

## Endoscopic classification of the capillary-vessel pattern of colorectal lesions by spectral estimation technology and magnifying zoom imaging

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**Background:** Colonoscopy with spectral estimation technology and magnifying zoom imaging allows the characterization of the fine superficial capillary pattern of normal mucosa and of colorectal lesions. The endoscopic distinction of the capillary pattern of colorectal lesions might contribute to the differential diagnosis among normal, hyperplastic, and neoplastic lesions.

**Objective:** By means of these latest technologic advances, the objective is to define a classification of the capillary-vessel pattern of colorectal lesions diagnosed during routine colonoscopy.

**Design:** A total of 309 colorectal lesions endoscopically or surgically resected were prospectively examined. The capillary pattern was divided into 5 subtypes according to the number, morphology, and distribution of the fine blood vessels. Capillary patterns types I and II were characterized by a few short, straight, and sparsely distributed vessels; types III to V were of numerous, elongated, and tortuous capillaries irregularly distributed.

**Results:** The overall accuracy of the capillary-vessel classification in determining the neoplastic or non-neoplastic nature of the colorectal lesions was 98.3% (304/309 lesions). Among 59 non-neoplastic lesions, 56 (94.9%) that showed patterns I or II were diagnosed as normal, inflammatory, or hyperplastic polyps. Of the 250 neoplastic lesions, 248 (99.2%) that had capillary pattern types III, IV, and V were diagnosed as adenomatous or carcinoma. The sensitivity of the capillary pattern classification for distinguishing neoplasia was 99.2% (95% CI, 98.2%-100%), and the specificity was 94.9% (95% CI, 92.5%-97.4%).

**Limitation:** A single-center study.

**Conclusion:** The endoscopic classification of the superficial capillary-vessel pattern of colorectal lesions is an accurate method of predicting the histopathologic findings.

The dramatic improvement on the resolution of the endoscopic image determined a greater detection rate of mucosal abnormalities. It also renewed the endoscopic challenge to differentiate among normal mucosa, inflam-

*Abbreviations:* B, blue; FICE, Fuji Intelligent Color Enhancement System; G, green; LST, lateral spreading tumor; NBI, narrow-band imaging; R, red; SET, spectral estimation technology.

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matory conditions, and hyperplastic lesions, and the subtle, flat, or depressed colorectal neoplastic lesions.<sup>1-3</sup> Chromoendoscopy improves the detection and characterization of colonic neoplastic lesions; however it is considered to be time consuming by most endoscopists.<sup>3-5</sup> On magnifying colonoscopy, it is possible to observe the morphology of the pit, the luminal openings of the mucosal crypts.<sup>6</sup> Image magnification is being used to differentiate neoplastic from non-neoplastic lesions and to predict the depth of neoplastic invasion with great accuracy by following a well-established and accepted pit pattern classification of colorectal lesions.<sup>4-10</sup> However, we believe that there still is room for improvement of these endoscopic techniques to obtain better image detail, reduce procedure time, and simplify endoscopic classification systems.<sup>8-10</sup>

Spectral estimation technology (SET) is a new endoscopic method that takes an ordinary digital endoscopic image from the video processor and arithmetically processes, estimates, and produces an image of a predetermined wavelength of red (R), green (G), and blue (B) signaling. Small vessels are very clearly contrasted as are the subepithelial capillaries and the microarchitecture (crests and pits) of the normal epithelium, which obviates the need for dye staining.

In the present article, we describe the utility of SET and magnifying zoom imaging in predicting the histologic features of colorectal lesions and suggest a classification of the superficial capillary-vessel pattern of colorectal lesions.

