Detección rápida de lesiones en el tracto genital femenino bajo, causadas por virus de papiloma humano, a través de técnicas de fluorescencia y procesamiento digital de imágenes

Rapid detection of lesions in the lower female genital tract, caused by human papilloma virus, through fluorescence techniques and digital image processing

A detecção rápida de lesões no trato genital inferior feminino, causada pelo vírus do papiloma humano, por meio de técnicas de fluorescência e de processamento de imagem digital

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Resumen

El cáncer cervicouterino continúa siendo un grave problema de salud en México: entre 95 y 99 % de los casos están asociados al virus del papiloma humano (Tovar-Guzmán, 2008). La detección oportuna de lesiones causadas por este virus es fundamental para la prevención y tratamiento de dicha enfermedad (Aguilar-Pérez, 2003). Una forma rápida de diagnosticar este tipo de enfermedades se puede lograr mediante el uso de técnicas no invasivas; en este sentido, las imágenes médicas representan la opción más viable, sin embargo, algunas de las desventajas de este método son el bajo contraste y la presencia de ruido, por lo que es importante desarrollar herramientas que contribuyan a la visualización y mejoramiento de las imágenes. El objetivo del presente trabajo es mejorar la capacidad diagnóstica de imágenes médicas producto del procedimiento colposcópico mediante el desarrollo de un software para la visualización, procesamiento y almacenamiento de video e imágenes médicas, específicamente para la detección rápida de lesiones en el tracto genital femenino ocasionadas por el virus del papiloma humano. Se implementaron filtros digitales para mejorar la visualización de dichas lesiones, los cuales incluyen filtrado manual y automático de fluorescencia para imágenes y la detección en tiempo real mediante el procesamiento de video.

Palabras clave: colposcopia, VPH, fluorescencia, procesamiento imágenes.

Abstract

Cervical cancer remains a serious health problem in Mexico: between 95 and 99% of the cases are associated with human papilloma virus (Tovar-Guzmán, 2008). The timely detection of lesions caused by this virus is essential for the prevention and treatment of the disease (Aguilar-Pérez, 2003). A quick way to diagnose such diseases can be achieved through the use of non-invasive techniques; in this sense, medical imaging represents the most viable option, However, some of the disadvantages of this method are the low contrast and the presence of noise, so it is important to develop tools that help display and enhancement of the images. The objective of this work is to improve the diagnostic capability of medical imaging product of the colposcopic procedure through the development of a software for the display, processing and storage of video and medical images, specifically for the detection fast of injuries in the female tract genital caused by the human papilloma virus. Digital filters were implemented to improve the

visualization of these lesions, which include filtering manual and automatic fluorescence imaging and detection in real-time video processing.

Key Words: colposcopy, HPV, fluorescence, processing images.

Resumo

O câncer cervical continua a ser um grave problema de saúde no México: entre 95 e 99% dos casos estão associados com papilomavírus humano (Tovar-Guzmán, 2008) de vírus. A detecção atempada de lesões causadas por este vírus é essencial para a prevenção e tratamento da doença (Aguilar-Pérez, 2003). Uma maneira rápida para diagnosticar estas doenças pode ser conseguida utilizando técnicas não invasivas; A este respeito, imagens médicas representam a opção mais viável, no entanto, algumas das desvantagens deste método são o baixo contraste e a presença de ruído, de modo que é importante para desenvolver ferramentas de reforço que ajudam a visualização e imagem . O objetivo deste trabalho é melhorar procedimento colposcópico produto imagiologia médica de diagnóstico através do desenvolvimento de software para visualização, processamento e armazenamento de vídeo e imagens médicas, especificamente para a rápida detecção de lesões no trato genital feminina causada por o vírus do papiloma humano. filtros digitais foram implementadas para melhorar a visualização dessas lesões, que incluem filtragem manual e automático para imagens e detecção de fluorescência, usando processamento de vídeo em tempo real.

Palavras-chave: imagens colposcopia, HPV, fluorescência, de processamento.

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Introduction

Cervical cancer is a disease of slow progression that develops as a result of persistent infection caused by any of the types of human papillomavirus (HPV), identified as high risk and linked with this cancer. Gradually these viruses cause epithelial lesions in the cervical region, which evolve in cervical cancer (Gutiérrez-Delgado et al., 2008).

