

[ ORIGINAL ARTICLE ]

## The Clinical Usefulness of the PillCam Progress Indicator for Route Selection in Double Balloon Endoscopy

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### Abstract:

**Objective** The utility of capsule endoscopy (CE) findings in the route selection for double balloon endoscopy (DBE) has not been adequately discussed. The PillCam Progress Indicator in the RAPID 6.5 software program graphically demonstrates the progress of the capsule endoscope through the small-bowel. This study aimed to clarify the usefulness of the PillCam Progress Indicator in choosing the initial DBE route.

**Methods** We retrospectively examined 50 consecutive patients with 50 target lesions detected on both CE and DBE at Hiroshima University Hospital from January 2011 to February 2018. In this study, we selected antegrade DBE on the basis of % Capsule Progress <50% as a clinical trial. The association between the PillCam Progress Indicator data and the DBE route to the target lesion was analyzed.

**Results** The target lesion was reached via the initial DBE route in 96% (48/50) of cases. The cutoff values for selecting an antegrade route for DBE were 50% for % Capsule Progress and 42% for % SB Time. At the cutoff value, the sensitivity, specificity, and positive and negative predictive values for route selection were 100%, 91%, 93%, and 100% for % Capsule Progress and 96%, 91%, 93%, and 95% for % SB Time.

**Conclusion** The PillCam Progress Indicator was useful for determining the appropriate initial DBE route.

**Key words:** capsule endoscopy, double balloon endoscopy, progress indicator, small-bowel

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### Introduction

Recently, technological advances have allowed for the visualization of the entire small-bowel using endoscopic systems, including capsule (1) and balloon (2) endoscopes. These endoscopes have been widely used in clinical practice (3) and have revolutionized the diagnosis and treatment of small-bowel diseases (4-7). The guidelines committee of the Japanese Gastroenterological Endoscopy Society (JGES) has developed the "Clinical Practice Guidelines for Enteroscopy." According to these guidelines, capsule endoscopy (CE) is the first-line small-bowel endoscopy tool for use in cases of occult gastrointestinal bleeding (OGIB) (3). This procedure is relatively simple, safe, and comfortable for patients. Indeed, the clinical utility of CE in the diagnosis of small-bowel diseases has been reported by various

groups (8-17). CE enables the observation of the small-bowel but does not provide the ability to perform biopsy for a histological analysis or therapeutic intervention.

Balloon endoscopy (BE) allows for histological specimens to be obtained using methods such as forceps biopsy, and interventional treatments including endoscopic hemostatic treatments, endoscopic resection, and balloon dilation can be performed. In 2001, Yamamoto et al. (2) first described double balloon endoscopy (DBE) as a new method for visualizing the entire small-bowel. Diagnostic and therapeutic DBE has been widely used for evaluating small-bowel diseases (4-7, 18-21).

CE has been reported to achieve total bowel enteroscopy in approximately 70-80% of cases (22, 23), with a total small-bowel observation rate using DBE of approximately 70% (24-26). Total bowel enteroscopy may be successfully carried out using either antegrade or retrograde BE. The

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**Table 1. Clinical Characteristics of Enrolled Patients.**

Sex	
Male	33 (66)
Female	17 (34)
Mean age±SD (years)	68.6±12.0
Mean height±SD (cm)	161±8.1
Mean body weight±SD (kg)	58.1±11.5
Mean body mass index±SD (kg/cm <sup>2</sup> )	22.4±3.4
Past history of abdominal surgery	
Present	19 (38)
Absent	31 (62)
Chief complaint	
Occult gastrointestinal bleeding	31 (62)
Abdominal symptoms	7 (14)
Abnormality on other imaging modality	5 (10)
Others	7 (14)

SD: standard deviation (%)

choice of an antegrade or retrograde approach is dependent upon the patient's symptoms and imaging examination results. When CE is performed before DBE, the findings from CE can be used predict where the lesion will be located in the small-bowel.

