

# Efficacy of Repeat Review with Flexible Spectral Imaging Color Enhancement in Patients with no Findings by Capsule Endoscopy

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## ABSTRACT

**Background/Aim:** The efficacy of flexible spectral imaging color enhancement (FICE) ch. 1 (F1) for the detection of ulcerative lesions and angioectasias in the small intestine with capsule endoscopy (CE) has been reported. In the present study, we evaluated whether F1 could detect incremental findings in patients with no findings in a standard review mode. **Patients and Methods:** In total, 52 patients (age: 60.1 ± 15.3 years; 30 males) with obscure gastrointestinal bleeding (OGIB) who underwent CE and in whom no lesion was detected in the small intestine in the standard mode (first review) were enrolled. Two experienced endoscopists independently reviewed CE videos again by F1 (second review). The following findings were defined to be significant: Ulcers, erosions, aphthas, angioectasias, tumors, and bleeding. Incremental findings at the second review were checked at F1 and in standard mode by the two reviewers (third review). Finally, the findings were confirmed by the agreement of the two reviewers at the third review. **Results:** F1 detected five significant lesions in three patients with overt OGIB; three erosions, one aphtha, and one angioectasia. For nonsignificant lesions, F1 detected 12 red mucosas and 16 red spots. Moreover, 29 patients with 71 findings were considered false positives. **Conclusion:** F1 detected incremental significant findings in a small percentage of patients with no findings in the standard review mode. In addition, F1 showed many false-positive findings. The incremental effect of a repeated review by F1 in patients with no findings in the first review is limited.

**Key Words:** Capsule endoscopy, flexible spectral imaging color enhancement, obscure gastrointestinal bleeding, repeat review, small intestinal lesion

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Flexible spectral imaging color enhancement (FICE), an image-enhanced endoscopy (IEE) technique, has been used widely in gastroscopy and colonoscopy.<sup>[1,2]</sup> FICE depends on optical filters and the use of spectral estimation technology to reconstruct images at different wavelengths based on images from white-light endoscopy. It has been reported that it improves the visualization of both neoplastic and non-neoplastic lesions in gastroscopy and colonoscopy.<sup>[3-5]</sup>

Capsule endoscopy (CE) has become an important examination of the small intestine.<sup>[6]</sup> The efficacy of CE for small intestinal diseases has been reported.<sup>[7-11]</sup> CE has demonstrated efficacy for patients with obscure gastrointestinal bleeding (OGIB). It can detect various kinds of disease states such as tumors, polyps, angioectasias, ulcers, and erosions.

Rapid 6.5 (Given Imaging Ltd., Yoqneam, Israel), a CE reading system, includes FICE.<sup>[12]</sup> Several studies have shown the effects of FICE in CE.<sup>[13-20]</sup> In a previous study, we found

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that FICE Ch. 1 (F1) detected a larger number of ulcerative lesions and angioectasias in the small intestine compared to a standard review.<sup>[16]</sup> However, little is known about the impact of FICE on CE in patients, with no findings in the standard mode CE. In the present study, we investigated whether F1 could detect incremental findings in patients with no findings in the standard review mode.

## PATIENTS AND METHODS

### Study design

This study was a retrospective analysis, conducted in accordance with the Declaration of Helsinki. All study participants provided written informed consent.

### Subjects

Between March 2008 and November 2011, 52 patients (age:  $60.1 \pm 15.3$  years; 30 males) with OGIB who underwent CE and in whom no lesion was detected in the small intestine in the standard mode (first review) were enrolled. OGIB was defined as recurrent or persistent overt/visible bleeding, iron deficiency anemia (IDA), or a positive fecal occult blood test (FOBT) with no bleeding source found during the initial endoscopic evaluation.<sup>[21]</sup> OGIB was classified as overt or occult OGIB. Overt OGIB was defined as clinically perceptible bleeding that recurred or persisted after a negative initial endoscopic evaluation by esophagogastroduodenoscopy (EGD) and colonoscopy. In comparison, occult OGIB was defined as IDA with or without a positive FOBT.<sup>[22]</sup>

