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# Diffuse Reflectance Image Enhancement For Cervical Cancer Detection - A Review

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**ABSTRACT:** Multi-spectral Diffuse Reflectance imaging provides information of the tissue transformation towards malignancy which can be studied by the diffused reflectance of the intense white light by the cervical tissues at the absorption peaks of the oxygenated haemoglobin at 545 and 575 nm. This technique can be used as a diagnostic tool for early detection of tissue abnormalities in cervical cancer. The presence of specular reflection and the motion artifacts associated with sequential recording of images degrade the quality of the DR images. This paper reviews the various image processing algorithms and assess their potential for improving the quality of multi-spectral DR images of cervix and the ability to identify the most malignant site for cervical tissue biopsy. This will help in the establishment of Multi-Spectral Diffuse Reflectance Imaging system as a screening technique for the early detection of cervical cancer.

**Keywords:** Diffuse Reflectance; Specular Reflection; Multi-spectral Diffuse Reflectance system; Segmentation; Monochrome; Inpainting; Image Ratio

## 1 Introduction

Cervical cancer is the second most common cancer among women worldwide [1]. Yearly more than 270,000 women die from cervical cancer. More than 85% of these deaths occur in low and middle income countries [1]. In India, one in every five women suffers from cervical cancer. Cervical cancer is mainly caused due to the presence sexually transmitted Human Papilloma virus (HPV) in the cervical region [3] which causes changes in the epithelial cells of the cervix, and can invade more deeply into the cervix and nearby tissues [2]. Cervical carcinoma is preventable and treatable, but poor access to screening and treatment services, leads to deaths in women living in low and middle income countries [1]. Current screening techniques based on Pap smear and Colposcopy burden the health care system with excessive costs, anxiety, and discomfort. Cervical biopsy is the gold standard for the detection of Cervical cancer [53].Since more than one biopsy is taken from the cervix to determine the presence of Cervical cancer, it leads to complications such as bleeding and infection and its laboratory results very often lead to false-negative or false-positive results. Therefore, there is a need to determine the exact location for the site of biopsy and develop a cost-effective and non-invasive screening strategy for the screening of cervical cancer. This would enable timely treatment so that surgical complications and mortality rates can be brought down. Information on the grade of malignancy can be obtained by spectral analysis of white light that is diffusely reflected by the cervical tissues. Diffuse reflection (DR) occurs due to the multiple elastic scattering of incident light due to the heterogeneity in the refractive index of the tissue components. During malignant transformation, the healthy tissue undergoes morphometric and cytologic changes, such as increase

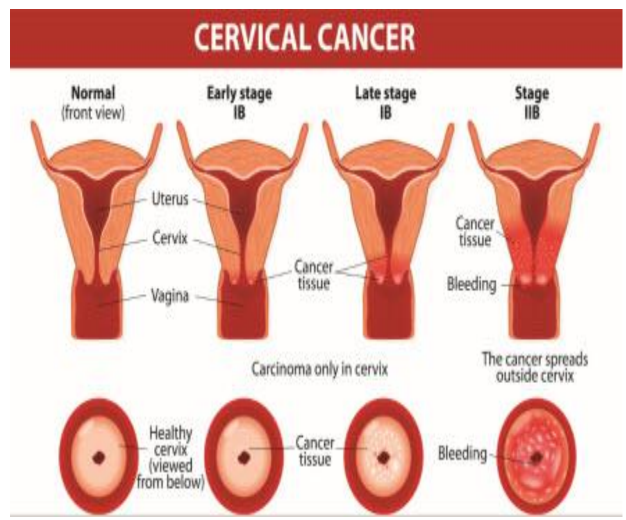


***Fig. 1.*** *Cervical Cancer stages and its bleeding symptoms Image Courtesy: [39]*

in epithelial thickness, nuclear size, nuclear to cytoplasmic ratio, changes in the chromatin texture and collagen content and angiogenesis. These along with changes in the absorption characteristics of oxygenated haemoglobin alter the diffusely reflected component of the incident light from cancerous cervical tissues. The presence of specular reflection and motion artifacts degrade the quality of DR images thereby leading to the false location of the site of biopsy and reducing the diagnostic accuracy of cervical cancer detection. In order to detect and locate the site of biopsy and accurately classify the suspected tissue into malignant or benign masses, image processing algorithms have to be developed for the image quality enhancement of the Cervical DR images. The algorithm developed need to be tested to evaluate the enhancement in diagnostic accuracies achieved in the detection and grading of cervical carcinoma.

