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endoscopy

# Indications for ESD/ Proposal for a white paper/guidelines from WEO's CRC SC

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*Endoscopy Division, National Cancer Center Hospital*



# Agenda

**Indication for ESD**

**ESGE guidelines**

**JGES guidelines**

**Proposal for WEO guidelines**



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# Agenda

## Indication for ESD

JGES guidelines

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Proposal for WEO guidelines



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**Indication for ESD**

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# **Endoscopic submucosal dissection for superficial gastrointestinal lesions: European Society of Gastrointestinal Endoscopy (ESGE) Guideline – Update 2022**

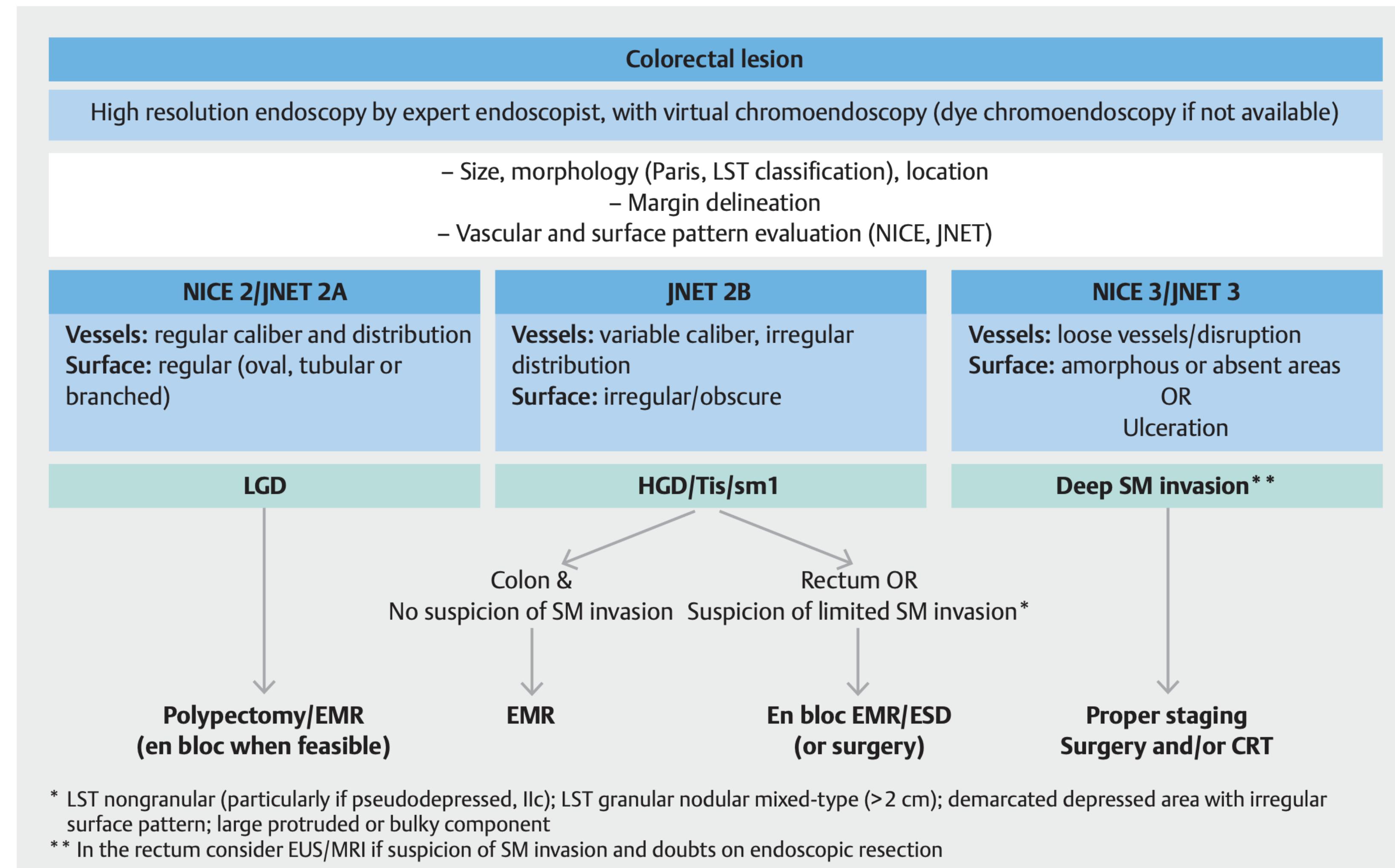


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► **Fig. 4** Endoscopic submucosal dissection (ESD) for superficial colorectal lesions: a decision algorithm. CRT, chemoradiotherapy; EMR, endoscopic mucosal resection; EUS, endoscopic ultrasonography; HGD, high grade dysplasia; JNET, Japan NBI Expert Team; LGD, low grade dysplasia; LST, laterally spreading tumor; MRI, magnetic resonance imaging; NICE, NBI International Colorectal Endoscopic.

