Update on Microscopic Image Processing: Detecting Successively Finer Structures— Architecture, Cells, Nuclei

William V. Stoecker[1] Haidar A. Almubarak[2], Sudhir Sornapudi[2], Peng Guo[2], Jason Hagerty[1,2], and R. Joe Stanley[2].
[1]Stoecker & Associates, Rolla, MO USA
[2]Missouri University of Science and Technology, Department of Electrical and Computer Engineering, Rolla, MO USA
{wvs, haa99d, ssbw5, pgp49, jrh55c, stanleyj}@mst.edu

INTRODUCTION

- Cervical cancer is the fourth most prevalent cancer globally, causing 250,000 deaths/year.
- The best test for cervical pre-cancer is histopathology evaluation by a pathologist.
- Most cervical cancer cases are in Africa, where there is a shortage of trained pathologists.
- New image processing techniques allow automated determination of cervical pre-cancer CIN1 to CIN4.

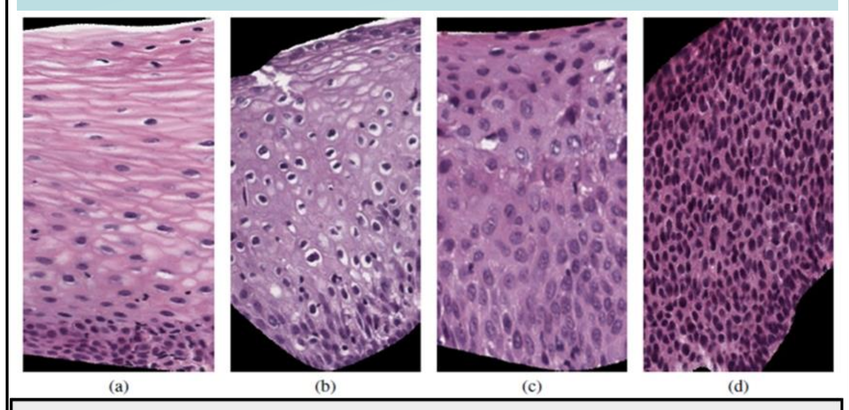
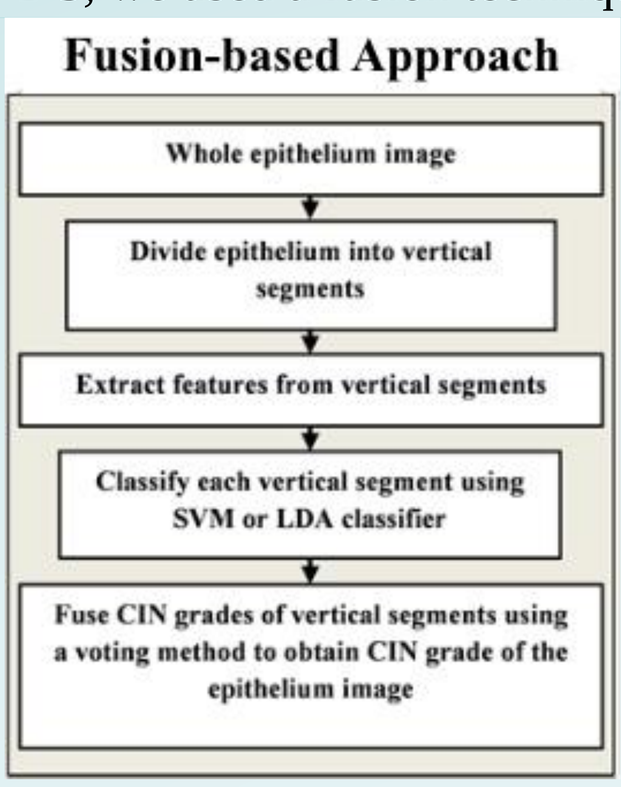