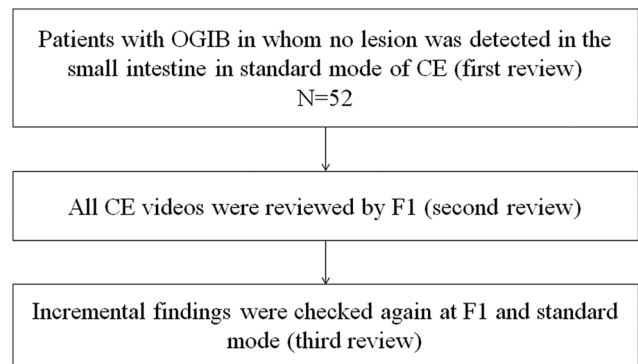
### Capsule endoscopy procedures

We used Pillcam SB or SB2 (Given Imaging Ltd., Yoqneam, Israel) in all study patients. Preparation for CE involved fasting for 12 h and administration of 40 mg simethicone immediately before CE. Eating was allowed after 5 h. During the examination, patients could move freely. CE was performed for approximately 8 h after ingesting, and sensor array and recording devices were then removed.

Two or more experienced endoscopists reviewed all CE videos independently in the standard mode (first review). CE images were reviewed using the Rapid 6.5 Access software (Given Imaging Ltd.). An independent review was performed to reach a consensus on CE findings [Figure 1].

### Flexible spectral imaging color enhancement on capsule endoscopy

Three modes of FICE (FICE ch. 1 [F1], FICE ch. 2 [F2], and FICE ch. 3 [F3]) are implemented within Rapid 6.5. Switching between the standard mode and each FICE mode can be achieved with a button click at the workstation. The spectral specifications of the FICE channels were as follows: F1 (wavelengths: Red 595 nm, green 540 nm, blue 535 nm),



**Figure 1:** Flowchart of the study

F2 (wavelengths: Red 420 nm, green 520 nm, blue 530 nm), and F3 (wavelengths: Red 595 nm, green 570 nm, blue 415 nm). Each spectral wavelength was determined for the following reasons: F1, to reduce interference with bile; F2, to emphasize blood; and F3, to emphasize the difference between bile and blood. We used standard mode and F1 because we previously reported the efficacy of F1 for the detection of ulcerative lesions and angioectasias in the small intestine at CE.<sup>[16]</sup>

### Data analysis

Two experienced endoscopists independently reviewed CE videos by F1 (second review) in patients with no findings in the standard review mode (first review). Incremental findings at the second review were checked again at F1 and standard mode by the two reviewers (third review). Finally, the findings were confirmed by agreement of the two reviewers at the third review. Findings judged not to be lesions in the third review were deemed to be false-positive lesions.

The following findings were defined as significant findings because these were at risk for bleeding: Ulcers, erosions, aphthas, angioectasias, tumors, and bleeding. Other findings, such as red mucosas and red spots, were defined as nonsignificant lesions.

We counted the number of incremental lesions detected at the second review and confirmed by the third review. The number of false-positive findings were also counted. Furthermore, we observed whether rebleeding occurred in patients. Follow-up care was performed at least once every 6 months. Rebleeding was defined as clinically perceptible bleeding after CE.

## RESULTS

### Baseline characteristics of the study patients

Baseline clinical characteristics of the study patients are summarized in Table 1. The mean age of the 52 patients (30 males, 22 females) was  $60.1 \pm 15.3$  years.

Of them, 27 (52%) had overt OGIB and 25 (48%) had occult OGIB. Fifteen patients (29%) had past histories of abdominal surgery, including gastrectomy, cholecystectomy, appendectomy, and uterine myomectomy. During the recording period, the CE reached the cecum in 45 (87%) patients.

### Additional lesions detected by flexible spectral imaging color enhancement ch. 1

F1 detected five significant lesions in 3 of the 52 patients; 3 erosions, 1 aphtha, and 1 angioectasia [Table 2; Figure 2a and b]. All three cases with significant lesions were patients with overt OGIB. Regarding nonsignificant lesions, F1 detected 12 red mucosas and 16 red spots.

### Misdiagnosed findings by flexible spectral imaging color enhancement ch. 1

In total, 29 cases with 71 findings were considered to be false positives [Table 2]. The following were misdiagnosed findings; 6 erosions, 42 red mucosas, 22 red spots, and 1 case of bleeding. For the 6 findings misdiagnosed as erosions, the correct diagnoses were; 2 residues [Figure 3a], 1 lymphoid

follicle, 1 bubble, 1 vessel, and 1 reflected light. For the 42 findings misdiagnosed as red mucosas, 32 were shadowed areas of normal mucosa, 4 were vessels, and 2 were bile. Approximately two-thirds of the 22 findings misdiagnosed as red spots were, in fact, residues, and others were bubbles and shadowed areas of normal mucosa [Figure 3b]. One finding misdiagnosed as bleeding was, in fact, bile [Figure 3c]. In many false-positive cases, residue or roughness of the mucosa was enhanced in red in F1.

