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Automatic detection of multi-level acetowhite regions in RGB color images of the uterine cervix

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ABSTRACT

Uterine cervical cancer is the second most common cancer among women worldwide. Colposcopy is a diagnostic method used to detect cancer precursors and cancer of the uterine cervix, whereby a physician (colposcopist) visually inspects the metaplastic epithelium on the cervix for certain distinctly abnormal morphologic features. A contrast agent, a 3-5% acetic acid solution, is used, causing abnormal and metaplastic epithelia to turn white. The colposcopist considers diagnostic features such as the acetowhite, blood vessel structure, and lesion margin to derive a clinical diagnosis. STI Medical Systems is developing a Computer-Aided-Diagnosis (CAD) system for colposcopy – ColpoCAD™, a complex image analysis system that at its core assesses the same visual features as used by colposcopists. The acetowhite feature has been identified as one of the most important individual predictors of lesion severity. Here, we present the details and preliminary results of a multi-level acetowhite region detection algorithm for RGB color images of the cervix, including the detection of the anatomic features: cervix, os and columnar region, which are used for the acetowhite region detection. The RGB images are assumed to be glare free, either obtained by cross-polarized image acquisition or glare removal pre-processing. The basic approach of the algorithm is to extract a feature image from the RGB image that provides a good acetowhite to cervix background ratio, to segment the feature image using novel pixel grouping and multi-stage region-growing algorithms that provide region segmentations with different levels of detail, to extract the acetowhite regions from the region segmentations using a novel region selection algorithm, and then finally to extract the multi-levels from the acetowhite regions using multiple thresholds. The performance of the algorithm is demonstrated using human subject data.

Keywords: Region segmentation, acetowhite, uterine cervical cancer, colposcopy

1. INTRODUCTION

Uterine cervical cancer is the second most common cancer in women worldwide, with nearly 500,000 new cases and over 270,000 deaths annually[1]. Colposcopy is the primary diagnostic method used in the US to detect cancer precursors and cancer of the uterine cervix, following an abnormal cytological screen (Papanicolaou smear). A colposcopic examination involves a systematic visual evaluation of the lower genital tract (cervix, vulva and vagina), with special emphasis on the subjective appearance of metaplastic epithelium comprising the transformation zone on the cervix[2]. For this purpose an optical colposcope is used, which has been in use for almost 80 years. A colposcope is a low powered binocular microscope with a built in white light source and objective lens attached to a support mechanism. A contrast agent, a 3-5% acetic acid solution, is used, causing abnormal and metaplastic epithelia to turn white. Cervical cancer precursor lesions and invasive cancer exhibit certain distinctly abnormal morphologic features that can be identified by colposcopic examination. Diagnostic features such as acetowhite, blood vessel structure and lesion margin are considered by physicians (colposcopists) to derive a clinical diagnosis[3]. These colposcopic signs, when considered aggregately, determine the severity of the neoplasia and discriminate abnormal findings from similarly appearing, anatomically normal variants.

The digital revolution in medical imaging is on its way, enabling more and more the use of sophisticated computer programs to assist the physicians with their diagnoses – Computer-Aided-Diagnosis (CAD). Examples of existing CAD systems can be seen in applications like mammography, chest-lung node detection and virtual colonoscopy[4]. STI Medical Systems is developing such a Computer-Aided-Diagnosis (CAD) system for colposcopy – ColpoCAD™ [5], a complex image analysis system that at its core assesses the same visual features as used by colposcopists. We conducted a technology exploration project for the development of a CAD system for colposcopy, prototyping image processing algorithms for glare removal, anatomic features detection, acetowhite region detection, lesion margin shape analysis, and blood vessel mosaic and punctation structure detection using RGB images from 111 human subjects participating in a clinical study of our Hyperspectral Diagnostic Imaging (HSDI™) instrument[6,7].

This paper presents our acetowhite region detection algorithm. The acetowhite feature is one of the most important individual predictors of lesion severity. Colposcopists assess the color of the acetowhite regions. But as most cervical imagery is not color calibrated, as was true for our data set, our analysis of the acetowhite region was limited to the detection of multi-level intensities in one feature image rather than analyzing the color information in more detail, which is only the first step. Note that the resulting defined acetowhite regions also serve as input for lesion margin shape analysis. Here, we present the details and preliminary results of a multi-level acetowhite region detection algorithm for RGB color images of the cervix, including the detection of the anatomic features: cervix, os and columnar region, which are used for the acetowhite region detection.

2. ALGORITHM DESCRIPTION

The image processing algorithm described in this paper detects multi-level acetowhite regions in RGB (Red-Green-Blue color space) images taken from an uterine cervix. We developed this algorithm using RGB images from 111 human subjects. The input image for the algorithm is a glare free RGB image from a uterine cervix, as shown in figure 1. Glare free imagery can be obtained either by cross-polarized image acquisition or glare removal pre-processing. We used a glare removal algorithm to remove the glare in figure 1.[8] The basic approach of the algorithm is to extract a feature image from the RGB image that provides a good acetowhite to cervix background ratio, to segment the feature image using novel pixel grouping and multi-stage region-growing algorithms that provides two region segmentations with different levels of detail, to extract the acetowhite regions from the region segmentations using a novel region selection algorithm, and then finally to extract the multi-levels from the acetowhite regions using multiple thresholds. At the same time we detect the following anatomic features: cervix, os and columnar region, which provide inputs to the acetowhite region detection. The steps of the acetowhite region detection and the detection of the anatomic features are described in detail in the following paragraphs. The outputs of the algorithm are binary image masks of the cervix, os and columnar regions, as well as a multi-level image mask of the acetowhite regions shown.

Figure 1: Glare free RGB image of the uterine cervix.

To assure proper processing at the image borders, the RGB image is extended to the top, bottom, left and right, and padded with the original image border values.

2.1 Cervix Region Detection

The cervix region, used as the Region-Of-Interest (ROI) for the processing, is detected using a hue color classifier that discriminates between cervix and vagina, and a watershed segmentation algorithm that precisely locates the low-intensity border around the cervix. The detected cervix region is shown as binary mask and overlay in figure 2.

a.  b. 

Figure 2: Cervix region – a. Mask, b. Overlay.

2.2 Acetowhite Pixel Feature

In order to improve the detection of the acetowhite regions a pixel feature image is calculated from the original RGB image that provides a high acetowhite to cervix background ratio. Acetowhite regions can be characterized by a white color and higher intensity. The cervix background of the acetowhite regions can be characterized by a reddish or pinkish color. To provide the acetowhite pixel feature image the green (G) channel from the RGB image is multiplied with the inverse of the saturation channel from the HSI color space transformed RGB image, shown in figure 3. The green (G) channel provides good intensity contrast and distinction between white vs. reddish and pinkish colors, and the saturation provides a good distinction between white vs. any other color.