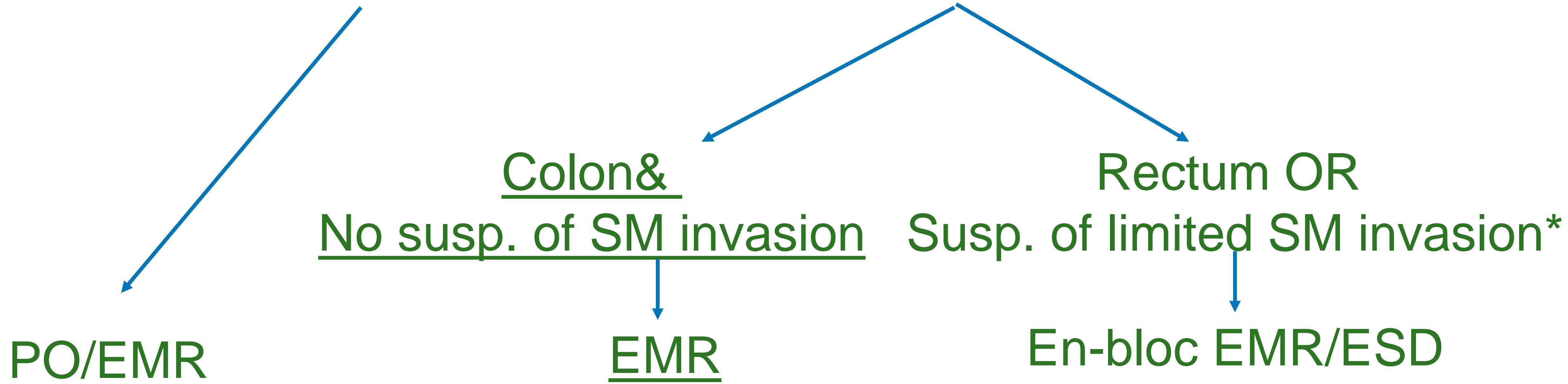


JNET 2A

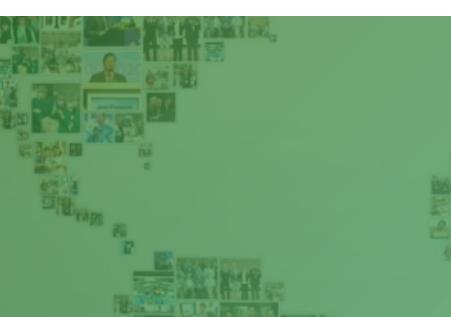
LGD

JNET 2B

HGD/Tis/sm1



- Colon&  
No susp. of SM invasion
- Rectum OR  
Susp. of limited SM invasion\*
- LST-NG (PD, IIc)  
• LST-G mix > 2cm  
• Demarcated depressed area with irregular surface pattern  
• Large protruded or bulky component



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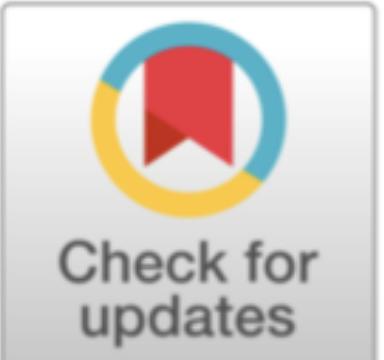


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## Guidelines

# Japan Gastroenterological Endoscopy Society guidelines for colorectal endoscopic submucosal dissection/endoscopic mucosal resection

Shinji Tanaka,<sup>1,2,3,4</sup> Hiroshi Kashida,<sup>1</sup> Yutaka Saito,<sup>1,2</sup> Naohisa Yahagi,<sup>1</sup> Hiroo Yamano,<sup>1</sup> Shoichi Saito,<sup>1</sup> Takashi Hisabe,<sup>1</sup> Takashi Yao,<sup>2</sup> Masahiko Watanabe,<sup>2,3</sup> Masahiro Yoshida,<sup>1,4</sup> Yusuke Saitoh,<sup>1</sup> Osamu Tsuruta,<sup>1</sup> Ken-ichi Sugihara,<sup>2</sup> Masahiro Igarashi,<sup>1</sup> Takashi Toyonaga,<sup>1</sup> Yoichi Ajioka,<sup>2</sup> Masato Kusunoki,<sup>3</sup> Kazuhiko Koike,<sup>4</sup> Kazuma Fujimoto<sup>1</sup> and Hisao Tajiri<sup>1</sup>

<sup>1</sup>*Japan Gastroenterological Endoscopy Society*, <sup>2</sup>*Japanese Society for Cancer of the Colon and Rectum*, <sup>3</sup>*Japanese Society of Coloproctology*, and <sup>4</sup>*Japanese Society of Gastroenterology, Tokyo, Japan*



**Table 2** Indications for ESD for colorectal tumors<sup>†</sup>

Lesions for which endoscopic en bloc resection is required

- 1) Lesions for which en bloc resection with snare EMR is difficult to apply
  - LST-NG, particularly LST-NG (PD)
  - Lesions showing a V<sub>i</sub>-type pit pattern
  - Carcinoma with shallow T1 (SM) invasion
  - Large depressed-type tumors
  - Large protruded-type lesions suspected to be carcinoma<sup>‡</sup>

