

2018 IASGO, ICUR & KSGC Joint Symposium Mar. 24th 2018 Seoul
Recent updates in colorectal cancer (CRC) prevention and screening

Endoscopic CRC prevention: screening using Image enhanced endoscopy (IEE) and colorectal ESD

Yokohama City University

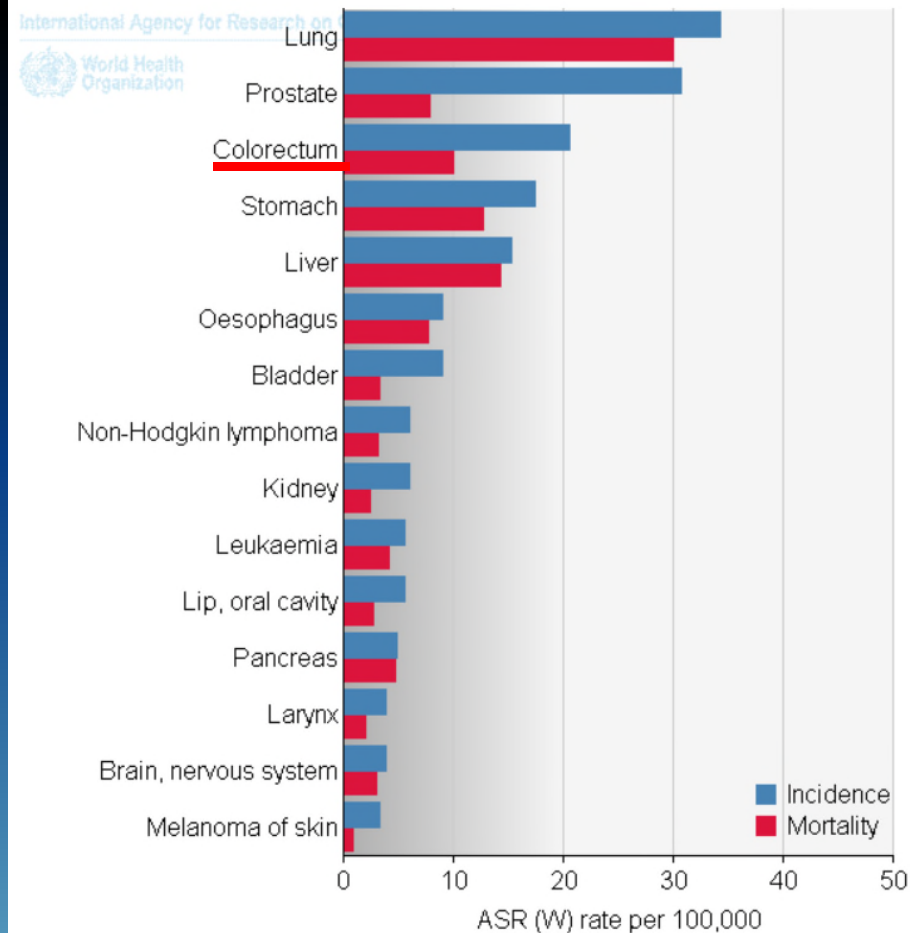
Takuma Higurashi

Topics

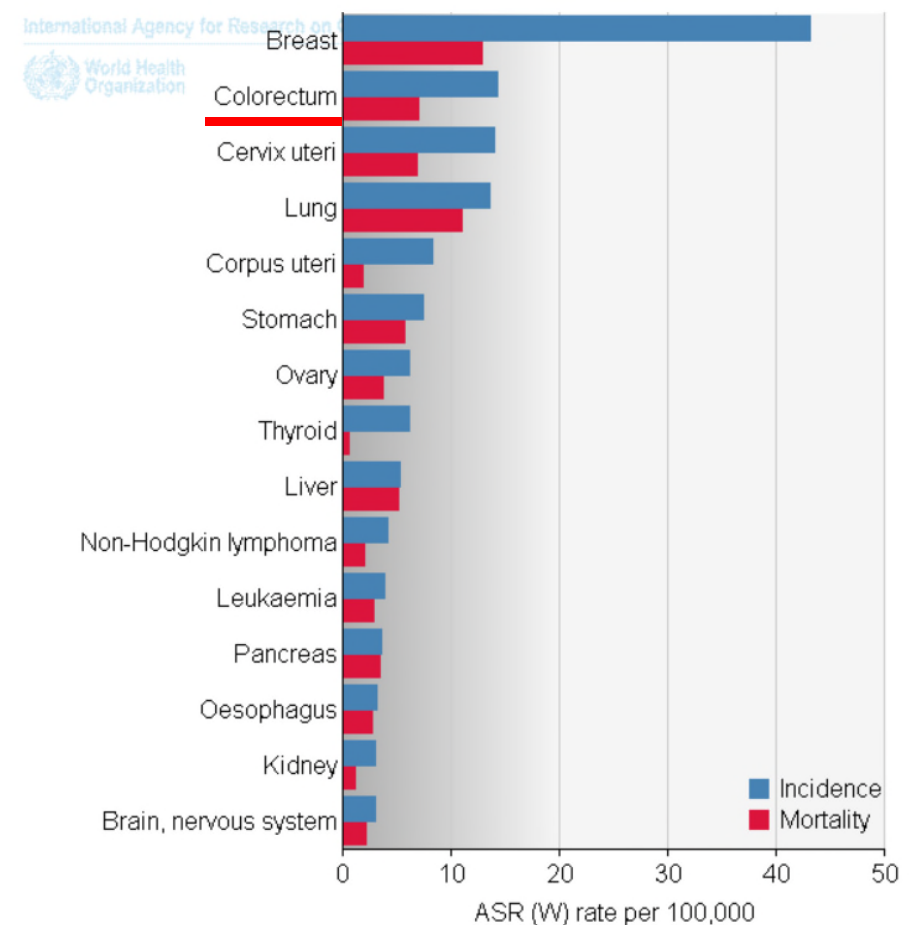
- Prevention of CRC using endoscopy
- Colorectal tumor with **image enhanced endoscopy (IEE)**
- Introduction of colorectal ESD

Cancer in the world

Estimated age-standardised incidence and mortality rates: men



Estimated age-standardised incidence and mortality rates: women



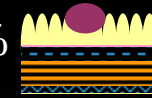
Outcome of CRC

Category of CRC progression

5-year survival rate

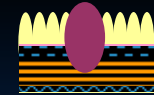
Stage 0 ⇒ Localized in the mucosa

: 95% ~ 100%



Stage I ⇒ Localized until the Proper muscular layer

: 90% ~ 95%



Stage II ⇒ Beyond the Proper muscular layer

: 80% ~ 85%

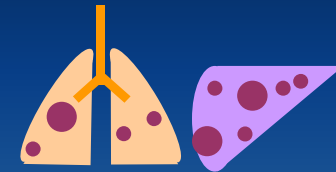


Stage III ⇒ exist lymph node metastasis

: 55% ~ 75%



Stage IV ⇒ exist liver, lung, and/or peritoneal L/N metastasis ~ 15%



The therapy is determined by stage and patients performance status.
Endoscopic therapy, Surgery, Chemotherapy and/or etc.

5-year survival rate of CRC is relatively high compared with other GI cancers.
CRC could be completely curative, if the lesion is detected in early stage.

(For example, in Gastric cancer, stage I: 85-95%, Stage II 65-85%, Stage III 30 ~ 50%)

Prevention of CRC

1. Primary Prevention

Health Promotion

Prevention of disease

2. Secondly Prevention

Early Detection & Diagnosis

Early Therapy



•CT

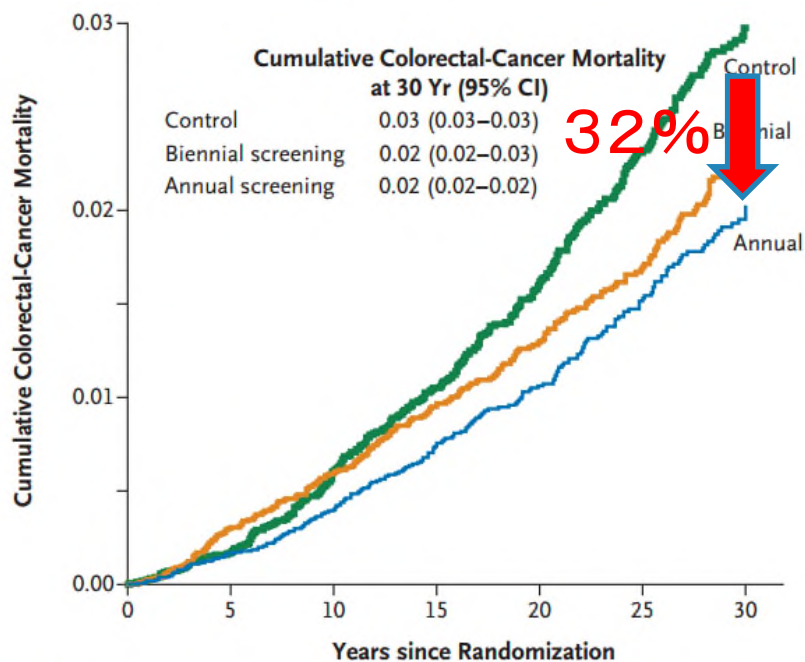
•Endoscopy

•Resection

(Polypectomy or Operation)

Long-Term Mortality after Screening for Colorectal Cancer

Aasma Shaukat, M.D., M.P.H., Steven J. Mongin, M.S., Mindy S. Geisser, M.S., Frank A. Lederle, M.D., John H. Bond, M.D., Jack S. Mandel, Ph.D., M.P.H., and Timothy R. Church, Ph.D.



