Bile pigment in small-bowel water content reflects bowel habits: a retrospective analysis of a capsule-endoscopy imaging series

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Abstract

Background Pigmented bile salts darken the small-bowel lumen and are present with bile acid, which is involved in the development of bowel habits. The small-bowel water content (SBWC) in the ileum could represent the colonic environment, although no studies have focused on this feature. However, measurement of the crude SBWC can be challenging because of the technical difficulty of the endoscopic approach without preparation. Our aim was to evaluate optically active bile pigments in the SBWC of patients with abnormal bowel habits using capsule endoscopy (CE), to investigate the impact of bile acid on bowel habits. In addition to conventional imaging, we used flexible spectral imaging color enhancement (FICE) setting 1 imaging, in which the effects of bile pigments on color are suppressed.

Methods The study population included 37 constipated patients, 20 patients with diarrhea, and 77 patients with normal bowel habits who underwent CE between January 2015 and May 2018. Patients with secondary abnormal bowel habits were excluded. Intergroup color differences of SBWC in the ileum (ΔE) were evaluated from conventional and FICE setting 1 images. Color values were assessed using the CIE L*a*b* color space. Differences in lightness (black to white, range 0 to 100) of SBWC were also evaluated.

Results Values of ΔE calculated from comparisons of conventional images of constipated and normal-bowel-habit patients, and patients with diarrhea and normal-bowel-habit patients were 11.3 and 10.7, respectively. These values decreased to 3.9 and 3.2, respectively, when FICE setting 1 images were evaluated. The SBWC lightness of patients with constipation and diarrhea was significantly brighter (34.0 versus 27.2, P < .0001) and darker (18.8 versus 27.2, P < .0001),
respectively, compared with the normal-bowel-habit patients. Examination of the FICE setting 1 images did not reveal significant differences in SBWC lightness between the constipated and normal-bowel-habit groups (44.7 versus 46.7, \( P = .33 \)) or between the diarrhea and normal-bowel-habit groups (44.7 versus 42.3, \( P = .39 \)).

Conclusions Differences in color and darkness of the SBWC in the ileum appear to be attributable to bile pigments. Therefore, bile pigments in SBWC could reflect bowel habits.

Background

Functional gastrointestinal disorders (FGIDs), also referred to as disorders of gut-brain interaction in Rome IV [1], negatively affect quality of life and impose a socioeconomic burden [2]. Although several endocrine, neurologic, and microbiome factors may result in FGID [3], obvious causes are not always evident. A deficiency of bile acid (BA) can contribute to the pathophysiology of constipation [4], while increasing intracolonic concentrations of BA can accelerate spontaneous peristalsis [5], with excessive BA resulting in loose stool consistency [6]. In the gastrointestinal (GI) tract, BA plays a role in the modulation of fluid and electrolyte absorption and the regulation of GI motility [7–9]. Through these functions, BA is important for the development of bowel habits. However, we were unable to find any previous studies that have investigated the contribution of BA in determining small-bowel water content (SBWC). To evaluate the role of BA in the development of abnormal bowel habits, we investigated SBWC just proximal to the colon.

Capsule endoscopy (CE) is an established modality, which is now considered the first choice for examination of small-bowel lesions. However, up to 30% of these lesions may be missed because of inherent limitations of the technology, especially
when there is increased gut motility and/or a lesion is captured in only one frame because of the rapid passage of the capsule through the bowel [10,11]. To increase the detection of small-bowel lesions that could be missed using conventional imaging, flexible spectral imaging color enhancement (FICE) has been developed [12]. FICE decomposes conventional CE images into 3 specific wavelengths (red, green, and blue) and then directly reconstructs the image. The assessor can easily switch between viewing conventional images and the 3 different settings of FICE images. The wavelengths for FICE settings that are used in the evaluation of CE images are as follows: setting 1 (red 595 nm, green 540 nm, blue 535 nm), setting 2 (red 420 nm, green 520 nm, blue 530 nm), and setting 3 (red 595 nm, green 570 nm, blue 415 nm) [13]. Among the 3 FICE settings, FICE setting 1 is optimized to reduce the interference of bile pigments, which contain bilirubin and darken the small bowel, impairing visibility. Specifically, as the wavelength for maximum absorbance of bilirubin is 455 nm, the spectrum of FICE setting 1 is designed to avoid the 400-500 nm wavelength range [14].