2) Mucosal tumors with submucosal fibrosis<sup>§</sup>

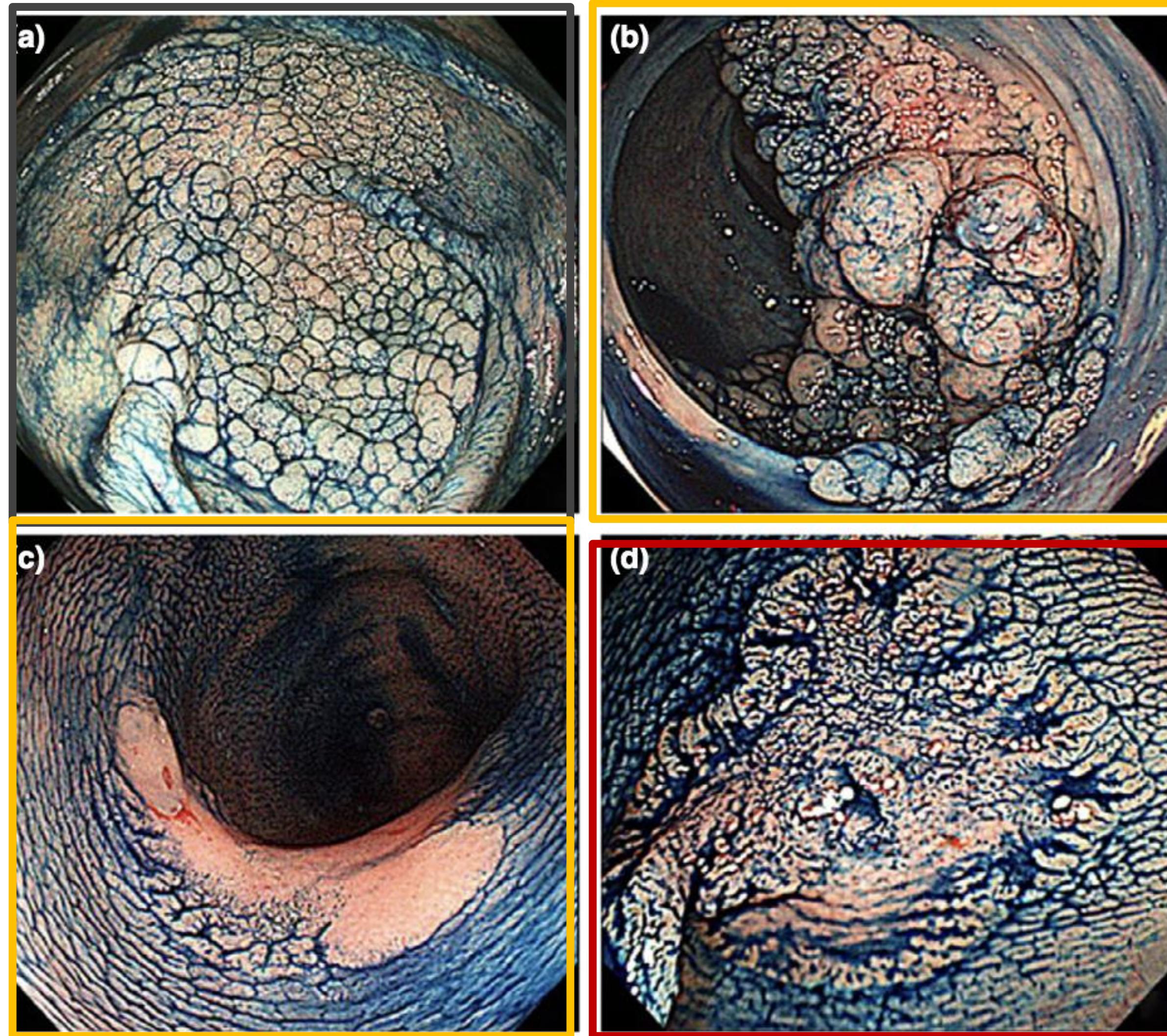
- 3) Sporadic localized tumors in conditions of chronic inflammation such as ulcerative colitis
- 4) Local residual or recurrent early carcinomas after endoscopic resection

<sup>†</sup>Partially modified from the draft proposed by the Colorectal ESD Standardization Implementation Working Group.

<sup>‡</sup>Including LST-G, nodular mixed type.

<sup>§</sup>As a result of a previous biopsy or prolapse caused by peristalsis of the intestine.

EMR, endoscopic mucosal resection; ESD, endoscopic submucosal dissection; LST-G, laterally spreading tumor granular type; LST-NG, laterally spreading tumor non-granular type; PD, pseudo-depressed; SM, submucosal.



f laterally spreading tumors (LST; classification should be done on the basis of image praying). LST-G, laterally spreading tumor granular type; LST-NG, laterally spreading tumor type LST-G (Homo); (b) nodular mixed-type LST-G (Mix); (c) flat-elevated-type LST-NG (PD).