No. at Risk

Control	14,497	13,103	11,320	9157	6741	4450
Biennial screening	14,635	13,243	11,445	9323	6802	4583
Annual screening	14,658	13,294	11,437	9219	6802	4498

Figure 1. Cumulative Colorectal-Cancer Mortality.

Cumulative colorectal-cancer mortality was assessed on the basis of Kaplan-Meier estimates, evaluated at monthly time points. Point estimates and 95% confidence intervals at 30 years are also shown.

Fecal Occult Blood Test

In the Minnesota Colon Cancer Control Study, 46,551 participants, 50 to 80 years of age, were randomly assigned to usual care (control) or to annual or biennial screening with fecal occult-blood testing.

Screening reduced colorectal-cancer mortality (relative risk with **annual screening**, 0.68; 95% confidence interval [CI], 0.56 to 0.82; relative risk with **biennial screening**, 0.78; 95% CI, 0.65 to 0.93) through 30 years of follow-up.

⇒ receiving **FOBT every year** reduce **32% of CRC death**

The NEW ENGLAND JOURNAL of MEDICINE

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SEPTEMBER 19, 2013

VOL. 369 NO. 12

Long-Term Colorectal-Cancer Incidence and Mortality after Lower Endoscopy

Reiko Nishihara, Ph.D., Kana Wu, M.D., Ph.D., Paul Lochhead, M.B., Ch.B., Teppei Morikawa, M.D., Ph.D., Xiaoyun Liao, M.D., Ph.D., Zhi Rong Qian, M.D., Ph.D., Kentaro Inamura, M.D., Ph.D., Sun A. Kim, M.D., Ph.D., Aya Kuchiba, Ph.D., Mai Yamauchi, Ph.D., Yu Imamura, M.D., Ph.D., Walter C. Willett, M.D., Dr.P.H., Bernard A. Rosner, Ph.D., Charles S. Fuchs, M.D., M.P.H., Edward Giovannucci, M.D., Sc.D., M.P.H., Shuji Ogino, M.D., Ph.D., and Andrew T. Chan, M.D., M.P.H.

Table 4. Colorectal-Cancer Mortality after Screening Lower Endoscopy.

Variable	No Screening Lower Endoscopy	Screening Sigmoidoscopy	Screening Colonoscopy [‡]
All participants			
All deaths from colorectal cancer			
No. of person-yr	1,182,248	302,330	357,008
No. of deaths	349	73	52
Age-adjusted hazard ratio (95% CI)	1.00	0.57 (0.44–0.73)	0.32 (0.24–0.44)
Multivariate hazard ratio (95% CI) [†]	1.00	0.59 (0.45–0.76)	0.32 (0.24–0.45)
Deaths from proximal colon cancer [‡]			
No. of deaths	121	46	25
Age-adjusted hazard ratio (95% CI)	1.00	1.04 (0.73–1.47)	0.49 (0.31–0.79)
Multivariate hazard ratio (95% CI) [†]	1.00	1.04 (0.73–1.48)	0.47 (0.29–0.76)
Deaths from distal colorectal cancer [‡]			
No. of deaths	195	21	16
Age-adjusted hazard ratio (95% CI)	1.00	0.29 (0.19–0.46)	0.18 (0.10–0.30)
Multivariate hazard ratio (95% CI) [†]	1.00	0.31 (0.20–0.49)	0.18 (0.10–0.31)
Men			
No. of person-yr	366,773	101,259	141,554
No. of deaths from colorectal cancer	131	30	26
Age-adjusted hazard ratio (95% CI)	1.00	0.57 (0.38–0.86)	0.34 (0.22–0.53)
Multivariate hazard ratio (95% CI) [†]	1.00	0.59 (0.39–0.90)	0.36 (0.23–0.56)
Women			
No. of person-yr	815,475	201,072	215,453
No. of deaths from colorectal cancer	218	43	26
Age-adjusted hazard ratio (95% CI)	1.00	0.56 (0.41–0.79)	0.31 (0.20–0.48)
Multivariate hazard ratio (95% CI) [†]	1.00	0.61 (0.43–0.85)	0.31 (0.20–0.48)

Screening Colonoscopy

Among 88,902 participants followed over a period of 22 years.

→ Screening colonoscopy reduce **68 %** CRC death

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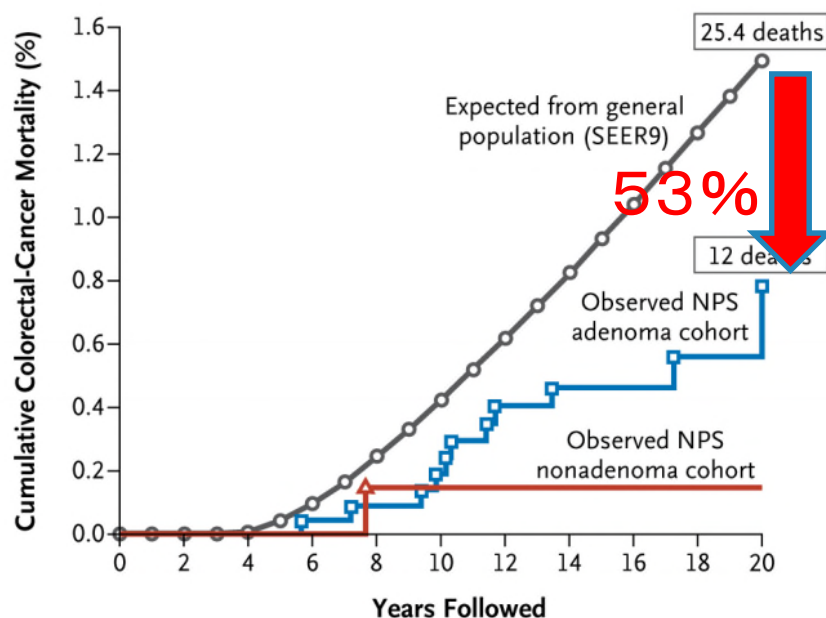
ESTABLISHED IN 1812

FEBRUARY 23, 2012

VOL. 366 NO. 8

Colonoscopic Polypectomy and Long-Term Prevention of Colorectal-Cancer Deaths

Ann G. Zauber, Ph.D., Sidney J. Winawer, M.D., Michael J. O'Brien, M.D., M.P.H., Iris Lansdorp-Vogelaar, Ph.D.,
Marjolein van Ballegooijen, M.D., Ph.D., Benjamin F. Hankey, Sc.D., Weiji Shi, M.S., John H. Bond, M.D.,
Melvin Schapiro, M.D., Joel F. Panish, M.D., Edward T. Stewart, M.D., and Jerome D. Waye, M.D.



No. at Risk

Adenoma	2602	2358	2100	1808	1246	461
Nonadenoma	773	733	678	632	420	164

Early Therapy Polypectomy

Among 2602 patients who had adenomas removed during participation in the study, after a median of 15.8 years, 1246 patients had died from any cause and 12 had died from colorectal cancer. Given an estimated 25.4 expected deaths from colorectal cancer in the general population, the standardized incidence-based mortality ratio was 0.47 (95% confidence interval [CI], 0.26 to 0.80) with colonoscopic polypectomy, suggesting a 53% reduction in mortality.

⇒ Polypectomy is effective for reducing 53% CRC death.

- Annual screening FOBT is effective
- Screening colonoscopy and polypectomy reduce CRC death

⇒ Is it enough just screening patients ? ?

The answer is . . .



NO!!!

Precise management of colonoscopy is very important

Adenoma Detection Rate (ADR)

The rate an endoscopist detects in one colonoscopy

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ORIGINAL ARTICLE

Adenoma Detection Rate and Risk of Colorectal Cancer and Death

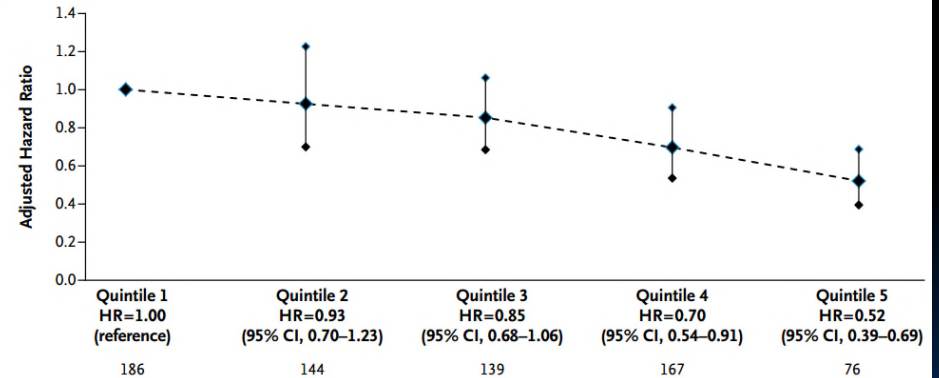
Douglas A. Corley, M.D., Ph.D., Christopher D. Jensen, Ph.D., Amy R. Marks, M.P.H., Wei K. Zhao, M.P.H., Jeffrey K. Lee, M.D., Chyke A. Doubeni, M.D., M.P.H., Ann G. Zauber, Ph.D., Jolanda de Boer, M.B., Bruce H. Fireman, Ph.D., Joanne E. Schottinger, M.D., Virginia P. Quinn, Ph.D., Nirupa R. Ghai, Ph.D., Theodore R. Levin, M.D., and Charles P. Quesenberry, Ph.D.