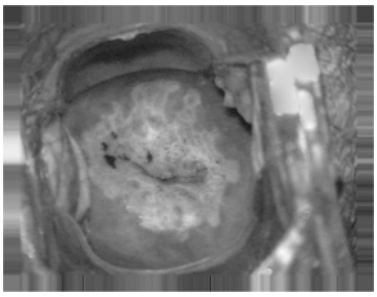
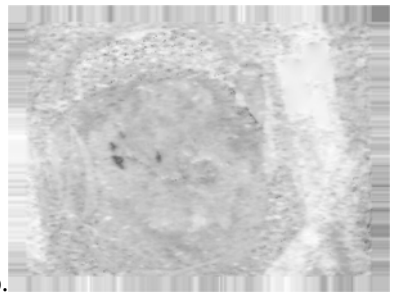
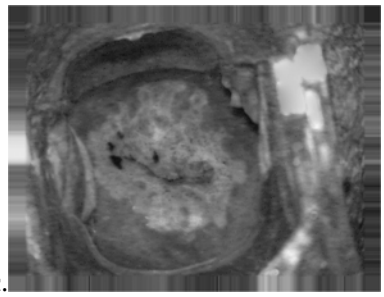
a.  b.  c. 

Figure 3: Acetowhite pixel feature - a. Green, b. Inverse saturation, c. Green multiplied with inverse saturation.

2.3 Acetowhite Pixel Grouping Segmentation

A sequence of an Alternating Sequential Filter (ASF), a toggle and an Alternating Sequential Filter (ASF), provides noise reduction and contour sharpening of the pixel feature in order to make the subsequent pixel segmentation and region growing algorithms more robust, see figure 4.

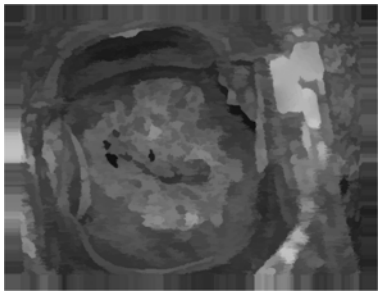


Figure 4: Noise reduced and contour sharpened acetowhite pixel feature image.

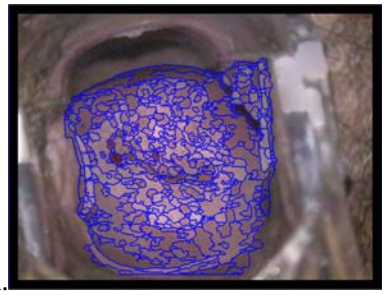
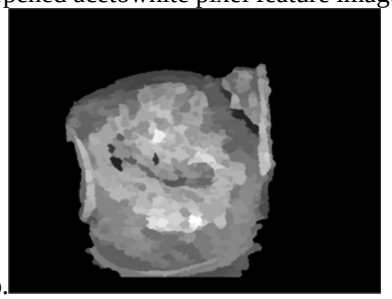
a.  b. 

Figure 5: Acetowhite pixel grouping segmentation – a. Overlay, b. Region average feature image.

The pixel grouping segmentation uses an iterative constraint watershed operation on the gradient feature image to regroup pixels in the image to regions that have contrast borders higher than a given threshold. The mask for the constraint watershed operation is obtained by calculating the region minima of the gradient of the region averaged feature image and eliminating basins lower than the threshold, combined with the frame of the image. At initialization, the noise reduced and contour sharpened pixel feature image is used as the region averaged feature image. At each iteration then, a new region averaged feature image is calculated based on the new region segmentation. The iterative process is stopped when the number of regions stops decreasing. Figure 5 shows the acetowhite pixel grouping segmentation as an overlay and the region average feature image.

2.4 Acetowhite Multi-Stage Region-Growing Segmentation

The region-growing algorithm segments a feature image into regions in multiple stages, providing region segmentations with different levels of detail from fine to coarse. The algorithm has a special feature that allows introducing contour constraints that inhibit the merging of adjacent regions. Currently the contour constraints are not yet use for the current acetowhite region detection. The algorithm is iterative and starts with an initial region segmentation of a feature image provided as a labeled region image. At each iteration, connected regions are merged when their average feature characteristics difference is below a threshold and there is no contour constraint between them. The threshold is incremented from iteration to iteration. The initial threshold and the threshold increments are provided as parameters. When contour constraints are used, those are provided as a binary contour image. The contours have to be located at the region boundaries of the labeled region image. The processing steps are shown in figure 6.

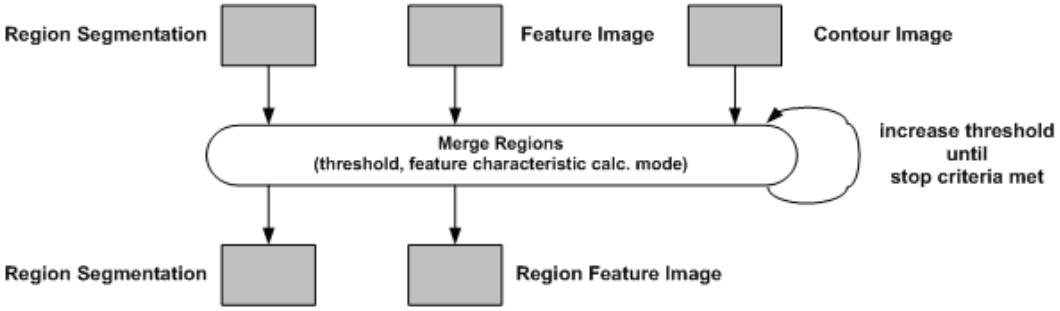


Figure 6: Region-growing processing steps.

The algorithm uses internal data structures in form of three (3) tables, shown in figure 7, the region feature table, the region merge table and the label merge barrier table, for the region growing process. The dimension of the tables depends on the maximum number of regions (N regions) determined by the highest label in the labeled region image. The region feature table, responsible for the feature characteristic determination, contains for each region the corresponding average feature characteristic and the number of pixels. The region merge table, responsible for the region merging, contains for each region the table entry index, a merged region label, and the merge region candidates. The label merge barrier table, responsible for the contour constraints, contains for each merged region label the corresponding label merge barriers introduced by the contour constraints. Note that there are two levels of region representations: the “original” regions and the merged regions. At initialization the merged regions are equivalent to the original regions. “Original” regions get the same “label” if they belong to a merged region - a merged region is identified with a unique merged region label. The merged region label corresponds to the smallest region index of the regions belonging to a merged region.