The best method for utilizing the CE results for BE route selection has not been adequately discussed. There have been some studies on the utility of the CE transit time for determining the DBE route (27-29). Kaffes et al. (30) and Hendel et al. (31) chose antegrade DBE to visualize two-thirds of the proximal small-bowel based on their experience and to assess the likelihood of reaching the relevant lesion. The PillCam Progress Indicator (Medtronic, Minneapolis, USA), operating on the RAPID 6.5 software program (Medtronic, graphically demonstrates the progress of a capsule endoscope through the small-bowel. The PillCam Progress Indicator is displayed during entire small-bowel observation. The system then reports the % Capsule Progress and % SB Time. The % Capsule Progress represents a percentage of the entire small-bowel images. The % SB Time represents a percentage of the entire small-bowel transit time. Although the PillCam Progress Indicator (Medtronic) estimates the location of the CE within the small-bowel, there are no reports concerning the usefulness of the PillCam Progress Indicator (Medtronic) for choosing the optimal DBE route.

The aim of this study was to clarify the usefulness of the PillCam Progress Indicator in selecting the initial DBE route.

## Materials and Methods

### Patients

We retrospectively examined 50 consecutive patients (male, n=33; female, n=17; mean age, 69 years, CE performed by SB2, n=26) with 50 lesions detected by both CE and DBE at Hiroshima University Hospital from January

2011 to February 2018. Patients in whom enteroscopy was achieved by CE and those in whom lesions were detected by both CE and DBE were enrolled. In our hospital, we usually perform CE prior to DBE, and the initial DBE route is determined based on the interpretation of the CE results.

Table 1 shows the clinical characteristics of the enrolled patients. The data for each patient were obtained by a retrospective medical record review and from stored endoscopic findings. The final diagnoses for all enrolled patients were included in the medical chart. Data on the examinations and procedures performed, including computed tomography (CT), small-bowel follow-through, CE, and DBE, along with the operative specimen results, were collected from the patients' medical records.

This study was performed in accordance with the Declaration of Helsinki. All patients were informed of the risks and benefits of CE and DBE, and each patient provided their written informed consent for the procedure to be performed. None of the patients refused the examinations during the study period. This study was approved by the Hiroshima University Hospital Institutional Review Board (registration number: E-1143).