Table 2. Adenoma Detection Rate and Risk of an Interval Colorectal Cancer among All Patients.

Adenoma Detection Rate	Interval Cancer no. of cases	Hazard Ratio (95% CI)*	Unadjusted Risk no. of cases/ 10,000 person-yr
Continuous rate	712	0.97 (0.96–0.98)	7.7
Rate quintile			
Quintile 1: 7.35–19.05%	186	1.00 (reference)	9.8
Quintile 2: 19.06–23.85%	144	0.93 (0.70–1.23)	8.6
Quintile 3: 23.86–28.40%	139	0.85 (0.68–1.06)	8.0
Quintile 4: 28.41–33.50%	167	0.70 (0.54–0.91)	7.0
Quintile 5: 33.51–52.51%	76	0.52 (0.39–0.69)	4.8

* Hazard ratios were adjusted for age, Charlson comorbidity score, sex (in the model including both men and women), and indication for colonoscopy, with clustering according to physician.

A Risk of Interval CRC



C Risk of Fatal CRC

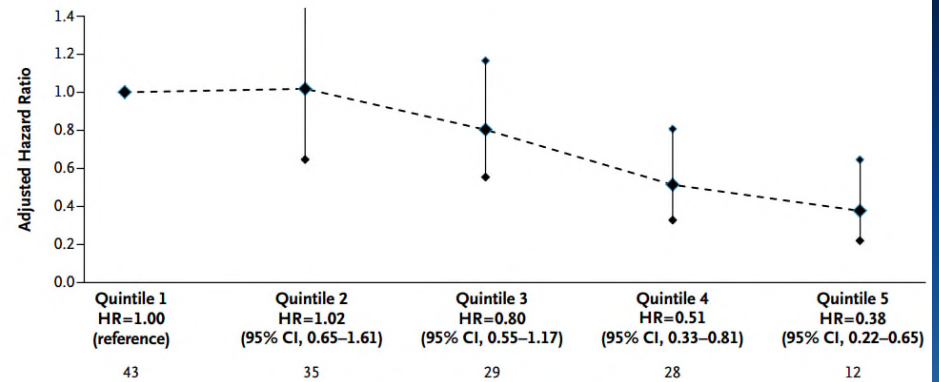


Figure 2. Hazard Ratios for Colorectal Cancer, According to Quintile of Adenoma Detection Rates.

Data were adjusted for sex, age, Charlson comorbidity index score, and indication for colonoscopy, with clustering according to physician. Vertical lines indicate 95% confidence intervals. HR denotes hazard ratio.

When ADR improves, CRC death will reduce

Longer Withdrawal Time Is Associated With a Reduced Incidence of Interval Cancer After Screening Colonoscopy



Aasma Shaukat,^{1,2,3} Thomas S. Rector,³ Timothy R. Church,⁴ Frank A. Lederle,³ Adam S. Kim,⁵ Jeffery M. Rank,⁵ and John I. Allen⁶

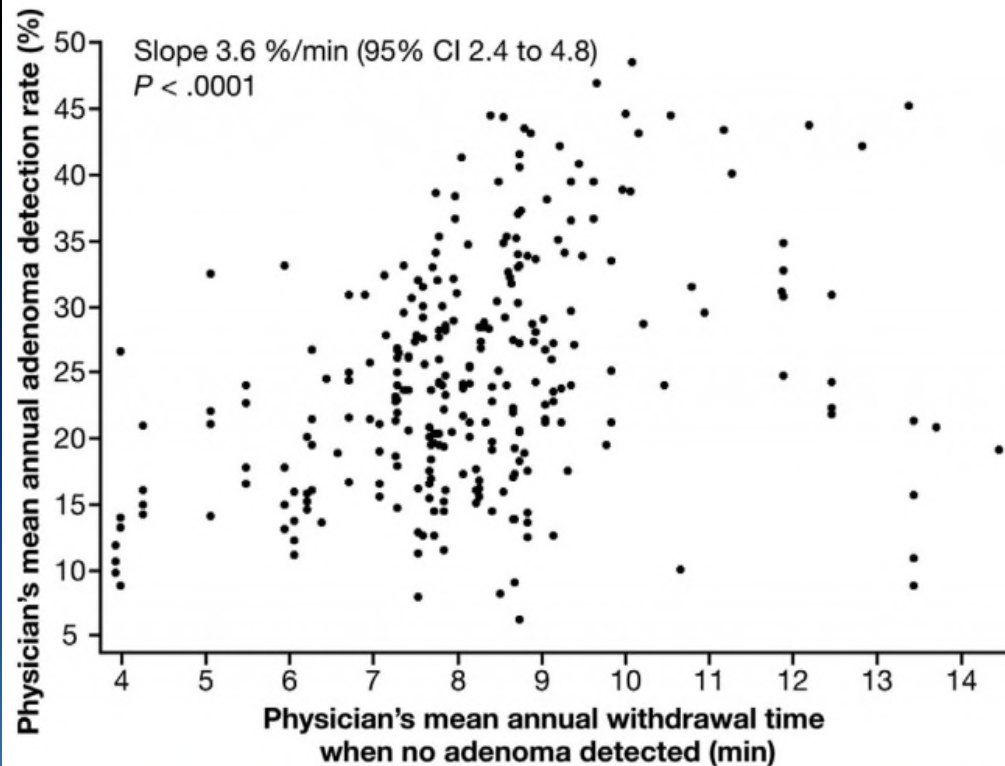


Figure 1. Relationship between physicians' annual withdrawal times and adenoma detection rates (ADRs).

The time of observation and ADR

- ADR improves 3.6% with 1 min extra for observation
- Observation time less than 6 min increases 2.3 times the risk of interval cancer (CRC detected at the next colonoscopy)

Factors of ADR

- colon cleansing level
- cecal intubation rate
- antispasmodic drug
- experience of endoscopists
- timing of the colonoscopy

(ADR decreases at latter half of AM and PM)

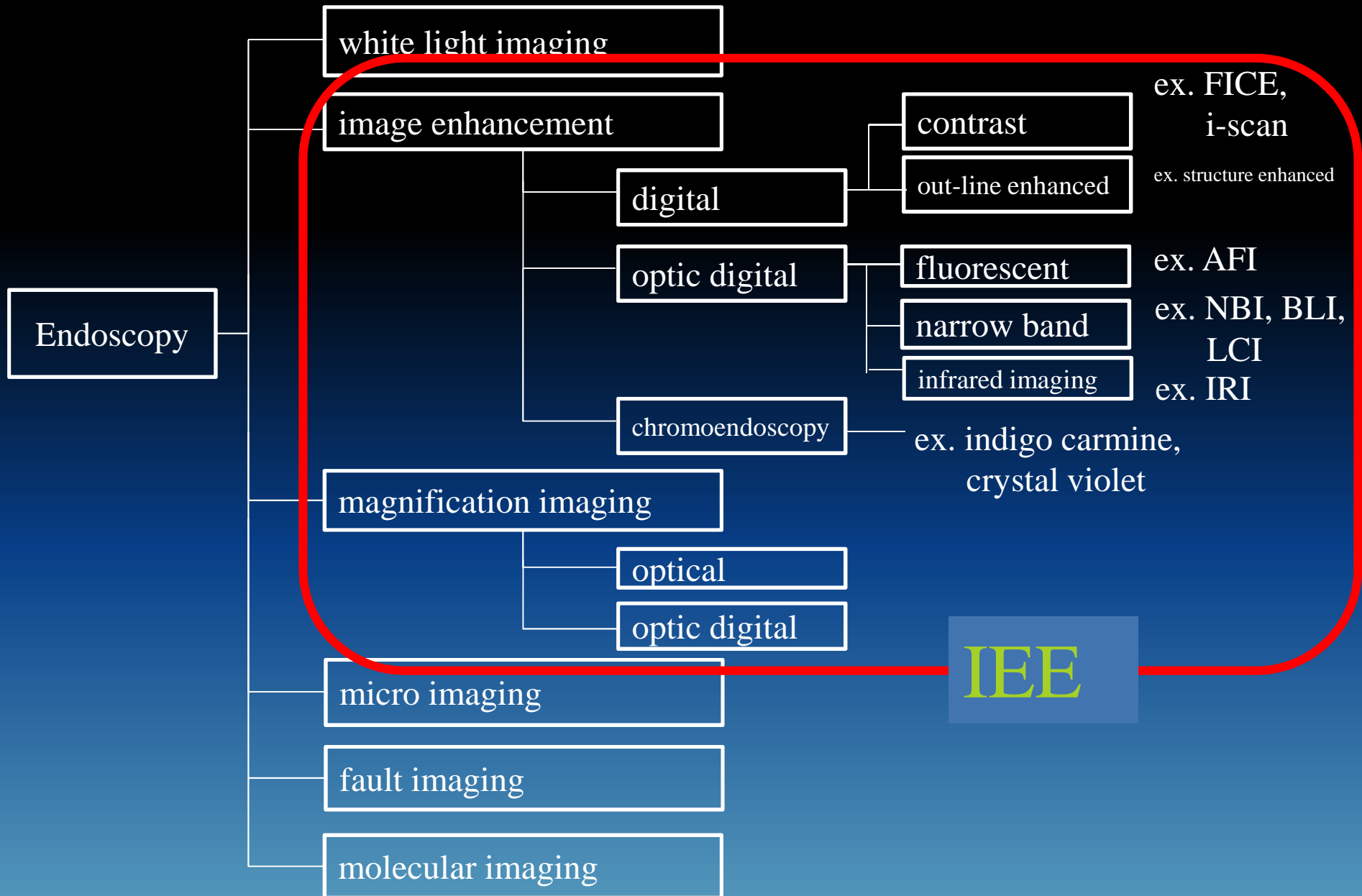
Lee TJ. et al. Endoscopy. 2014;46(3):203-11.