Cervical cancer is the second most common gynecologic cancer in the world and it is estimated that 275 000 women die each year from cervical cancer (Bourgioti et al., 2016). On the other hand, considered that the female population of Latin American origin is at high risk of developing cervical cancer. Comparative studies show that the highest with respect to this type of cancer mortality rates correspond to Chile and Mexico. In our country, cervical cancer is the leading cause of death from neoplasms in women over 25 years old (Hidalgo-Martínez, 2006). It should be noted that this type of cancer is a preventable disease if diagnosed in a timely manner and will provide treatment appropriate to premalignant lesions (Aguilar-Pérez, 2003).

Order to improve cervical scans and establish the initial forms of cervical cancer, Hans Hinselman designed in 1924 the first colposcope, an apparatus which is performed a procedure known as colposcoapy, with which you can examine the epithelium of female genital tract (Vera Gaspar et al., 2013).

The traditional colposcopies have the disadvantage that its false positives fluctuate between 4 and 33% and between 40 and 62% false negatives. These fluctuations are mainly due to information obtained from a traditional colposcopy has a high degree of subjectivity and the diagnosis depends on the interpretation of the colposcopist (Aroch Calderón et al., 2005).

The use of techniques of fluorescence allows better visualization of lesions caused by the human papillomavirus, using acetic acid as agent mordent and specific fluorochromes. In this case is used Fluorescein isothiocyanate (FITC), a reactive with nucleophiles, including groups amine and sulfhydryl protein, with a range of maximum 492nm excitation and minimum of 320nm. The maximum emission is carried out to the 518nm in the blue-green region of the spectrum. The technique of detection of HPV lesions through application of FITC is based on an increased presence of proteins embedded in cells infected with HPV and treated with acetic acid, which generates a greater absorption of the fluorochrome (Vera Gaspar et al., 2013).

To be able to observe the fluorescence properly and with sufficient contrast should attenuate the excitation light but not the fluorescence signal. This requires the use of filters. Commonly used optical filters that are physically present on the devices (Reichman, 2012). He objective of this work is develop a software that allow view best such fluorescence and, accordingly, that facilitate the detection of lesions caused by HPV. In this case the use of digital filters allows to better visualize the fluorescence, avoids the need to physically change the different filters and reduces noise in the image, so it also reduces the likelihood of false positives. Similarly, the development

and use of other filters can improve the visualization of lesions after applying traditional techniques in colposcopic processes.

MATERIALS AND METHODS

Description of method

The software developed together with the application of filters to improve the visualization of lesions is able to automatically detect certain lesions in the images produced by the colposcopic process. To detect such lesions, the following procedure was performed: first, a resolution change was made to the acquired image and the most appropriate color space was selected; Then a thresholding and filtering was done in the frequency domain, then an emphasis was placed on high frequencies and a multiscale analysis was then applied through the wavelet transform; Finally the coordinates for the detection and visualization of the lesion were located.

Implementation of filters

To improve the visualization of lesions, the implementation of decay and signal processing filters was carried out using different filters with specific objectives for each one. A grayscale filter was then generated, where the image is decomposed into RGB (Red, Green, Blue) by applying brightness gradations to the pixels, with an option from zero to one.

A negative filter was generated to improve the visualization of acetoblanqueo of the tissue for lesion detection, which was generated using the complement of the value of each pixel of the image. Fluorescence composition in the RGB color space (Red, Green, Blue) in the wavelength ranges in which the FITC has its maximum emission was considered later for fluorescence visualization generated by the FITC. In this way a filter was created that improves the contrast and visualization of this fluorescence, reducing the bands of blue and red colors.

The first step was to equalize the images in order to redistribute the histogram values of the image. In the filter for manual fluorescence display, the RGB decomposition (Eq. 1) is performed based on a user-marked threshold, described in Eq. 2:

$$R(x,y) = img(:,:,1) \qquad (1)$$
$$G(x,y) = img(:,:,2)$$
$$B(x,y) = img(:,:,3)$$

$$img \quad (2)$$

$$= \begin{cases} R = R(x,y) * \left(\frac{1}{\alpha\Delta + 1}\right), & R < \theta \\ G = G(x,y) * (\beta\Delta), & G < \theta \\ B = B(x,y) * \left(\frac{1}{\alpha\Delta + 1}\right), & B < \theta \end{cases}$$

