Novel segmentation method for cervix classification

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Introduction

Cervical cancer is the second leading cause of cancer death in women aged 20 to 39 years, although it is a theoretically preventable disease. [1] Around 500,000 women are diagnosed with cervical cancer each year worldwide [2] with nearly 300,000 death cases arising annually. [3] Cervical cancer is the most common cancer among women in Eastern and Middle Africa. Nine in ten cervical cancer deaths occur in less developed regions. [4] This situation could be attributed to the limited access to cervical cancer screening in these regions. With multiple early detection and treatment methods, cervical cancer is already one of the most preventable cancers today. FDA approved vaccines such as Gardasil and Cervarix are highly effective in preventing cervical cancer among girls and young women before infection. [5] Even diagnosed with cervical cancer, proper treatment can improve the 5-year survival rate up to 75%. [3] Early detection and treatment of precancerous changes of the cervix can prevent cancer development.

Early detection of cervical cancer normally goes through the Papanicolaou (Pap) test first, which is also known as the Pap smear. It is cytology based screening that detects abnormal cells before they develop into cancer cells. [6] With appropriate follow-up, cervical cancer deaths can be reduced up to 80%. [7] Despite its high false positive rates, visual inspection with acetic acid is another choice when Pap smear is not affordable. Abnormal cells would turn white after application of 3%-5% acetic acid. [8] More than 90% of cervical cancer cases are due to human papillomavirus (HPV) infection. [9] DNA tests for HPV, which checks for the virus rather than the cells, are usually combined with the Pap smear to increase the sensitivity of cervical pre-cancer detection. [10] When the HPV test is positive and the Pap test shows abnormal cells, colposcopy is considered as the primary diagnostic method for further examination.

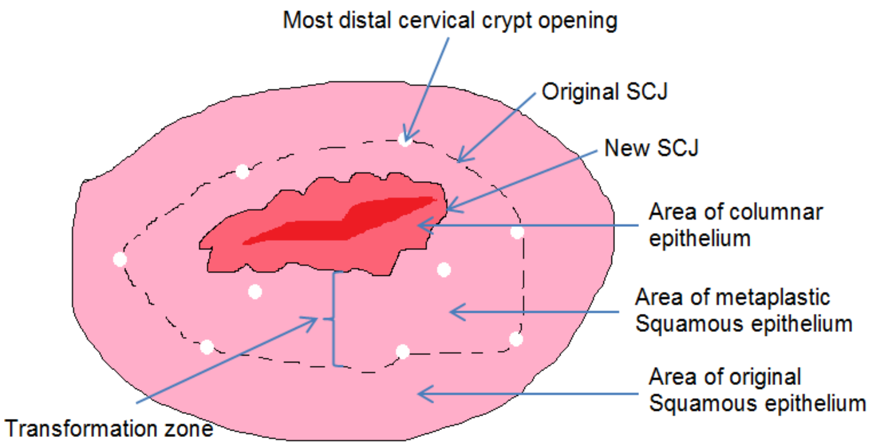

Fig1. Cervix basic anatomy

Colposcopy examination employs the colposcope, which is an instrument that has magnifying lenses, to visually check the surface of the vagina and the cervix closely and clearly, with the emphasis on the transformation zone (TZ) where HPV infection and cervical pre-cancer are most likely to start. [11] Fig 1 is an illustration for cervix basic anatomy. The squamo-columnar junction (SCJ) is where the squamous epithelium of the ectocervix meets the columnar epithelium of the endocervix and the cervical area between the original SCJ and the new SCJ is referred to as the transformation zone (TZ). The SCJ and TZ are fundamental landmarks of metaplasia. [12] Colposcopy helps physicians to identify different cervix types and rank the severity of lesions. Fig 2 displays three cervix types that need different treatments. The accuracy of colposcopy highly depends on colposcopists' expertise. Nowadays digital colposcope is used to produce the high-resolution cervix image, also known as cervigram, for automatic identification of neoplastic tissue in a quantitative manner and minimization of the variability among colposcopists. [13] A great many algorithms have been developed for cervigram processing and detection of cervical cancer. [13-17]

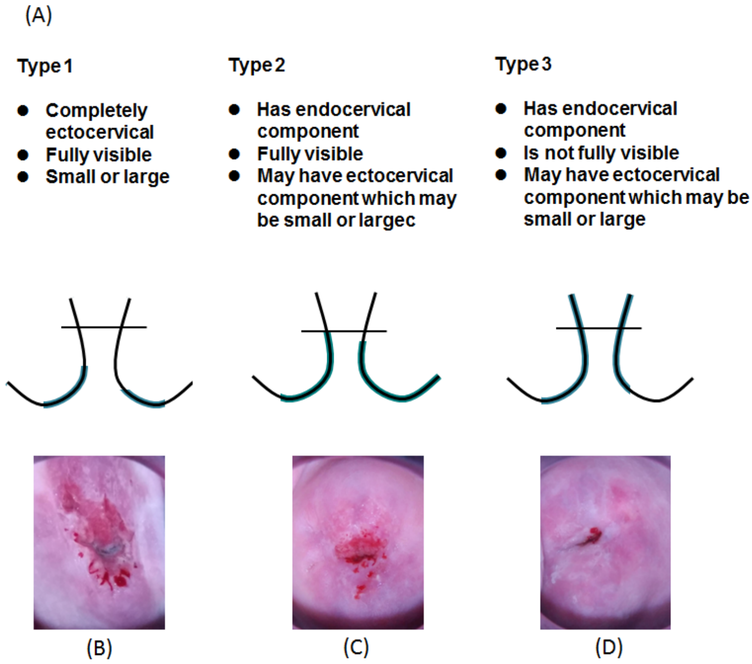

Fig 2. 3 cervix types to be classified. (A) detailed description of type 1 (B), type 2 (C) and type 3 (D) cervix