- the use of image enhanced endoscopy (IEE)



Today's topic

Grouping of endoscopy



ADR and chromoendoscopy

- Indigo carmine spraying improves ADR

Pohl J. et al. Gut 2011;60:485-490.

Charles JK. et al. Am J Gastroenterol 2010; 105:1301–1307

→ however the observation time expands

⇒ any simple methods?

NBI and BLI only requires just pressing

the button during the observation

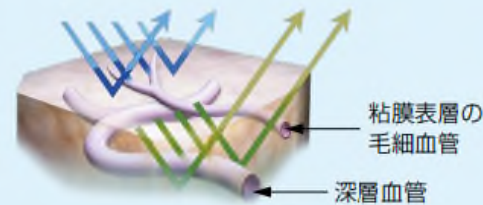
And provide the further information

Narrow Banding Imaging (NBI)

Narrow Band Imaging (NBI) system (Olympus Medical Co., Tokyo, Japan). A narrow wave (415nm and 540nm) which is absorbed in blood, microvascular and microsurface pattern are enhanced.

●血管走行が強調表示されるNBI

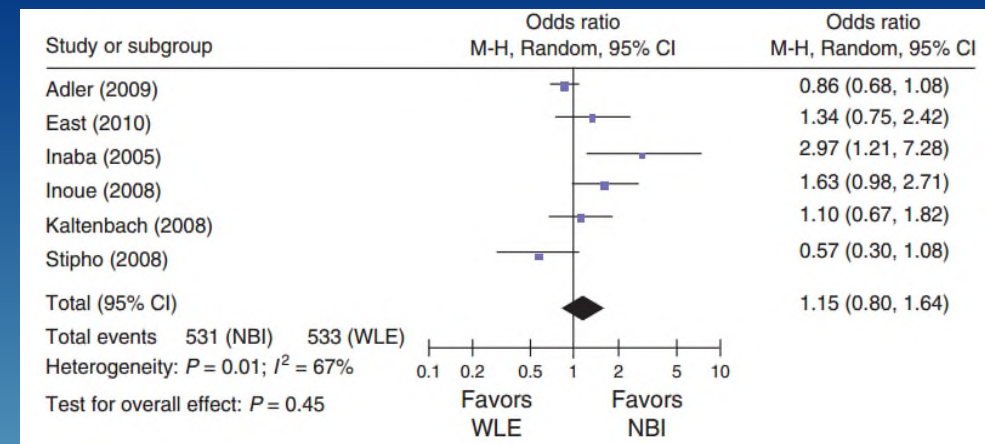
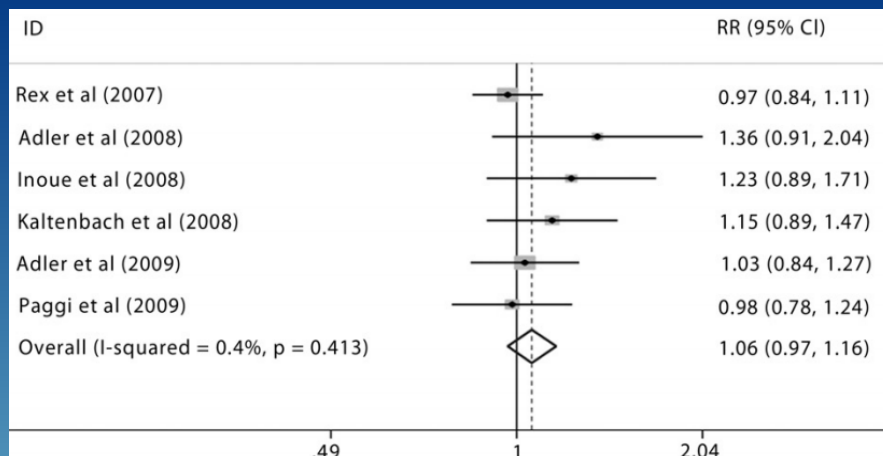
NBI(Narrow Band Imaging)は粘膜表層の毛細血管や表面微細構造が強調表示される、オリンパス独自の光デジタル法による画像強調観察機能です。2つの狭帯域化された光が、ヘモグロビンによって強く吸収され、血管と背景粘膜とのコントラストを強調。モニター上では粘膜表層の毛細血管が茶色調に、深層血管がシアン(青緑)調に表示されます。



NBIモード時のモニター画像

- 茶色調: 粘膜表層の毛細血管
- シアン調: 深層血管

NBI and ADR



Dinecen L, et al. Gastrointest Endosc 2012;75(3):604-11.

Pasha SF, et al. Am J Gastroenterol 2012;107(3):363-70.

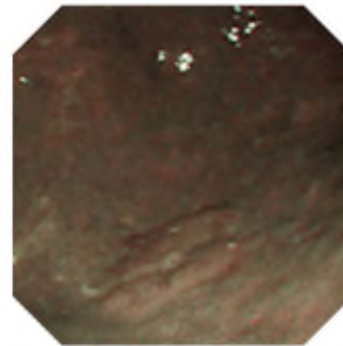
New generation NBI (2012~)



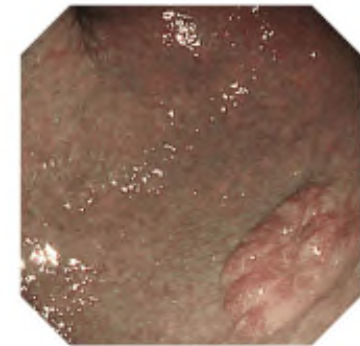
明るくなったNBI (Narrow Band Imaging)

粘膜表層の血管走行が強調表示されるNBI。観察深度の大幅な向上により、従来製品*に比べて遠点の部位も明るく映し出し、より詳細な観察をサポートします。EVIS LUCERA ELITEでは、すべてのスコープと内視鏡システムがNBIに標準対応しています。

*従来製品：EVIS LUCERA SPECTRUM



EVIS LUCERA SPECTRUM



EVIS LUCERA ELITE

With the new generation NBI, Polyp detection rate (PDR) and ADR improves. NBI 35.4% vs non-NBI 20.1% $p=0.01$

Lee TJ. et al. Endoscopy. 2014;46(3):203-11.

BLI and ADR



Detectability of colorectal neoplastic lesions using a novel endoscopic system with blue laser imaging: a multicenter randomized controlled trial

Hiroaki Ikematsu, MD, PhD,¹ Taku Sakamoto, MD,² Kazutomo Togashi, MD, PhD,³ Naohisa Yoshida, MD, PhD,⁴ Takashi Hisabe, MD, PhD,⁵ Shinsuke Kiriya, MD, PhD,⁶ Koji Matsuda, MD, PhD,⁷ Yoshikazu Hayashi, MD, PhD,⁸ Takahisa Matsuda, MD, PhD,² Shozo Osera, MD, PhD,¹ Kazuhiro Kaneko, MD, PhD,¹ Kenichi Utano, MD, PhD,³ Yuji Naito, MD, PhD,⁴ Hiroshi Ishihara, MD,⁵ Masayuki Kato, MD, PhD,⁷ Kenichi Yoshimura, PhD,⁹ Hideki Ishikawa, MD, PhD,¹⁰ Hironori Yamamoto, MD, PhD,⁸ Yutaka Saito, MD, PhD²

Japan

Gastrointestinal Endoscopy 2017 86(2):386-394.

TABLE 2. Detected polyps in the WLI and BLI groups

	WLI group (n = 474)	BLI group (n = 489)	P value
No. of adenomas per patient, mean ± SD	1.01 ± 1.36	1.27 ± 1.73	.008
Adenoma detection rate, %	52.7	54.8	.521
No. of polyps per patient, mean ± SD	1.43 ± 1.64	1.84 ± 2.09	.001
Polyp detection rate, %	62.4	68.3	.056

WLI, White-light imaging; BLI, blue-laser imaging; SD, standard deviation.