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## 2 DETECTION TECHNIQUES

The challenge for the early detection of cervical cancer is to identify women who have the potential to progress to Cervical cancer and those who do not. This can be accomplished by the help of the screening and the diagnostic tests for cervical cancer such as:

1. **Pap test:** The outside of the cervix and vagina is scrapped for samples of the cells for testing.
2. **The Liquid-Based Cytology Test:** A thin layer of cells is transferred onto a slide after the removal blood or mucus from the sample. Because the sample is preserved, other tests, such as the HPV test can be conducted at the same time.
3. **Auto Pap:** It is the computerized scanning for the detection of abnormal cells in the cervix.
4. **Pelvic Examination:** Physical examination of a woman's uterus, vagina, ovaries, fallopian tubes, cervix, bladder and rectum is done for the detection of any unusual changes.
5. **HPV Typing:** HPV testing is done on sample of cells from the patient's cervix for the detection of HPV 16 and HPV 18.

Pap test and the HPV test together provide a diagnosis of Cervical cancer which is further verified by the following diagnostic tests:

1. **Colposcopy:** Colposcope gives a magnified view of the tissues of the vagina and the cervix.
2. **Visual inspection using acetic acid (VIA):** 3–5% solution of acetic acid is applied on the epithelial cells of the cervix. This leads to the appearance of acetowhite areas which are examined using a torch or halogen focus lamp [18].
3. **Visual inspection using Lugol's iodine (VILI):** Lugol's solution causes black or dark brown staining in the mature Squamous epithelial cells which aids in the inspection of the cervix [18].
4. **<u>Biopsy</u>:** Biopsy is done as a method of differential diagnosis. Biopsy performed can be a Colposcopic biopsy or a cone biopsy.

If biopsy indicates the presence Cervical cancer, additional tests are recommended to see if the cancer has spread beyond the cervix or not. These tests include the re-examination of the pelvic region, intravenous urography, CT scan, MRI, PET scan, Cystoscopy, Proctoscopy and Laparoscopy.

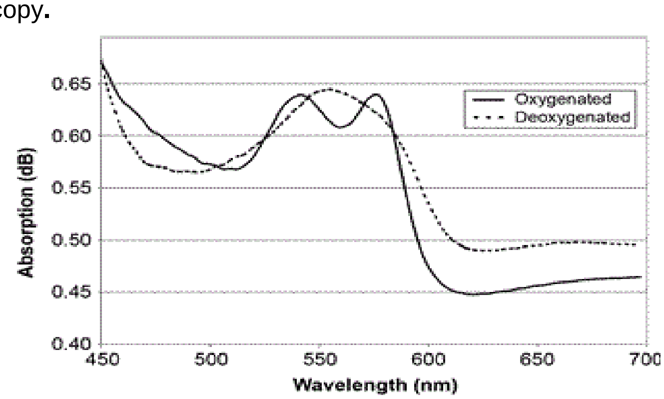


***Fig. 2.** Spectral Absorption Response of Oxygenated and Deoxygenated Hemoglobin. Image Courtesy: [41]*

Conventional techniques of Cervical cancer detection have significant limitations. Colposcopic image and VIA interpretation rely on the visual interpretation by the doctors [7], [11], and is subjective [20], [21], [22], [23]. Multiple visits and discomfort from biopsy prevent women from attending regular screening [19]. Most of the diagnostic tests are expensive and when performed, can lead to false-negative results. This causes a delay in seeking medical attention. These tests could also lead to false-positive results, which causes anxiety and increase the risks when follow-up tests are performed. Therefore an approach should be taken to reduce such errors and develop an effective and affordable screening strategy for the early detection of cervical carcinoma [17]. Optical Imaging provides spatial diagnostic information of the morphological and biochemical changes related to the progression of cancer in the tissue. The advances in image processing algorithms have given way to high quality optical imaging systems. Diagnostic image analysis tools have been established as methods to discriminate neoplastic cervical tissue from normal tissue. Multi-spectral DR imaging at the oxygenated haemoglobin absorption peaks has the potential to be used in cervical cancer screening as the amount of oxyhaemoglobin and deoxyhaemoglobin in cervical tissue vary due to the transformation of the tissue to its malignant state [12].