## PATIENTS AND METHODS

From July 2006 to October 2007, with a magnifying colonoscope (EC-490/590 ZW5; Fujinon Fujifilm Corporation, Saitama, Japan) attached to a processor (4400 Processor; Fujinon), we performed total colonoscopy in 166 patients (110 women; 33-88 years old, mean [SD] age  $61.53 \pm 11.21$  years), and a total of 309 colorectal lesions consecutively and prospectively diagnosed were included in the study. The study enrolled consecutive patients clinically suspected of a colorectal condition because of presenting symptoms or referral by another health care professional. Patients with inflammatory bowel disease ( $n = 15$ ) and familial adenomatous polyposis ( $n = 1$ ), as well as cases with insufficient tissue specimens ( $n = 2$ ), were excluded from the study. Written informed consent was given by all patients before the colonoscopic examination.

Macroscopic classification of the colorectal lesions was followed as defined by the Paris Consensus<sup>11</sup> as polyp, superficially flat or depressed lesion, and lateral spreading tumor (LST). The advanced cancers underwent surgical resection; all the other lesions were endoscopically resected and examined by a single pathologist blinded to the endoscopic findings. Lesions were stored in small flasks that contained 10% formalin. In the case of multiple lesions, each lesion was identified and placed into a separate flask. The methodology of the study was approved by an independent ethical committee.

Recognition of the capillary pattern of the colorectal lesions was undertaken with the Fuji Intelligent Color Enhancement System (FICE) (Fujifilm Corporation), a digital system that uses SET. Briefly, the image captured by the charge-coupled device of the colonoscope is sent to the spectral estimation matrix processing circuit in the processor unit, where various pixelated spectra of the image are separated. Because the spectra by pixels are known, it is possible to implement imaging on a single wavelength for each R, G, and B of the digital signal. Such single wavelength images are randomly selected and assigned to the

### Capsule Summary

#### What is already known on this topic

- Colonoscopy with spectral estimation technology and magnifying zoom imaging allows the differentiation of the fine superficial capillary pattern of both normal mucosa and colorectal lesions.

#### What this study adds to our knowledge

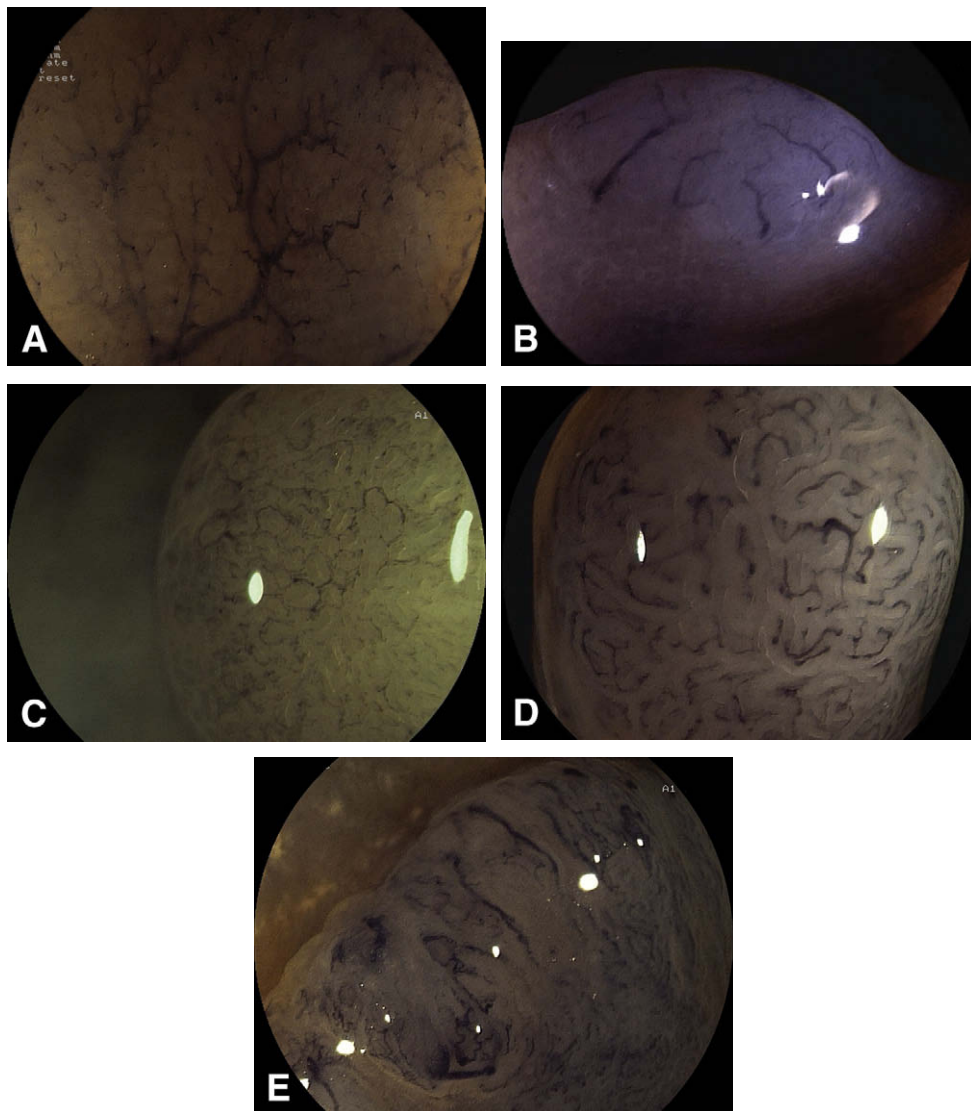
- A proposed endoscopic classification of the superficial capillary pattern of colorectal lesions achieved an overall accuracy of 98%.