Where:

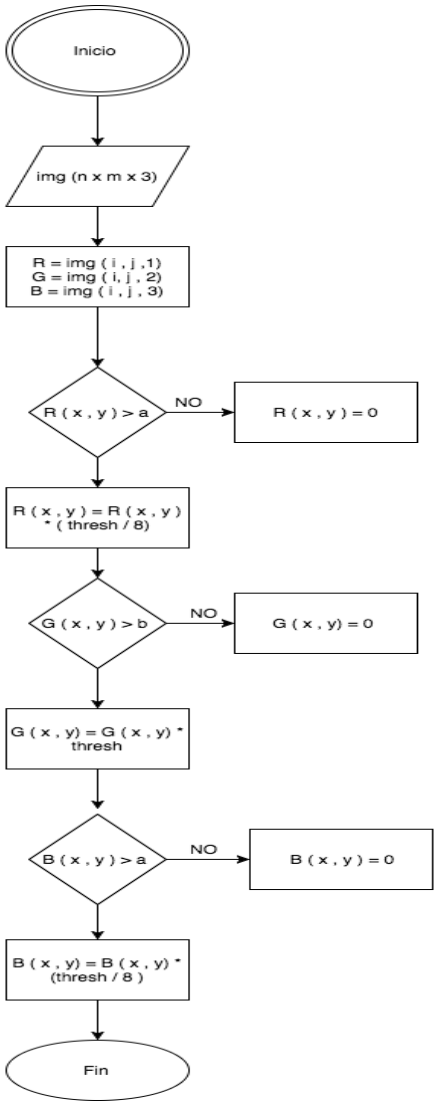
Δ : Increase given by user

$\alpha\ y\ \beta$: Coefficients given for the suppression and increase of bands.

img: Matrix source of nxmx3 dimensions

For the fluorescence display filter the software automatically evaluates the composition of the image and highlights the color spectrum that describes a coordinate with fluorescence presence. This is achieved by setting a limit (a) for the value of R and B, and a limit (b) for the value of G. If the value of R or B is greater than a, its value is multiplied by 0. In In case the value is below a, the value of R will be reduced. If the value of G is greater than b, its value is multiplied by a set value. In this way the value of the G component is intensified and the values of the R and B components are attenuated, allowing a better visualization of the FITC fluorescence, as it is in the blue green area of the spectrum. The values of R and B are only attenuated and not suppressed since they form part of the G component (Figure 1).

Figure 1. Fluorescence Detection Filter Flowchart.



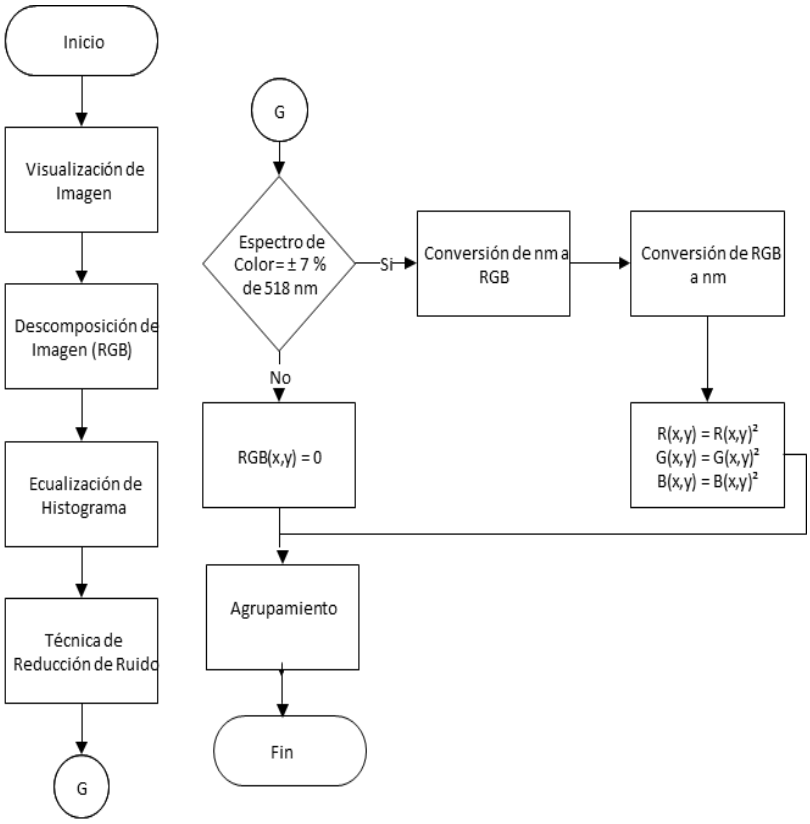
The figure shows the process that the software performs for the detection and visualization of fluorescence in images acquired by colposcopy.