# Introduction of CREAT-J

*Yutaka Saito, MD, PhD, FJGES, FASGE*



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Presenter; SAITO, YUTAKA, E-mail: [ytsaito@ncc.go.jp](mailto:ytsaito@ncc.go.jp)

# LONG-TERM OUTCOMES AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION FOR COLORECTAL EPITHELIAL NEOPLASMS: A JAPANESE PROSPECTIVE MULTICENTER COHORT TRIAL

CREATE-J

Presentation Time: 8:10 AM to 8:17 AM

Presentation Time: 8:10 AM to 8:17 AM, 11:43

AM to 11:46 AM

**YUTAKA SAITO, OHATA K, KOBAYASHI N, HARADA K, TAKEUCHI Y, CHINO A, Takamaru H, Kodashima S, HOTTA K, IKEMATSU H, URAOKA T, MURAKAMI T, DOYAMA H, ABE T, KATAGIRI A, HORI S, MICHIDA T, SUZUKI T, FUKUZAWA M, KIRIYAMA S, FUKASE K, MURAKAMI Y, ISHIKAWA Hideki, & The Colorectal ESD Activation Team of JAPAN (CREATE-J)**



# BACKGROUNDS 1

CREATE-J  
CBIVLH-J

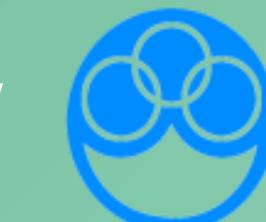
- It has been reported that p-EMR lowers the incidence of local recurrence by ablating the mucosal defect margin. <sup>1)</sup>
- Recurrence after p-EMR is, however; difficult to treat with EMR and often requires surgery even for benign adenomas. <sup>2)</sup>