To reduce the cost of screening, improve reproducibility and help colposcopists to overcome subjectivity in their diagnosis, automated cervigram analysis algorithms are gaining interests from several research groups in recent years. Sun *et al.* reported a diagnostic image analysis algorithm that automatically identifies histologically neoplastic tissue areas in the colposcopic images. It is a two-steps approach. Cervigrams are firstly segmented into similar local regions using K-means clustering algorithm. An ensemble classifier is then used to estimate whether lesions are present. This method displayed a sensitivity of 79% and specificity of 88%. [15] Simoes *et al.* developed a hybrid neural network using Kohonen self-organizing maps (SOM) and multilayer perceptron (MLP) network for colposcopic images classification on dot pattern. They used 170 samples and 72.15% of the images have been correctly classified. [16] Claude *et al.* constructed a MLP network with back-propagation algorithm to classify contours of lesions from colposcopic images and achieved an accuracy of 95.8% using 283 samples. [17] For the purpose of automatically detecting cervix lesions in cervigrams, image-preprocessing steps that remove specular reflections (SR) caused by camera flash and isolate the region of interest (ROI) are essential.

MobileODT has collected over eight thousand cervigrams from their Enhanced Visual Assessment (EVA) System. In collaboration with Kaggle, these cervigrams are available for the public to develop an algorithm that accurately identifies the cervix types. The images are pre-divided into training data and test data. Images in the training set are labelled according to the cervix type shown in Fig 2. In this work, we evaluated the segmentation procedure developed by Greenspan [18] on a subset of the cervigrams and compared with two novel methods we developed on the performance of cervix type classification using neural network model.

Methods and Materials

The overall workflow is illustrated in Fig 3. After performing a classical image preprocessing step that removes specular reflection (SR) and regions obscured by blood on the tissue surface, cervigrams are resized into small scale (compression). And then, features of input images are transformed into 3-dimensional numpy arrays using opencv. Image segmentation is performed using different methods and algorithms including colour recognition, clustering to crop ROI from input images. In the model training section, CNN model is used for image recognition and classification based on different segmentation results. Some image augmentation procedures such as image rotation and amplification are introduced for our small data set to reduce overfitting. Finally, loss and accuracy are used as metrics to compare the performance of different segmentation methods and also choose the best epoch in CNN model training.

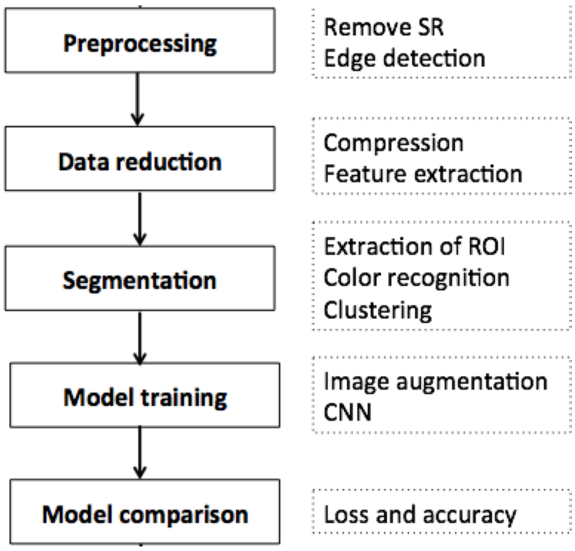

Fig 3. The workflow of our model building process

Benchmark segmentation

A normal cervix of a woman viewed with a vaginal speculum shows that the external os is surrounded by the functional SCJ and the irregular demarcation between the lighter and darker shades of pink mucosa is also visible. Two important areas of the cervix are SCJ where two different types of epithelial meet and TZ which between the original SCJ and the new SCJ [19].

In this work, we first introduce a benchmark image processing algorithm by Greenspan *et al.* [18] to detecting the region of interest (ROI). It intends to extract a rough area without irrelevant information (medical equipment, other tissues, text and frames) [20] to the utmost extent, which could confuse the automatic detection of the cervix, while making sure of the target, the entire cervical region, not being excluded. Thus, the region of anatomical and medical interest could be defined by this detection and it is made possible for further analysis to focus on the cervix region itself. There are two steps for the detection: the first is to quantize the degree of ‘redness’ of the colour space within the image (the darker red the pixel colour results in the greater value), and the second is to calculate the distance between a pixel and the image centre. After wiping off small bias of the image by smoothing the colour channel, we normalized the two values and made clustering analysis. The computed results spread into a coordinate system and are clustered into 2 groups by k-means clustering (k=2). One is high in ‘colour’ (darker red) but low in distance, and the other is low in ‘colour’ (light red) but high in distance.

In current work, the noisy parts of the cervigram images have been eliminated, which largely meets the judgemental criteria of presenting a coarse ROI remaining the entire cervix region. However, the contour of the cervix is still uneven, rugged, full of irrelevant edges. To solve this problem, there are previous works using a positive principal curvature k which is calculated based on the convexity of cervix boundary. And the rough contour line is marked white, so the concave parts are white or light grey and the convex parts are black or dark grey. Then k is normalized labelled as k ranges from 0 to 1, and k near 1 means concave parts (inward bending), on the contrary, k near 0 means convex parts (outwards bending) [18]. Active contour model (ACM), which is robust and applicable on rough images [21], is introduced into the algorithm to smooth the boundary. And a prior shape model is also integrated into this segmentation framework due to the limitations of ACM (slow convergence and leaking problems) [22]. The combination allows the evolution of the curve and provides a smoothing effect on the edges.