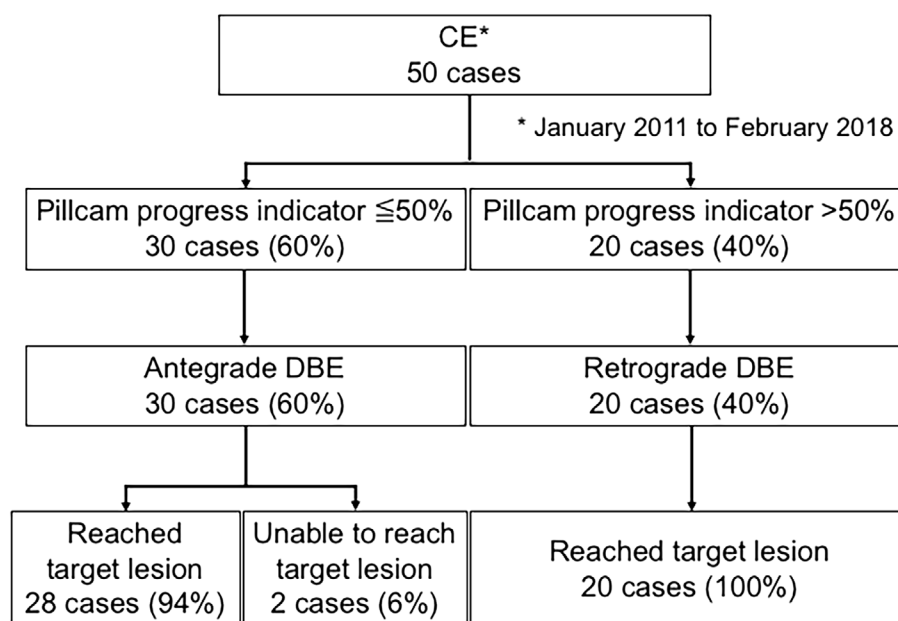
### CE procedure

Capsule endoscopy was performed using the PillCam SB2 or SB3 (Medtronic). The capsule endoscope was swallowed with a solution of dimethicone after an overnight fast. Sodium picosulfate and magnesium citrate were administered for bowel preparation the night before swallowing the capsule endoscope. For patients with renal dysfunction, only sodium picosulfate was prescribed. The patients were allowed to drink clear liquids every 2 hours and to eat a light meal 4 hours after swallowing the CE. CE recordings were reviewed using the RAPID 6.5 or 8.0 software (Medtronic).

Total enteroscopy by CE was considered successful when the capsule endoscope reached the cecum or the site of anastomosis in the ileocecal area within the recording time. The % Capsule Progress and % SB Time were defined as the percentages of the initial images that confirmed the target lesion endoscopically. The capsule recordings were reviewed by 2 experienced physicians, each of whom had read more than 30 capsule videos.

### DBE procedure

The DBE system (FUJIFILM Medical, Tokyo, Japan) consisted of a video endoscope with a flexible overtube and a pressure-controlled pump system. In this study, we used the EN-450P5 endoscope with the TS-12140 overtube or the EN-450T5 or EN-580T5 endoscope with the TS-13140 overtube. Antegrade DBE was performed after an overnight fast. Retrograde DBE was performed after bowel preparation with oral electrolyte lavage used for regular lower gastrointestinal endoscopy. For bowel preparation and oral lavage, the patient consumed 250 mL of magnesium citrate (Magcorol; Horii Pharmaceutical Ind., Osaka, Japan) on the day before the examination, followed by 2 L of magnesium cit-



**Figure 1.** A flowchart of the decision-making process regarding the initial DBE route according to the PillCam Progress Indicator and the frequency of reaching the target lesions. CE: capsule endoscopy, DBE: double-balloon endoscopy

**Table 2.** Final Diagnoses of Enrolled Patients.

Angioectasia	12 (24)
Polyp	6 (12)
Ulceration of unknown origin	6 (12)
Malignant lymphoma	5 (10)
Gastrointestinal stromal tumor	4 (8)
Anastomotic ulceration	3 (6)
Primary small bowel cancer	2 (4)
Metastatic tumor	2 (4)
Lymphangioma	2 (4)
Others	8 (16)
Total	50 (100)

(%)

rate, 2 L of polyethylene glycol solution (Niflec; Ajinomoto Pharma, Tokyo, Japan), or 1 L of high-concentration polyethylene glycol solution (Moviprepp; Ajinomoto Pharma) on the morning of the examination. For both approaches, intestinal looping was checked fluoroscopically. Patients were sedated with midazolam and pentazocine, if necessary. Blood pressure, heart rate, and oxygen saturation were monitored during the DBE procedure. The endoscopic findings were evaluated by 2 physicians who had experienced more than 100 DBE studies.

### Evaluations

We evaluated the following: PillCam Progress Indicator (% Capsule Progress and % SB Time), the frequency of reaching the target lesions according to the PillCam Progress Indicator, and the cutoff values for % Capsule Progress and % SB Time used to choose antegrade DBE.

We defined the target lesion as the lesion detected by CE

that corresponded to the lesion detected by 2 physicians on DBE. Lesions identified on only CE or DBE were excluded. Cases with multiple lesions were excluded from this study.

### Statistical analyses

Continuous data are reported as the mean  $\pm$  standard deviation and range. Comparisons were performed using the chi-squared test for categorical data. Receiver-operating characteristic (ROC) curves were created to determine the optimal cutoff values for the % Capsule Progress and % SB Time used for the initial choice to perform antegrade DBE. P values of  $<0.05$  were considered statistically significant. The JMP Pro 13 software program (SAS, Cary, USA) was used to perform for the statistical analyses.