The following methods were used for the automatic fluorescence detection filter:

- Adaptive Histogram Equalization with Limited Contrast (CLAHE). This method seeks to reduce the noise produced by Adaptive Histogram Equalization in homogeneous areas.
- Non-Local Means Denoising Method (Buades et al., 2011).

Fuzzy C-Means Clustering was used to eliminate noise in the form of distant dots, in which the distances between the pixels with fluorescence were used and the points whose membership function was below average were eliminated (figure 2).

Figure 2. General diagram for fluorescence detection.



The diagram shows the sequence of steps used from the acquisition of the image and all processing steps for fluorescence detection.

Software Testing

Tests were performed with software generated to test the functionality of the filters and the lesion detection system. For this, we used images acquired from previously performed colposcopy videos and in which the acetic acid, Schiller test and FITC application techniques were used. Then the filters of the generated software were applied to the corresponding images from the technique used in each image and the images were compared before the application of the filter, as well as the application of the filter to observe a better distinction of the lesions present in the images. Fluorescence detection was emphasized manually and automatically by the software,

seeking the selective display of the FITC emission wavelength range. The same was done when evaluating the noise elimination in the filter for the fluorescence display through the automatic filter.

RESULTS

Test scores

The application of the different filters included in the software was successful, so that the original images and images processed after the application of the filter could be observed through the graphic interface of the software (figure 3 for the grayscale filter And Figure 4 for the negative filter).

Figure 3. Grayscale filter

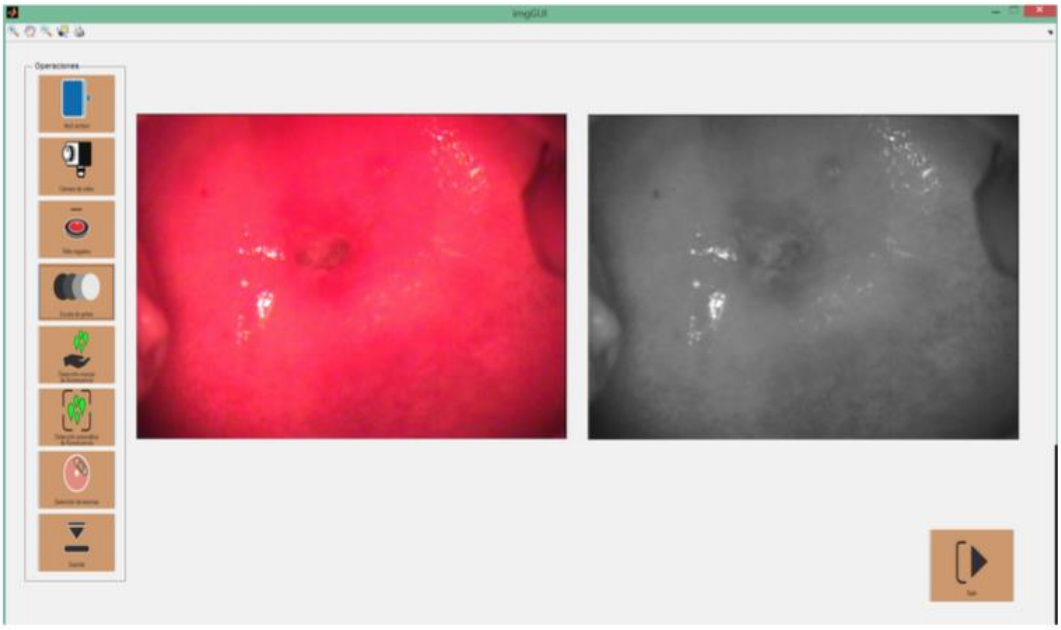
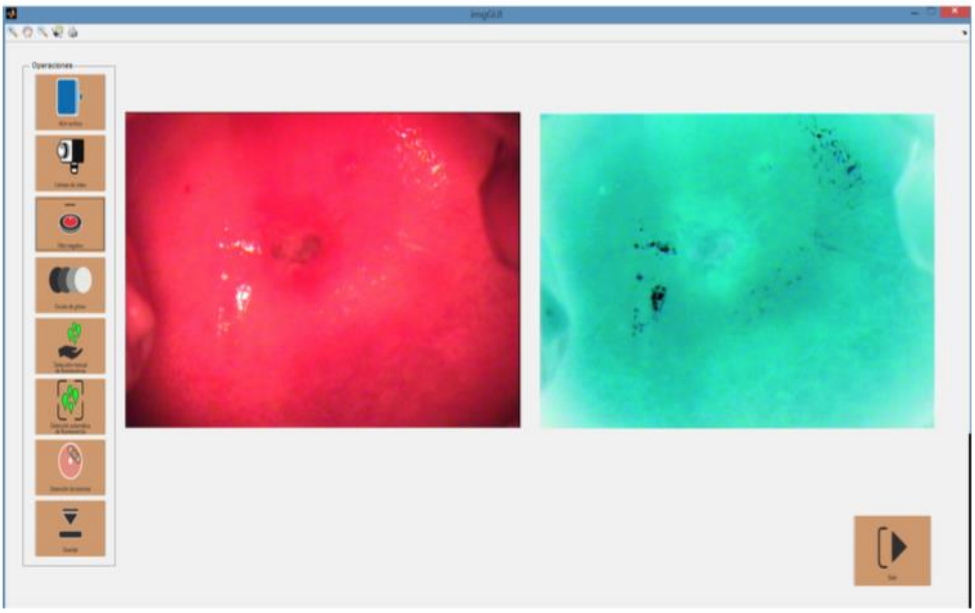