Fig. 1 CIN grades (a) Normal, (b) CIN1, (c) CIN 2, (d) CIN 3

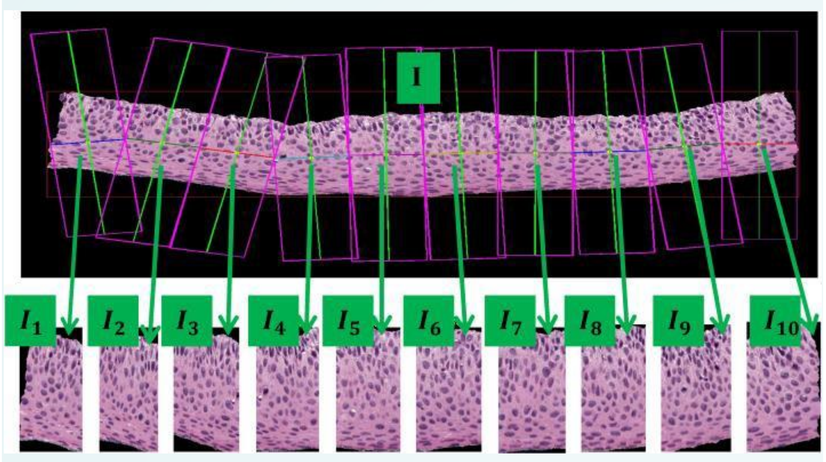
METHODS

To determine of CIN1 grade: Normal, CIN 1-3, we used a fusion technique:



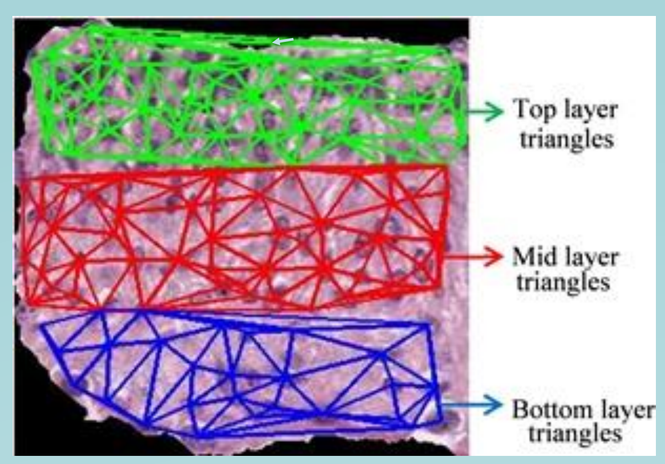
SEGMENT ARCHITECTURE

- The epithelium segments contain the classification information.
- Bounding box for epithelium found.
- Epithelium re-oriented by medial axis
- Divide along axis to find vertical segments I_1-I_{10}