The benchmark segmentation procedure for cervigrams is adapted from [18], and the raw python code for this procedure is provided by chattob on Kaggle (url: https://www.kaggle.com/chattob/cervix-segmentation-gmm). This benchmark method is checking the main interest field of the cervix picture by sorting out the main contour (max area size) of the cervix. First step: Margin check, aim to find out the max area of the cervix in the picture and erase the black margin around it. In this process, it uses OPENCV to find out the largest contours and cut out the max rectangle without the black margin. Second step: Using K-means clustering to separate the different cervix region, and the final step is to identify the maximum bounding rectangle of the particular cervix field (with the largest contour size) in the image.

Cervigram pre-processing

Before segmentation for images, it is necessary to remove outliers and noisy images from the training set. After manually checking all the training pictures, we found that not all of these images had a clear view of cervix, and some of the pictures were quite not clear to see the cervix part (3085.jpg). By using HSV threshold setting, filtered out red region of interest. If the image is night vision image, then next segmentation step will not find any contour in the image. So these night vision images are treated as noisy images, which could only have negative influence for further recognition. Apart from that, we also found some irrelevant images (3086.jpg) from the training set which appeared to be no help for recognition.

Because these cervical cancer pictures were recorded under different circumstances, neither the brightness nor background colour is quite different with each other. However, one thing can be sure is that the most interest field we focus on is cervix. And for all the cervix part in the picture appear to be red colour with various saturation and value. We assume that use RGB or HSV (Hue, Saturation and Value, a type of color space.) colour space will be a great help to do the segmentation by filtering out the cervix part with red colours.

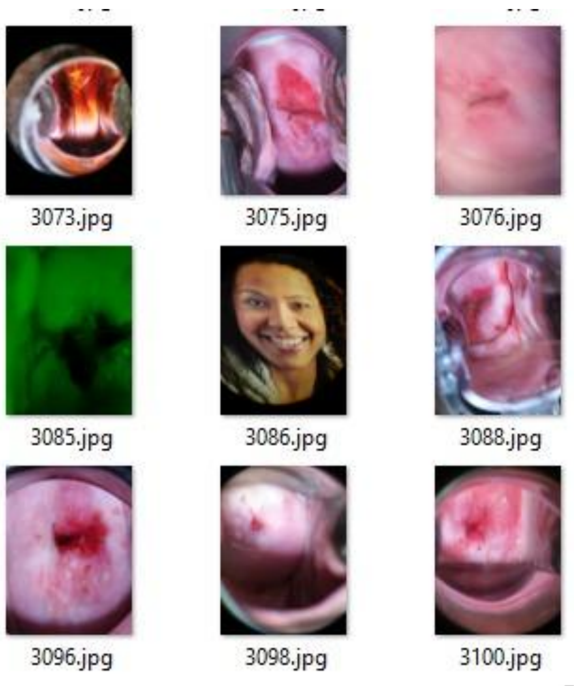

Fig 4. Example cervigram images

Comparing the benchmark segmentation method and HSV colour filter + margin check method, the aim of these two algorithm are to extract the cervix part (interest field) from the pictures. Our method focus more on the colour space filter rather than only double checking the contours.

HSV filter + margin check Segmentation method

HSV colour filter + margin check method is to transform the RGB colour space into HSV colour space filtering out the red region of the picture. Then find out the main contour in the red region(cervix field) with the largest size.

First step: Transform the picture into HSV colour space. Set the lowest red colour threshold and the highest red colour threshold in order to filter out the red colour region of the cervical picture. We used OpenCV library in python to set the lower_red colour into [90,0,0], which means setting the lowest hue in 90, saturation in 0 and value in 0. And set the upper_red color into [180,255,255], which means setting the highest hue in 180,saturation in 255 and value in 255. Created a mask for HSV threshold and by using cv2.bitwise_and (img=img, mask=mask) function, Other irrelevance colors were replaced by value of 0 which means it turns other irrelevant colors into pure black colour (value 0). In that case, we found that there are several picture were taken by night vision in training data, because only few of these night vision picture, we consider them as the noise for this HSV method. HSV threshold also helped us remove the high light spot in the interest field (red cervix region).

Second step: After we filtered out the red region of these pictures. After transforming HSV back to RGB colour space, and turned RGB colour space into grayscale image. then setting cv2.threshold(gray,10, 255, cv2.THRESH_BINARY) for grayscale image which means to apply global thresholding for a value of 10 to transform gray scale image into binary image. Then using cv2.findContours function by setting parameters: cv2.RETR_TREE(find out the hierarchy for each contour like whether it has parent contours and children contours or not) and cv2.CHAIN_APPROX_NONE (store all contours points into the vector). by this approach, found the boundary between each white and black region due to binary image and store the boundaries as contours in vectors.

Third step: After Finding out the contours in the picture, we sorted the max area size of these contours and carry out the main contour as the region of interest (ROI), and copy the main contour into a zero matrix with same size of the image. Then using cv2.floodFill function to impute value 1 inside the main contour then by using ourself written function maxRect() to check top,bottom,left and right side of this matrix from margin to centroid of image to find the bounding rectangle of this main contour. After that, crop the bounding rectangle of the main contour from the RGB version of this image to get the ROI eventually.