The tables are initialized using the feature image, the labeled region image and the contour image, illustrated in figure 7. Each region label in the labeled region image gets a table entry in the region feature table, the region merge table and the label merge barrier table. At initialization each region gets a merged region label that is identical to the region table entry index. For each region the number of pixels and the average feature characteristic in the feature image is calculated and stored in the region feature table. For each region the neighborhood regions are calculated. All regions are evaluated if there is a contour segment from the contour constraints separating them from any of their neighborhood regions. In the case of a contour constraint separation, the merged region label (identical to the neighborhood region index at initialization) of the neighborhood region is stored as a label merge barrier for the merged region label of the region (identical to the current region index at initialization) under evaluation. In the case of no contour constraint separation, and that the neighborhood region index is smaller than the current region index, the neighborhood region index is stored as a merge region candidate in the region merge table.

At each iteration of the algorithm, all regions are evaluated for a possible merge with their merge region candidates, their neighborhood regions. When a region and a merge region candidate are evaluated for a possible merge, the minimum of their respective merged region labels is considered as the new label and the maximum as the old label – using always the smaller label as the new label. In the case where both merged region labels are the same, both regions have already been merged and do not need any further considerations. The test for a possible merge consists of evaluating the difference of the two regions’ corresponding feature characteristics against the current threshold and

checking for a possible contour constraint between the regions' corresponding merged regions. The contour constraints are captured in the label merge barrier table. A contour constraint between two merged regions is checked by looking for the old label in the label merge barriers of the new label entry. The threshold is incremented after each iteration.

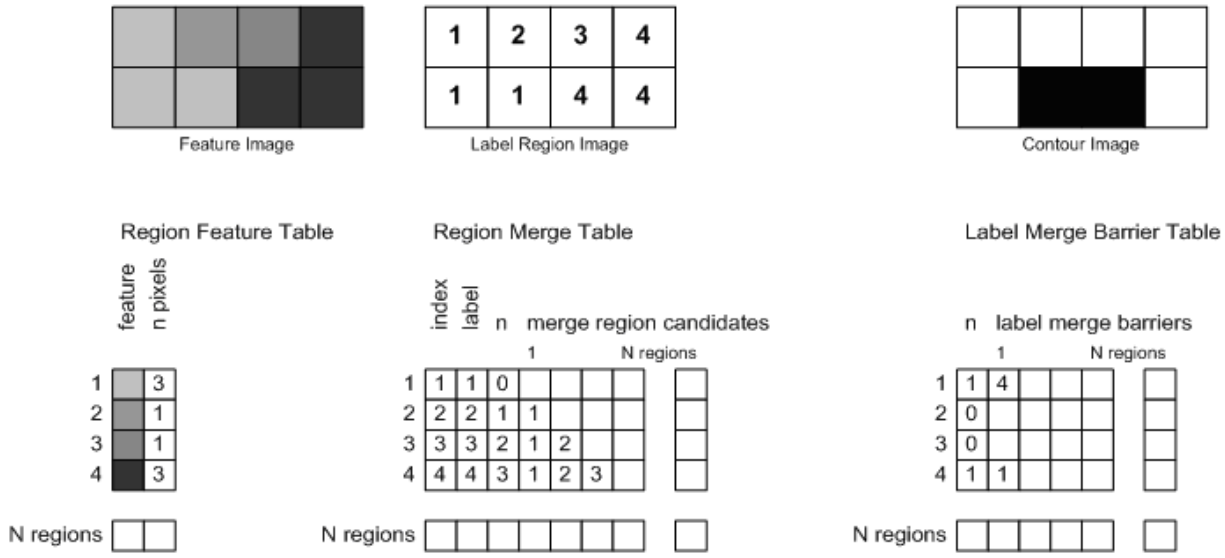


Figure 7: Region growing data structures - Initialization.

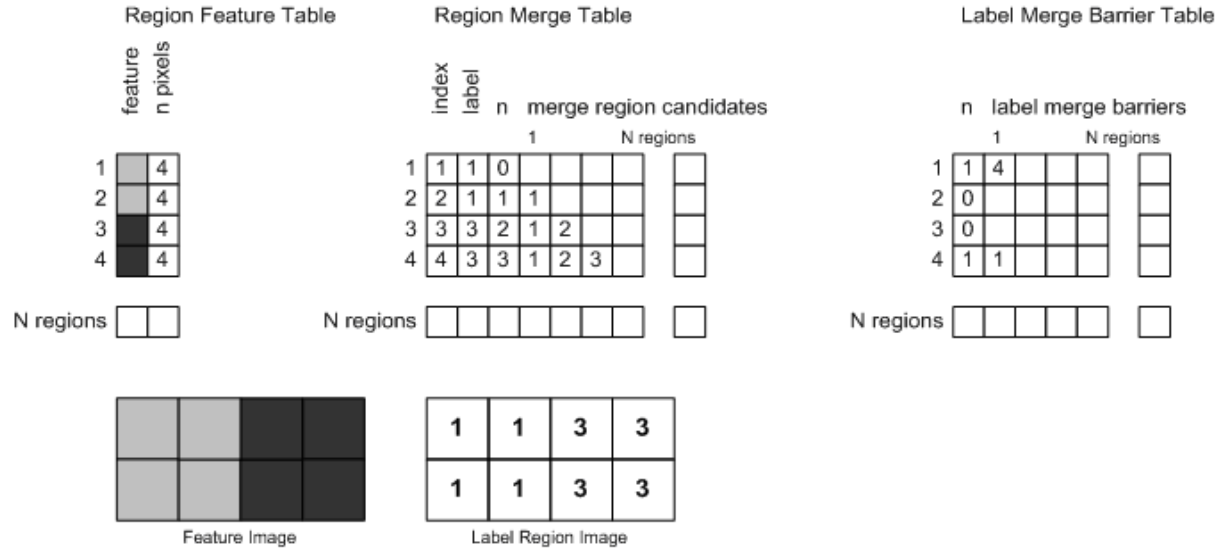


Figure 8: Region growing data structures - Merge.

The feature characteristics of the regions to be considered for a merge can be calculated in two (2) different ways: (a) using the individual regions' average feature characteristics, or (b) using the merged regions' average feature characteristics. Consider the regions' feature characteristics in figure 7 and 8. The regions under consideration for a merge are 2 and 3. It can be seen that in the case of an individual region based calculation the difference between the feature characteristics of region 2 and 3 is smaller and therefore more likely to be merged than in the case of the merged region based calculation.

Once it has been determined that two regions can be merged, the merged region labels of all regions in the region merge table that are equal to the old label are updated with the new label. When the merged regions' average feature characteristic based calculation has been chosen, the feature characteristics and number of pixels of the old label entry and the new label entry in the feature table are used to calculate the new merged region average feature

characteristic and number of pixels. The feature table entries of all regions having the new merged region label are updated with the new merged region average feature characteristic and number of pixels. Updating the label merge barrier table – propagating the contour constraints from the "original" regions to the merged regions, or merged regions to the new extended merged regions - consists of adding the label merge barriers from the old label entry to the label merge barriers of the new label entry and replacing the old labels referencing back in the label merge barriers of the label merge barriers of the old label with the new label. Note that the label merge barrier table contains the contour constraint in both merged region entries. This is redundant but provides an easy update mechanism of replacing the old label with the new label. Note that the region merge table contains the neighborhood relationship between regions only in the region with the higher region index. The merge process is shown with an example from figure 7 to 8.

