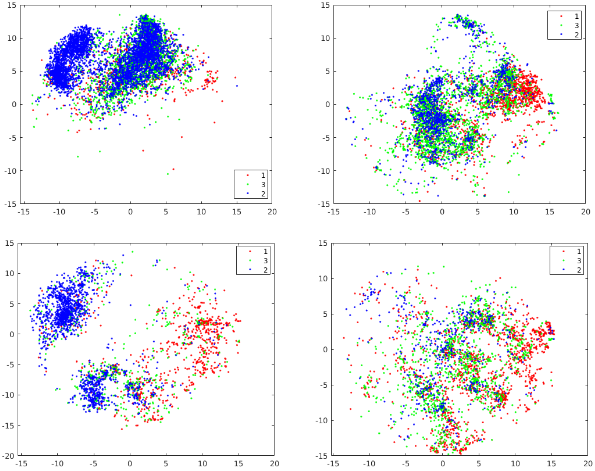
- Each multiscale representation is used as a **document** for build a PLSA model to find some topics
- T-sne is used to visualize the original space and the PLSA generated

Visual Results - Original Space



Visual Results - Space by topic



Research Group

The Computer Imaging and Medical Applications Laboratory (CIM@LAB) is a research group devoted to solve pertinent medical problems by combining artificial vision and machine learning techniques.

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Professors: 2
Doctoral Students: 9
Master Students: 19

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cim@lab
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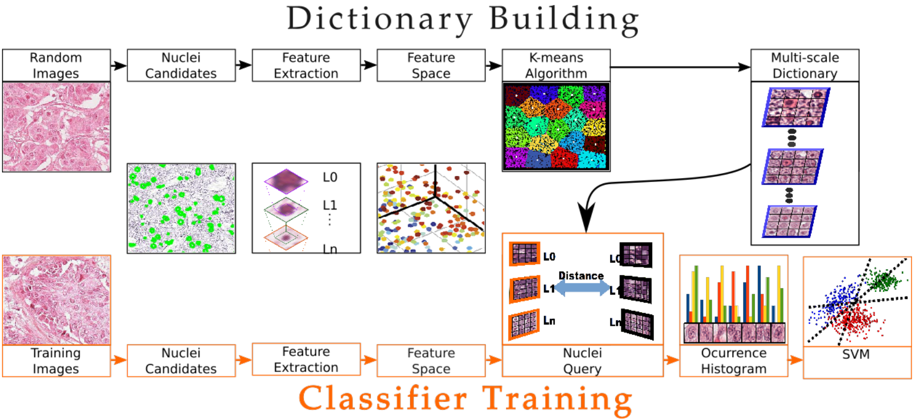
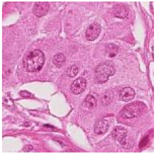
Finished PH.D. thesis: 9
Finished M.Sc. thesis: 46
International indexed journals: 37
International peer reviewed conferences: 100
Books & charapters: 8
Colombian journals: 15
Colombian conferences: 21

First Aproach



Nuclei Detection

- Using a color deconvolution technique the Hematoxylin (H) and eosin (E) stains are estimated



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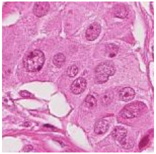

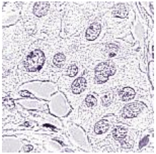

Nuclei Detection

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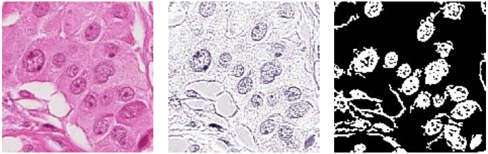
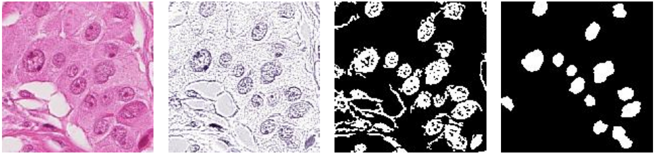
- Watershed algorithm is used to detect nuclei candidates in H stain