Increasing attention is being paid to assessment of the small bowel, with the identification of small-bowel lesions being used to assess the occurrence of systemic diseases and other conditions [15–17]. The SBWC in the ileum could be a significant indication of the colonic environment, although measurement of crude SBWC can be challenging due to the technical difficulty of ileum endoscopy without preparation. It is well-known that the excretion of bilirubin could parallel that of BA [18,19]. Moreover, bile pigment can be considered to be colorimetrically dominant in the SBWC [20]. Therefore, the present retrospective study aimed to evaluate optically active bile pigments in the SBWC of patients with abnormal bowel habits using CE, and to indirectly assess whether BA involvement is associated with
abnormal bowel habits. The method of color analysis used in the study has been assessed and validated by several endoscopists in previous studies demonstrating the usefulness of image-enhanced endoscopy for gastrointestinal neoplasms [21,22].

Methods

Aim of study

This retrospective study aimed to analyze the contribution of BA in the SBWC in the ileum to the development of abnormal bowel habits using optical effects observed in color analysis of capsule endoscopy images.

Study population

A total of 223 consecutive patients who underwent small-bowel exploration by CE between January 1, 2015, and May 30, 2018, were included. After excluding 15 patients who presented with blood or opacity in the small bowel, 17 were excluded on the basis of medication use: sodium chenodeoxycholate in 7 and magnesium oxide in 10, both of which can influence SBWC. Following these exclusions, 172 patients were eligible for image evaluation. Patients with abnormal bowel habits secondary to other conditions were then excluded. After 29 patients with enteritis or colitis including inflammatory bowel disease were excluded, 5 patients with specific systemic diseases were also excluded. These diseases were Parkinson’s disease in 1 patient, thyroid function abnormalities in 3 patients, and diabetic neuropathy in 1 patient. An additional 2 patients who underwent bowel resection and 2 who underwent cholecystectomy were excluded. No patients with advanced colorectal cancer were included in the initial population.

The study population included 134 patients (74 males and 60 females; mean age,
64.6 years [range, 10–88 years]) who underwent CE at Hiroshima City Asa Citizens Hospital, between January 2015 and May 2018. Of these 134 patients, 37 were constipated, 20 had diarrhea, and 77 normal bowel habits (not being categorized into either the constipation or diarrhea group). Patients were classified on the basis of their predominant bowel habits, which were assessed by a questionnaire administered before CE examination. The initial indications for CE were suspected bleeding from the small bowel, unexplained abdominal symptoms, abnormal findings on other abdominal imaging techniques, and abnormal laboratory findings. The flow chart of patient enrollment is shown in Fig. 1.

This study conformed to the principles of the 6th revision of the Declaration of Helsinki (2008), and the study and its protocols were approved by the institutional review board (IRB) of the Hiroshima City Asa Citizens Hospital, which also granted us permission to access the patients’ information on October 16, 2018 (IRB No. 30–4–6).

**Capsule endoscopy**

For examination of the small bowel, CE was performed using a PillCam™ SB3 video capsule (Medtronic, Dublin, Ireland). The capsules were swallowed with a solution of dimethicone after a 12-hour overnight fast, without any other preparation. Once the capsules were swallowed, patients continued with their routine daily activities. Patients were able to drink clear liquids and eat a light meal 2 and 4 hours after swallowing the capsules, respectively. After 9 hours, the sensor arrays and recording devices were removed, and images were analyzed using Rapid™ for Pillcam™ software that was installed on a Rapid Workstation R8.0 (Medtronic, Dublin, Ireland), with FICE software incorporated. Captured CE images were
reviewed and analyzed, independent of clinical background, by 2 endoscopists who had previously reviewed CE images of more than 500 cases. Evaluation of the images was based on mutual agreement. The entire small bowel was divided in half on the basis of the capsule transit time; with images in the first part considered to be of the jejunum, with those from the latter part from the ileum.

**Image acquisition**

The latter half of the small bowel, defined as the ileum in the present study, was further divided into equal thirds on the basis of the capsule transit time. Three eligible CE images showing small-bowel water pooled in the lumen were selected from the initial, middle, and terminal parts of the ileum from each patient. During the image selection procedure, the endoscopists were blinded to patients’ clinical information. These images were extracted from the regions whose colors were dominant in the color-bar on the Rapid Workstation. Images, with optical artifacts and/or significant amounts of floating residue not considered in the selection. The images for FICE setting 1 were acquired by converting the selected conventional CE images. Three pairs of conventional and corresponding FICE setting 1 images were selected from the ileum of each patient.