The algorithm runs until the selected stop criterion is met:

1. Maximum threshold
2. Minimum number of peaks in histogram
3. Minimum number or regions
4. (2) or (3)

At each iteration the stop criteria is evaluated. The maximum threshold is provided as input parameter. The number of regions is determined by counting the number of entries in the region merge table for which the table index is equal to the label. The number of peaks in the histogram is intended to relate to the number of region characteristics the algorithm should distinguish. Therefore the histogram needs to be adjusted for the fact that regions with similar but not equal characteristics might not get merged during the region growing process due to a contour constraint or their spatial distance. A raw histogram of the current region growing iteration is calculated from the region feature table. The histogram gets adjusted by merging peaks in the histogram that lie in a distance smaller than half (1/2) the current threshold by convolving the raw histogram with a rectangle function of a length of half (1/2) the current threshold. An illustration of this process can be seen in figure 9.

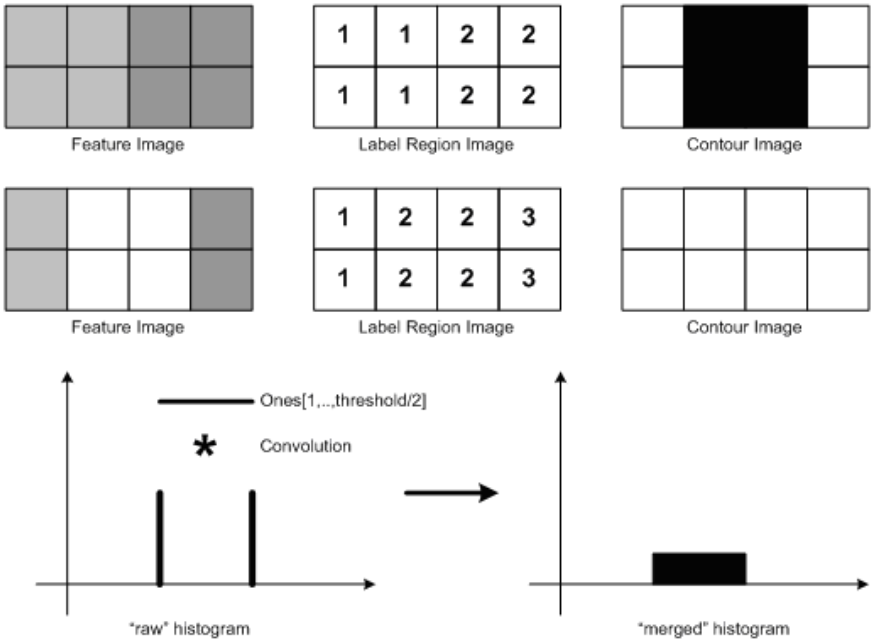


Figure 9: Merged histogram.

The algorithm provides the ability to continue the region growing with a new execution of the algorithm. For this purpose either the internal data structures can be exported and used as input to continue the region growing or the new execution of the algorithm is initialized with the region labeled image output. A sequence of region growing steps provides the ability to optimize the region growing parameters (feature characteristics calculations and contour constraints), for different phases of the region growing which depend on the characteristics of the data for the application at hand. A multi-stage execution of the iterative region growing segmentation algorithm provides different levels of region details for the feature extraction algorithms.

The current implementation of our acetowhite region-growing sequence is simple with only two stages, FIRST and SECOND, and not yet taking advantage of the possible parameter adaptation or the contour constraints to control the region-growing. The region-growing for the SECOND stage uses the minimum number of peaks in the histogram and the minimum number or regions stop criteria, and the merged regions' average feature characteristic calculation. The minimum number of peaks in the histogram is based on a scene model that assumes seven (7) distinct regions: os, columnar, squamous, and up to four distinct acetowhite level regions, to be distinct in the histogram. Figure 10 illustrates the underlying scene model histogram. The minimum number of regions assumes a maximum of four (4) spatially separated regions per distinct region in the histogram limiting the number of total regions to twenty-eight (28). The stop criteria for the FIRST stage is simply half the number of iterations than used for the SECOND stage.

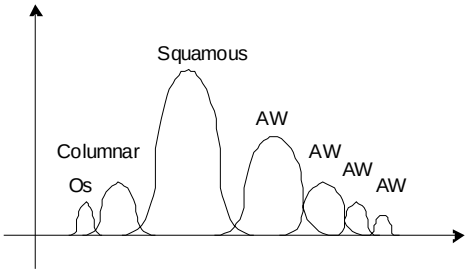


Figure 10: Scene model histogram.