## Results

Fifty patients underwent CE and DBE for 50 target lesions. We divided the patients into two groups based on the initial DBE route selected according to the % Capsule Progress (antegrade,  $n=30$ ; retrograde,  $n=20$ ). In this study, antegrade DBE was usually selected when the PillCam Progress Indicator showed a % Capsule Progress value of  $<50\%$  as a clinical trial. Fig. 1 shows a flowchart of the decision-making process for the initial DBE route according to the PillCam Progress Indicator and the frequency of reaching the target lesions. Table 2 shows the final diagnoses of all patients. Angioectasia was the most common disease in this series.

The average times to reach to the target lesions from the pyloric ring in antegrade DBE and from the ileocecal valve in retrograde DBE were 21.8 minutes and 24.4 minutes, respectively. There were no significant differences between an-

**Table 3. Comparison Value of % Capsule Progress and % SB Time between Both Groups.**

	Route		Total
	Antegrade	Retrograde	
% Capsule Progress	18.6±15.3 %	79.4±13.5 %	42.9±33.4 %
% SB time	16.8±14.4 %	74.8±15.9 %	40.0±32.3%

**Table 4. Frequency of Reaching the Target Lesions by Double Balloon Endoscopy according to % Capsule Progress.**

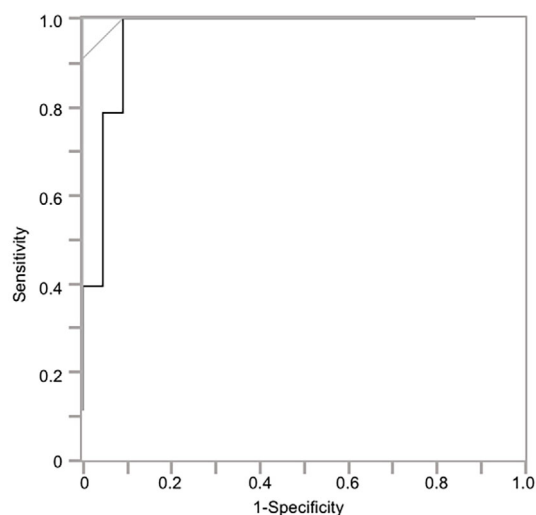
% Capsule Progress	Route		Total
	Antegrade n=30	Retrograde n=20	
≤50%	93% (28/30)		93% (28/30)
>50%		100% (20/20)	100% (20/20)
Total	93% (28/30)	100% (20/20)	96% (48/50)

**Table 5. Frequency of Reaching the Target Lesions by Double Balloon Endoscopy according to % SB Time.**

% SB time	Route		Total
	Antegrade n=30	Retrograde n=20	
≤50%	93% (28/30)	100% (1/1)	93% (29/31)
>50%		100% (19/19)	100% (20/20)
Total	93% (28/30)	100% (20/20)	96% (48/50)

tegrade and retrograde DBE. The mean % Capsule Progress and % SB Time values in the two groups are shown in Table 3. The frequency of reaching the target lesion by DBE in each group, according to the % Capsule Progress and % SB Time, is shown in Tables 4 and 5, respectively. When the % Capsule Progress and % SB Time were <50%, the frequency of reaching the target lesion by antegrade DBE was 93% and 94%, respectively. Retrograde DBE was not selected for any cases with a % capsule value of <50%. In the case of retrograde DBE, all lesions were reached during the initial DBE procedure. In total, 96% of the target lesions were reached. In 2 cases in which the antegrade route was selected for the initial DBE procedure, route changes were required to reach the target lesion. In both of those cases we reached the target lesions by retrograde DBE.