2-layer Contouring segmentation

The purpose of image segmentation is to exact the cervix region from individual cervigram images to facilitate following classification model building. Due to the reason that the benchmark segmentation procedure fails to detect the ROI using K-means clustering under the a-R feature space for some cervigram images (Fig 7), we develop a new segmentation procedure with two sequential contouring steps: The first step is to determine an adaptive threshold, which is the weighted sum of neighborhood values in a Gaussian window. Then we identify the contour with the largest area in a binary image transformed under such adaptive threshold. In the 2nd step we draw the same contour lines identified in step 1 on a blank image with the same size as the input image, and then performed the 2nd round contouring to identify the largest middle area, which is supposed to be the cervix region and ROI. At last, we draw the bounding rectangle around the 2nd contour identified in step 2 and extract it for following model training.

We use opencv library in python to implement all image processing and segmentation. Due to the high resolution of input cervigrams, we first resize them to dimension 256×192 to increase the efficiency of image processing. To identify the first contour, ADAPTIVE_THRESH_GAUSSIAN_C is used as the adaptive thresholding algorithm with block size 11 and a constant subtraction 2 within the thresholding function cv2.adaptiveThreshold. cv2.findContours is then used for contour detection with cv2.RETR_EXTERNAL as the contour retrieval mode and cv2.CHAIN_APPROX_NONE as the contour approximation method. In identifying the 2nd contour, the input image is first transformed from BGR scale to gray scale using cv2.cvtColor, and then the hard threshold 127 is set within cv2.threshold for following contour detection. The 2nd contour is then detected using the same retrieval mode and approximation method as the first contour.

Conventional Neural Network

Conventional Neural Network (CNN) is a typical feed-forward artificial neural network, in which the artificial neurons are capable of responding to a restricted region of space. CNN ignores the complex preprocessing of images; thus, the original image can be directly recognized. It has outstanding performance and been widely used in image recognition and processing.

CNN consists of multiple alternation convolutional layers and pooling layers. In the convolutional layer, the neuron input of each layer is connected with receptive fields, and extract features of this partial region, so that the output delivers a higher-resolution representation of the original image, and this process repeats in each layer. The pooling layer is for feature mapping. Neurons on each mapping layer share same weight, which means the same filter is used for each pixel in the layer, this reduces free parameter numbers and improves performance.

The shared weight achieves parallel learning, and it outperforms traditional neural networks in voice recognition and image processing. Moreover, the shared weight also decreases the complexity of neural networks, especially when processing multidimensional images.

Results

Our training dataset consists of 1481 cervigrams including 250 type_1, 781 type_2 and 450 type_3 labelled cervixes. All these cervigram data was downloaded from Kaggle competition “Intel & MobileODT Cervical Cancer Screening”. There are three different dimensions / resolutions of these cervigrams: 3264×2448, 4128×3096 and 4128×2322. In this study, we presented two novel segmentation procedures and compared their prediction performance with the benchmark method provided by chattob.

We first applied chattob’s benchmark segmentation procedure to process all training cervigrams. And the classification model built based on cervigrams after segmentation using this procedure was treated as the benchmark. Next, we generated segmentation results using two different methods: HSV+margin check method and 2-layer contouring procedure.

(A) (B)

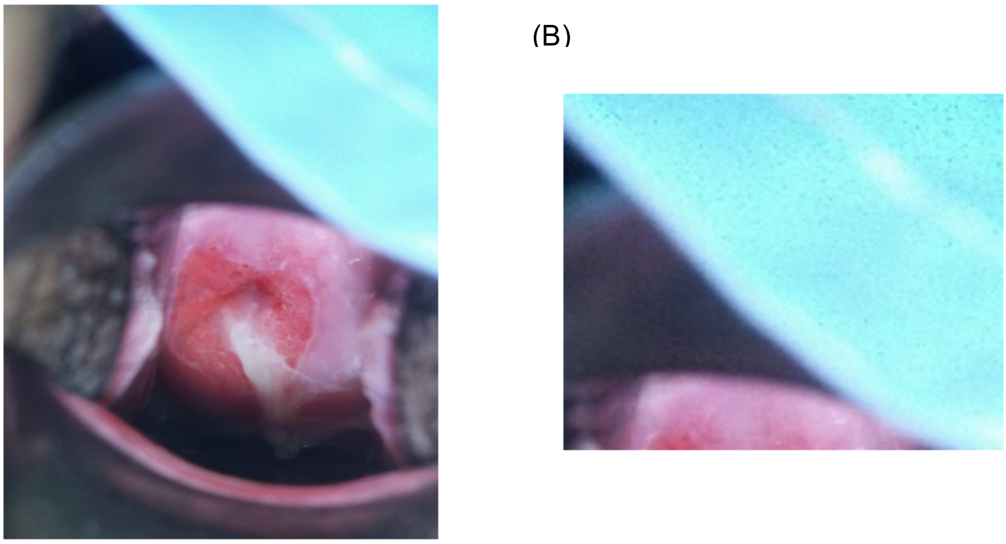

Fig 5. A) Raw image and B) Artifact of irrelevant large contours

(A) (B)