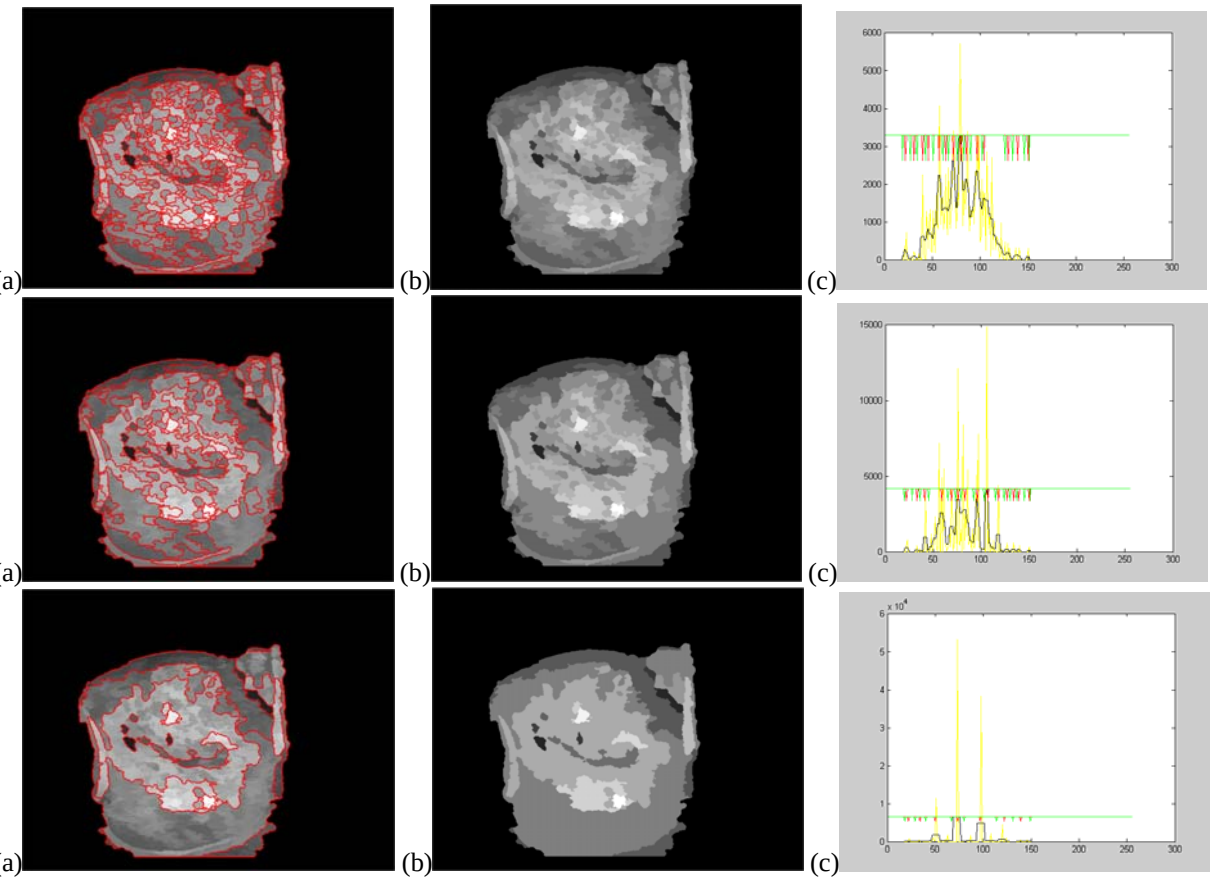


Figure 11: Region-growing segmentation iterations 1, 8 and 16.

The threshold is incremented by 1 until the stop criterion is met. Figure 11 shows (a) the region segmentation overlaid on the feature image, (b) the region averaged feature image and (c) the histogram for the iterations 1, 8 and 16 of region growing. Iteration 8 corresponds to the FIRST stage and iteration 16 to the SECOND stage. The final result of the FIRST region growing stage is shown in figure 12 and that of the SECOND region growing stage in figure 13.

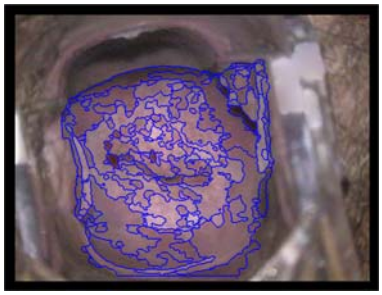
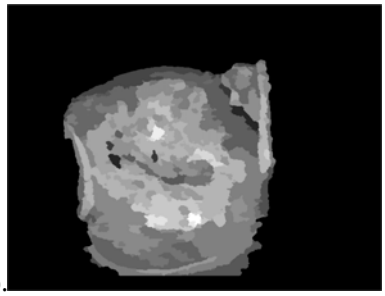
a.  b. 

Figure 12: FIRST stage region segmentation – a. Overlay, b. Region average feature image.

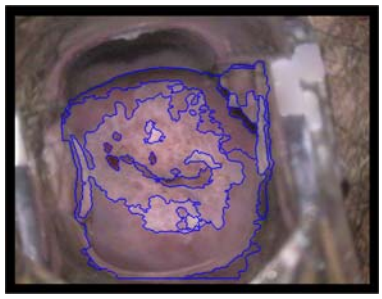
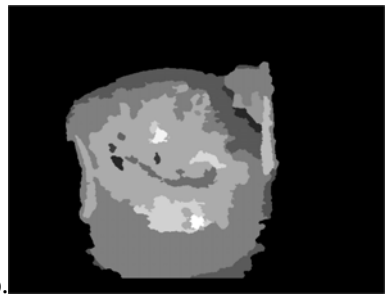
a.  b. 

Figure 13: SECOND stage region segmentation – a. Overlay, b. Region average feature image.

2.5 Os Region Detection

The os region detection uses the same pixel feature calculation, pixel grouping and region-growing processing steps as the acetowhite region detection. We use the red (R) channel from the RGB color image as the pixel feature image and use only one stage of the region growing with the maximum threshold stop criteria. It is assumed that the os region is entirely located inside the cervix region and that it has the lowest feature values in the image. Therefore we detect the valleys or "holes" in the feature image and the regions of low feature values. We extract the hole regions in the pixel feature image and the region segmentation from the region-growing algorithm, by calculating the fill values of a mathematic morphology grayscale close hole operation. The feature values in those regions are then thresholded using a histogram based adaptive threshold to keep only the regions with the lowest feature values. All thresholded regions are combined and cleaned up by eliminating regions at the cervix region border and small regions under a given threshold. The feature values in the detected region are then thresholded again with an adaptive threshold derived form the surrounding columnar region feature values to determine the final os region. The detected os region is shown as binary mask and overlay in figure 14.

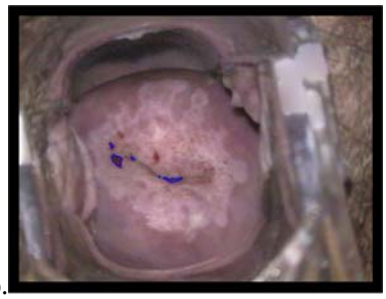
a.  b. 

Figure 14: Os region – a. Mask, b. Overlay.

2.6 Columnar Region Detection

To detect the columnar region, we make the assumption, that the columnar region is entirely located inside the cervix region and that it has lower feature values than the surrounding regions, in particular the acetowhite regions. Therefore we detect the valleys or "holes" in the feature images. We extract the hole regions in all region segmentations provided from the multi-stage acetowhite region-growing and the os region-growing, by calculating the fill values of a mathematic morphology grayscale close hole operation. All hole regions and the detected os region are combined, holes in the regions are closed, small regions are eliminated and the regions that include the os region are extracted as the columnar region. The detected columnar region is shown as binary mask and overlay in figure 15.

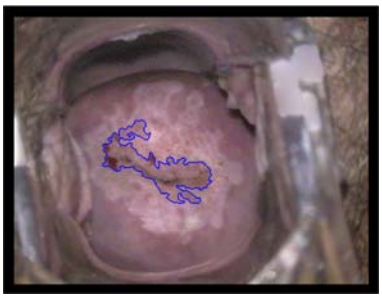
a.  b. 

Figure 15: Columnar region – a. Mask, b. Overlay.

2.7 Acetowhite Region Selection

The acetowhite region selection process uses a feature image, a region segmented feature image, a region image, and a region mask. The feature image is used to calculate the feature characteristics for the region selection process. The feature image consists of the original pixel feature image where the maximum values outside the cervix region are limited to the mean value of the cervix region of the region segmented feature image. Using this maximum value for the region outside the cervix region makes the selection process for regions on the cervix border more robust. The region segmented feature image is initialized with the region segmentation from the region-growing algorithm and is updated at each iteration. Selected regions are eliminated (zeros) and regions under consideration that are not selected are set to a neighboring region's lower feature value to be part of a region at a lower feature value. The region mask, initialized with ones, is used to mask out the regions (zeros) that have already been selected, and are no longer used in the processing. The region image, initialized with zero, is used to store the selected regions.