### Follow-up of patients

We followed the study patients for  $46.7 \pm 7.5$  months. There was no case of rebleeding.

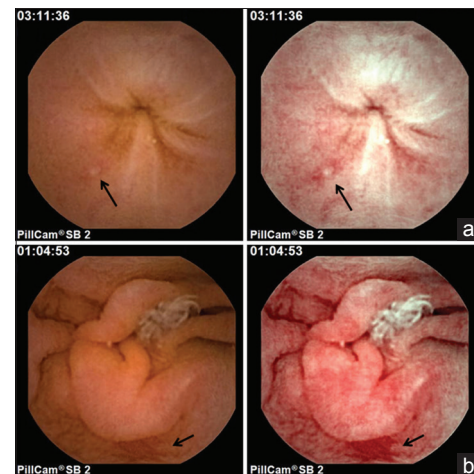
### DISCUSSION

We assessed whether FICE ch. 1 could detect incremental small-intestinal findings in patients with no findings by

**Table 1: Baseline characteristics of the study patients (n=52)**

Age (years)*	60.1±15.3
Male/Female	30 (58%)/22 (42%)
Indications of CE	
Overt OGIB	27 (52%)
Occult OGIB	25 (48%)
Past history of abdominal surgery	15 (29%)
Percentage of capsule obtained cecum image	87%
Daily using drugs	
NSAIDs	3 (6%)
Antiplatelet agent	5 (10%)

CE, capsule endoscopy; OGIB; obscure gastrointestinal bleeding; NSAIDs, nonsteroidal anti-inflammatory drugs; \*Mean±SD

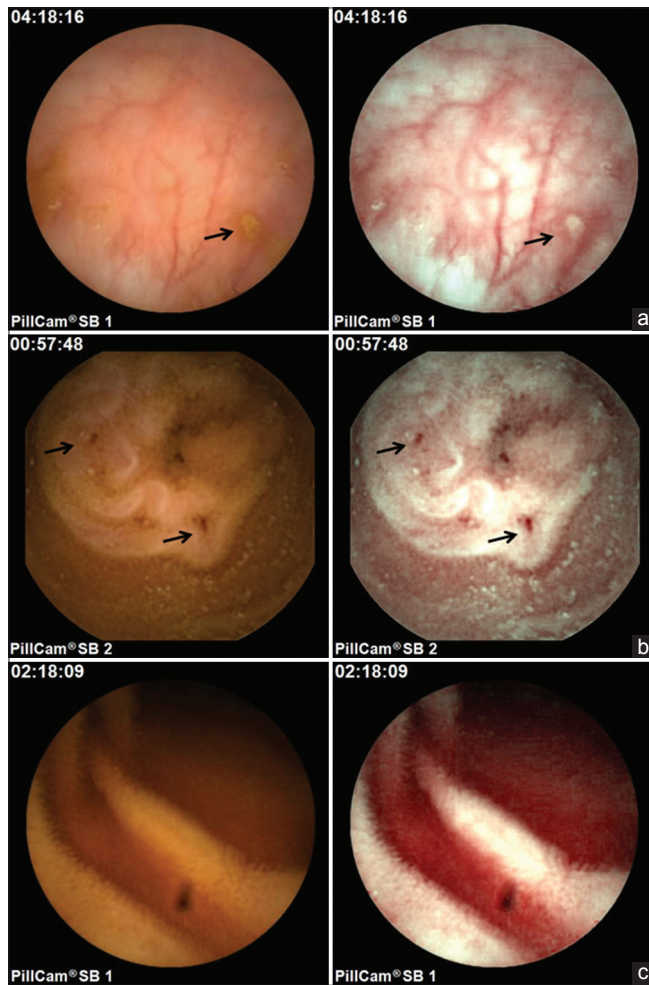


**Figure 2:** Capsule endoscopy images of small-intestinal significant lesions detected at the second review (left; standard mode, right; F1). (a) erosion (b) angioectasia

**Table 2: Additional lesions and misdiagnosed findings detected by F1 in patients with no findings by capsule endoscopy**