## 3 DIFFUSE REFLECTANCE SPECTROSCOPY (DRS)

### 3.1 Principle of DRS System

Diffuse reflectance spectroscopy (DRS) can be utilized to non-invasively quantify the optical properties of epithelial tissues from the absorption and multiple scattering of intense white light by the tissue constituents. The light reflected from the tissue, consists of specularly reflected and diffusely reflected components [13]. The angle of specular reflection of light is

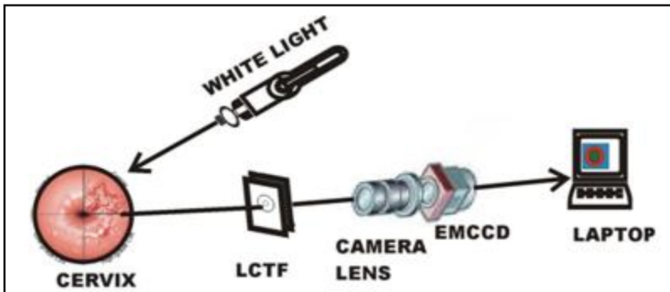


***Fig. 3.** Schematic DR imaging of the Cervix Image Courtesy: [25]*

equal to the angle of incident light rays [15], therefore the intensity of the specular component is always higher than that of the intensity of the light scattered and reflected from the tissue inhomogenieties. The diffusely reflected components contain information of the optical properties of scattering of the collagen fibers and the absorption of light by haemoglobin [14] which forms the important information for the location of the site of cervical biopsy thus leading to an early detection of cervical cancer. Decrease in hemoglobin concentration is noticed in cancer cells owing to the reduced production of the enzyme ferrochelatase involved in the biochemical transformation of

Protoporphyrin IX to heame. This lowers the concentration of oxy and deoxy heamoglobin in cancer tissues. With increasing dysplasia there is an enhancement in tissue vasculature leading to increased multiple elastic scattering, which reduces the intensity of the diffusely reflected light component. Less amount of light to propagates into the connective tissue which leads to decrease in scattering. This is associated with angiogenesis that is linked with some types of early cancers [13]. Subhash et al. observed that the DR ratio (R545/R575) of the oxygenated haemoglobin absorption dips at 545 and 575 nm which increases during tissue transformation towards malignancy. This characteristic feature of the cancer cells at the epithelium, which has been used to distinguish between different grades of oral cavity cancer, can be extended for detection and grading of cervical cancer lesions [12].

### 3.2 Types of DRS System

DRS system can be of two types i.e., the Point monitoring system and the Multi-spectral Diffuse Reflectance system. The Point monitoring system [24] based on fiber optic probes, is simple and efficient, but the probe tip on contact with cervix exerts a mild pressure during measurement which causes bleeding and obscures the information on tissue transformations from the light collected from the surface of the cervical tissue. Further, it is time consuming to screen an entire area of the cervix by point monitoring of DR light. Therefore Multispectral Diffuse Reflectance imaging is preferred as it can collect diffuse reflected light from an entire irradiated sample automatically in a fraction of a second in the preferred oxygenated haemoglobin absorption wavelengths.

## 4 Multi-spectral Diffuse Reflectance System

Subhash et al. [42] conducted a clinical trial at Regional Cancer Centre (RCC), Thiruvananthapuram after obtaining the ethical approval of the Human Ethic Committee of RCC (No. HEC No-28/ 2011). The study was afterwards registered in the Clinical Trial Registry of India (REF/ 2013/ 10/ 005904). The trial was carried out using Multi-spectral Diffuse Reflectance Imaging system (MDRIS) which consists of an electron multiplying charge coupled device (EMCCD) camera with a Nikon AF 35-70 zoom camera lens and a liquid crystal tunable filter (LCTF) of 7 nm bandwidth that can be tuned electronically to any wavelength in the 400-720 nm range [42]. The patient is made to lie in lithotomic position and a Cusco vaginal speculum is inserted with the help of a lubricating gel, for the effective visualization of the cervix. In order to avoid high chances of specular reflection, excess mucous is removed by the application of the saline-soaked cotton into the patient's vagina. The cervix region is then illuminated with white light from a tungsten halogen lamp (3V, 12W) and the DR images are recorded sequentially at 545 and 575 nm with the help of the LCTF control software [42].

