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Research Article

# Linked Color Imaging Increases the Color Difference Between Normal Mucosa and Colorectal Polyps

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## 2. Key words

Linked color imaging; Color difference; Color contrast; Adenoma detection rate; Polyp detection; Colorectal polyp; Colon adenoma

## 1. Abstract

**1.1. Introduction:** HD-White Light Endoscopy (WLE) is the gold standard in the detection of colon adenoma. Recently, Linked Color Imaging (LCI) was developed which combines special light and computational post processing in one imaging modality. First study results show improved visibility and a higher adenoma detection rate using LCI compared to WLE.

**1.2. Aim:** Evaluation of color difference between colon adenoma and the surrounding mucosa in WLE, BLI and LCI as a potential explanation for differences in the adenoma detection rate.

**1.3. Methods:** Prospective acquisition of images of colon polyps in the three light modes WLE, Blue Light Imaging (BLI) and LCI.

Transformation of the images into L*a*b* color space. Measurement of color values of polyps and the surrounding mucosa. Calculation of the color difference (Delta-E) between both areas.

We used paired t-test for statistical analysis.

**1.4. Results:** In total, 267 images of 89 polyps were evaluated. Delta-E in WLE was lowest (12.34± 6.73). The highest Delta-E value was calculated for LCI (16.83 ± 10.85). The Delta-E using BLI was 14.38 ± 11.42. The difference between LCI vs BLI and BLI vs WLE was not statistically significant. The difference between WLE and LCI was highly significant (p=0.002).

**1.5. Conclusion:** Only linked color imaging leads to a significant increase of the color contrast of colon adenoma. This is a feasible explanation for the reported increased adenoma detection rate using LCI.

## 3. Introduction

White Light Endoscopy (WLE) remains the gold standard in gastrointestinal endoscopy for the detection of colorectal polyps [1]. However, still adenoma is missed in about 1 of 5 cases even during careful examinations [2]. Numerous technologies such as chromoendoscopy and Virtual Chromoendoscopy (VCE) have been developed to overcome these problems. VCE either consists of filtered light using only light of certain wave lengths or it consists of post- processing of the images that have been captured with standard white light. A combination of both technologies has not been established before.

The most commonly used VCE method is Narrow Band Imaging (NBI). NBI is highly effective in the characterization of polyps [3]. But there is no clear evidence that the use of NBI leads to an increase of the adenoma detection rate or decrease of the adenoma miss rate [1]. Therefore, WLE is still recommended as general standard for polyp detection.

A naturally occurring limitation to WLE in the gastrointestinal tract is the narrowed color space of the mucosa that is the result of the spectral wavelength of human mucosa that is mostly composed of different red tones. Thus, the detection and differentiation of relevant mucosal findings on the basis of color tones is limited.

Upcoming technologies in the field of endoscopy such as Linked Color Imaging (LCI) have been developed to overcome this limitation.

LCI uses special light with emphasis on the absorption max-

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-imum of hemoglobin in combination with a post processing tool, which reallocates colors in the color space. Therefore, LCI widens the spectrum of colors used in an endoscopic image. In theory, increasing the width of a color space should lead to an increased color contrast. Mathematically, color contrast can be expressed as the distance of two-color values in a color space. However, color values cannot be expressed in a linear relation easily. Most of the color spaces that are used in modern computing systems have a non-linear linkage of color values and brightness values and the difference of colors are therefore different to express.

A commonly used method to calculate color differences is to convert the colors of an image into the so-called L*a*b* color space (EN ISO 11664-4) in which the difference between two colors includes the physiological difference in color recognition. In this color space the color difference can be expressed as the three-dimensional distance between two points in the color space.

Studies have already evaluated this method and have shown that LCI increases color difference [4]. These studies have all been performed using a laser based light source. LED based light source equipped with LCI has not been studied yet.

The aim of our study is to evaluate the change in color contrast of colon polyps compared to the adjacent mucosa using WLE, BLI and LCI with the LED based light source and contemporary processor software.

## 4. Methods

We prospectively acquired images of colon polyps during standard colonoscopies. Patients with known chronic inflammatory bowel disease were excluded. Only cases with comparable high-quality images of the same polyps in WLE, LCI and BLI after irrigation with water were included in the analysis.

All investigations were performed using the ELUXEO® System and 700 Series endoscopes (EC-700ZP/L or EC-700R/L Fujifilm Europe, Germany). Images were stored on the internal hard drive of the processor in tagged image format. All patients provided written informed consent before colonoscopy. The local ethics committee approved the study (Number 152/17). The study adheres to the 2nd revision of the Helsinki declaration and is in concordance with the European law of data protection.