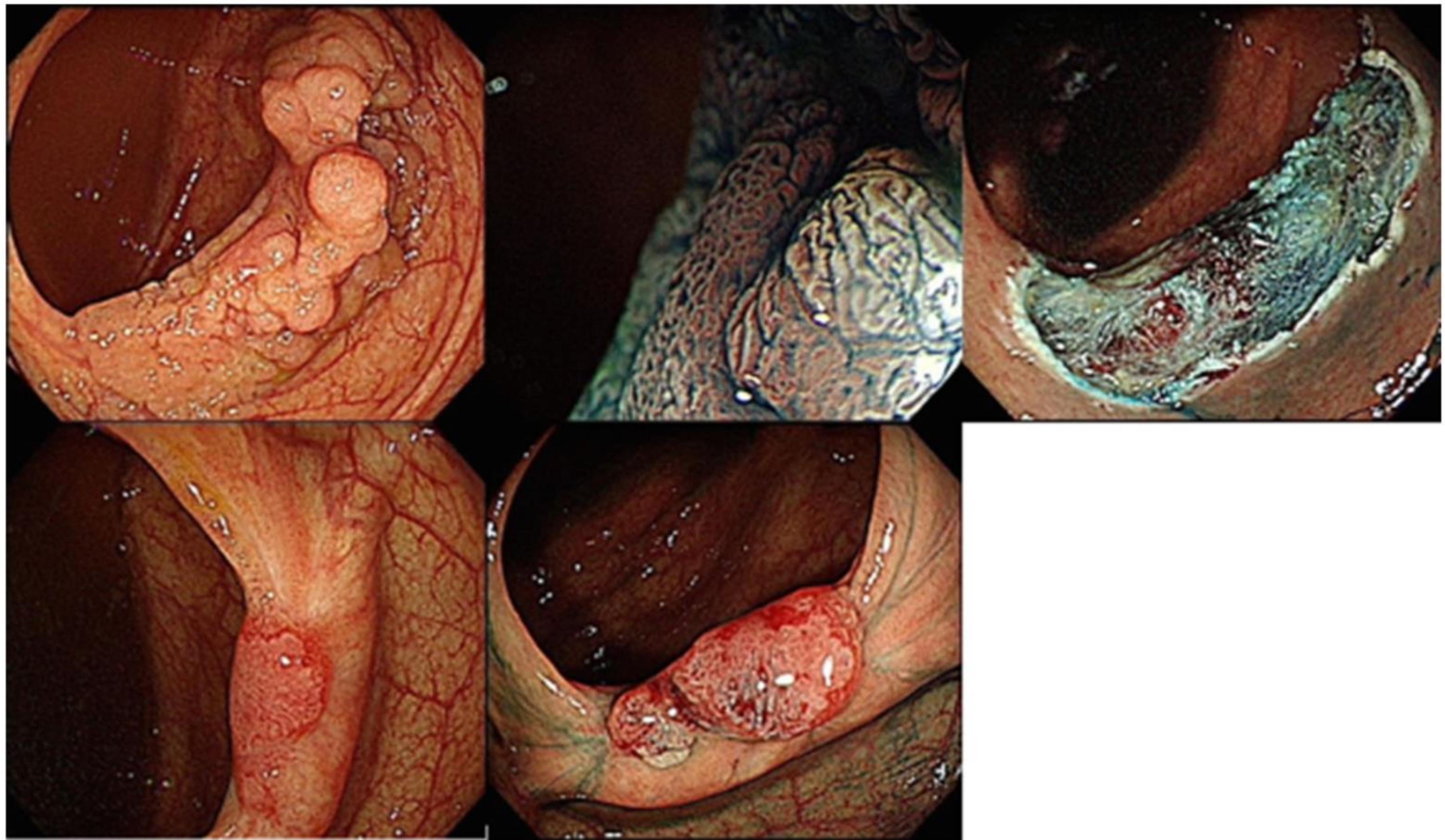




# Optimal surveillance interval after piecemeal endoscopic mucosal resection for large colorectal neoplasia: a multicenter randomized controlled trial

Takeshi Nakajima<sup>1</sup> · Taku Sakamoto<sup>1</sup> · Shinichiro Hori<sup>2</sup> · Shinya Yamada<sup>3</sup> · Hiroaki Ikematsu<sup>4</sup> · Keita Harada<sup>5</sup> · Han-Mo Chiu<sup>6</sup> · Shinsuke Kiriyma<sup>7</sup> · Tomoki Michida<sup>8</sup> · Kinichi Hotta<sup>9</sup> · Naoto Sakamoto<sup>10</sup> · Takashi Abe<sup>11</sup> · Akiko Chino<sup>12</sup> · Masakatsu Fukuzawa<sup>13</sup> · Nozomu Kobayashi<sup>14</sup> · Kazutoshi Fukase<sup>15</sup> · Takahisa Matsuda<sup>1</sup> · Yoshitaka Murakami<sup>16</sup> · Hideki Ishikawa<sup>17</sup> · Yutaka Saito<sup>1</sup> 





**Fig. 4** Representative images of case #6. The 0-Is + IIa (LST-G) lesion was treated via piecemeal endoscopic mucosal resection (p-EMR, 10 pieces). At the 3-month follow-up colonoscopy, a recur-

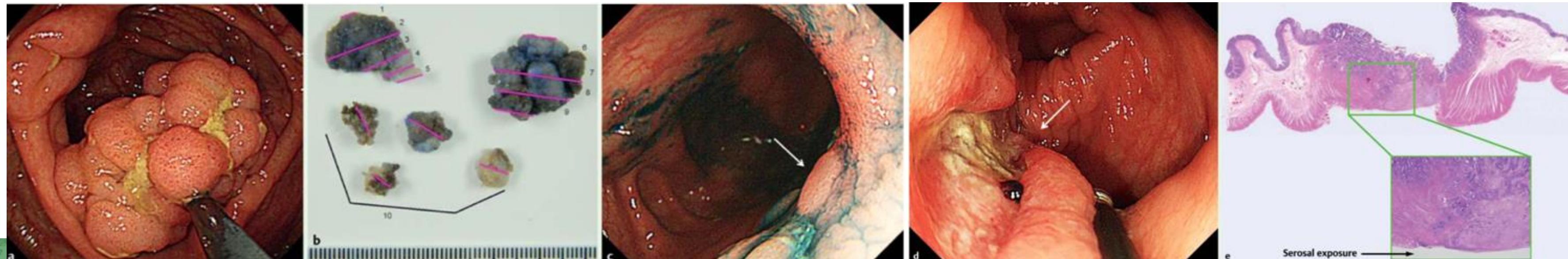
rent lesion was detected and cancerous recurrence was confirmed via intentional diagnostic EMR. Laparoscopic resection was then performed accordingly.



# BACKGROUNDS 2

CREATE-J  
CREATIVE-J

- In addition, in the case of p-EMR, it is difficult to accurately diagnose SM invasion & LYV, and there is a risk of missing an appropriate subsequent treatment.<sup>2)</sup>



# BACKGROUNDS 3

- ESD is the solution to solve these problems <sup>1)</sup>.
- Although good short-term outcomes have been reported from the West as well as Asia <sup>2-4)</sup>, and single center long-term outcomes <sup>5)</sup>, there have been no long-term prospective multicenter outcomes.



- 1) Saito Y, Abe S, Inoue H, et al. Gastroenterology. 2021 Aug;161(2):405-410.
- 2) Kobayashi N, Takeuchi Y, Ohata K, et al. Dig Endosc. 2021 Dec 28. doi: 10.1111/den.14223.
- 3) Fleischmann C, Probst A, Ebigbo A, et al. Gastroenterology. 2021 Oct;161(4):1168-1178.
- 4) Draganov PV, Aihara H, Karasik MS, et al. Gastroenterology. 2021 Jun;160(7):2317-2327.e2.
- 5) Yamada M, Saito Y, Takamaru H, et al. Endoscopy. 2017 Mar;49(3):233-242.