**Image processing**

Color processing and image analysis were performed using Adobe Photoshop Elements 10 (Adobe Systems Inc, California, United States). The region of interest (ROI) was defined as the area of pooled water in the lumen, avoiding halation and shadowing, to represent the entire SBWC in the image (yellow boxes in Fig. 2). The position of the ROI was set on the conventional image after agreement between the 2 endoscopists and applied to the corresponding FICE setting 1 image. Color
information was extracted from the ROI in the form of Red, Blue, Green (RBG), then converted to the Commission Internationale d’Eclairage (CIE) L*a*b* color values [23]. Three pairs of conventional images and corresponding FICE setting 1 images were processed in this manner, and the average L*a*b* values were calculated for each pair. These were considered representative values for each patient and were calculated for every patient in the study (Supplementary Table 1).

Color analysis

The color value for each image was expressed using the 3-dimensional color parameters L* (black to white; range, 0 to 100), a* (green to red; range, 128 to 127), and b* (blue to yellow; range, 128 to 127) (Fig. 3). The relative perceptual difference between any 2 colors can be approximated by the color distance between them. Color differences (ΔE) of SBWC between groups were calculated using the following equation [24]:

\[ \Delta E = \sqrt{(\Delta L^*)^2 + (\Delta a^*)^2 + (\Delta b^*)^2} \]

The value of ΔE was calculated for each comparison and classified into units of color difference according to the evaluation criteria of the National Bureau of Standards (NBS), using the following equation [21,25]:

\[ \text{NBS units} = \Delta E \times 0.92 \]

The NBS defines the units of color difference as follows: 0–0.5 = trace, 0.5–1.5 = slight, 1.5–3.0 = noticeable, 3.0–6.0 = appreciable, 6.0–12.0: much, 12.0 and above = very much.

Study comparisons

Patients were classified into 3 groups: constipation, diarrhea, and normal bowel habits, according to their answers to the questionnaire administered before CE
examination. The questionnaire asked details regarding stool frequency and bowel habits over the last 3 months, based on information maintained by each patient in a daily diary. Patients were provided with the definition of constipation and diarrhea before completing the questionnaire to improve the reliability of the information provided. Constipation was defined as fewer than 3 spontaneous bowel movements per week or difficulty in >25% of defecation events. Diarrhea was defined as loose or watery stools occurring in >25% of defecation events [26]. The questionnaire also asked about the presence of abdominal pain related to defecation. “Presence” of pain was defined as having pain at least one day per week for the last 3 months. The patients’ demographic and clinical characteristics were evaluated. These included: age; sex; alcohol consumption, and smoking habits; comorbidities including hypertension, diabetes mellitus, hyperlipidemia, cardiovascular disease, chronic liver disease, and chronic kidney disease; and current medications, including non-steroidal anti-inflammatory drugs, antithrombotic agents, and proton pump inhibitors. The mean defecation frequency of each group was calculated, and the capsule transit time in the small bowel, evaluated.

The ΔE values for the SBWC of the ileum of the constipation and diarrhea groups were compared to those of the normal-bowel-habit group. The median values of L*a*b* and NBS units of ΔE were compared between groups for both the conventional and FICE setting 1 images.

The average lightness (L*) of SBWC of the ileum for the constipation and diarrhea groups were also compared to that of the normal-bowel-habit group for both conventional and FICE setting 1 images.

Statistical analyses

Student’s t test was used to compare quantitative data using JMP software, version
The chi-squared test, with a $3 \times 2$ contingency table, was used to compare categorical data using Microsoft Excel 2008 for Mac (Microsoft, Redmond, WA), with Yates’ correction when required. All of tests were 2-sided, and a $P$ value of $<.05$ was considered statistically significant.

Results

The clinical characteristics of all groups are presented in Table 1. Univariate analysis indicated that there were no statistically significant differences among the groups in demographics, psychosocial histories, comorbidities, or medications. The mean frequency of defecation was 1.1 times daily for the normal-bowel-habit group, 0.5 times daily for the constipation group and 3.0 times daily for the diarrhea group. Abdominal pain was present in 11 of patients in the normal-bowel-habit group, 6 in the constipation group and 4 in the diarrhea group. The mean [standard deviation (SD)] capsule transit times in the small bowel were not significantly different, either between the constipation and normal-bowel-habit groups (307.0 [117.9] versus 288.1 [109.7], $P = .50$), or between the diarrhea and normal-bowel-habit groups (306.9 [94.3] versus 288.1 [109.7], $P = .37$).