### 4.1. Calculation of Color Difference

To calculate the difference of color values between polyp and adjacent mucosa on each polyp we captured three types of images, LCI, BLI and WLI mode of each polyp (Figure 1). Afterwards images were transformed from Adobe RGB color space into the L*a*b* color space using an image processing software (Adobe Photoshop CS3, Adobe, San José, CA, USA)

The calculation of color difference was performed with the same software. To measure the color values, an endoscopist (JW) placed two measurement points corresponding to a respective 31 x 31-pixel matrix each in the lesion and surrounding mucosa. Dark areas and reflection highlights were spared out. This process was repeated for each of the three images of one polyp (Figure 1). The color difference (Delta-E) was calculated as the Euclidean distance of the colors in the Lab color space using the following formula.

$$Delta\text{-}E_{p,v}{}^2 = (L^*_p - L^*_v)^2 + (a^*_p - a^*_v)^2 + (b^*_p - b^*_v)^2$$

*For color differences between the two colors* $(L^*a^*b^*)_p$ *and* $(L^*a^*b^*)_v$

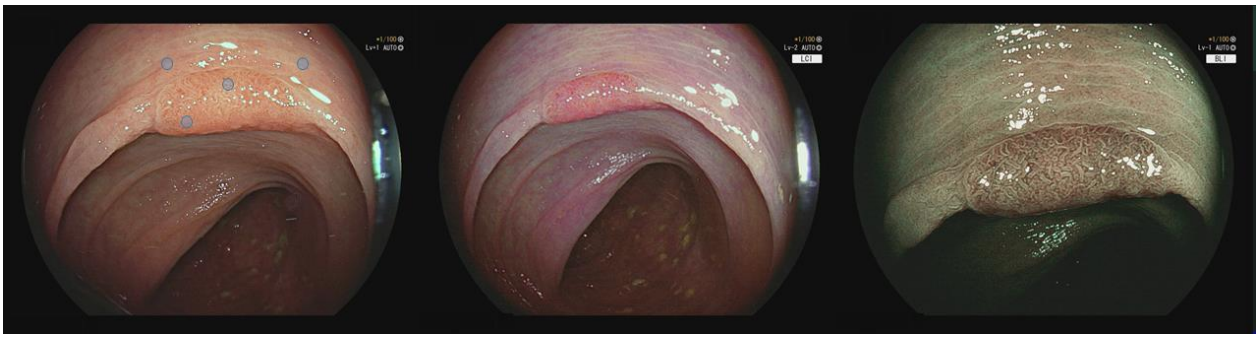

**Figure 1:** Corresponding images of the same flat adenoma with WLE and LCI, BLI (from left to right). Measurement of two points, covering the surface area of the lesion and the surrounding mucosa, for each color mode. Here expressed only in the image.

### 4.2. Data Analysis and Statistics

Sample size was calculated for Delta-E values for WLE of 12 ± 6 and an increase using BLI or LCI of > 4. Assuming an alpha value of 0.5 and a power of 0.8 a sample size of > 70 polyps was calculated.

Delta E values were compared using paired one-sided t-test. A p-value of <0.05 was considered to represent significance levels.

## 5. Results

In total, 267 images of 89 polyps were analyzed as image triplets.

The median size of polyps was 7 mm, ranging from 2 mm to 40 mm.

Eleven polyps were classified as NICE I, 68 polyps were classified as NICE II and 6 polyps were classified as NICE III. Overall, 4 polyps were correctly classified as Sessile Serrated Adenoma (SSAp).

The Delta-E value between polyp and surrounding mucosa with WLE was lowest with 12.34 ± 6.73. Values were highest for LCI (16.83 ± 10.85). BLI showed Delta-E values of 14.38 ± 11.42. There was no statistically significant difference between the Delta-E values for LCI and BLI (p = 0.064). This was also the case for the comparison between BLI and WLE (p = 0.12). The Delta-E using LCI was significantly higher compared with WLE (p = 0.002). Main results are illustrated in (Figure 2).

For the 4 SSAp, Delta-E values in BLI mode were higher compared to average BLI values and showed no differences in the other light modes. Due to small numbers no, statistical test was performed. Delta-E values in SSAp were 12.65 ± 8.19 for WLE, 18.50 ± 11.73 for LCI and 12.71 ± 9.10 for BLI.