Nuclei Detection

- Using a color deconvolution technique the Hematoxylin (H) and eosin (E) stains are estimated
- Watershed algorithm is used to detect nuclei candidates in H stain
- Final candidates are found after morphological operations



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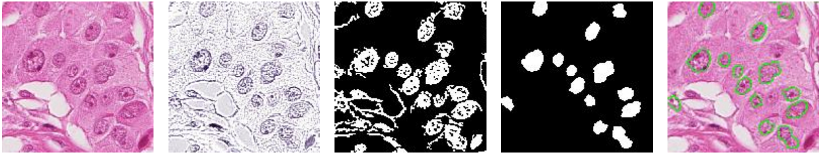
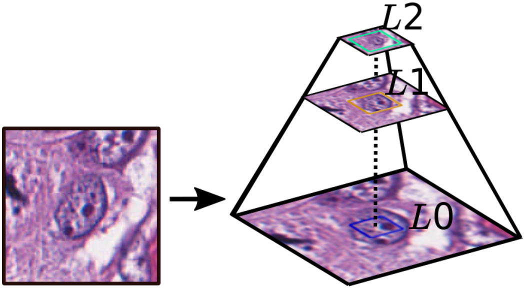


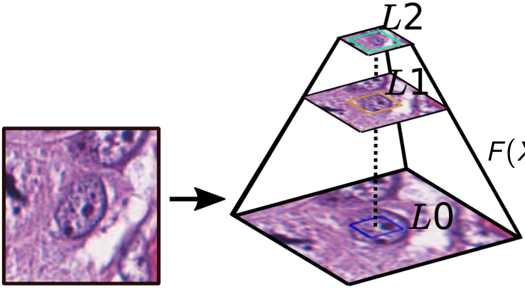
Multi-scale Feature Extractor

- The characterization of each nucleus candidate was performed by analyzing multiple scales



Multi-scale Feature Extractor

- The characterization of each nucleus candidate was performed by analyzing multiple scales
- The feature vector corresponds to the information from RGB patches which are concatenated along one dimension.



$$F(X_i) = \{L0, L1, L2\}$$

Results F1-Score

The F-score is used to evaluate the classification

$$F_{\beta} = (1+\beta^2).\frac{precision.recall}{(\beta^2.precision)+recall} \tag{1}$$

$\beta = 1$ is used this is the harmonic mean between precision and recall

Dataset - Mitos Atypia 14

Grade	#40X images
NP 1	92
NP 2	900
NP 3	208

Table: *Training and validation - 11 cases for training*

Grade	# 40X images
NP 1	152
NP 2	252
NP 3	92

Table: *Test dataset - 5 cases*

Results

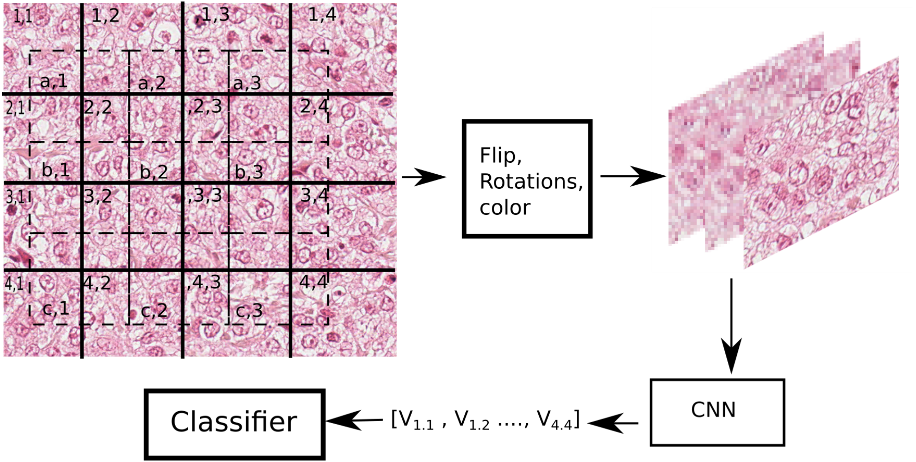
Experiment/S.Patch	32x32 L2	20x20 L2
1 vs 2 and 3	**0.593**	0.434
3 vs 1 and 2	**0.642**	0.47
1 vs 2	**0.7128**	0.47
1 vs 3	0.660	**0.7029**
2 vs 3	**0.6759**	0.5813