Figure 4. Negative filter



The fluorescence was also successfully detected selectively for the FITC emission wavelength. In the manual detection version, a greater amount of fluorescence and scattered spots were observed, which could indicate presence of noise and generate false positives. In the case of the automatic detection, the fluorescence was also detected in the emission wavelength of the FITC, however, a smaller amount of scattered fluorescence points was observed in the image, showing a good noise elimination in the image and a decrease in the Probability of generating false positives (figure 5).

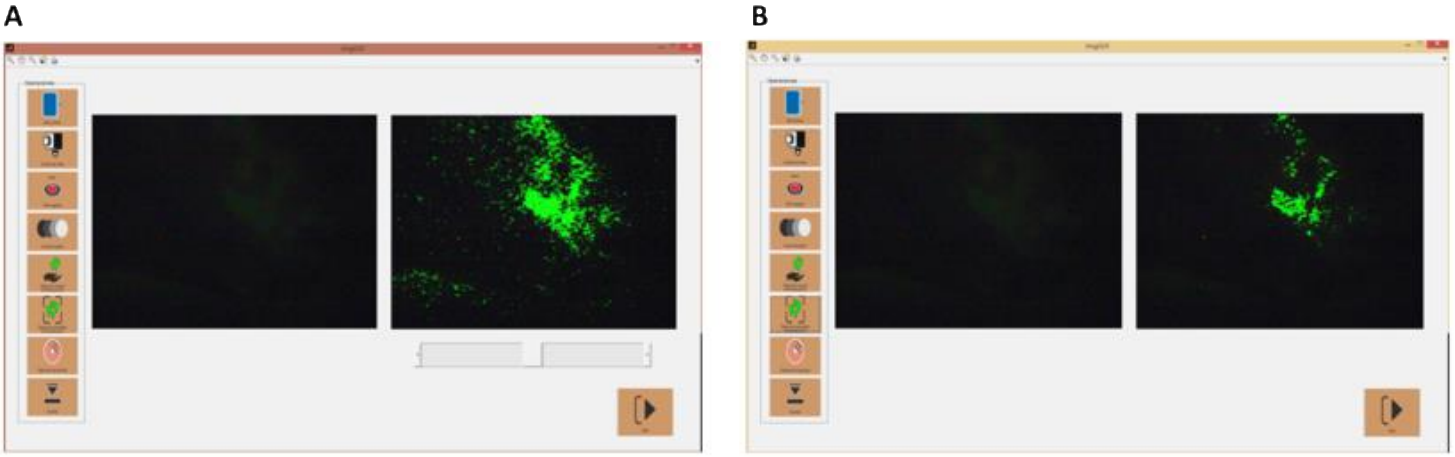
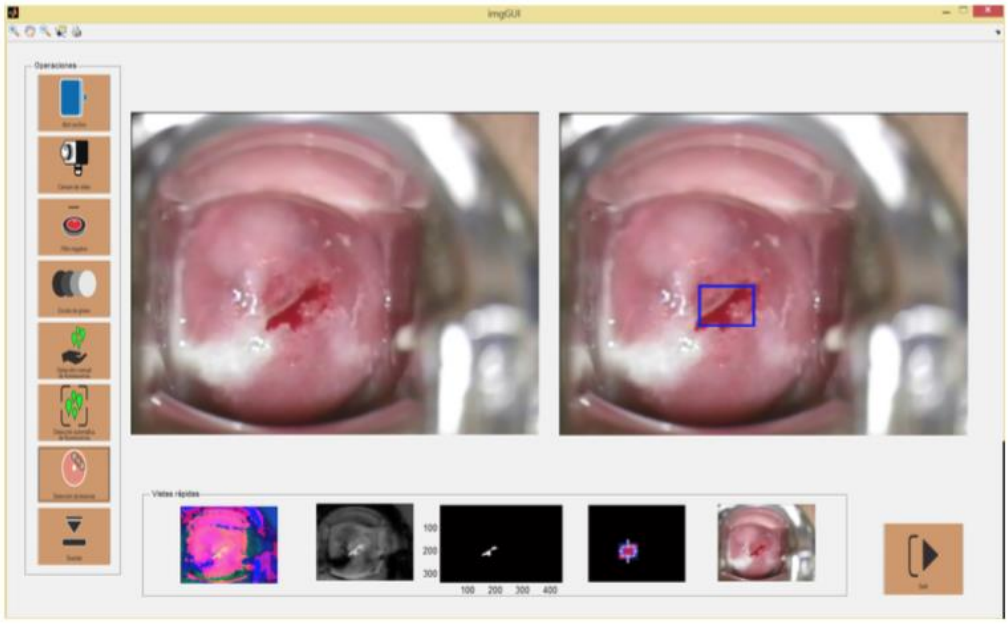


Fig. 5. Filtros de detección de fluorescencia manual y automático. La figura muestra los resultados de la detección de fluorescencia a través del filtro manual A y a través del filtro automático B. Observándose menor puntos de fluorescencia dispersos en el filtro automático.

It was also observed that the software was able to identify lesions automatically, but only in lesions that were shown as high frequency points in the image (figure 6).

Figure 6. Automatic injury detection



Software Description

This work generated a software to detect lesions caused by the human papilloma virus in the lower female genital tract. This software can be integrated into colposcopes that use the most common techniques in colposcopic studies, including visualization of lesions after saline application, acetic acid or lugol application, as well as colposcopes using the FITC application to visualize lesions Of HPV.

DISCUSSION