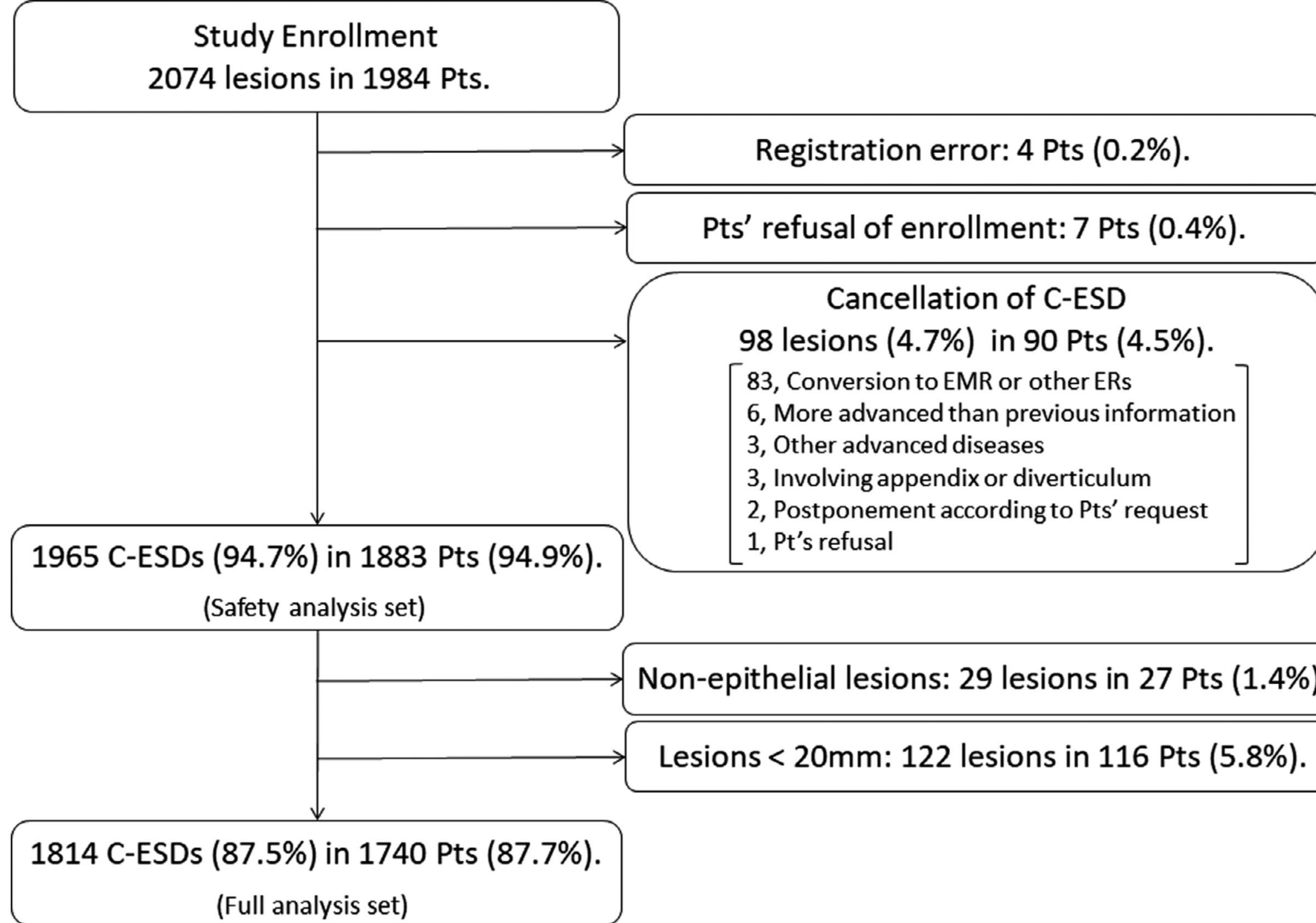


**Original Article**

# Outcomes of endoscopic submucosal dissection for colorectal neoplasms: Prospective, multicenter, cohort trial

Nozomu Kobayashi,<sup>1</sup> Yoji Takeuchi,<sup>2</sup> Ken Ohata,<sup>5</sup> Masahiro Igarashi,<sup>6</sup> Masayoshi Yamada,<sup>7</sup> Shinya Kodashima,<sup>8</sup> Kinichi Hotta,<sup>14</sup> Keita Harada,<sup>15</sup> Hiroaki Ikematsu,<sup>16</sup> Toshio Uraoka,<sup>9,19</sup> Naoto Sakamoto,<sup>10</sup> Hisashi Doyama,<sup>21</sup> Takashi Abe,<sup>3,22</sup> Atsushi Katagiri,<sup>11</sup> Shinichiro Hori,<sup>23</sup> Tomoki Michida,<sup>2,4</sup> Takehito Yamaguchi,<sup>17,18</sup> Masakatsu Fukuzawa,<sup>12</sup> Shinsuke Kiriyama,<sup>20</sup> Kazutoshi Fukase,<sup>24,25</sup> Yoshitaka Murakami,<sup>13</sup> Hideki Ishikawa<sup>26</sup> and Yutaka Saito<sup>7</sup>





**Figure 1** Study flow chart. C-ESD: colorectal endoscopic submucosal dissection. EMR, endoscopic mucosal resection; ER, endoscopic resection.