The ROC curves for the % Capsule Progress and % SB Time for the DBE route selection are shown in Figs. 2 and 3. In the ROC curve for % Capsule Progress, the cutoff value for selecting antegrade DBE was 50%. At this cutoff value, the sensitivity, specificity, positive predictive value, and negative predictive value for route selection were 100%, 91%, 93%, and 100%, respectively. The area under the ROC curve (AUC) for % Capsule Progress was 0.963. In the ROC curve for % SB Time, the cutoff value for selecting antegrade DBE was 42%. At this cutoff value, the sensitivity, specificity, positive predictive value, and negative predictive value for route selection were 96%, 91%,

**Figure 2. The receiver-operating curve (ROC) for % Capsule Progress in the selection of the route for initial double-balloon endoscopy. The cutoff value for selecting antegrade DBE was 50%. At this cutoff value, the sensitivity, specificity, positive predictive value, and negative predictive value for route selection were 100%, 91%, 93%, and 100%, respectively. The area under the ROC curve (AUC) value for % Capsule Progress was 0.963.**

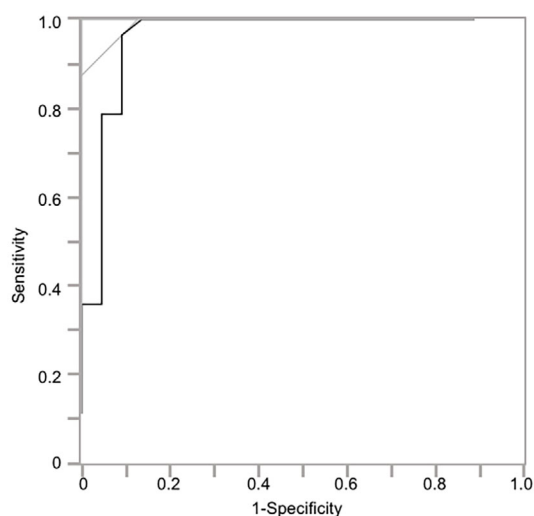
93%, and 95%, respectively. The area under the ROC curve (AUC) for % Capsule Progress was 0.960. The differences were not statistically significant.

In 2 cases, we were unable to reach to the target lesions during the initial antegrade DBE procedure (Table 6). These cases required route changes to reach the target lesions. We reached the target lesions during secondary retrograde DBE in both cases. In one patient diagnosed with hemangioma, the patient underwent CE for OGIB. The CE showed a bluish submucosal tumor when the % Capsule Progress and % SB Time values were both 34%. We initially selected antegrade DBE, but could not reach the target lesion. Next, we

performed retrograde DBE and were able to reach the target lesion. Due to repeated gastrointestinal bleeding, this patient underwent partial small-bowel resection. Intraoperatively, the target lesion was located in the lower small-bowel, 50 cm cephalad from the cecal bulb. In the second patient, the % Capsule Progress and % SB Time values of the target lesion were 6% and 12%, respectively. Although it was estimated that the target lesion would be located in the upper small-bowel because of the low progress indicator values, we could not reach the target lesion during the initial antegrade DBE procedure. We therefore performed retrograde DBE to reach the target lesion. The target lesion in this patient was considered to be located in the lower small-bowel based on computed tomography performed after DBE.

## Discussion

Our study revealed that the % Capsule Progress and % SB Time values are useful as accurate indicators for DBE route selection. With our protocol, the target lesion was reached during the initial DBE procedure in 96% of the cases in this study. The % Capsule Progress and % SB Time used to choose antegrade DBE were approximately 50%. The average time to reach the target lesions in antegrade and retrograde DBE did not differ to a statistically significant



**Figure 3.** The receiver-operating curve (ROC) for % SB Time in the selection of the initial double-balloon endoscopy route. The cutoff value for selecting antegrade DBE was 42%. At this cutoff value, the sensitivity, specificity, positive predictive value, and negative predictive value for route selection were 96%, 91%, 93%, and 95%, respectively. The area under the ROC curve (AUC) value for % Capsule Progress was 0.960.

extent. Our results also indicated that we could reduce the detection time required during DBE by selecting the initial DBE route with reference to the PillCam Progress Indicator.

DBE is an invasive method and sometimes antegrade and retrograde procedures are required to observe the entire small-bowel. The selection of a high yielding initial DBE route can affect the duration, compliance, and cost. Currently, there is no standard method for DBE route selection. It has been reported that the time index in CE is useful for DBE route selection (27-29). However, we considered that this indication was uncertain because the speed of the capsule endoscope in the small-bowel is not constant. Thus, it was necessary to standardize more accurate indications for DBE route selection. The % Capsule Progress represents the percentage of images taken of the entire small-bowel. The % Capsule Progress value enabled us to estimate the location of the capsule endoscope within the whole small-bowel. We considered that the accuracy of the indications was improved by adding the % Capsule Progress to the time index from the duodenal bulb to the cecum (in this study, we called this the % SB Time).