RGB signal to build and display an enhanced digital color image. In this system, 10 different combinations of RGB signaling are available.

All colonoscopies were performed by 2 experienced endoscopists (C.R.T. and R.S.T.), both having performed more than 20,000 examinations to date. Histopathologic examinations were performed by an experienced pathologist (E.B.T.), who has performed more than 20,000 histologic examinations of colorectal lesions by following the guidelines of the World Health Organization classification of colorectal tumors.<sup>12</sup> Our study followed, as strictly as possible, the Standards for Reporting of Diagnostic Accuracy statement to improve the quality of reporting of studies of diagnostic accuracy.<sup>13</sup>

The present classification system of the capillary pattern was based on our previous experimental and clinical observational studies.<sup>14,15</sup> Evidence from experimental observations showed that colorectal neoplastic lesions present a typical vascular architecture, so called tumor-type specific angiogenesis phenotype.<sup>15,16</sup> Our initial observations with multiple FICE settings led the examiners to characterize the neoplastic and non-neoplastic capillary-vessel patterns of colorectal lesions and to choose FICE setting no. 4, which determines the wavelengths for R 500 nm, G 520 nm, and B 405 nm, as the one providing the best imaging of the capillary vessels. No other FICE setting was used in our classification. The size of the lesions was estimated at the time of colonoscopy under standard magnification with the help of an opened standard biopsy forceps (7 mm), which served as the parameter for small lesions. Lesions resected by EMR and surgery were measured with a ruler.

Besides FICE, the capillary pattern of all colorectal lesions was determined with the assistance of zoom technology. Optical zoom magnification is essential for a detailed evaluation of the capillary-vessel morphology. The magnification used for a qualitative diagnosis of the capillary-vessel pattern ranged from  $\times 30$  to  $\times 100$ . The determinations of the capillary-vessel pattern were all made in real time and before the histopathologic