BLI and ADR



Detectability of colorectal neoplastic lesions using a novel endoscopic system with blue laser imaging: a multicenter randomized controlled trial

Hiroaki Ikematsu, MD, PhD,¹ Taku Sakamoto, MD,² Kazutomo Togashi, MD, PhD,³
 Naohisa Yoshida, MD, PhD,⁴ Takashi Hisabe, MD, PhD,⁵ Shinsuke Kiriyama, MD, PhD,⁶
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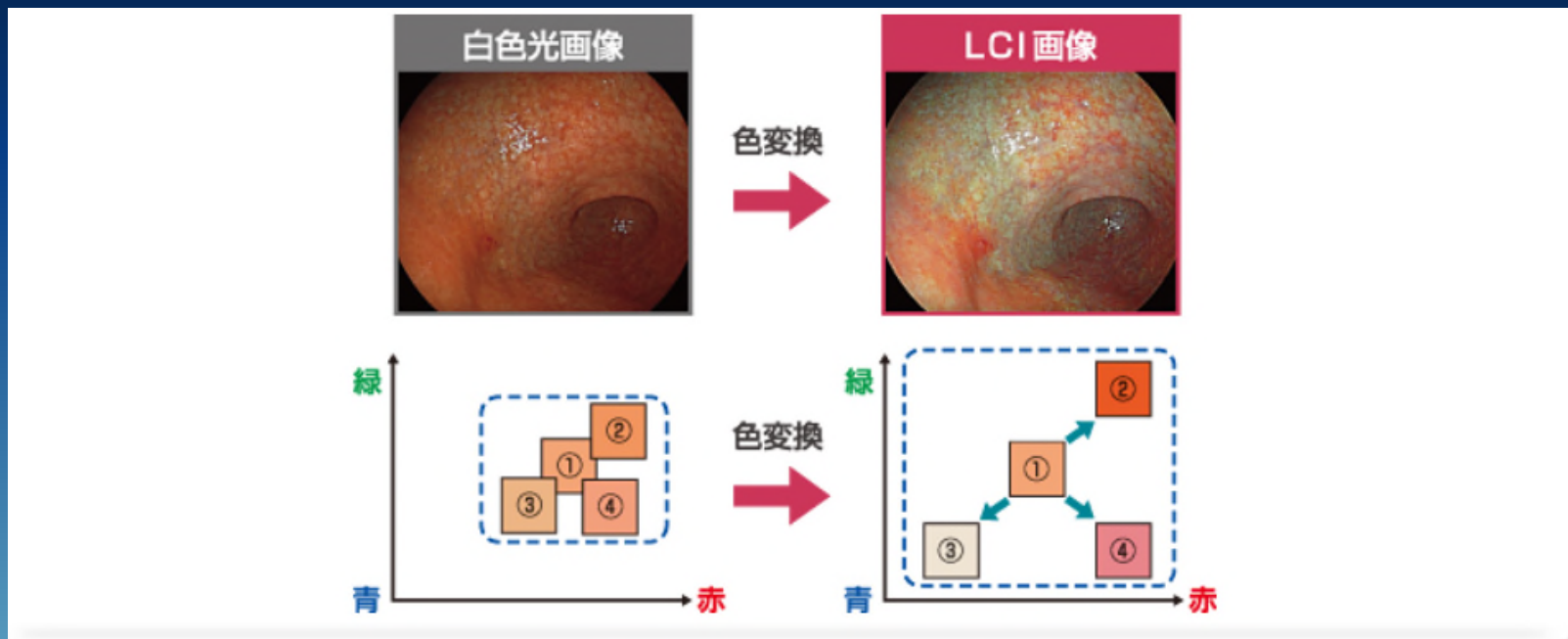
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Linked Color Imaging(LCI)



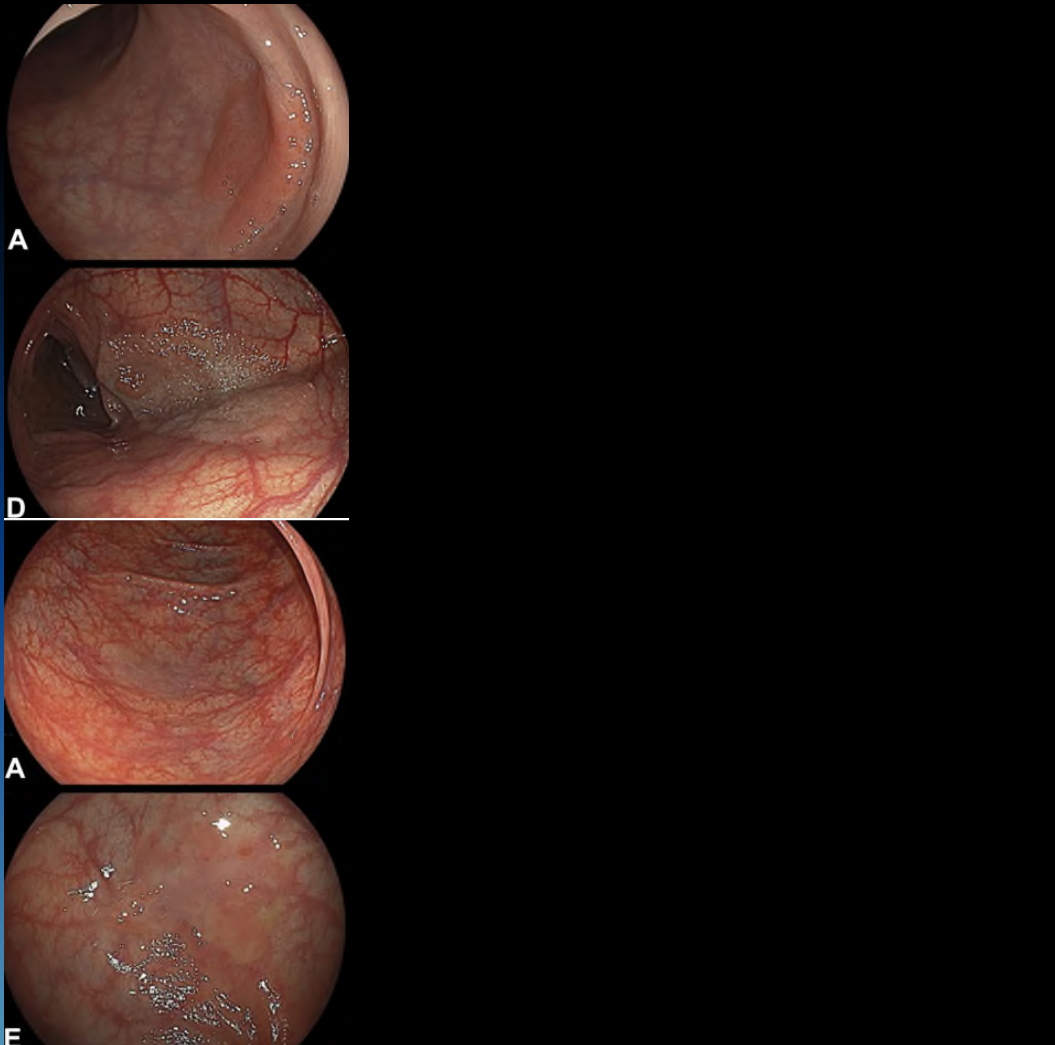
In 2012, Fujifilm produced “LCI”.
LCI differentiates the red color spectrum more effectively than White Light imaging thanks to its optimal pre-process composition of light spectrum and advanced signal processing. The increased color contrast improves detection of inflammation and results in more accurate delineation.



The usefulness of about BLI and LCI

Linked-color imaging improves endoscopic visibility of colorectal nongranular flat lesions

Takuto Suzuki, PhD, MD,¹ Taro Hara, PhD, MD,² Yoshiyasu Kitagawa, MD,¹ Hideyuki Takashiro, MD,³ Rino Nankinzan, MD,³ Osamu Sugita, MD,³ Taketo Yamaguchi, PhD, MD³



BLI and LCI improve the visibility of colorectal lesions.