Two (2) thresholds are used; an absolute minimum feature value threshold for a region to be considered, and a minimum contrast threshold between the region border and the background border in order to select a region. The absolute minimum feature value threshold is calculated as the minimum in the final region-growing histogram to the left of the mean of the cervix region of the region segmented feature image. The minimum contrast threshold is defined as a percentage of the maximum stop value of the region-growing process.

The region selection algorithm is iterative and stops when no more region maxima are found. At each iteration, the region maxima of the region segmented feature image that are above the absolute minimum feature value are calculated. Note that the region segmented feature image is updated at each iteration. Each region maxima is evaluated for selection. A 3 pixel wide (4-neighborhood) border is determined inside (region) and outside (background) the region under consideration. First it is evaluated if there is a background border that is part of the region mask and inside the cervix region. Then the average feature values are calculated from the feature image for the region border and the background border that is part of the region mask. If the average feature value of the region border is higher than the average feature value of the background border by at least the given contrast threshold then the region is selected. A selected region is added to the region image, eliminated from the region segmented feature image and eliminated from the region mask. Should the region not be selected then its values in the region segmented feature image are set to the maximum value of the region's background region in the region segmented feature image. This way the region is considered as part of the region with a lower feature value in the next iteration. If there is no background border that is part of the region mask and inside the cervix region, the region is selected if the region value of the region segmented feature image is above the mean of the cervix region of the region segmented feature image. In any case, this region is eliminated from further considerations by eliminating it from the region mask and setting its values in the region segmented feature image to zero. Figure 16 illustrates the region selection processing steps.

We use different contrast thresholds for the regions inside and outside the columnar region, therefore we need the columnar region as an input to the region selection process. The acetowhite region selection process is applied to the FIRST and SECOND region segmented feature images and then the results are combined (union). The processing of two different levels of detail provides robustness against varying illumination conditions. Figure 17 shows the intermediate results of the region selection process, at iteration 1, 2 and 11, for the SECOND region segmented feature image. The region maxima are identified as red contours. Figure 19 shows the final acetowhite region (blue) with the os (green), columnar (green) and cervix (black) regions in a cervix segmentation overlay on the original RGB image.

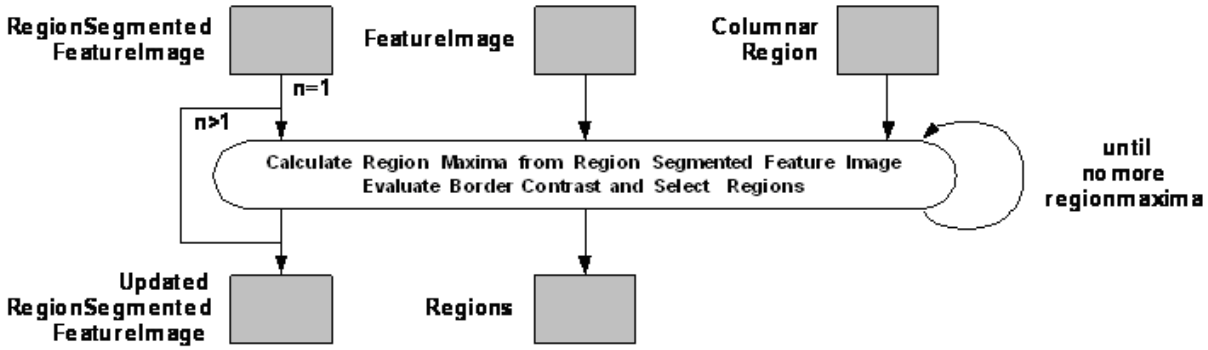


Figure 16: Region selection processing steps.

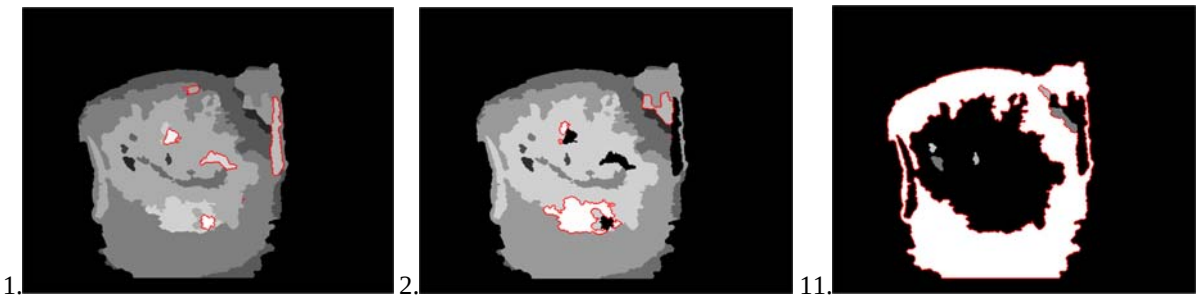


Figure 17: Region segmented feature image maxima - iteration 1, 2 and 11.

2.8 Multi-Level Acetowhite Region Detection

Acetowhite regions with different intensity levels are extracted from the FIRST region segmented feature image using the histogram minima of the SECOND region segmented feature image as thresholds. Figure 18 shows the different thresholding results and figure 19 shows the final multi-level acetowhite regions as overlay on the original RGB image.

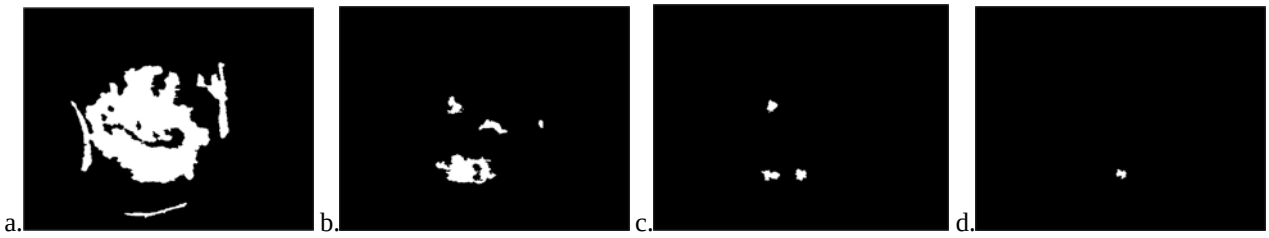


Figure 18: Acetowhite region segmented feature image thresholded using histogram minima.