The $\Delta E$ values of SBWC of the ileum for all groups are presented in Table 2. Examination of the conventional images revealed the $\Delta E$ between the constipation and normal-bowel-habit groups to be 11.3, defined as “much” difference by the NBS rating system. On the other hand, examination of the FICE setting 1 images—all of which were adjusted to reduce bile-pigment effects—revealed $\Delta E$ to be decreased to 3.9—an “appreciable” difference. Comparison of the diarrhea and normal-bowel-habit groups showed a similar trend, with $\Delta E$ of the conventional images being 10.7 (“much” difference), and FICE setting 1 images suggesting $\Delta E$ to be 3.2
Comparison of the mean lightness (L*) of SBWC in the ileum between groups is illustrated in Fig. 4. Examination of the conventional images indicated the mean [SD] lightness of SBWC of the constipation group to be significantly higher (appearing brighter) than that of the normal-bowel-habit group (34.0 [7.4] versus 27.2 [7.2], \( P < .0001 \)). On the other hand, the mean [SD] lightness of SBWC of the diarrhea group was significantly lower (i.e., appeared darker) than that of the normal-bowel-habit group (18.8 [5.2] versus 27.2 [7.2], \( P < .0001 \)). Examination of the FICE setting 1 images did not reveal a significant difference between the mean [SD] lightness of SBWC of the constipation and normal-bowel-habit groups (44.7 [11.1] versus 46.7 [9.5], \( P = .33 \)). Similarly, the mean [SD] lightness of SBWC was not significantly different between the diarrhea and normal-bowel-habit groups (44.7 [11.1] versus 42.3 [9.8], \( P = .39 \)).

Discussion

The pathophysiology of FGID, including irritable bowel syndrome (IBS), is multifactorial in nature and may include altered sensation, psychosocial factors, colonic motility, and mucosal factors [1]. Interaction of these factors generates functional gastrointestinal symptoms due to “leaky” intestinal barrier, abnormal permeability, and signaling amplification [27]. In particular, luminal factors, such as BA, may induce changes in the mucosal, motor, and sensory functions [28]. Interaction of the microbiota with dietary constituents that are mixed with BA can generate biologically active molecules that influence gut motility and secretion and could play a fundamental role in the formation of bowel habits [3].

In the present study, we aimed to indirectly evaluate the contribution of BA to
abnormal bowel habits in the ileum, which has not—to the best of our knowledge—been the focus of any published studies to date. To this end, we used an optical approach involving CE which did not require sampling of the small-bowel water and subsequent biochemical analyses. We evaluated the BA involvement of SBWC indirectly by assessing the darkening of the lumen, which can be attributed to bile pigments. This was achieved by analyzing the color difference between conventional and FICE setting 1 images and performing between-group comparisons. The use of all 3 FICE settings has not been reported to significantly improve the overall delineation or detection rate of small-bowel lesions; however, the usefulness of FICE setting 1 has been demonstrated in the detection of vascular lesions [29]. Moreover, the lesion-detection rate using FICE setting 1 has been reported to be unaffected by the presence of bile pigments [30]. This suggests that the use of this setting can suppress the effects of bile pigment on the color of SBWC and enhance the appearance of reddened lesions. For these reasons, the use of FICE setting 1 was deemed clinically appropriate for the present study.

Quantitative analysis of the color difference was carried out by assessing the CIE L*a*b* color values; an approach that has previously been used to demarcate lesions from the surrounding mucosa during endoscopy [21,31]. In the present study, the color differences (ΔE) of SBWC in the ileum between the constipation and normal-bowel-habit groups were found to be 11.3 and 3.9, respectively, using conventional and FICE setting 1 images. Similarly, the ΔE values between the diarrhea and normal-bowel-habit groups were 10.7 and 3.2, respectively, calculated from conventional and FICE setting 1 images. The ΔE values decreased for both comparisons when the FICE setting 1 (minimizing bile-pigment interference) images were used; therefore, these differences were deemed to be produced by bile
pigments in the SBWC. Significant values of ΔE were observed when significant differences in the lightness of SBWC were observed. In other words; the SBWC of constipated patients appeared brighter than that of patients with normal bowel habits, suggesting lower concentrations of bile pigments associated with constipation. Similarly, the SBWC of diarrhea patients appeared darker, suggesting higher concentrations of bile pigments than that found in patients with normal bowel habits.