Location	n	SM-invasion	OR	95% CI	T1b	OR	95% CI
Right colon	922	13.6%	1	Ref.	5.6%	1	Ref.
Left colon	338	17.2%	1.32	0.94-1.85	8.0%	1.45	0.90-2.35
Rectum	414	17.6%	1.37	0.99-1.87	11.8%	2.25	1.5—3.37

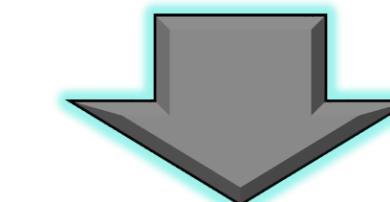
#### Combination of location & morphology

Right, LST-G	467	8.1%	1	Ref.		3.9%	1	Ref.	
Right, LST-NG	382	17.5%	2.4	1.58-3.66	<0.001	5.2%	1.38	0.73-2.62	0.333
Right, non-LST	73	27.4%	4.26	2.32-7.82	<0.001	19.2%	5.92	2.83-12.39	<0.001
Left, LST-G	130	11.5%	1.47	0.79-2.75	0.228	9.2%	2.54	1.21-5.34	0.013
Left, LST-NG	168	18.5%	2.56	1.54-4.25	<0.001	4.2%	1.09	0.46-2.58	0.853
Left, non-LST	40	30.0%	4.84	2.31-10.18	<0.001	20.0%	6.24	2.58-15.17	<0.001
Rectum, LST-G	301	14.6%	1.93	1.22-3.06	0.005	10.0%	2.76	1.52-5.01	0.001
Rectum, LST-NG	51	29.4%	4.7	2.39-9.29	<0.001	13.7%	3.97	1.61-9.81	0.002
Rectum, non-LST	62	22.6%	3.29	1.68-6.46	<0.001	19.4%	5.99	2.77-12.99	<0.001

# STUDY PROTOCOL

Ohata K, Kobayashi N, Saito Y. Gastroenterology. 2022 Jul 8:S0016-5085(22)00751-X.

Registration of all Colorectal ESD Pts. 1,984



Perform colorectal ESD

1,883

Pathological assessment

(1,965 lesions)



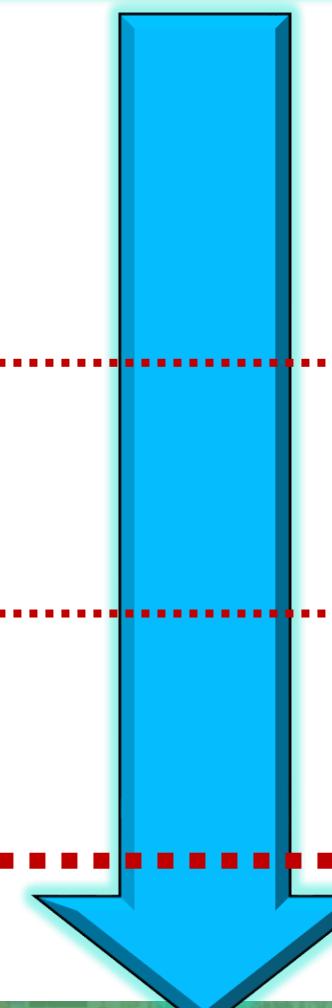
Curative (JSCCR guidelines\*)

Non-curative

\* JSCCR guidelines Curative

- No POR/MUC component
- Ly(-) V(-)
- Invasion Depth < 1000 $\mu$ m
- BD1
- VM0

Additional Surgery



1y  
3ys  
5ys



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Endoscopy Division, National Cancer Center Hospital

(Clinical Trial Registration: UMIN000010136)



# Patient and Lesion Characteristics

## -91% Curative Resection-

	Total	Adenoma	Tis	T1a	T1b -
Number of lesions, n	1814	40%	39%	7%	8%
Curability, n (%)					
<b>Complete CR (%)</b>	<b>79%</b>	87%	86%	75%	0
<b>Incomplete CR</b>	<b>12%</b>	13%	13%	10%	0
<b>non-CR</b>	<b>9.6%</b>	0.4%	1.0%	14%	100%

### Definitions:

Intramucosal cancer, corresponding to high-grade dysplasia and mucosal high-grade neoplasia in the WHO classification, was defined as Tis.

Submucosal invasion < 1000 µm was defined as T1a, and invasion ≥ 1000 µm was recorded as T1b.

CR was achieved when there was no submucosal deep invasion ≥ 1000 µm, lymphovascular invasion, tumor budding, nor a poorly differentiated component.