Summary

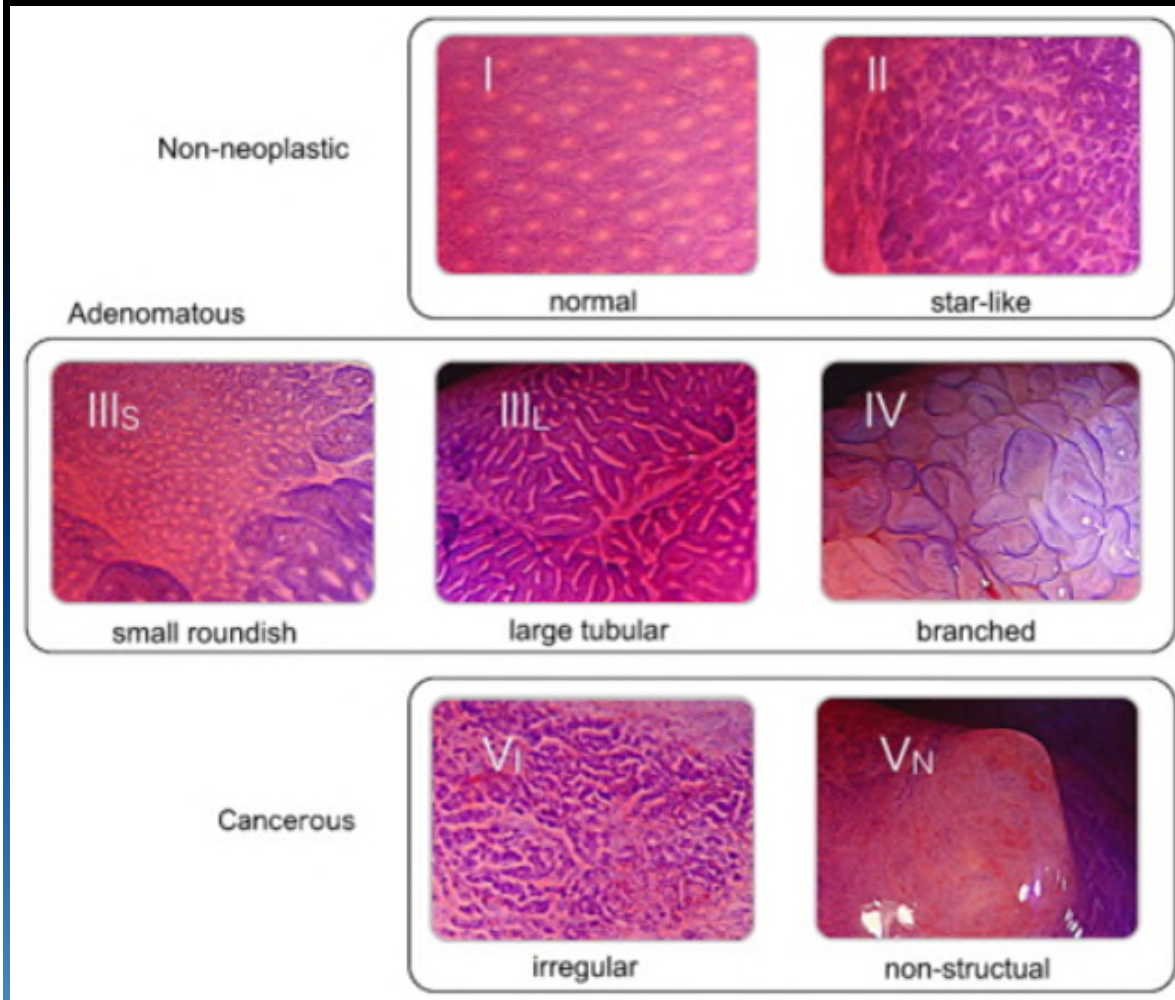
- ADR improves with the use of IEE



⇒ How is the ability of qualitative diagnosis for colorectal neoplasms with IEE?

The ability of IEE for the qualitative diagnosis of colorectal neoplasms

Pit pattern with crystal violet



Golden standard for recent

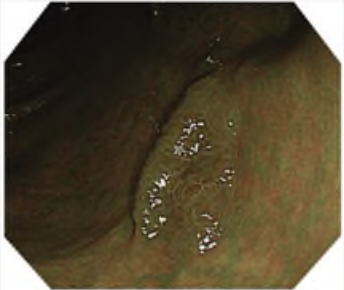
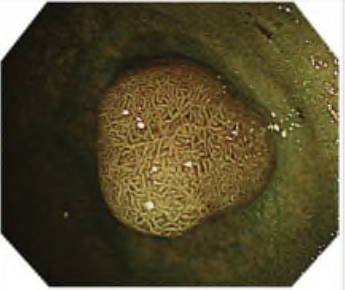
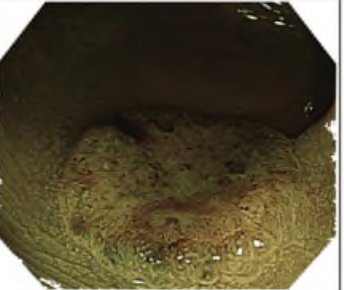

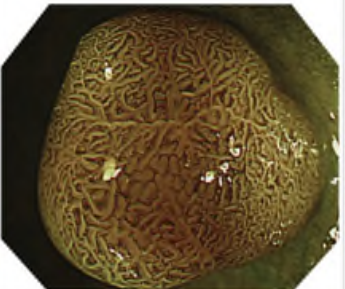
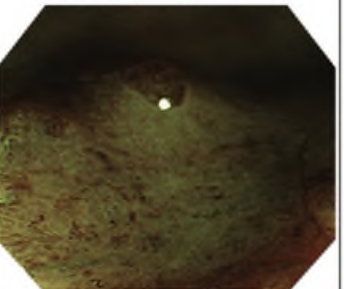
Precise diagnosis rate
is 85 ~ 98.7%

agenda

- the hassle procedure
- long observation time
- cost

The ability of NBI(non-magnification)

NBI International Colorectal Endoscopic (NICE) Classification*

	Type 1	Type 2	Type 3
Color	Same or lighter than background	Browner relative to background (verify color arises from vessels)	Brown to dark brown relative to background; sometimes patchy whiter areas
Vessels	None, or isolated lacy vessels coursing across the lesion	Brown vessels surrounding white structures**	Has area(s) of disrupted or missing vessels
Surface Pattern	Dark or white spots of uniform size, or homogeneous absence of pattern	Oval, tubular or branched white structure surrounded by brown vessels**	Amorphous or absent surface pattern
Most likely pathology	Hyperplastic	Adenoma***	Deep submucosal invasive cancer
Examples			
			

* Can be applied using colonoscopes with or without optical (zoom) magnification

** These structures (regular or irregular) may represent the pits and the epithelium of the crypt opening.

*** Type 2 consists of Vienna classification types 3, 4 and superficial 5 (all adenomas with either low or high grade dysplasia, or with superficial submucosal carcinoma). The presence of high grade dysplasia or superficial submucosal carcinoma may be suggested by an irregular vessel or surface pattern, and is often associated with atypical morphology (e.g., depressed area).

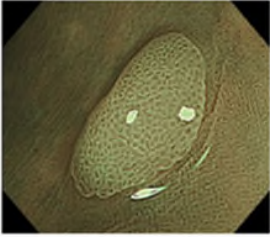
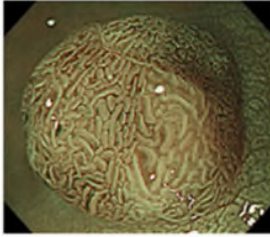
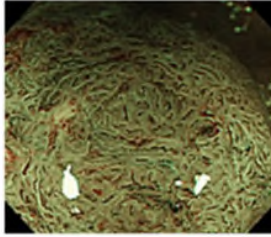
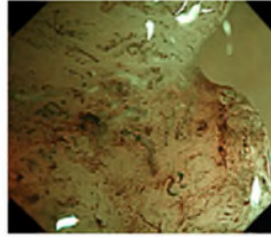
Precise diagnosis rate is 89-92%

David HG, et al Gastroenterology 2012;143:599 – 607

Hayashi N, et al. Gastrointest Endosc 2013;78:625-32.

The ability of NBI (magnification)

The Japan NBI Expert Team (JNET) classification.

	Type 1	Type 2A	Type 2B	Type 3
Vessel pattern	· Invisible* ¹	· Regular caliber · Regular distribution (meshed/spiral pattern) * ²	· Variable caliber · Irregular distribution	· Loose vessel areas · Interruption of thick vessels
Surface pattern	· Regular dark or white spots · Similar to surrounding normal mucosa	· Regular (tubular/branched/papillary)	· Irregular or obscure	· Amorphous areas
Most likely histology	Hyperplastic polyp/ Sessile serrated polyp	Low grade intramucosal neoplasia	High grade intramucosal neoplasia/ Shallow submucosal invasive cancer * ³	Deep submucosal invasive cancer
Endoscopic image				

*1. If visible, the caliber in the lesion is similar to surrounding normal mucosa.

*2. Micro-vessels are often distributed in a punctate pattern and well-ordered reticular or spiral vessels may not be observed in depressed lesions.

*3. Deep submucosal invasive cancer may be included.

Sano Y, et al. Digestive Endoscopy 2016; 28: 526–533

TABLE 3. Performance characteristics of each type of the JNET classification*

JNET classification	Sensitivity	Specificity	PPV	NPV	Accuracy
Type 1	87.5 (81.9-93.1)	99.9 (99.8-100.0)	97.5 (94.8-100.3)	99.4 (99.1-99.7)	99.3 (99.0-99.6)
Type 2A	74.3 (72.6-76.0)	92.7 (90.2-95.1)	98.3 (97.7-98.9)	38.7 (35.7-41.6)	77.1 (75.5-78.6)
Type 2B	61.9 (58.1-65.6)	82.8 (81.2-84.3)	50.9 (47.5-54.4)	88.2 (86.9-89.6)	78.1 (76.6-79.6)
Type 3	55.4 (48.7-62.1)	99.8 (99.6-100.0)	95.2 (91.4-98.9)	96.6 (95.9-97.3)	96.6 (95.9-97.2)

*Values are percents with 95% confidence interval in parentheses.