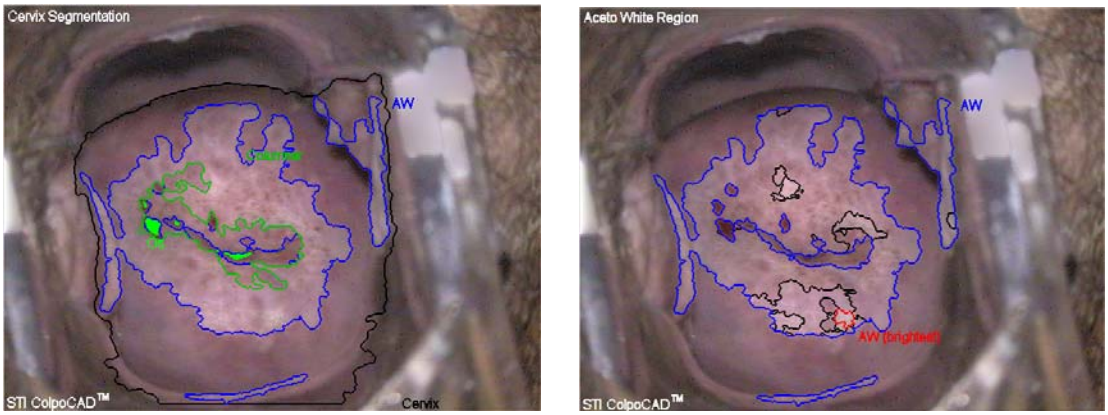
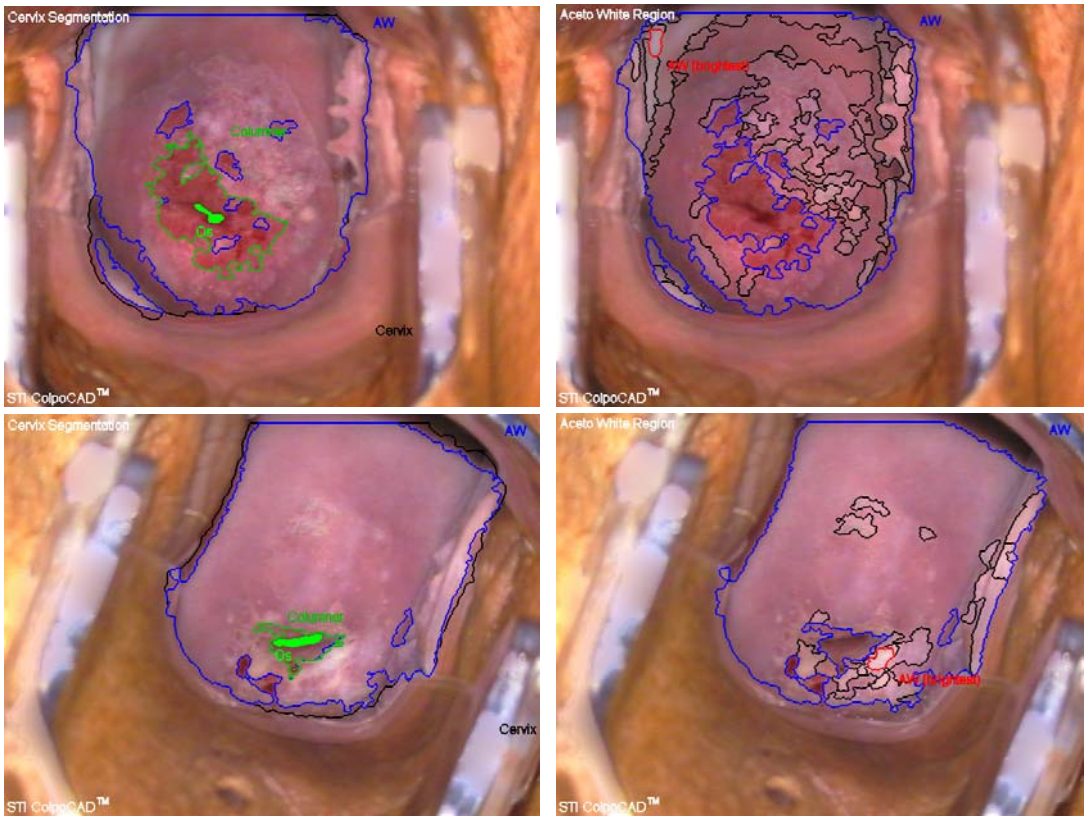


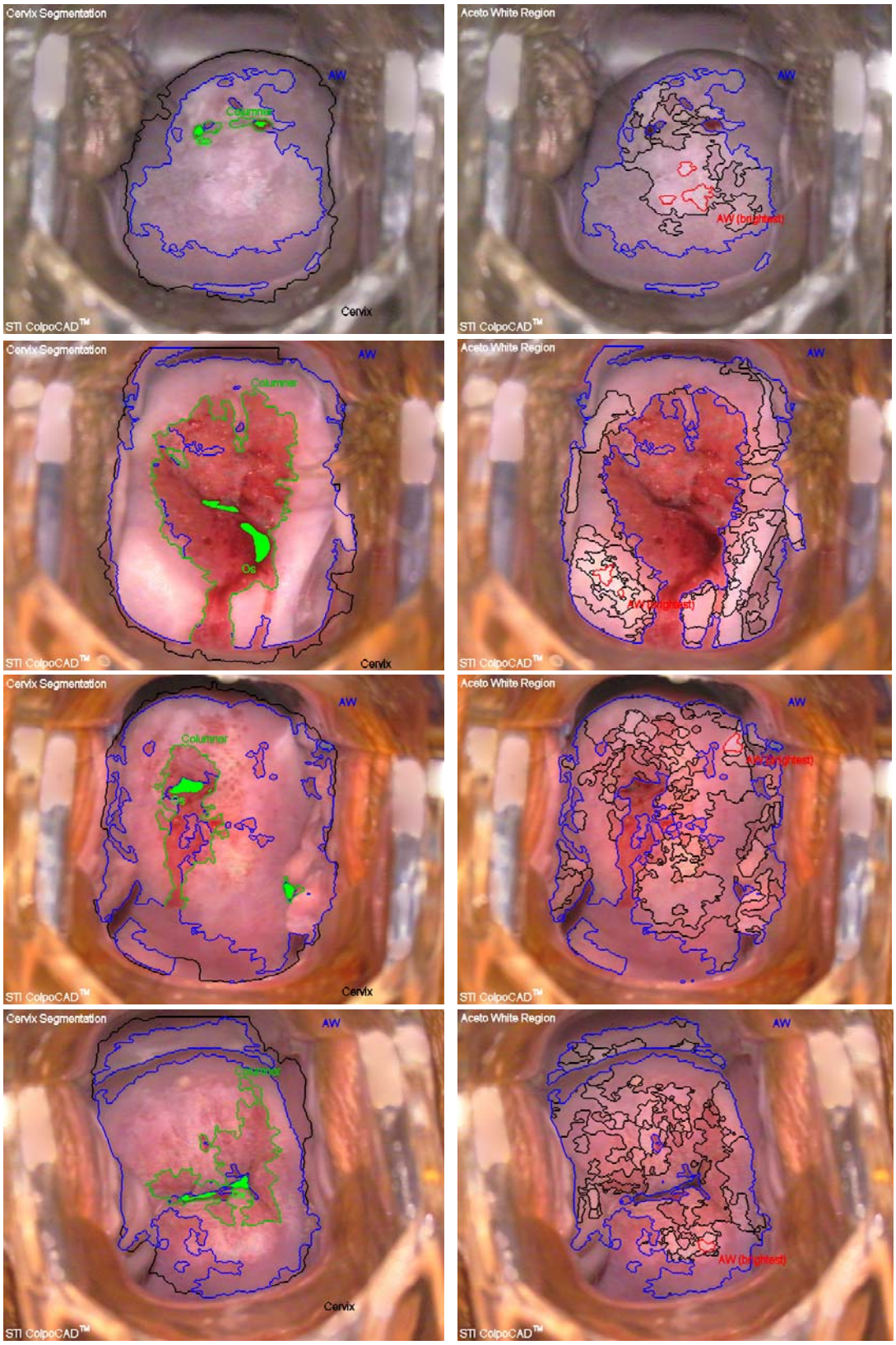
Figure 19: Cervix segmentation and multi-level acetowhite region overlays on original RGB image.