## 5 Image Processing Techniques for the Detection of Location of the Site of Biopsy in Cervical DR Images

The LCTF is scanned sequentially to the oxygenated heamoglobin peaks at 545 and 575 nm while recording the DR images of the cervix with MDRIS. Specular reflection from the surface of the cervix, which gets enhanced due to vaginal secretions and motion artifacts associated with sequential recording of images must be removed to enhance the image quality and improve classification accuracies.

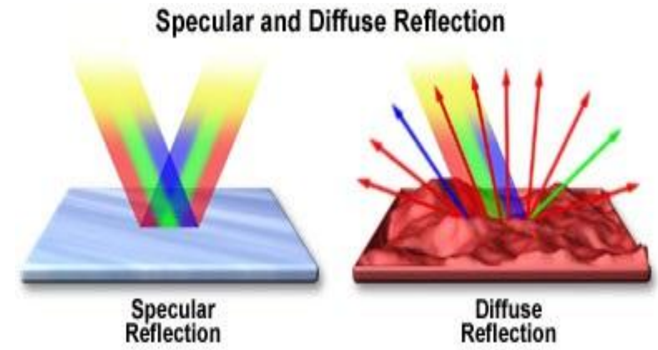


***Fig. 4.*** *Specular and Diffuse Reflection Image Courtesy: Reference [42]*

The various processes involved in algorithm developed are:

### 5.1 Segmentation of Cervical ROI image from the DR image

The cervical region of interest (ROI) in the recorded image involves only about half of the Diffuse Reflectance (DR) image. Other parts of the image contain irrelevant information, such as equipment parts, frames, and vaginal wall, which can confuse the automatic identification of the tissues within the cervix [16]. This creates a need for the segmentation of Cervical ROI from the DR images. According to Abhishek et al. [16], a Colposcopic image contains many visible features that can distinguish normal tissue from cancerous tissue. These images are in RGB format thereby making it easier for segmentation by the method of K-mean Clustering. Cervical ROI can also be segmented by taking into consideration that the region around the cervix is the speculum which is surrounded by the vaginal walls, but these factors cannot be determined in a monochrome DR image of the cervix.

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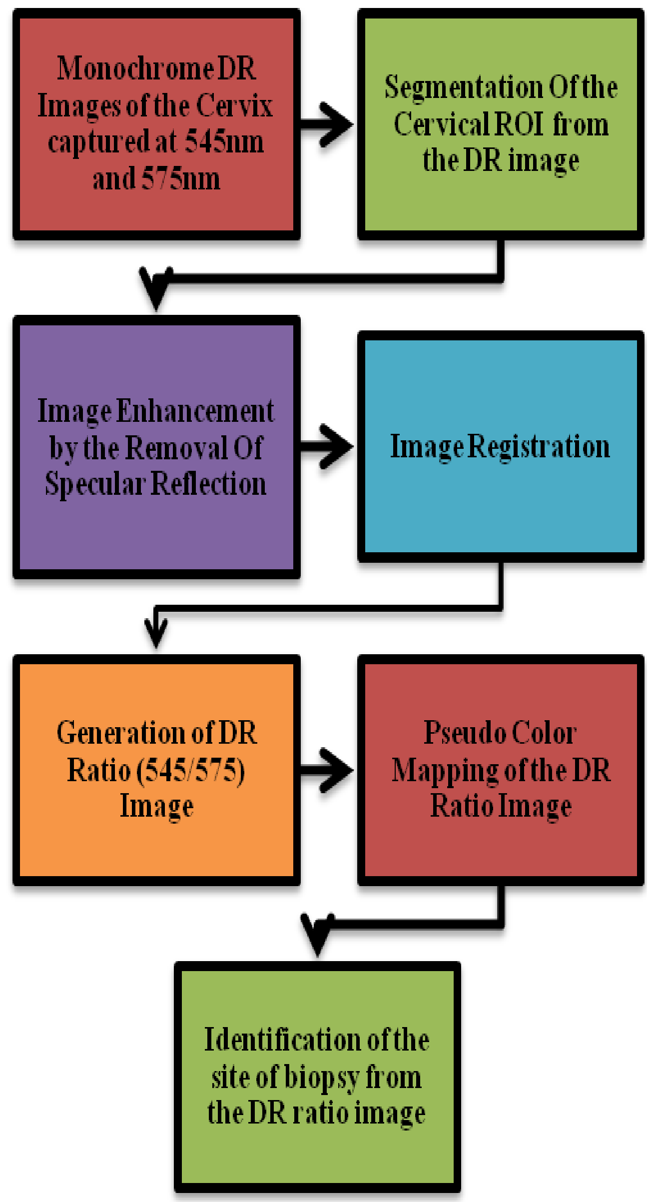