Gay et al. previously reported that the indication for route selection during push-and-pull enteroscopy used a time index of 0.75; in that study, the lesion location was defined as a percentage of the mouth-to-cecum time (27). Li et al. evaluated the ability of CE to guide the choice of insertion route for DBE (28). They used the time index, which was defined as a percentage equivalent to the pylorus-to-lesion time per pylorus-to-ileocecal valve time. They reported that a time index of 0.6 was accurate and practical. Nakamura et al. reported that the CE transit time was useful for determining the DBE route in OGIB (29). In this study, the best cut-off values for route selection according to the CE transit time from the intake to the cecum and duodenal bulb to the cecum were 60% and 50%, respectively, using an ROC curve.

We used the % Capsule Progress and % SB Time to determine the initial DBE route. The % Capsule Progress was displayed by the PillCam Progress Indicator when reviewing the RAPID video, and the % SB Time was displayed in the CE report in the RAPID software program. These indices were displayed after the first duodenal and cecal images were landmarked in automatic mode for the SB2 and SB3 videos. The automatic mode can cut down on the reviewing times and reduce the burden on reviewers by eliminating redundant images. The % Capsule Progress may indicate where the capsule endoscope moved from the duodenum, representing a percentage of all small-bowel images. In this study, we calculated the cutoff value of % Capsule Progress

**Table 6.** Summary of 2 Cases Requiring Route Change to Reach the Target Lesions.

No.	Age (years)	Sex	Chief complaint	Past history of abdominal surgery	Target lesion	% Capsule Progress	% SB time	Route
1	70	Female	Anemia	Absent	Hemangioma	34%	34%	Antegrade→retrograde
2	74	Male	Anemia, melena	Absent	Lymphangioma	6%	12%	Antegrade→retrograde

and % SB Time for selecting antegrade DBE using ROC curves. The cutoff values of the % Capsule Progress and % SB Time were 50% and 42%, respectively. In general, the capsule endoscope moves more rapidly in the duodenum and proximal jejunum in comparison to the other parts of the small-bowel (32). Thus, it might be assumed that the % SB Time value would be lower than the % Capsule Progress value. In fact, the ROC curves of the % Capsule Progress and % SB Time values did not differ to a statistically significant extent, and the usage of both values might be more useful for selecting the route for DBE.

Our data showed that two target lesions were not reached when an antegrade route was used in the initial DBE procedure. In these cases, the lesions were located more distally in the small-bowel than was reflected during CE. Thus, it is preferable to determine the initial DBE route on the basis of the PillCam Progress Indicator findings as well as other data, such as CT, ultrasound, or enteroclysis.

The present study was associated with some limitations. First, it was a single-center retrospective study. The retrospective design could have resulted in a recruitment bias and have led to a significant bias in patient selection because of the exclusion criteria of this study. Second, the number of participants was relatively small. Third, the endoscopy devices and review software were not the same in all cases. For example, the SB3 was found to have superior image resolution in comparison to the SB2. The SB3 also has an adaptive frame rate (AFR) feature that automatically changes the imaging frame rate, depending on the capsule speed, and expands the shooting area. Thus, differences in the devices may have affected the results in the cases involving proximal jejunum lesions. In previous studies, it was reported that the SB3 could increase diagnostic yields (33, 34). However, Xavier et al. reported that the SB3 did not improve the overall diagnostic yield in comparison to the SB2 (35). Thus, this difference might not have affected our results. Further large prospective cohort studies will provide more evidence for selecting the most appropriate initial DBE route.

In conclusion, the PillCam Progress Indicator of CE was useful for determining the appropriate initial DBE route.

**The authors state that they have no Conflict of Interest (COI).**

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