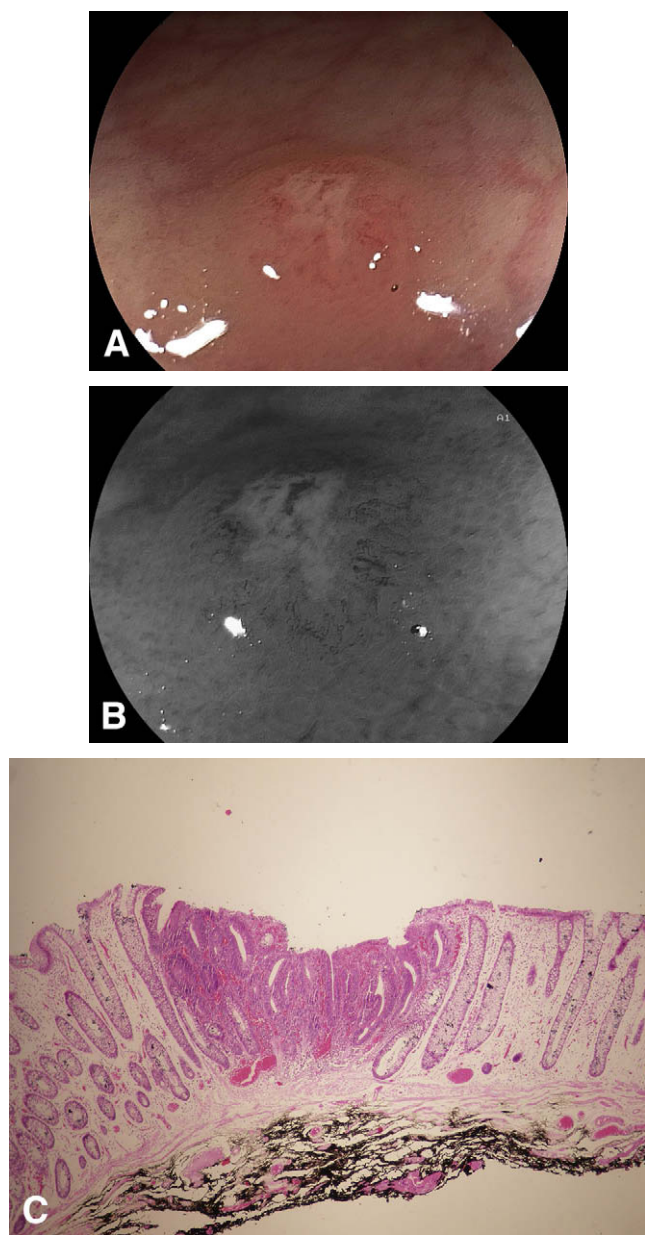


**Figure 1.** Endoscopic capillary-vessel pattern classification. The characterization of vessels was defined in relation to the morphology and arrangement of the normal vascular pattern of the colorectal epithelium. **A**, Type I: normal pattern composed of thin subepithelial capillary vessels with a linear shape and regular arrangement surrounding the mucosal crypts. **B**, Type II: this pattern exhibits hypovascularity or marginal capillaries of a thicker diameter, curved or straight but uniform, without dilatations, and the pericryptal arrangement is not remarkable. **C**, Type III: numerous capillaries of thinner diameter, irregular and tortuous, with frequent point dilatations, and tapering like a spiral shape, showing remarkable periglandular arrangement. **D**, Type IV: numerous long, spiral, or straight blood vessels with a thicker diameter, and sparse dilatations, running upright, surrounding the villous glands. **E**, Type V: pleomorphism of capillaries and abnormal distribution and arrangement; numerous heterogeneous thick vessels with chaotic arrangement are the predominant feature.

report. In the vast majority of our cases, less than 30 seconds was the average time spent to determine the capillary pattern. The tip of the colonoscope should be placed very close to the lesion, and, in case of excessive bowel movement and difficult focusing, the use of a biopsy forceps gently grasping the contiguous mucosa helped in holding onto the lesion for a clear detailed zoom examination of the superficial structures, which saved time during the procedure. The capillary pattern was grouped into 5 subtypes according to the number, morphology, and arrangement of the fine epithelial blood vessels (Fig. 1).