Additional lesions detected by F1	Number of lesions	Misdiagnosed findings by F1	Number of lesions (Correct diagnosis)
Significant lesions		Erosion	6 (2 residues, 1 lymphoid follicle, 1 bubble, 1 vessel, 1 reflect light)
Erosion	3	Bleeding	1 (bile)
Aphtha	1	Res mucosa	42 (32 shadowed areas of normal mucosa, 4 vessels, 3 residues, 2 bile, 1 bubble)
Angioectasia	1	Red spot	22 (16 residues, 3 bubbles, 3 shadowed areas of normal mucosa)
Nonsignificant lesions			
Red mucosa	12		
Red spot	16		

F1, Flexible spectral imaging color enhancement ch. 1



**Figure 3:** Capsule endoscopy images of false-positive findings detected at the second review (left; standard mode, right; F1). (a) a residue misdiagnosed as an erosion (b) shadowed areas of normal mucosa misdiagnosed as red spots (c) bile misdiagnosed as bleeding

the standard review mode of CE. F1 did detect additional significant lesions in 3 of 52 patients with no findings in the standard review mode. However, there was no case of rebleeding during the follow-up period.

Several previous studies have reported the efficacy of FICE in CE for detecting angioectasia and ulcerative lesions. We previously reported the efficacy of F1 for detecting ulcerative lesions and angioectasias in the small intestine.<sup>[16]</sup> Imagawa *et al.*<sup>[14]</sup> also reported that F1 and F2 had higher detectability for angioectasias. Konishi *et al.*<sup>[17]</sup> showed that F1 and F2 were more useful for the detection of erosions than the standard mode. In the present study, the incremental small-intestinal findings by F1 were 3 erosions, 1 aphtha, and 1 angioectasia, which is consistent with previous studies.

However, we showed that F1 also picked up many false-positive findings. The following were misdiagnosed

findings; 6 erosions, 42 red mucosas, 22 red spots, and 1 case of bleeding. The reasons for the misdiagnoses are thought to be similar to those for the incremental findings. In many false-positive cases, residues and roughness of the mucosa were enhanced in red with F1. Furthermore, while FICE enhances the color contrast to avoid interference by bile, this reduces the quality of the image's resolution. Such diminished resolution interferes with the correct diagnosis.

All 3 cases with significant lesions were patients with overt OGIB, although it made no sense to analyze the data statistically because of the small number of cases. Several studies have reported that the diagnostic yield of CE for small intestinal lesions in patients with overt OGIB is significantly higher than that in patients with occult OGIB.<sup>[23-26]</sup> However, other studies have shown that there is no difference in the diagnostic yield of CE between patients with previous overt and occult OGIB.<sup>[27-29]</sup> Although the difference in the diagnostic yield of CE between patients with overt and occult OGIB is controversial, a higher prevalence of small intestinal lesions in overt OGIB may be associated with this result.

It is unclear whether we should review videos at F1 practically in patients with no finding in the standard mode. Although incremental findings were detected at the second review, there was no case of rebleeding during the follow-up period ( $46.7 \pm 7.5$  months). Hence, it would seem that a detailed examination or hemostatic therapy was not required in these cases. Therefore, a second review by F1 may not be necessarily required in terms of clinical practice according to the present study. However, we did not analyze the data statistically because of the small number of cases. Clinically, management change such as close follow-up or a detailed examination could decrease rebleeding rate if further experience is accumulated. Furthermore, it takes twice as long to review CE videos in both F1 and standard mode. Although reviewing CE in both F1 and standard mode may be unrealistic until a computer-aided diagnosis system is established, further experience is needed to assess the feasibility and efficacy of reviewing in both modes. At present, the efficacy of FICE in CE is such that FICE improves the detectability of ulcerative lesions or angioectasias in patients with small bowel lesions, as reported previously.<sup>[13-18]</sup> Additional review by FICE should be performed only in cases where significant lesions were detected in the standard review for enhanced visualization, which may improve lesion diagnosis.

Potential limitations of our study should be noted. First, the study was retrospective and relatively few patients



were enrolled. Second, a detailed examination, such as a balloon enteroscopy, was not performed in any patient with additional significant lesions by FI because this was a retrospective study.

## CONCLUSION

Among patients with OGIB, FI detected incremental small intestinal lesions in a small percentage of patients with no findings in the standard review mode. However, it also detected many false-positive findings. The incremental effect of repeated review by FI in patients with no findings in the first review is limited.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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