Our study included 11 patients with abdominal pain in the normal-bowel-habit group, 6 in the constipation group and 4 in the diarrhea group. These patients would be categorized as having IBS according to Rome IV. However, in the clinic it may not be possible to confidently separate the disorders into separate entities, for example differentiating IBS-C (constipation) from functional constipation and IBS-D (diarrhea) from functional diarrhea. Thus, Rome IV considers that these disorders exist on a continuum rather than in isolation [32,33].

Our results are supported by the study of Shin et al. [34], who compared traits of IBS with the fecal BA levels of IBS patients and healthy volunteers. The authors reported that fecal levels of BA were significantly higher in subjects with IBS-D. Moreover, they found that subjects with IBS-C had lower fecal levels of BA compared with healthy volunteers. Normalization of bowel function, either by BA supplementation or sequestration in IBS-C and IBS-D, respectively, confirms that characterization of fecal BA composition may be necessary to clarify the pathogenic role of BA [6,35]. In IBS-D or functional diarrhea, increased fecal BA may result from increased synthesis of BA, possibly due to deficient negative-feedback inhibition of BA synthesis or genetic variation [36,37]. These facts suggest that BA involvement in the small bowel still has an impact on the development of bowel habit, although
95% of BA is recycled in the terminal ileum. Elobixibat is a minimally absorbed ileal bile-acid-transporter inhibitor and is used clinically to treat constipation by augmenting the level of BA that flows to the colon. Increased dosage causes an increased frequency of diarrhea and corresponding abdominal symptoms [38], as BA can affect stool consistency or cause liquefying of the stool. Although it has been reported that FGID may be associated with motility abnormalities, such as rapid intestinal transit in IBS-D [39], FGID is defined using a symptom-based, rather than a motility-based, approach [1]. The capsule transit time in the small bowel showed no significant differences among groups in the present study and thus, it did not seem to be correlated with bowel habits. Our study has some limitations: First, we did not compare SBWC among the patients in vitro. An association between the indirect assessment of BA concentration and the real BA concentration in the ileum is lacking in the present study. Second, we did not evaluate the Bristol Stool Scale [40]. The reason for this was because we did not aim to subclassify IBS patients but rather simply to compare the study subjects with abnormal bowel habits. Third, this was a single-center retrospective study. We recognize that local biological factors, including genetics, microbiome, environmental hygiene, cytokines, and central-nervous-system effects, could have an impact on symptom generation, manifestation, and interpretation. Therefore, a large-scale prospective study is needed to address these limitations.

Conclusions
Pigmentation of the SBWC in the ileum could be formed by bile. Moreover, the degree of bile pigmentation affects bowel habit.
Abbreviations

BA, bile acid

SBWC, small-bowel water content

CE, capsule endoscopy

FICE, flexible spectral imaging color enhancement

FGIDs, functional gastrointestinal disorders

GI, gastrointestinal

IRB, institutional review board

ROI, region of interest

CIE, Commission Internationale d’Eclairage

NBS, national bureau of standards

SD, standard deviation

IBS, irritable bowel syndrome

NSAIDs, non-steroidal anti-inflammatory drugs

PPI, proton pump inhibitor

Declarations

Ethics approval and consent to participate

This study conformed with the principles of the 6th revision of the Declaration of Helsinki (2008), and the study and its protocols were approved by the institutional review board (IRB) of the Hiroshima City Asa Citizens Hospital, which also granted us permission to access the patients’ information on October 16, 2018 (IRB No. 30-4-6).

Consent for publication
Consent was obtained from all subjects whose imaging data were published in this study.

Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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The work described herein was supported by departmental resources only. The authors report no conflicts of interest.

Authors’ contributions
TA designed the study and drafted the article. AF made the conception and design of the study. KS, NA, and SM made the analysis and collection of the data. SN made supervised the procedure and made the final approval.

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Tables

Table 1. Baseline demographic and clinical patient characteristics

| Defecation phenotype | Normal bowel habitsa n = 77 | Constipationa n = 37 | Diarrheaa n = 20 | P va |
|----------------------|-----------------------------|----------------------|------------------|------|
| Demographics         |                             |                      |                  |      |
| Age ≥75 years        | 28 (10)                     | 10 (27)              | 5 (25)           | .6   |
| Male sex             | 44 (57)                     | 19 (51)              | 11 (55)          | .5   |
| Psychosocial history |                             |                      |                  |      |
| Smoking              | 11 (14)                     | 8 (22)               | 4 (20)           | .7   |
| Alcohol consumption  | 27 (35)                     | 11 (30)              | 9 (45)           | .6   |
| Comorbidity          |                             |                      |                  |      |
| Hypertension         | 37 (48)                     | 20 (54)              | 6 (30)           | .2   |
| Diabetes mellitus    | 8 (10)                      | 6 (16)               | 5 (25)           | .4   |
| Hyperlipidemia       | 19 (25)                     | 5 (14)               | 4 (20)           | .5   |
| Cardiovascular disease | 17 (22)                    | 12 (32)              | 3 (15)           | .4   |
Chronic liver disease$^b$ & 4 (5) & 1 (3) & 2 (10) & .83 \\
Chronic kidney disease$^c$ & 26 (34) & 10 (27) & 4 (20) & .62 \\