## RESULTS

The size of the 309 colorectal lesions ranged from 1 to 50 mm. There were 242 lesions (78.3%) that were 1 to 5 mm in diameter, 49 lesions (15.8%) were between 6 and 20 mm, and 18 lesions (5.8%) were larger than 20 mm in diameter. The median size was 5 mm (25% lower quartile = 4 mm; 75% upper quartile = 5 mm), and the average (SD) size was  $7.7 \pm 9.6$  mm. According to the Paris Consensus<sup>11</sup> on the macroscopic classification of colorectal lesions, there were 270 polyps, 5 flat lesions (IIa), 7 depressed lesions (IIc), 3 mixed-type IIa + IIc, and 9 LST.



**Figure 2.** **A**, A depressed-lesion type IIc located at the rectum and 3 mm in diameter. Its surface is covered by thick whitish mucus, which prevents the observation of the pit pattern. **B**, However, with SET and magnifying zoom imaging, the capillary-pattern type III could be readily identified, which indicated that the lesion was neoplastic in nature. **C**, EMR was performed and a minute adenocarcinoma in situ was revealed by histopathologic examination (H&E, orig. mag.,  $\times 40$ ).

The other lesions were 12 advanced colorectal tumors, 2 postpolypectomy scars, and 1 mucosal erosion.

The 6 lesions with type I capillary pattern were diagnosed as 3 cases of edema of the mucosa, 2 cases of regenerative fibrous tissue, and 1 inflammatory infiltrate. Among 52 lesions with type II capillary pattern, 50 (96.1%) were diagnosed as hyperplastic polyps and 2 (3.8%) were adenomas with low-grade dysplasia.

At histologic examination of 224 lesions seen with capillary-pattern type III, 3 lesions (1.3%) were found to be

non-neoplastic (2 hyperplastic polyps and 1 inflammatory polyp) and 221 (98.6%) were neoplastic lesions: 197 lesions (87.9%) were adenomas with low-grade dysplasia, 21 (9.3%) were adenomas with high-grade dysplasia, and 3 (1.3%) were early stage adenocarcinomas.

The 8 lesions with capillary-pattern type IV were neoplastic lesions: 3 lesions were adenomas with low-grade dysplasia, and the other 5 were adenomas with high-grade dysplasia. All 19 lesions that exhibited capillary-pattern type V were adenocarcinomas: 7 lesions were early colorectal adenocarcinomas, and the other 12 lesions were advanced cancers. The histopathologic findings in relation to the capillary pattern are summarized at Table 1.

Considered as a group of 59 non-neoplastic lesions that exhibited capillary pattern I or II, 56 lesions (94.9%) were histologically confirmed as non-neoplastic (normal and/or edematous, inflammatory, or hyperplastic polyps). Of the 250 lesions presenting blood-vessel pattern types III to V, 248 (99.2%) were histologically diagnosed as neoplastic lesions. When considering the overall accuracy of the capillary classification in determining the neoplastic or non-neoplastic nature of the colorectal lesions, it was observed that 304 lesions (98.3%) were correctly diagnosed in their histopathologic nature. The sensitivity of the capillary pattern for distinguishing neoplasia was 99.2% (95% CI, 98.2%-100%), and the specificity was 94.9% (95% CI, 92.5%-97.4%). The positive and negative predictive values were 98.8% (95% CI, 97.6%-100%) and 96.6% (95% CI, 94.6%-98.6%), respectively.

With regard to the diagnosis of colorectal carcinoma, we evaluated 22 cases: 19 lesions (86.3%) showed capillary-pattern type V, and 3 colorectal carcinomas (13.6%) were classified as capillary-pattern type III; nonetheless, both were neoplastic patterns of capillary vessels (Fig. 2). The sensitivity and specificity of type V capillary pattern for the diagnosis of carcinoma were 86% (95% CI, 83%-90%) and 99% (95% CI, 98%-100%), respectively.