Table: *Results Bag Of Features*

Current Work

- **To enhance the automatic nuclear pleomorphism grading**
- To find out if there is a relationship between the nuclear grade quantification with the cancer recurrence

CNN Framework



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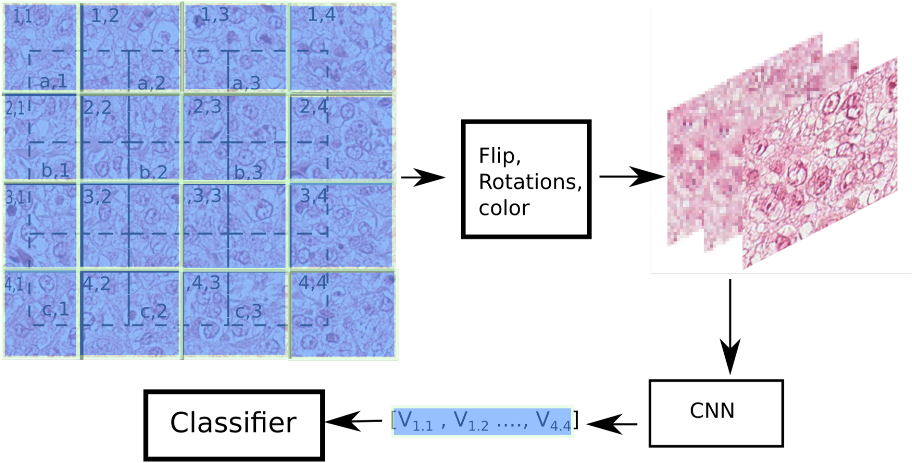


Dataset- Mitos Atypia 14

Grade	#40X images	Total Patches 344x344 pixels	Train	Validation
NP 1	92	21,344	18,144	3,200
NP 2	900	22,500	19,096	3,404
NP 3	208	20,800	17,764	3,036

Table: *Training and validation - 11 cases for training*

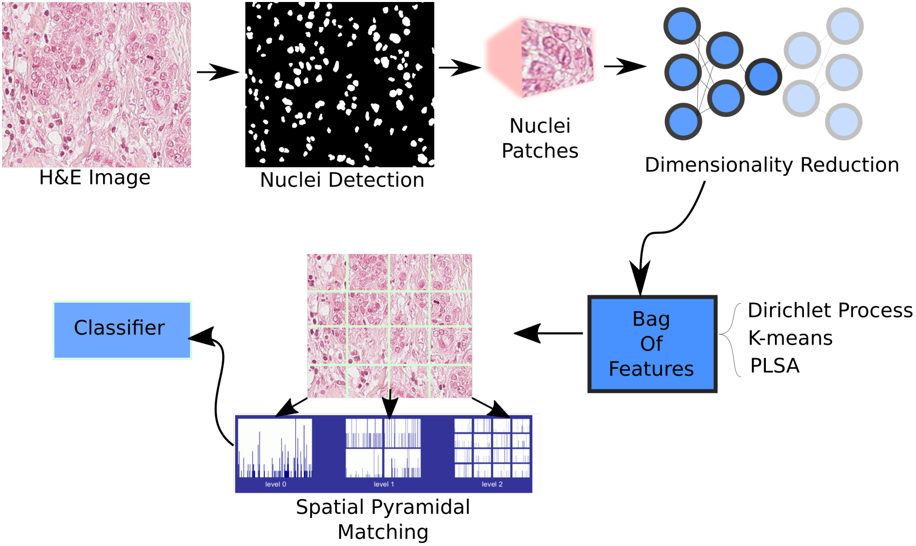
Grade	# 40X images
NP 1	152
NP 2	252
NP 3	92