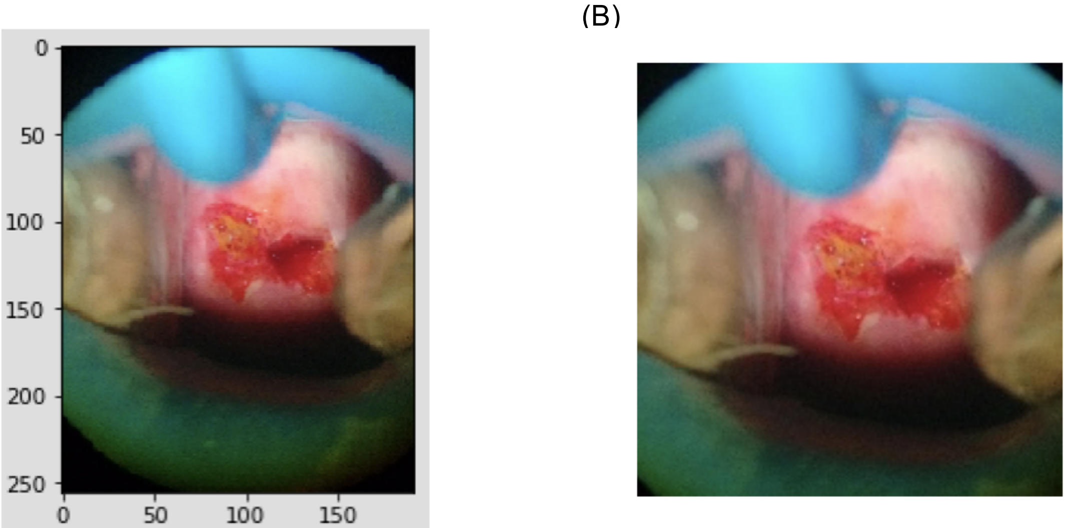

Fig 6. A) Raw image and B) Artifact of other irrelevant colours

Segmentation using the benchmark method

From Fig 5A and Fig 6A we can see that the raw image have some other blue, green, yellow colours which could result in extracting some useless patterns like blue colour surgical tools with the interest part, the cervix, as shown in Fig 5B and Fig 6B by original segmentation method. The irrelevant colour items will interfere the second step of checking the maximum area of those contours. Another problem of using these pictures to train the CNN is that it can be very time-consuming. Since we will transform the 3 channels RGB picture into array, other irrelevant colour value will affect the training result in a negative way and increase the training time.

Segmentation using HSV+margin check method

From Fig 7 and Fig 8, by filtering with HSV colour space, we turned these irrelevant colours into black, in other word, we replaced these irrelevant pixels' value with 0. By setting the threshold of brightness value, we can erase some high light white spot from the picture. Because most of these high white spot value may cause the massive worry calculation when training CNN.

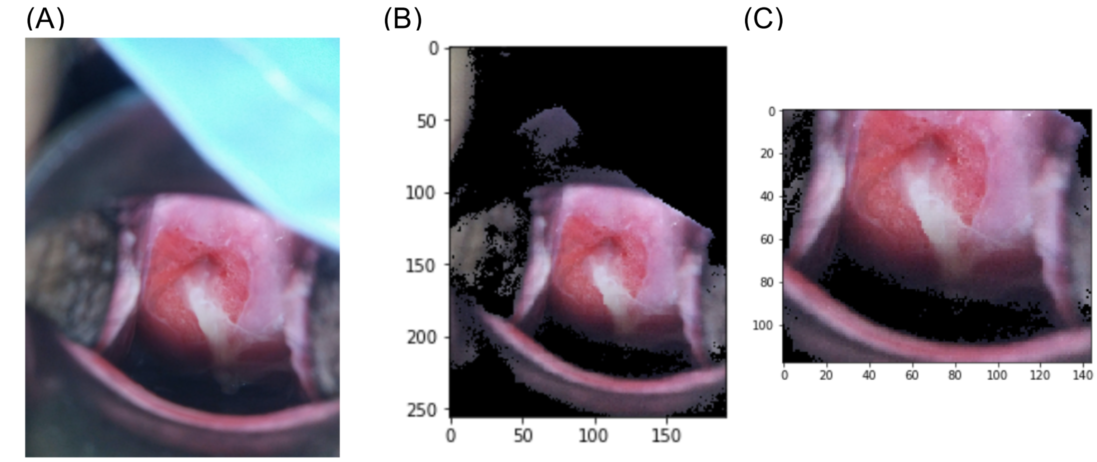

Fig 7. Removal of irrelevant regions by HSV filter

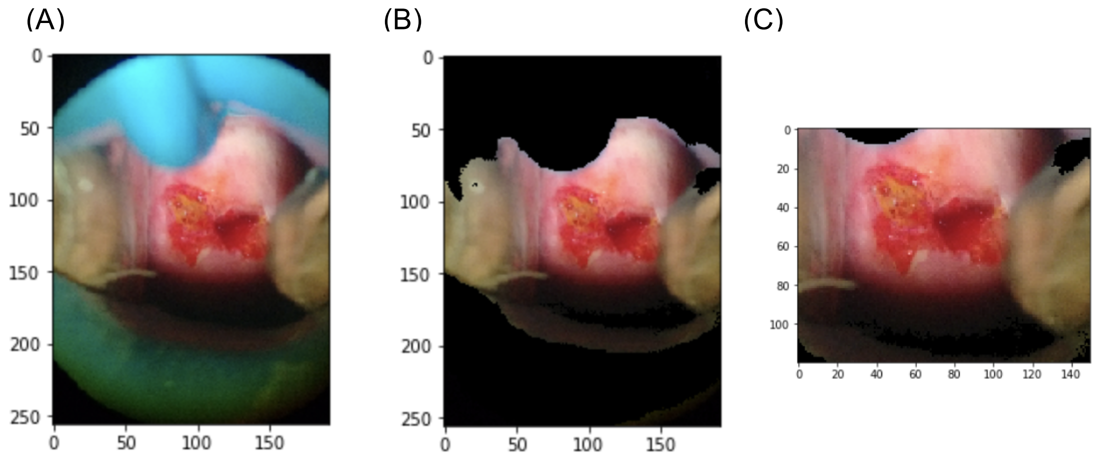

Fig 8. Removal of irrelevant colours by HSV filter

After this step, we cleared the background of the raw picture. Then the detected largest contours will no longer be interfered by other irrelevant colours. For training CNN model, the convolution process will be quicker than the original one. We can see that the segmentation result is better than the former one using original method.