### Interobserver agreement on the classification of the capillary pattern

The lesions observed by each endoscopist in real time were documented and recorded as digital imaging files. High-quality digital images recorded from each lesion were selected, unidentified, and presented on a 14-inch liquid crystal display monitor to the endoscopist, who was blind to the initial determination of the lesion type reported by the other examiner (C.R.T. or R.T.). In this way, 162 colorectal lesions were evaluated by both main examiners, and the results were compared, and the kappa coefficient was analyzed by a third independent investigator (M.T.C.). The 2 observers had a significant agreement on the classification of the capillary pattern (kappa [SD] =  $0.85 \pm 0.04$ ,  $P < .01$ ). There was disagreement in only 8.6% of all the lesions evaluated. The crude learning curve of our classification proved to be rather a flat plateau, with high accuracy rates being observed from the beginning:

**TABLE 1. Histopathologic findings according to capillary-vessel pattern of colorectal lesions**

Endoscopic capillary pattern	No. lesions (%)				Total no.
	Non-neoplastic	Low-grade neoplasia	High-grade neoplasia	Carcinoma	
I	6 (100)	0	0	0	6
II	50 (96.15)	2 (3.85)	0	0	52
III	3 (1.33)	197 (87.94)	21 (9.37)	3 (1.33)	224
IV	0	3 (37.5)	5 (62.5)	0	8
V	0	0	0	19 (100)	19
Total no.	59	202	26	22	309

with 74 lesions examined, we reached an accuracy rate of 97.2% (72/74). Within the first validation set, the accuracy rate was 98.1% (109/111), and 98.3% (304/309) was reported at this large sample evaluation.<sup>14</sup> Therefore, we considered that the examination of 100 lesions should enable the endoscopist to achieve over 95% accuracy rate in diagnosing a colorectal lesion by its capillary-vessel pattern.

## DISCUSSION

There has been increasing emphasis on the colonoscopic detection of discrete flat and depressed lesions, on the endoscopic distinction between neoplastic and non-neoplastic lesions, and on the endoscopic recognition of early, endoscopically resectable cancer without invasion of the deep submucosa (Paris consensus<sup>11</sup>). However, not every flat lesion is neoplastic, and, the higher the resolution of endoscopic imaging, the higher the likelihood of diagnosis of incidental findings or lesions within the normal human range that must be discriminated from true neoplastic ones when deciding to perform a biopsy or polypectomy. Chromoendoscopy is a validated endoscopic method that enhances the subtle surface irregularities that flat lesions produce, increasing the sensitivity of the colonoscopic examination, and it alone can provide clues as to whether or not lesions are neoplastic.<sup>3</sup> Magnifying endoscopy can be added to chromoendoscopy to improve the analysis of the surface architecture of the epithelium with the pit pattern classification. Based on this classification system, one can accurately differentiate between non-neoplastic (pit patterns I and II) and neoplastic lesions (types III and IV).<sup>6</sup> However, the majority of endoscopists do not routinely use these techniques, because the benefits are considered to be worth less than the time spent in performing them.

The capillary-pattern classification should be practical and is designed to make easier the *in vivo* endoscopic distinction of commonly diagnosed colorectal lesions. The

normal mucosa, hyperplastic lesions, tubular and villous adenomas, and cancerous lesions should all be addressed in the classification system. Therefore, we designed a 5-subtype classification of capillary pattern in a structure that parallels the pit pattern classification to facilitate correlations with histopathologic findings. As with other important macroscopic aspects, such as size, morphology, and pit pattern, the characterization of the capillary-vessel pattern of colorectal lesions might add substantial information to the endoscopic diagnosis.