3. PRELIMINARY RESULTS

In our technology evaluation project, we used RGB images from 111 human subjects for the development of the acetowhite region detection algorithm. The algorithm performance was assessed by qualitative subjective inspection of the processed images. The algorithm appears to perform very well over the entire data set. The performance of the acetowhite region detection algorithm can be assessed by looking at the cervix segmentation and multi-level acetowhite regions as overlays on the original RGB images as shown in figure 20.

The quantitative performance of the acetowhite region detection algorithm will be assessed as part of our ColpoCAD™ development, when we will have acquired data sets with comprehensive annotations from expert colposcopists and pathologists, including "ground truth" for the acetowhite regions.




Cervix Segmentation
AW
Columnar
Cervix
STI ColpoCAD™
Aceto White Region
AW
AW (brightest)
STI ColpoCAD™
Cervix Segmentation
AW
Columnar
Os
Cervix
STI ColpoCAD™
Aceto White Region
AW
AW (brightest)
STI ColpoCAD™
Cervix Segmentation
AW
Columnar
Cervix
STI ColpoCAD™
Aceto White Region
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STI ColpoCAD™
Cervix Segmentation
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STI ColpoCAD™
Aceto White Region
AW
AW (brightest)
STI ColpoCAD™

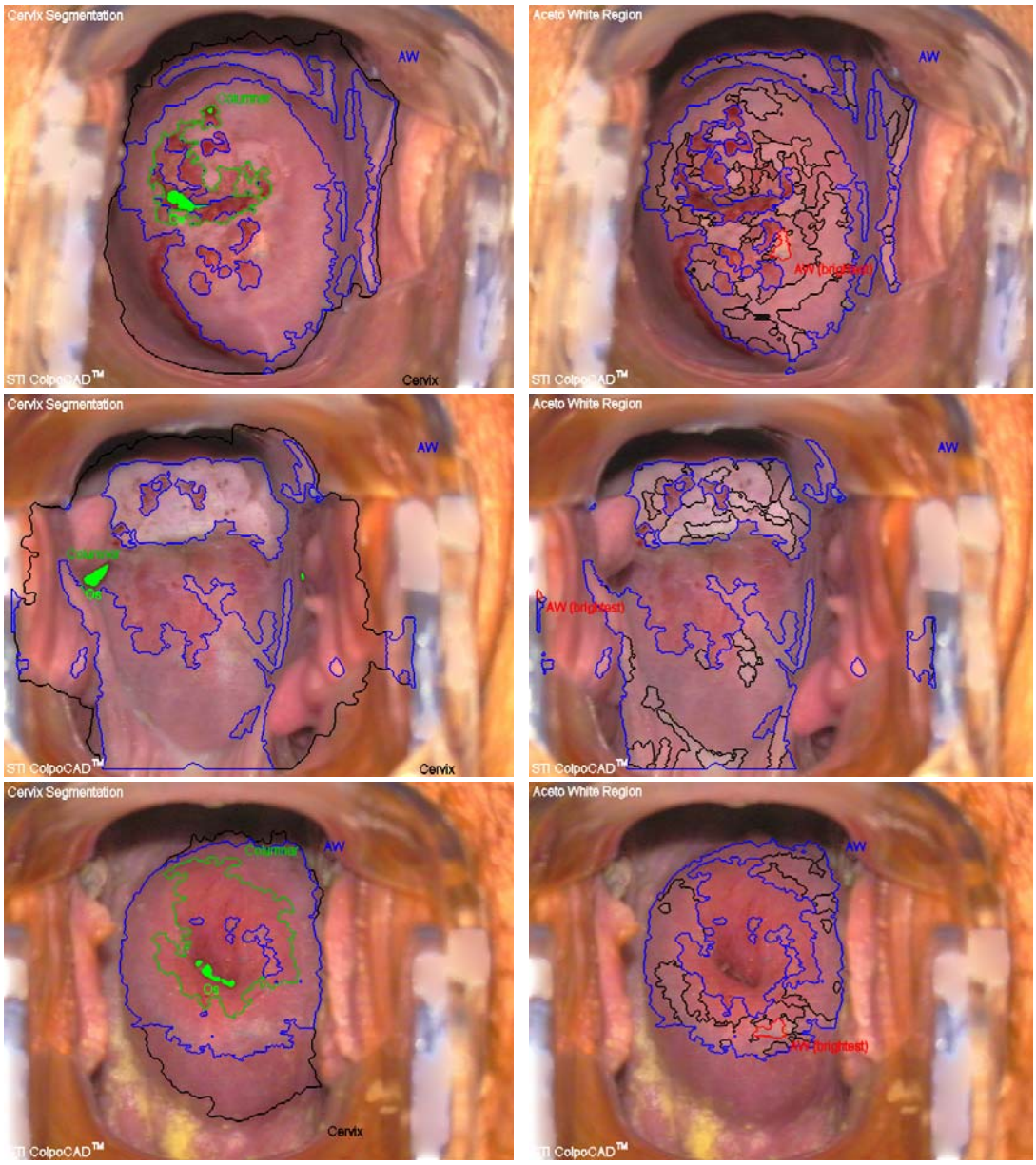

Figure 20: Cervix segmentation and multi-level acetowhite region overlays on original RGB images.

4. CONCLUSIONS

We presented the details and preliminary results of a multi-level acetowhite region detection algorithm for RGB color images of the uterine cervix. We used RGB images from 111 human subjects for the development of the acetowhite region detection algorithm. Our preliminary results demonstrate the feasibility of this approach, which we plan to refine with calibrated and "ground truth" annotated imagery that will also enable a quantitative performance analysis.

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