***Fig. 5.*** *Methodology of the Image Processing Techniques for the detection of Cervical cancer from the DR images.*

Histogram Thresholding [43] is one of the most widely used techniques for the segmentation of ROI in monochrome images [44]. The highest number of pixels containing a particular intensity can be selected. This intensity value provides information of the region of cervical ROI in the DR image. Otsu method of thresholding is also used for the segmentation of monochrome images [43]. Iris images of the eyes are monochrome in nature. The segmentation of the Iris ROI from the eye images are done by Hough transform [45] by considering the circular nature of the pupil and the iris. A binary image is generated based on the circularity detection of the iris. Holes in the binary image are removed by the application of Morphological flood-filling operation. The binary image is then used for the segmentation of Iris ROI from the eye images. Since the cervix is opened up by the cylindrical speculum, which makes the cervix in the DR image appear circular, this feature can also be used for the segmentation of the Cervical ROI from the DR image.

### 5.2 Specular Reflection Removal

Specular reflections (SR) in Cervical DR images occur due to the presence of moisture on the cervix surface. These reflections act like mirrors reflecting the light from the illumination source. They lead to the appearance of bright regions in the acquired images and are undesirable and lead to erroneous results during segmentation [15]. According to Abhishek et al. [16], the Colposcopic images are separated into Red, Green and Blue Planes. The specular reflections are selected from each of the planes and are eliminated by logically AND-ing them. A morphological method of dilation is also used which is then followed by a Filling algorithm to smoothly interpolate inwards the region of specular reflections with the information of the pixels on the boundary of the region containing specular reflections. This can be done by solving the Laplace's equation.

$$\Delta y = 0 \qquad (1)$$

where $\Delta$ is the *Laplace operator.*

According to McConnon et al. [33], specular reflections detected by Intensity Thresholding are removed by the morphological operations of dilation and closure. Danbing Jai et al. [29] suggested a method to detect specular reflections by converting the RGB image to HSI color model as the pixels in the HSI model have greater illumination and less saturation values.

$$I = (R + G + B)/3 \qquad (2)$$

$$S = 1 - (3(R + G + B)) * a \qquad (3)$$

where a is the minimum of R, G and B

$$H = \{\theta, G > B \text{ and } 2\pi - \theta, G \leq B\} \qquad (4)$$

$$\theta = cos\text{^}(-1)\{(1/2[(R-G)(R-B)])/\sqrt{((((R-G)\text{^}2 + (R-B)(G-B))))}\} \qquad (5)$$

A minimum and a maximum threshold levels are selected for the detection of specular reflections. The surrounding pixels affected by the reflections are included for removal by using the morphological operation of dilation. The specular reflections are removed by using TV based inpainting methods which is solved using the FISTA algorithm. Fabiane et al. [28], proposed a method of SR removal based on Sparse and Low Rank decomposition where the input image is divided into the three color planes, R, G and B and the RPCA decomposition algorithm is applied to each of the color channel images such that

$$D_r = A_r + E_r \qquad (6)$$

$$Dg = Ag + Eg \qquad (7)$$

$$D_b = A_b + E_b \qquad (8)$$

The error images $E_r$, $E_g$ and $E_b$ of endoscopic images contain the information of the pixels containing specular reflection and

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some very low values of pixels intensities which are then eliminated by calculating their standard deviations $\square_r$, $\square_g$ and $\square_b$ and converting to zero all pixel values, which are smaller than these standard deviations. Finally, the low-rank components $A_r$, $A_g$, and $A_b$ are reformulated and combined to get an endoscopic image free from specular reflections. According to Othmane et al. [46], specular reflections are removed by first enhancing, denoising the histogram of the image and finding the last bump in the denoised histogram. This is done to determine the different areas that correspond to specular reflections. The Specular reflections are then removed by erosion and diffusion processes. Stéphane et al. proposed that specular reflections are detected better by taking the Bilinear Histogram of the image in order to generate a specular mask. The specular mask and input image are then used for the elimination of the specular reflections by using Naiver Stokes algorithm of image inpainting [32].