Table: *Test dataset - 5 cases*

Results

	CNN (1024dim)	CNN (3dim)	VGG16	Alexnet	Resnet50
3Vs.1 and 2	0.635	0.523	0.629	0.493	**0.685**
1Vs.2 and 3	**0.676**	0.645	0.564	0.581	0.573
1 Vs 2	0.637	**0.664**	0.453	0.623	0.592
2 Vs 3	0.570	0.567	0.544	0.619	**0.670**
1 Vs 3	0.666	**0.672**	0.620	0.649	0.563

Spatial Pyramidal Characterization

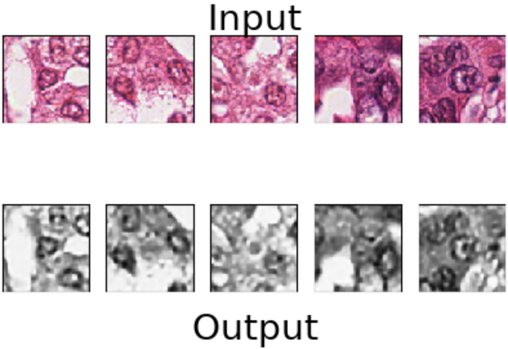


Nuclei Detection

- Color deconvolution to find hematoxylin channel (Macenko et al.)
- Watershed Algorithm to find connected components at different scales (Veta et al.)
- Patches are extracted using the nuclei centroid as seed (72x72 pixels)

Dimensionality Reduction- Convolutional autoencoder

- 3 convolutional layer for encoding and 3 for decoding
- 2048 dimensions in coded representation for nuclei (22.5 compresion factor)
- 6300 dim feature vector (LO,L1,L2)



Autoncoder Reconstruction

Results

	PS.	PS L0	PS L01	PS L2	BOF PY	BOF PY L0	BOF PY L1
3 Vs. 1 and 2	0.578	**0.630**	0.565	0.53	0.624	0.593	0.583
1 Vs. 2 and 3	0.624	0.564	0.520	0.489	**0.692**	0.642	0.678
1 Vs 2	0.473	0.597	0.542	0.573	0.650	**0.713**	0.660
2 Vs 3	0.560	0.603	0.606	0.632	0.722	0.660	**0.729**
1 Vs 3	0.623	0.716	0.639	0.632	0.628	0.675	**0.740**

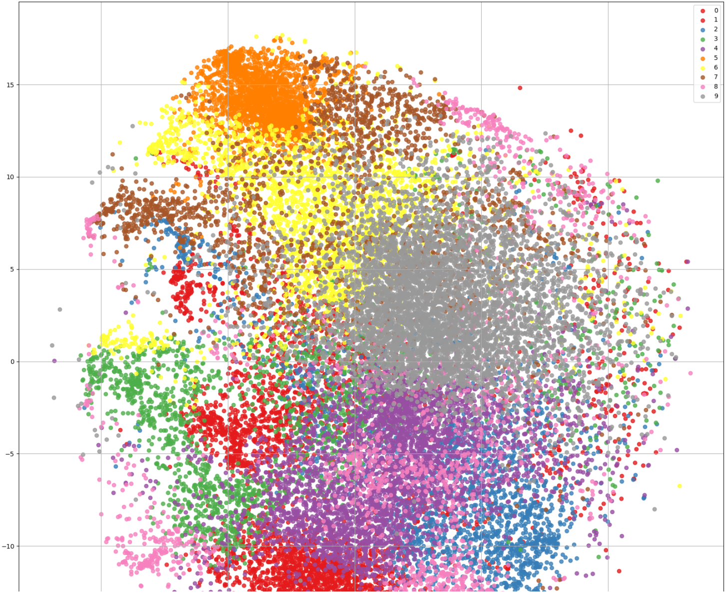
New Dataset

Grading	# Marked Areas
Grade 1	135
Grade 2	132
Grade 3	39
Total Cases	**24**

Final Remarks

- The Slightly variation between the NP grades and the high tissue variability makes difficult to find an adequate model.
- The CNN model could be improved if take advantage of the spatial information
- The auto-encoder representation and vocabulary construction maybe is not the most appropriate.

Thank you...


0
1
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−5
−10

Proposed Grading Methodology