Segmentation using 2-layer contouring

The detail of 2-layer contouring procedure was described in Methods. All cervigram images were processed by this procedure individually. From Fig 9 we showed two sample results from the benchmark and the new segmentation method. In Fig 9A, the benchmark method failed to detect the vertex region with medical instruments remained in their final results. Using our 2-layer contouring procedure we first detected a complex contour outline under an adaptive threshold as shown in the figure. And it is clear that the ROI is the central region of this contour. After generating a white background with the same contour outline, we performed the 2nd round contouring and detected the largest contour area within the first contour, from which the whole medical instrument was successfully excluded. Finally, the bounding rectangle of the second contour was extracted as the ROI and proceeded to following steps. Fig 9B showed another example with a similar scenario, where the benchmark segmentation method failed to detect the ROI and exclude the medical instrument. Similarly, our new segmentation procedure performed quite well in removing the artifact of medical instrument and narrow down the cervix region. However, we also observed that the shading artifact due to a strong flashlight may have some negative effect on the detection of ROI.

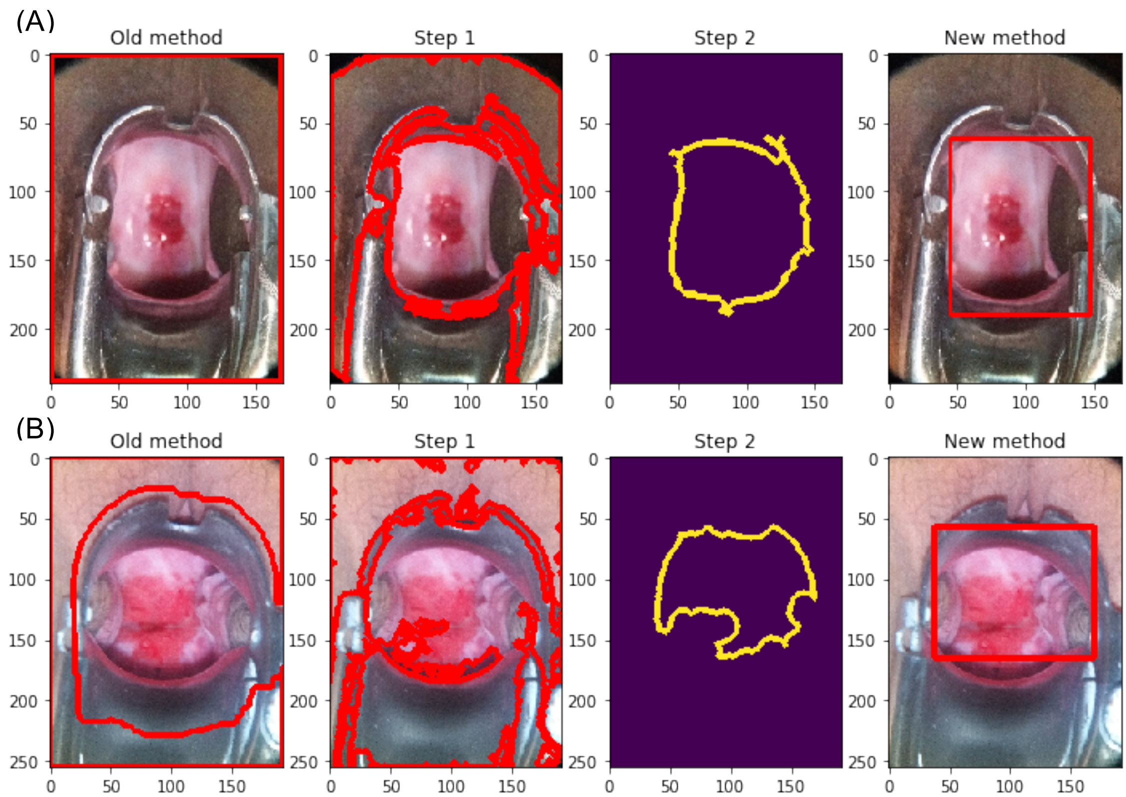

Fig 9. Two example images were processed using the benchmark and the 2-layer contouring method. Label "old method" represents the benchmark method. "Step 1" stands for the first round contouring. "Step 2" stands for the result of the 2nd round contouring. The final result of 2-layer contouring is shown with the label "New method".

Classification model using CNN

The architecture of our network is summarized in Fig 10. It contains five learned layers – three convolutional and two fully-connected. The output of the last fully-connected layer is fed to a 3-way classifier which produces types of cervical cancer. ReLU is introduced as activation function in all layer for its nonlinearity and faster learning performance except for the last fully connected layer. Max pooling is introduced for non-linear down-sampling, which serves to progressively reduce the spatial size of the representation, to reduce the number of parameters and amount of computation in the network, and hence to also control overfitting. Dropout is also introduced to reduce overfitting and it could improve the performance of our model.