### 5.3 Image Registration

Image registration is the process of overlaying two or more images of the same object taken at different time intervals from different fields of view [48], [49]. One of the most challenging aspects is the proper registration of the two images before image division. As the Cervical DR images are captured at different angles, directing dividing one image by the other, results in false ratio values in the DR ratio image, which will lead to the false indication of the location of the site of cervical biopsy [50]. García-Arteaga J. D. et al. [51], proposed an algorithm which is called as an optimization over a set of continuous deformation vector fields. It is formulated as a minimization of a criterion J with respect to a vector field $h$ representing a 2D geometrical transformation.

$$h^* = \arg\min_{h^*}\left(J(f,g,h)\right) \tag{9}$$

$$J(f,g,h) = J_D(f,g,h) + \alpha J_R(h) \tag{10}$$

where $h^*$ is the optimal solution and $f$ and $g$ are the images to be registered, $J_D$ is a cost function measuring the dissimilarity between the images, $J_R$ is a regularization term and $\alpha$ is a proportionality constant determining how much of regularization will be used. Darío Ramírez-Garcés et al. [48], proposed two complementary ways to perform image registration process. The first one is a 'global registration' and the second one is a 'local registration', which are complementary to each other. The global registration is applied with the aim of improving noise arising due to the movement during the capture of the image sequence. The local registration is then applied to further improve the quality of the registration process. H. Lange et al. [52] proposed a method of image registration by using the information of reflectance and fluorescence of tissue. This method requires a specific instrument called Hyper Spectral Diagnostic Imaging and does not work if reflections are present in the images. Othmane et al. [46] proposed a robust registration method which takes into account the specular reflections. It does not need any specific instrument for image registration. The image registration method is based on opponentSIFT descriptor. This descriptor worked perfectly for Colposcopic image registration as it is invariant to changes in illumination, image noise, rotation, scaling, and small changes in viewpoint [46], [47].

### 5.4 Generation of DR ratio(545/575) image

Image division, also called ratioing, is a technique used for the detection of changes between two images of the same object of interest. It gives the ratio between corresponding pixel values of image A and image B. The two Cervical DR images captured at 545nm and 575nm are divided pixel by pixel to generate a Cervical DR ratio (545/575) image. Division of images introduces noise in the regions where the intensity in the either image is too low to be use. Various masking operations are used to counter the noise added to the images. The simplest masking method is to set areas outside the ROI to zero by manually drawing an outline of the ROI. Alternately, masking can be done based on the exclusion of pixels below a user specified minimum intensity level. After proper shading correction and background subtraction, the intensity versus pixel number histogram will show a large distinct peak for low intensity pixels and a spread of high intensity pixels that comprise the ROI image. Floating point errors must be considered during the final division that produces the ratio image [50].

### 5.5 Pseudo-color Mapping and Location of the Biopsy Site on the Cervix

The pseudo-color display of the ratio image is scaled to emphasize and study certain intensity ranges which helps in bringing out different features in the image. A monochrome image without its pseudo-color scale complicates medical analysis as it is difficult to differentiate different features of the monochrome ROI image [50]. According to Li Buhong et al. [31], fluorescence image of lung cancer is converted to color image by pseudo-color mapping, which highly enhanced the discrimination of lung cancer. It is important to preserve the relative intensity information between different regions of the medical images. Hence applying schemes to color map them may result in loss of diagnostically useful information. In order to preserve the relative intensity between regions of the monochrome or ratio image, a pseudo-color scheme is used. In pseudo-color mapping, each of the gray levels is matched to a point in the color space. F(x, y) is the input gray value of the monochrome image. $T_R(.)$, $T_G(.)$, and $T_B(.)$ are the transformation functions of the three primary colors and their gray value.