The software is able to process the images acquired through a camera or video integrated to the colposcope. Image processing includes the application of four filters: a grayscale filter, a negative filter, a manual fluorescence filter, and a filter for automatic fluorescence display. It can also automatically detect some types of tissue injuries that are displayed as high frequency spots. The negative filter aims to improve the visualization of the aceto-whitewash generated in the lesions after the application of acetic acid. The grayscale filter has the objective of improving the

visualization of the state of the genital tract by minimizing the interference of brightness caused by the illumination of the colposcope. The manual fluorescence filter allows the fluorescence to be displayed in the specific spectrum of the FITC and the automatic detection filter allows this display while being able to reduce image noise. In addition, the software has a user-friendly graphical interface, allowing images to be saved after processing and applying the filters, so that they can be included in patient records.

CONCLUSIONS

The generation of this software can serve as a support tool in the detection of lesions caused by the human papillomavirus in the lower female genital tract and also for the rapid diagnosis or prevention of cervical cancer. Therefore, this software has been shown to be useful in detecting such lesions and decreasing the subjectivity of colposcopic studies, with special emphasis on the technique of applying FITC specific for HPV-generated lesions. It is recommended to improve the automatic detection of lesions, so it is necessary to establish patterns in the images that may be related to lesions caused by HPV.

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