Even excluding SSAp from the overall analysis including all polyps, did not change the results significantly (WLE: 11.09 ± 6.18; LCI: 15.27 ± 11.29; BLI: 13.84 ± 11.95).

In 6 polyps, Delta-E was notable higher in BLI compared to LCI. In a sub analysis we found that in 5 of these cases the polyp was larger than 10 mm and presented with a high vascular pattern intensity.

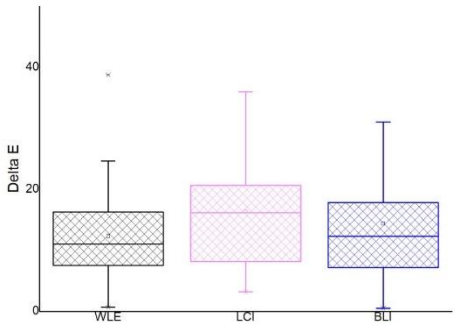


**Figure 2:** Main results demonstrating a significant higher Delta E in LCI images. WLE and BLI show similar results.

## 6. Discussion

Our study is the first using the LED based light source equipped with LCI in a prospective European cohort and is in concordance with the results of Yoshida et al. [4] that demonstrates the superiority of LCI when compared with WLE and BLI in terms of increasing the color contrast.

Although the different technologies used in both studies show similarities, the outcome may not be predicted and transferred from one technology to the other.

The overall values of color difference from normal mucosa and polyps were notable lower in the study performed by Yoshida et al. This can be attributed to the general color values produced by the endoscopy system. All available studies have been performed using a laser-based system, which does not use LED light and therefore uses a slightly different but obviously notable color range. In addition to that, the endoscopes used in the study by Yoshida were equipped with a CCD sensor. The endoscopes used in our study were equipped with a CMOS sensor and thus images include less noise and speckles compared to CCD derived images which has an impact on color range measurements. In an abstract presented on UEGW 2019 [5] the overall Delta E Values were reported to be around a value of 8 in under-water conditions, showing a significant variability in general. Therefore, in future studies the systems should be comparable and in addition the settings and image processing procedures should be equal in comparative and especially multicenter trials on this topic.

Yoshida et al. investigated the visibility of polyps and showed a significant increase of polyp visibility with LCI but not with BLI [4]. Another study prospectively investigated in 101 adenoma and showed an increased visibility [6]. Both studies used an investigator dependent visibility score. Min et al. [7] proved an increase in polyp detection and adenoma detection rate with LCI in a cross-over study. An increased detection by using LCI was also found in a study investigating sessile serrated adenoma [8]. A reduction in adenoma miss rate using LCI was shown in a study that supports these data strongly [9]. All these data are in accordance with our thesis that LCI is superior to WLE in detecting colorectal polyps.

Many endoscopic studies use different and therefore hard to compare endoscopy units with obvious differences in image quality, while image quality still is a fundamental factor influencing the adenoma detection rate. Thus the overall data quality regarding comparability of image quality is suboptimal.

A certain strength of our study is the use of a single endoscopic unit with stable settings that enables the best comparability of imaging data and may overcome the above described weakness.

One might argue that these data are different to transfer to clinical use but another study by Yoshida could clearly show the advance of LCI towards WLE and investigated the yield of only 30 seconds extra inspection with LCI in a cross over design to WLE [10]. In this study only in the LCI group and not in the white light group an increase in ADR was found. In summary the increased ADR was not attributed to the second look effect but to LCI use. Non granular flat lesions in the colon also seem to be detected better with LCI compared to white light endoscopy [11].

Also, studies that repost an advantage of NBI over LCI in the detection of colon adenoma have recently published [12]. These data need to be interpreted with caution as in metanalysis NBI has not shown to be superior to WLE and therefor has never been advocated as a tool for polyp detection.

The main limitation of our study is the fact that the results can only interpret the results as an explanation for reported polyp detection rate but cannot prove this relationship. The best way to identify a causal relationship is a crossover tandem study that investigates on the color difference of polyp's hat have additionally been found

with LCI and were overseen in WLE. With our data we justify the conduction of such a study.

In summary our study can bring up a potential explanation for the increased detection rate using LCI. In our study BLI, as in many studies before NBI could not increase ADR which is in accordance with our data that do not show an increase in color difference between a polyp and surrounding mucosa in BLI.

These results point out the crucial role of color difference for the ability to detect a lesion beside other features like size, and shape, which can be assumed to be comparable in images of the same polyp that use different light modes.

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