The first convolutional layer filters 32 x 32 RGB input images with 4 kernels of size 3x3x3 (height x width x depth). The first max pool size of window is 2x2, selecting the max value of each window on the entire layer. The second convolutional filters the output of max pooling procedure with 8 kernels of size 3x3x4. The second max pool size of window is 2x2, selecting the max value of each window on the entire layer. The third convolutional layer filters with 16 kernels of size 1x1x8. Finally, after several convolutional and max pooling layers, the high-level reasoning in the neural network is done via dense (fully connected layers). In the first dense, we extracts 12 hidden units by ReLU. At last, the output of final fully connected layer refers to 3 hidden units as classifier, which indicates the categorical probability distribution of 3 types of cervical cancer.

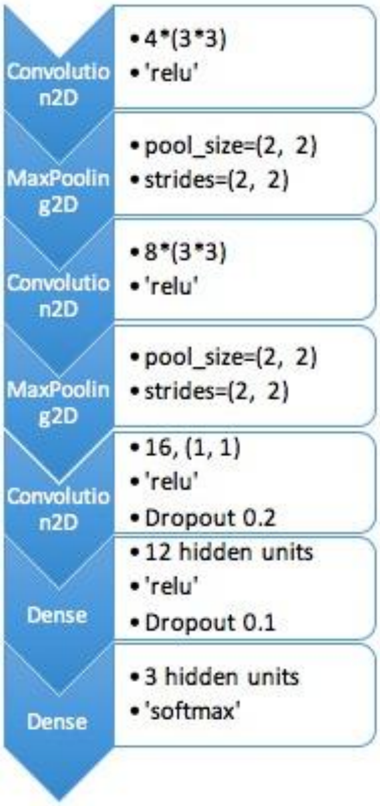

Fig. 10 Architecture of Network

In order to compare different methods of segmentation, control variant method is introduced to select the best performance of accuracy and loss. During our experiment, all procedures and parameters remain unchanged except for pre-processing segmentation image data. Images with different segmentation firstly will be transformed into numpy array in normalization format and the labels of each types of cervical cancer will be recoded as 0,1,2 into numpy array named train_target. Then we use the same random seed in order to keep random sampling when splitting our data into train and validation set for cross-validation. The goal of cross validation is to define a validation dataset to "test" the model in the training phase, in order to limit problems like overfitting.

The accuracy refers to percentage of accuracy. Higher accuracy, the better model is.
The loss is calculated on training and validation and its interpretation is how well the model is doing for these two sets. Loss is not in percentage as opposed to accuracy

and it is a summation of the errors made for each iteration in training or validation sets. In the case of neural networks the loss is usually negative log-likelihood for classification

After processing CNN model, 200 iterations have been run and accuracy and loss outcomes have been generated accordingly in each iteration and mapped into curve line chart for visualization as shown in Fig 11. The left side is accuracy curve of percentage of accuracy of training data (‘acc’, blue line) and validation data (‘val_acc’, green line). The right side is loss curve of training data (‘loss’, blue line) and validation data (‘val_loss’, green line)