$$R(x,y) = T_R\{[f(x,y)]\} \tag{11}$$

$$G(x,y) = T_G\{[f(x,y)]\} \tag{12}$$

$$B(x,y) = T_B\{[f(x,y)]\} \tag{13}$$

The intensity of the three primary colors at coordinates (x, y) of an image will be denoted by R (x, y), G (x, y) and B (x, y) respectively. Thus, each pixel in a color image will be considered as an additive combination of these three-intensity values at the coordinates of the pixel. The transformation functions are described as below [31].

$$T_R = \begin{cases} 0, & (0 < x < 128) \\ 4x - 512, & (128 < x < 192) \\ 255, & (192 < x < 256) \end{cases} \tag{14}$$

$$T_G = \begin{cases} 4x, & (0 < x < 64) \\ 255, & (64 < x < 192) \\ 1024 - 4x, & (192 < x < 256) \end{cases} \tag{15}$$

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$$T_B = \begin{cases} 4x, & (0 < x < 64) \\ 512 - 4x, & (64 < x < 128) \\ 0, & (128 < x < 256) \end{cases} \quad (16)$$

This technique can also be applied to other fluorescence or ratio images for the detection and localization of human diseased tissue sites in situ. The pseudo colored mapped ratio image facilitates easy identification of the most malignant site in the lesion for biopsy. Tissue biopsy can be taken from the identified site which will then be sent for histopathological examination [42].

## FUTURE SCOPE

Although LCTF has the inherent property of transmitting light of a single polarization, it is not able to completely filter out specular reflection from the tissues illuminated with white light. Polarizers can be added both on the transmitting and the receiving section of the LCTF to minimize specular reflections. Bright areas on the Cervical DR images, caused by light reflection from the moisture present on cervical tissue surface can be reduced by new innovative image processing algorithms, thereby increasing diagnostic accuracies for the early detection of Cervical cancer. Results of the histopathological testing of the biopsied cervical tissue can be used to create a scatter plot to check the accuracy of the location of the site of cervical tissue biopsy and in turn classify these results into different stages of Cervical cancer. Further studies should be planned to test the MDRIS on a larger population with a view to refine this modality for non-invasive detection of cervical malignancies during its early stages.

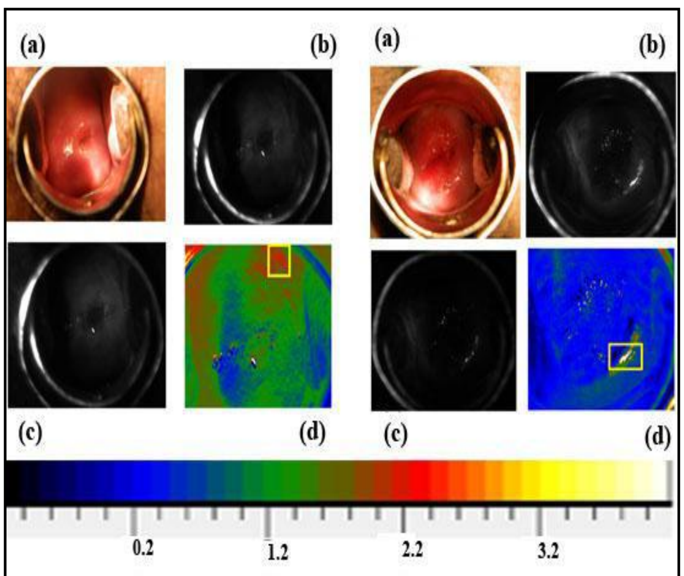


***Fig. 6.*** *Images for a typical low-grade (left) and high-grade (right) cervical intraepithelial neoplasia; (a) digital color photo,( b) monochrome image at 545nm, (c) monochrome image at 575nm, (d) zoomed ratio image showing biopsy site in a rectangular box. The color palette shows the range of median pixel intensity values for tissue discrimination [42].*

## CONCLUSION

Quantitative detection of cervical intraepithelial lesions of the cervix without the need for tissue removal is of great clinical significance and leads to less mental stress and the reduction in the number of biopsies on the female patients. MDRIS establishes the potential of DR imaging at the oxygenated hemoglobin absorption peaks and utilizes the DR image ratio of R545/R575 for the screening and the identification of the most malignant site in the cervix for tissue biopsy and pathology. This use of DR imaging as a screening method can lessen healthcare costs by facilitating detection of cervical cancer during its early stages and also reduce the number of patients lost during the follow up tests.

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