Current medications

NSAIDs & 7 (9) & 3 (8) & 2 (10) & .96 \\
Antithrombotic agents & 16 (21) & 8 (22) & 3 (15) & .96 \\
PPI & 20 (26) & 13 (35) & 7 (35) & .70 \\

$^a$Data are expressed as numbers and (%) of patients. $^b$Viral etiologies included infection with the hepatitis B or C virus. Non-viral etiologies included alcoholic hepatitis and autoimmune hepatitis. There were no patients with decompensated cirrhosis in the initial population. $^c$Sustained renal malfunction defined as an estimated glomerular filtration rate of $< 60$ mL/min.1.73 m$^2$. $^d$The chi-square test for the 3 2 contingency table was used to compare categorical data.

NSAIDs, Non-steroidal anti-inflammatory drugs; PPI, proton pump inhibitor.

Table 2. Color differences between the small-bowel water content of constipation and diarrhea patients and normal-bowel-habit patients
### Defecation phenotype

|                         | Constipation | Diarrhea |
|-------------------------|--------------|----------|
| **Conventional images** |              |          |
| ΔE (color difference) compared with normal-bowel-habit | 11.3         | 10.7     |
| NBS unit                | 10.4         | 9.9      |
| Rating by NBS evaluation criteria<sup>a</sup> | Much         | Much     |
| **FICE setting 1 images** |            |          |
| ΔE (color difference) compared with normal-bowel-habit | 3.9          | 3.2      |
| NBS unit                | 3.6          | 2.9      |
| Rating by NBS evaluation criteria<sup>a</sup> | Appreciable  | Noticeable |

<sup>a</sup> NBS classification: 0–0.5, trace; 0.5–1.5, slight; 1.5–3.0, noticeable; 3.0–6.0, appreciable; 6.0–12.0, much; 12.0 and above, very much.

**Abbreviations:** FICE, flexible spectral imaging color enhancement; NBS, National Bureau of Standards.

**Supplementary table 1. Median of representative L<sup>*</sup>a<sup>*</sup>b<sup>*</sup> values of the small-bowel water content in constipation and diarrhea group and normal-bowel-habit group**

|                         | Normal bowel habits | Constipation | Diarrhea |
|-------------------------|---------------------|--------------|----------|
| **Conventional images** | (27.5, 7.5, 27.5)   | (34, 15, 33) | (19.75, 3.5, 21.2) |
| **FICE setting 1 images** | (44.5, 1, 10.5)    | (47.5, 3.5, 11) | (45, -1.75, 9) |

Data was expressed as (L<sup>*</sup>a<sup>*</sup>b<sup>*</sup>).

**Figures**
223 patients who underwent capsule endoscopy  
From 2015 January to 2018 May

<Exclusion criteria affecting image analysis>
- Incomplete entire small bowel exploration (19 cases)
- Presence of blood or poor visual image due to opacity of the small bowel (15 cases)
- Use of medication that affects small bowel water content (17 cases)

172 patients with acceptable image evaluation

<Exclusion criteria affecting bowel habits>
- Enteritis or colitis including inflammatory bowel disease (29 cases)
- Presence of systemic disease causing defecation disorder (5 cases)
- Surgery of the intestine or biliary system (4 cases)

134 patients enrolled
- 37 constipation
- 20 diarrhea
- 77 normal bowel habits

Figure 1

Patient enrollment flow chart Medications considered to affect small-bowel water
Figure 2

Small-bowel water content in the ileum Representative raw conventional images

(a) with normal bowel habit, (b) with constipation setting 1 images shown in (d), (e), and (f) respectively. Yellow boxes indicate the regions of interest.
Commission Internationale d’Eclairage (CIE) L*a*b* color Color is expressed as 3-dimensional real-number space; therefore, any color variation can be expressed in L*a*b* coordinates.
Figure 4

Between-group comparison of lightness of small-bowel water contents in the ileum

(a) Conventional images

(b) FICE setting 1 images