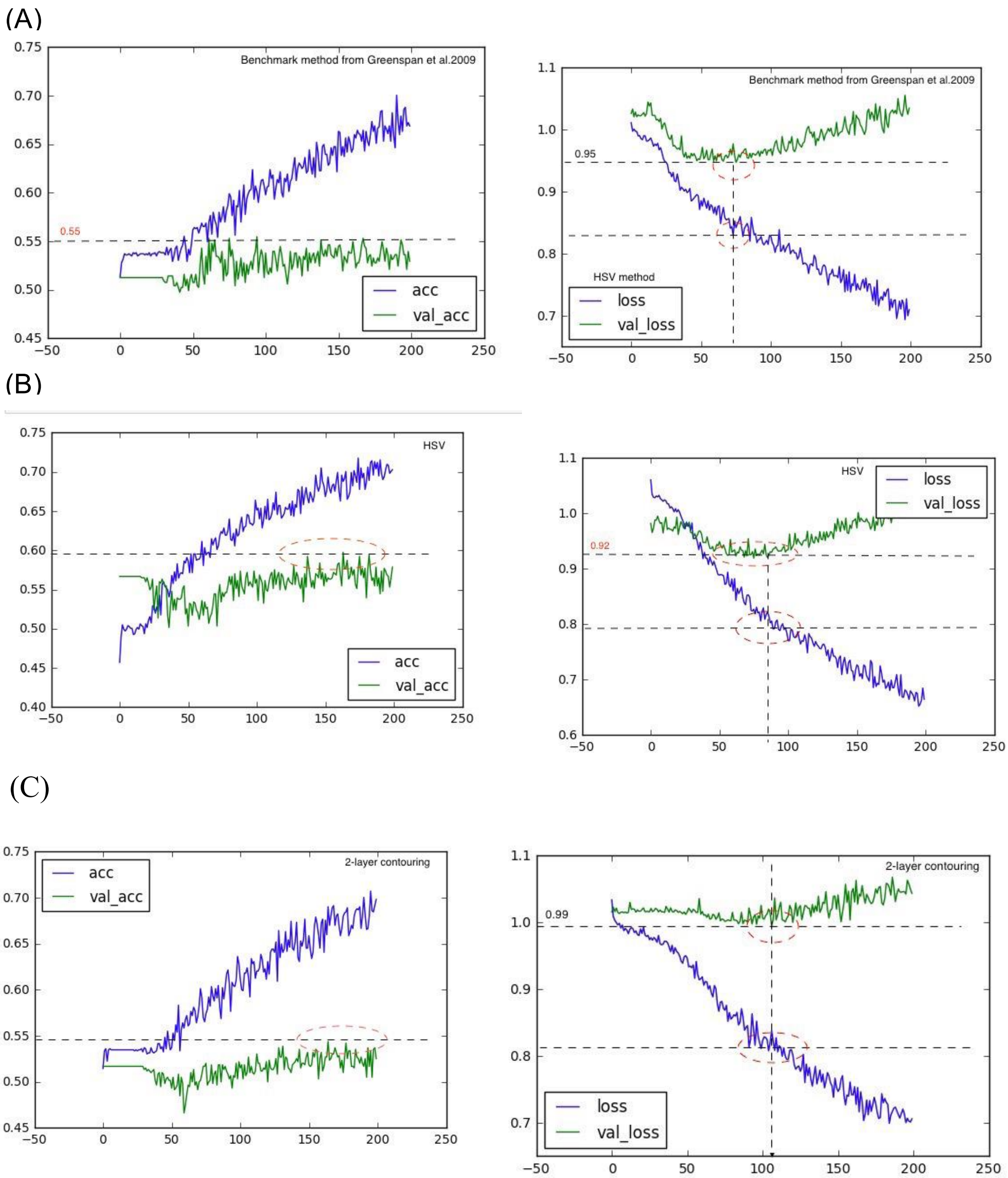

Fig 11. Accuracy and loss of CNN models. (A) Benchmark method from Greenspan et al.2009 (B) HSV (C) 2-layer contouring

During these three methods for segmentation, the best performance is method of HSV method, followed by the Greenspan’s method and 2-layer contouring method. It is shown that highest validation accuracy of HSV method can achieve almost 60%, the Greenspan's method and the 2-layer contouring can not reach over 55%. When comparing the loss performance, the lower the Loss, the better a model. The HSV method also performs best, because when the validation loss (val_loss) reaches the lowest level near 0.92 between 50 to 100 iterations, the training loss (loss) drops down below 0.8. However, the lowest validation loss point in the Greenspan's is higher than 0.92, in the same time training loss can not reach under 0.8, and it is the same result as the 2-layer contouring method. All in all, the HSV method of segmentation has the best performance.

Discussion

Worldwide, cervical cancer is the fourth-most common cause of death from cancer in women, but if detected early, it is one of the most successfully treatable cancers. However, limitations of contour recognition in existing detecting method may lead to imprecision on diagnosis. In this experiment, we are trying to make enhancement on original algorithm to improve overall accuracy. 2 novel methods (2-layer contouring procedure, HSV method) is used to make enhancement to image process algorithm in detecting the ROI and color recognition, by using classification algorithm of CNN, we found improvements on the precision of diagnosis. The best performance is HSV method, both in segmentation and classification accuracy.

The novelty of our methods is two fold: First, HSV method creatively target on the red ROI firstly rather than focusing on finding the contours of the image. Because most of these images consist of red cervix cancer region, by using HSV method, will not lose the target region (ROI) from the very beginning to the end of the segmentation and also can remove those night vision images (viewed as noise image), and will replace the interference from other irrelevant colors and the high light spot with pure black color (which pixels value of 0 with RGB color space) in the picture, in that case, it also reduce the calculation time when training CNN model because of all pixels value equal to 0 in other irrelevant part.

Second, our 2-layer contouring method creatively applies two rounds of sequential contour detection to better identify the cervix region and exclude the artefact of clinical instruments, which is a challenging task for any segmentation method with only one layer contouring.

For pre-processing step, there are lots of other processing methods, which could make the training images more clear and help us extract the cervix part more precisely. Such as Laplacian transform (Laplace of Gaussian) and Canny filter to make images more smoothly and remove noise from it. And for many images, it is necessary to identify the centroid of cervix by using colour or brightness value threshold. That will be more helpful for segmentation by knowing the specific position of cervix.

Sometimes, when cutting the bounding rectangle out of the image, it is not suitable to use rectangle for each image segmentation. For some images, it will lose less feature pattern using bounding circle to crop the cervix part rather than bounding rectangle to do the work. Because segment method in this thesis is based on normal pictures taken by normal flash, we cannot handle any night vision pictures. In that case, it is advisable to repaint those night vision pictures by using some adjustable colour imputation algorithm.

We used hard thresholding for the HSV filter of images, which should be better if we set this hard threshold with adjustable value. We can check the red colour distribution to find out the cervix part belongs to which scope. Then depending on the distribution findings, we set the adjustable value for HSV filter may improve the segmentation.

Although our new 2-layer contouring procedure outperforms the existing benchmark method in detecting cervix regions with the artifact of clinical instruments, its limitation is that it may not be general and robust enough due to the large variability of existing cervigram images. The challenge of automated segmentation of cervigrams comes from many sources, including the strong shading artifact due to the camera flash, the specular reflection (SR) artifact, the viewing angle of camera, the shape and size of the medical instruments, the narrow dynamic range of colors, the variability of cervix tissue content, and no clear boundaries between tissue regions [18]. We haven't conducted a comprehensive test on the performance of our new method in processing images with artifacts as listed above. It is also likely that the contour with the largest area in the 2nd layer contouring may not always be the ROI, so that a dynamic selection of the right contour is necessary to improve the accuracy of ROI detection. Moreover, previous studies and our results suggest that no single method can be used alone and performs well enough in the segmentation of cervigrams with large variability. Therefore, one possible future development could be the combination of multiple segmentation methods, where the major type of artifact will be classified first for individual images and the best suitable segmentation method will then be applied to extract the ROI.

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