Strategy for endoscopic diagnosis and treatment

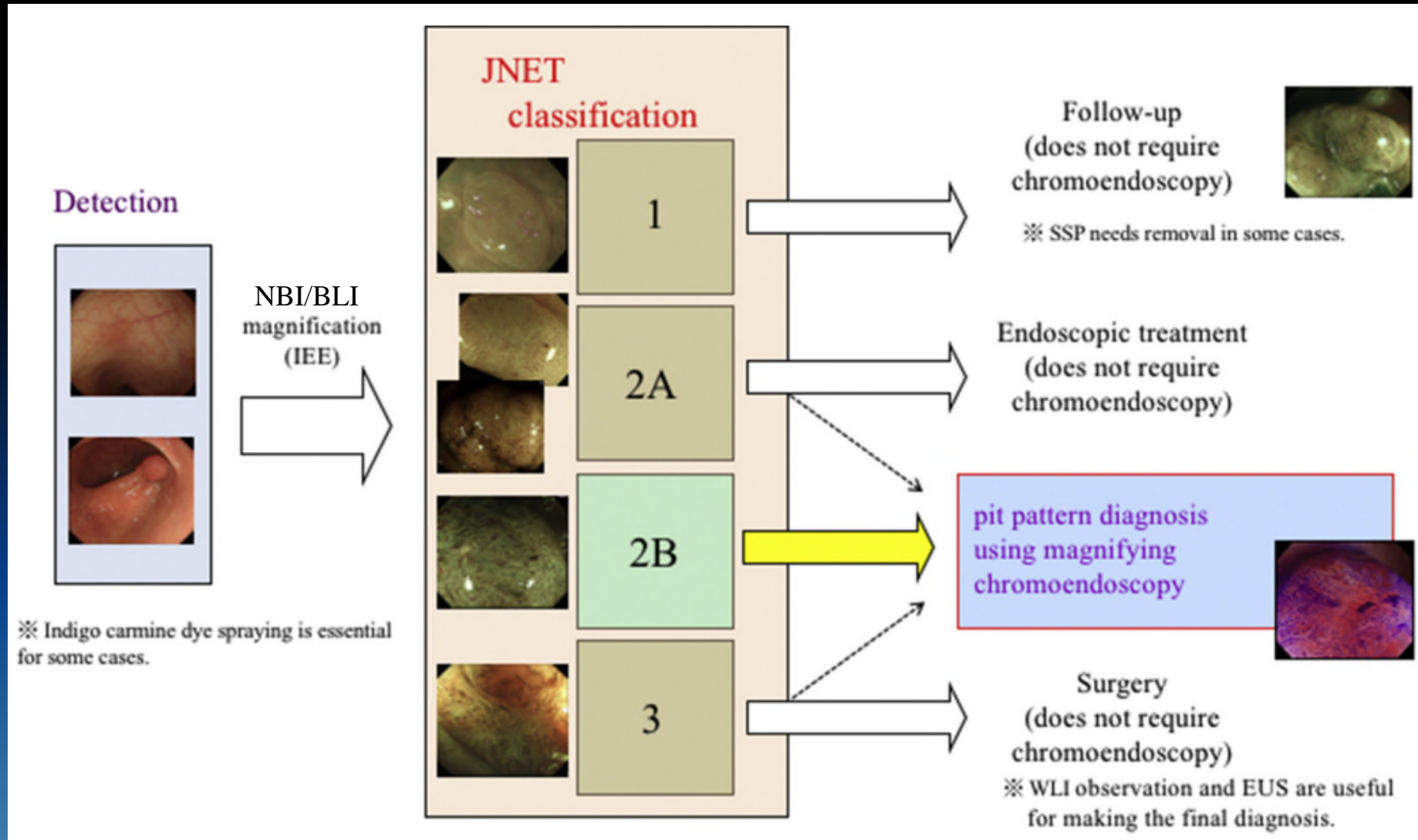
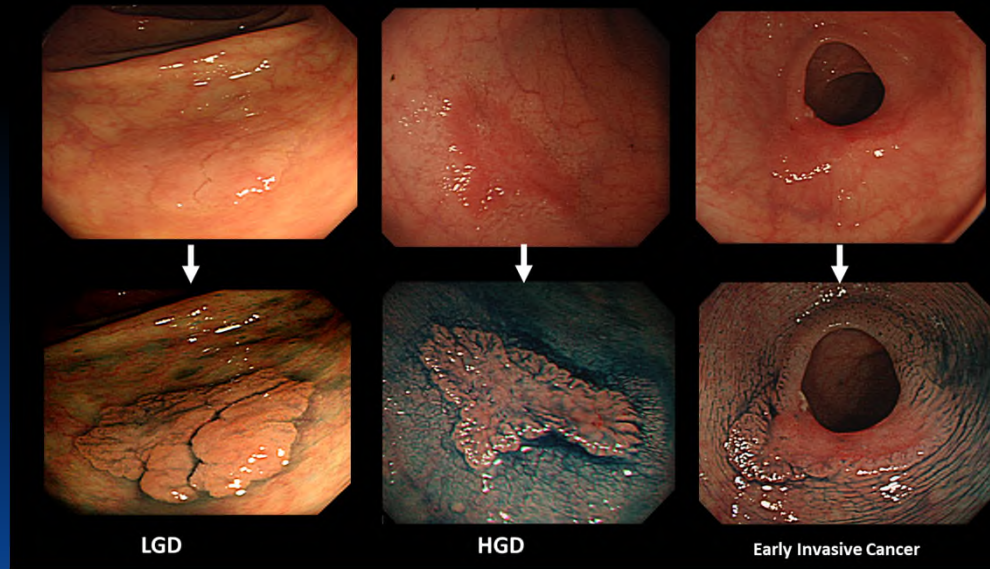


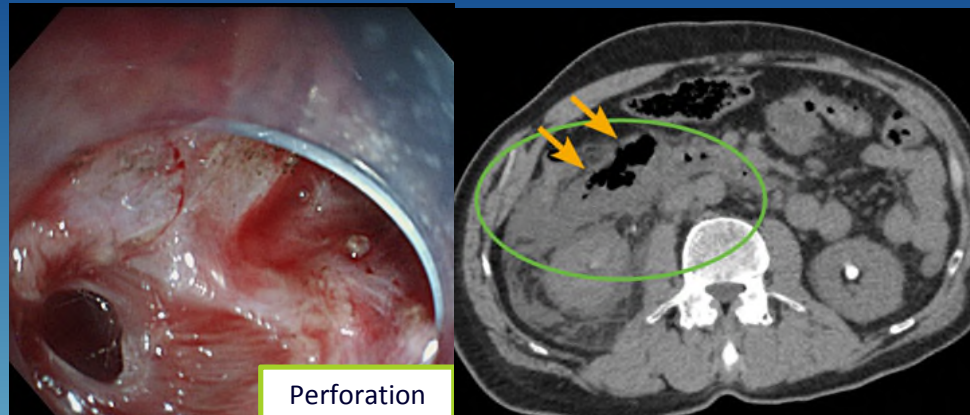
Figure 2. Strategy for endoscopic treatment of colorectal lesions. *NBI*, narrow-band imaging; *IEE*, image-enhanced endoscopy; *WLI*, white light imaging; *EUS*, endoscopic ultrasonography.

The most important point to introduce colorectal ESD
is . . .

Precise diagnosis for the target lesion of Colorectal ESD



Because . . . colorectal ESD sometimes causes complication
such as perforation



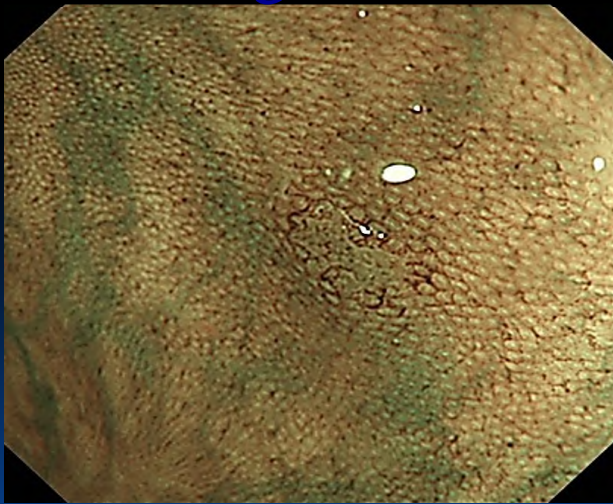
The target lesion of Colorectal ESD

The lesion that preferred to endoscopic En bloc resection
Of which . . .

- 1) difficult to en bloc resection by EMR
 - LST-NG, especially Pseudo Depressive type
 - showed V₁ pit pattern
 - SM slight invasion
 - Large depressed tumor
 - Large protruded lesion suspected cancer
- 2) involve fibrosis in submucosal layer
- 3) associate chronic inflammation such as UC
- 4) local residual lesion after endoscopic resection