Vertical segments of epithelium

LAYERED ARCHITECTURE

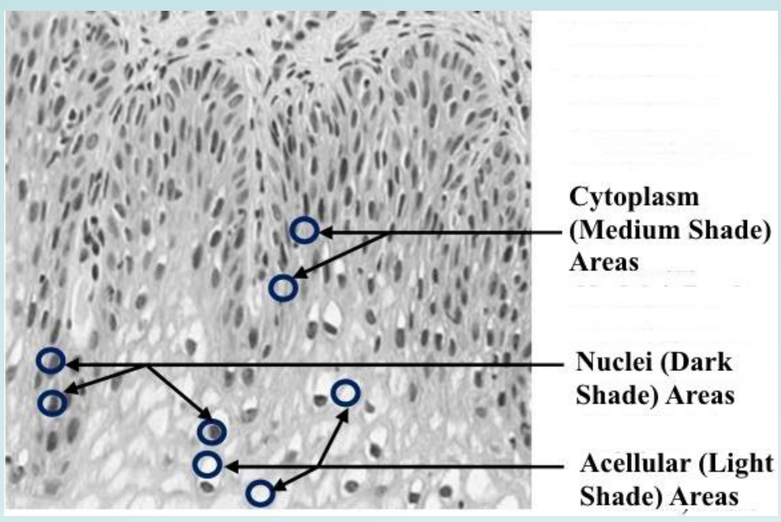


Delaunay triangles for layer description

PRE-CANCER STRUCTURES

3 structures were detected by Intensity

- Cytoplasm
- Nuclei
- Acellular features



CLASSIFIER FEATURES

Label	Description
F1	**Contrast of segment**: Intensity contrast between a pixel and its neighbor over the segment image.
F2	**Energy of segment**: Squared sum of pixel values in the segment image.
F3	**Correlation of segment**: How correlated a pixel is to neighbors over the segment image.
F4	**Segment homogeneity**: Closeness of the distribution of pixels in the segment image to the diagonal elements.
F5, F6	**Contrast of GLCM**: Local variation in GLCM in horizontal and vertical directions
F7, F8	**Correlation of GLCM**: Joint probability occurrence (periodicity) of elements in the segment image in the horizontal and vertical directions
F9, F10	**Energy of GLCM**: Sum of squared elements in the GLCM in horizontal and vertical directions.
F11	**Acellular ratio**: Proportion of object regions within segment image with light pixels (acellular).
F12	**Cytoplasm ratio**: Proportion of object regions within segment image with medium pixels (cytoplasm).
F13	**Nuclei ratio**: Proportion of object regions within segment image with dark pixels (nuclei).
F14	**Average nucleus area**: Ratio of total nuclei area over total number of nuclei
F15	**Background to nuclei area ratio**: Ratio of total background area to total nuclei area
F16	**Intensity ratio:** Ratio of average light area image intensity to background intensity
F17	**Ratio R:** Ratio of average light area red to background red
F18	**Ratio G:** Ratio of average light area green to background green
F19	**Ratio B:** Ratio of average light area blue to background blue
F20	**Luminance ratio:** Ratio of average light area luminance to background luminance
F21	**Ratio light area:** Ratio of light area to total area
F22	**Light area to background area ratio:** Ratio of total light area to background area
F23	**Ratio acellular number to nuclei number**: Ratio of number of light areas to number of nuclei
F24	**Ratio acellular area to nuclei area**: Ratio of total light area to total nuclei area
F25	**Triangles in top layer:** Number of triangles in top layer
F26	**Triangles in mid layer:** Number of triangles in middle layer
F27	**Triangles in bottom layer:** Number of triangles in bottom layer

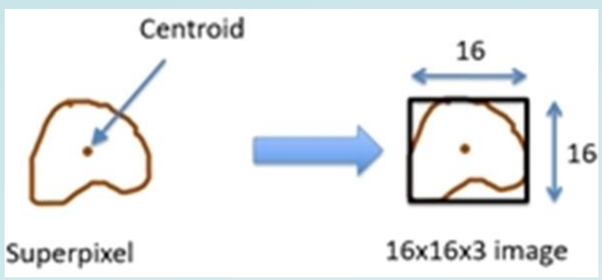
CLASSIFIER RESULTS

- Two classifiers, linear discriminant analysis (LDA) and support vector machines (SVM) were used to classify 61 CIN images
- Exact-class labeling was 83.6% accurate and labeling at least within one grade (off-by-one) was 98.4% accurate [1]

	Fusion-based classification	
	SVM	LDA
Exact Class Label	78.69%	83.61%
Normal vs. CIN	96.72%	96.72%
Off-by-One	98.36%	98.36%

DEEP LEARNING NUCLEI DETECTION

- In another study, patch-based deep learning was used to improve nuclei detection[2]



Patch-based deep learning technique

The deep learning technique compared favorably to six other methods[2]:

- Multi-scale convolutional neural network (MSCNN-GC)
- Generalized LaPlacian of Gaussian (gLoG)
- Ellipse voting
- Stacked sparse auto-encoder (SSAE)
- Multi-scale transform adaptive transform (MATDK)
- Scale-selection, adaptive (SSDCVR-CNN)

Study	# Nuclei	Precision	Recall	F1	JAC
MSCNN-GC	13749	83.86	87.09	85.42	74.67
gLoG	13749	88.55	83.77	86.00	75.58
Ellipse Voting	13749	88.00	84.25	86.02	75.67
SSAE	750000	88.84	82.85	85.74	75.04
MATDK	3381	80.02	88.11	83.87	72.22
SSDCVR-CNN	4748	76.14	89.86	82	70.12
Current	**108635**	**97.62**	**98.43**	**98.02**	**96.13**

CONCLUSIONS

Image processing can detect critical cellular features for automatic pre-cancer classification[1,2].

References

1. Sornapudi S, Stanley RJ, Stoecker WV, Almubarak H, Long R, Antani S, Thoma G, Zuna R, Frazier SR. Deep Learning Nuclei Detection in Digitized Histology Images by Superpixels. J Pathol Inform. 2018 Mar 5;9:5.

2. Guo P, Banerjee K, Joe Stanley R, Long R, Antani S, Thoma G, Zuna R, Frazier SR, Moss RH, Stoecker WV. Nuclei-Based Features for Uterine Cervical Cancer Histology Image Analysis With Fusion-Based Classification. IEEE J Biomed Health Inform. 2016 Nov;20(6):1595-1607