The microvasculature of the normal colorectal epithelium is composed of vessels on the order of 5 to 10  $\mu\text{m}$  in diameter.<sup>16</sup> To recognize such microstructures, high-magnification imaging is required. Some cases of hyperplastic and adenomatous lesions might show minute superficial capillary vessels as well. Therefore, when considering the density of the capillary vessels of colorectal lesions without magnification (greater than  $\times 100$ ), it might be possible to underestimate the nature of lesions by not visualizing the minute capillary vessels with neoplastic morphology. The importance of magnification was highlighted in a study by Pohl et al<sup>17</sup> that used FICE with low and high magnification in small colorectal lesions, which achieved better accuracy rates in distinguishing non-neoplastic from neoplastic lesions by using high magnification. Rastogi et al<sup>18</sup> used narrow-band imaging (NBI) with low magnification, and, by a combination of surface and vascular characteristics, classified colorectal polyps into 5 different patterns and reported an overall 92% accuracy rate in diagnosing adenomas and hyperplastic colorectal polyps. These studies differ from ours in that the capillary-vessel morphology was evaluated according to vascular density or surface morphology. Both previous studies did not look at the vascular pattern of carcinomatous lesions. Our data showed that colorectal cancer exhibits an increase in the number of capillary vessels that turn into irregular, larger, and thicker vessels in a disordered arrangement.

Although we consider our cases representative of the usual lesions that endoscopists face in daily practice, the uncommon lesions, such as mixed hyperplastic-

adenomatous polyps and serrated adenomas, were not specifically addressed, because there were only a few cases among our study sample. The differential diagnosis between these lesions and their homogeneous counterpart, based on the capillary pattern, as well as on the pit pattern, represents a professional challenge. Previously, investigators who used NBI in the diagnosis of colorectal lesions proposed a classification of the capillary pattern based on vascular density.<sup>18-20</sup> FICE and NBI are distinct technologies that produce similar clinical effects by promoting a clearer endoscopic visualization of the mucosal capillary vessels. Both technologies are noninvasive, practical, and obviate the use of dye-contrast spraying in the mucosa, which in turn saves time and resources spent on the performance of chromoendoscopy. The reported sensitivity and specificity of NBI and FICE to discriminate colorectal lesions were similarly high.<sup>17-20</sup> We emphasized that FICE with high zoom magnification is essential for a detailed diagnosis of the capillary pattern of colorectal lesions, which results in a higher diagnostic accuracy rate. We believe the same occurs with NBI. FICE and NBI eliminate the need for dye spraying of a contrast agent; however, we consider both techniques as magnification dependent for a high-quality endoscopic examination.

Our data showed that the interobserver agreement was good, and the learning curve of the classification of capillary-vessel pattern was short; with 100 lesions examined, the accuracy rate in diagnosing colorectal lesions was over 95%.

We believe that our classification is easy to learn and works equally for the experienced colonoscopist and the average colonoscopist. Certainly, a combination of the type of capillary pattern, magnification, high-resolution image, and gross lesion morphology were all involved to obtain our excellent results in distinguishing colorectal lesions. The differential diagnosis of small colorectal polyps is much more challenging than that of larger lesions. Almost 80% of our lesions were less than 5 mm in diameter, and the average size was 7.7 mm. Lesions larger than 2 cm in diameter were included in our study, because villous and cancerous lesions routinely diagnosed are large lesions. Therefore, our classification system covered a broad range of commonly diagnosed colorectal lesions, and the accuracy rate in predicting the histopathologic findings is very high and independent from the size of the lesion.

Herein, we showed that the classification of the capillary pattern is highly accurate; in 98.3% of the colorectal lesions examined, the correct histopathologic nature of the colorectal lesion was diagnosed. For the examination of the capillary pattern, along with SET, we used optical zoom, and the magnifying power needed to differentiate the capillary pattern in the vast majority of the lesions approached  $\times 100$  magnification. Our results were as accurate or superior to those reported by investigators who used magnifying chromoendoscopy and the pit pattern

classification of colorectal lesions.<sup>4-10</sup> However, we should mention that the present classification of capillary-vessel patterns of colorectal lesions needs confirmation in larger studies before being recommended to be used clinically. Randomized multicenter controlled trials should be used for the analysis of the clinical impact of this technique in surveillance and screening colonoscopies.

In the present study, based on SET and magnifying zoom imaging, we proposed a new endoscopic classification of the superficial capillary pattern of colorectal lesions that correlates significantly with the histopathologic findings.

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