Flow of the diagnosis

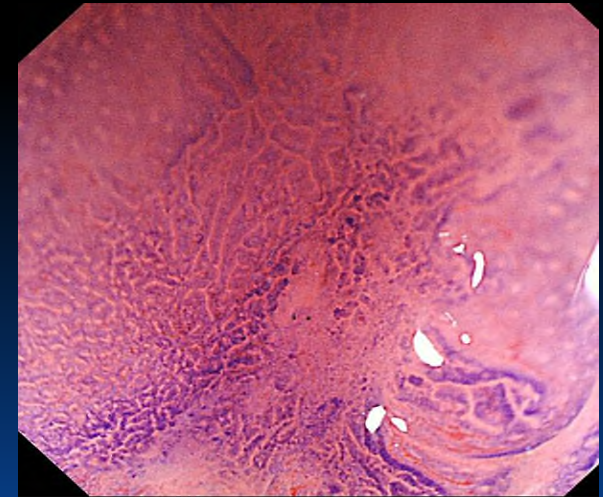
presence
diagnosis



qualitative
diagnosis



invasion depth
diagnosis



Non-Magnifying
Endoscopy

Conventional endoscopy



NBI/BLI



Chromoendoscopy



Magnifying
Endoscopy

NBI/BLI

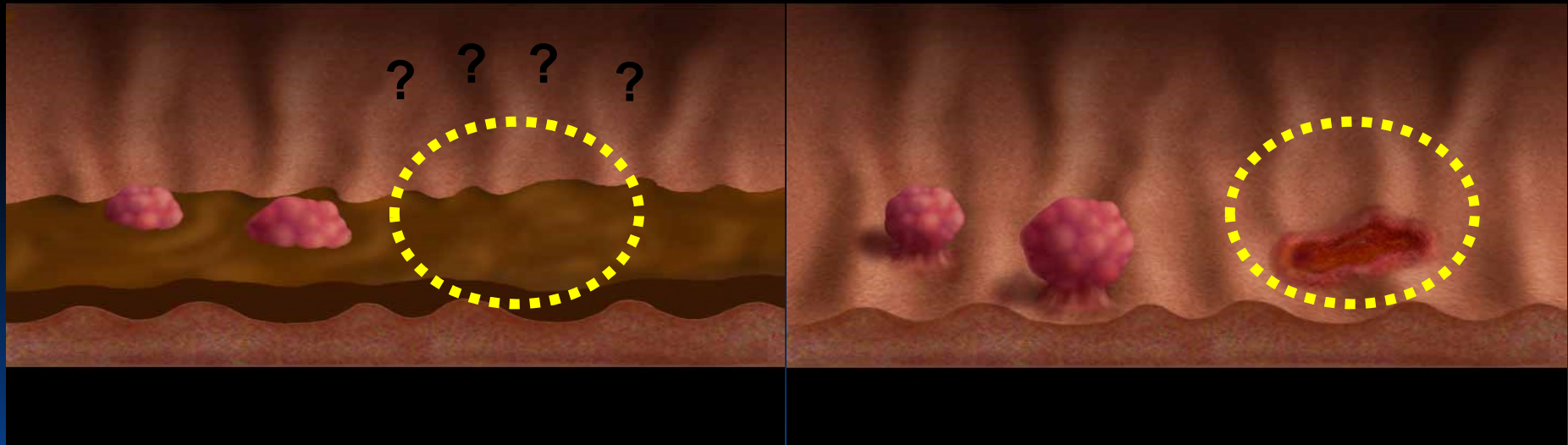


Chromoendoscopy



presence
diagnosis

Bowel Preparation



**Good Bowel Preparation is Indispensable
to Detect “Flat and Depressed” Lesions**

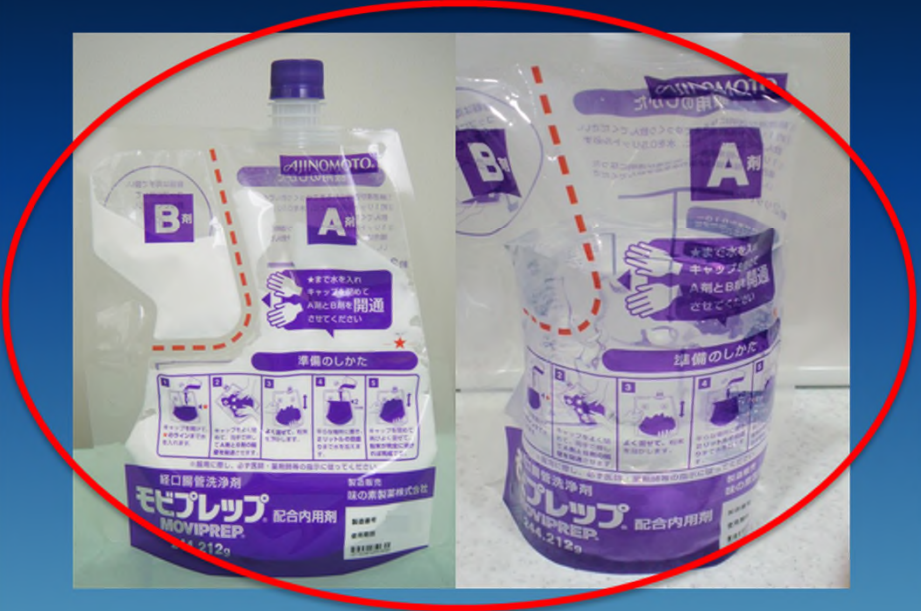
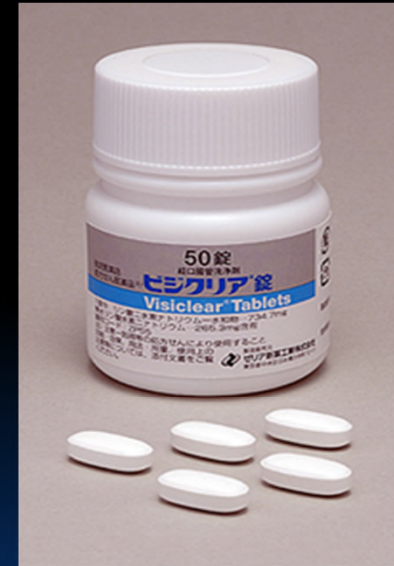


**Polyethylene glycol electrolyte lavage solution
(PEG-ELS) 2 -3 Liters**

• • • On the Examination's Day Morning

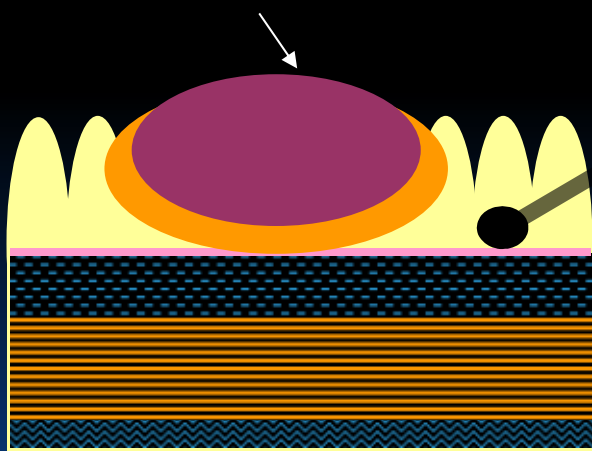


前処置 (preparation)

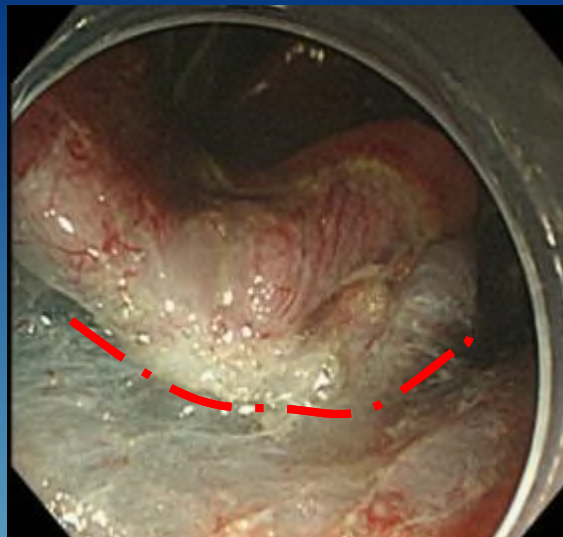
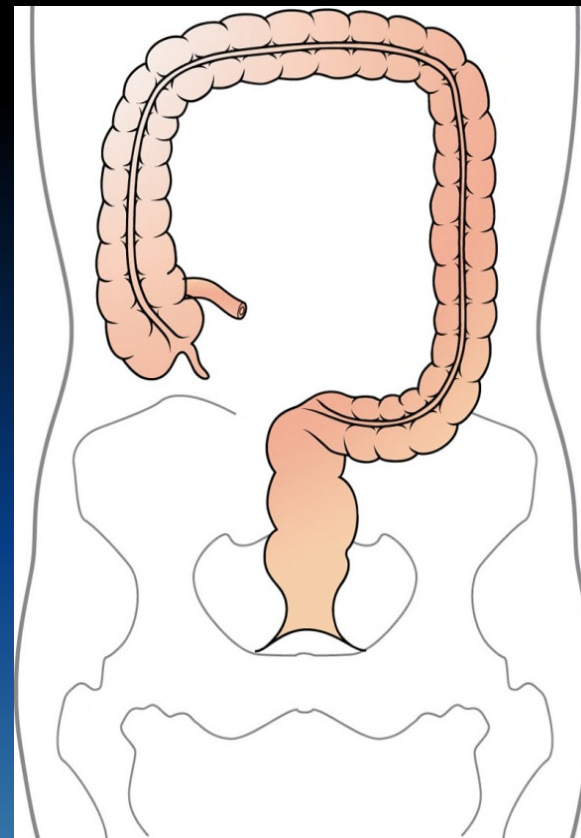


Points to start colorectal ESD

Malignancy(cancer)



Mucosa
Muscular layer of mucosa
Submucosa
Proper muscular layer
Serosa



Cutting devices

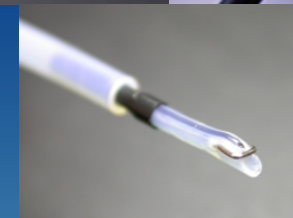
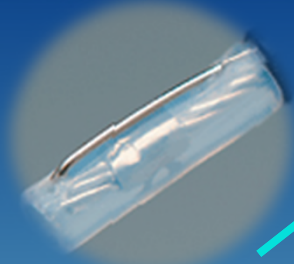
Blade type



Needle type



Grasping type



Take home message

- CRC is a disease increasing world wide and we need to lower the burden
- Screening colonoscopy reduces CRC death
- It is important to manage the quality control of colonoscopy
- Chromoendoscopy is useful for detection and diagnosis for colorectal neoplasms, however the procedure is hassle, so NBI and BLI is worthy of note.

Take home message

Precise diagnosis for the target lesion of Colorectal ESD
(Pit pattern, NBI/BLI JNET classification)

- Be aware of colorectal anatomy focus on layer, which differs on the location of colon
(mucosal layer, muscularis mucosae, submucosal layer)
- Understand the characteristic of various cutting devices
(Blade type, Needle type, Grasping type)
- Know as much about the prevention and treating method for complications
(hemorrhage, perforation)