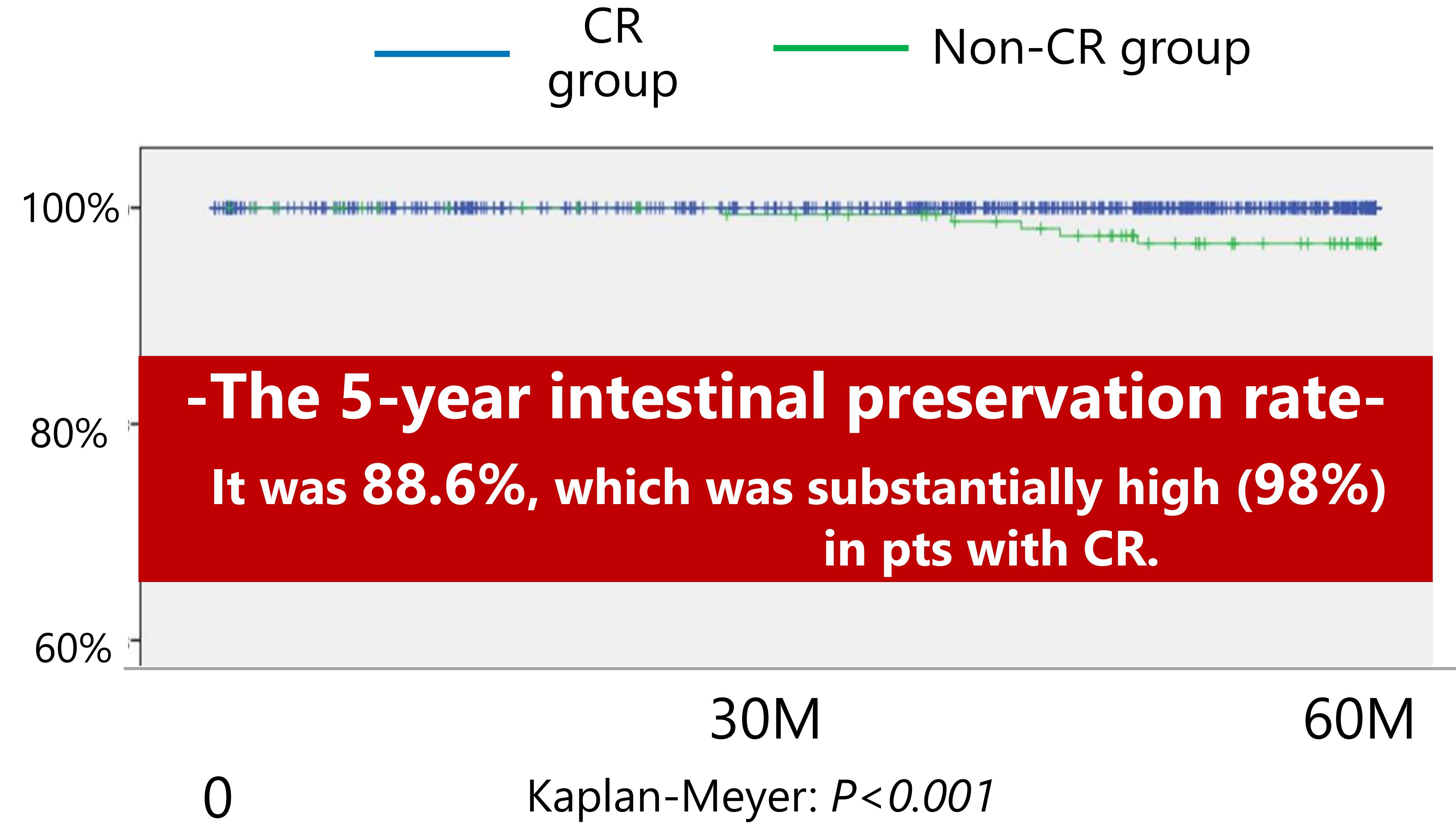
Complete CR was defined as a CR free of tumor at both lateral and horizontal margins of the specimen.

Incomplete CR was defined as CR with lateral margin presence or cannot be determined because of coagulation artefacts.

Adenoma includes serrated lesions.



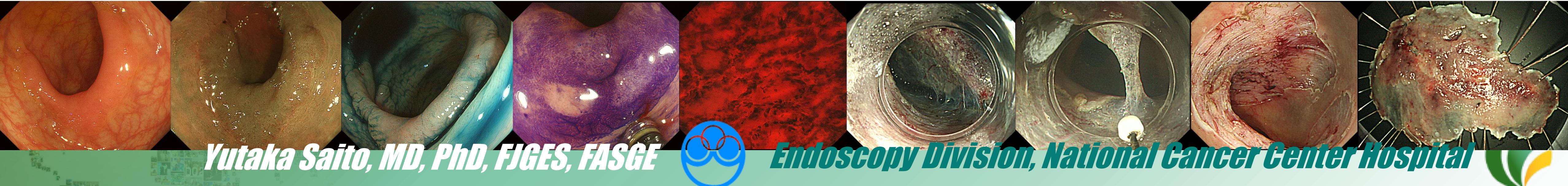
# ➤ The primary outcomes: Comparison of Disease-free Specific Survival



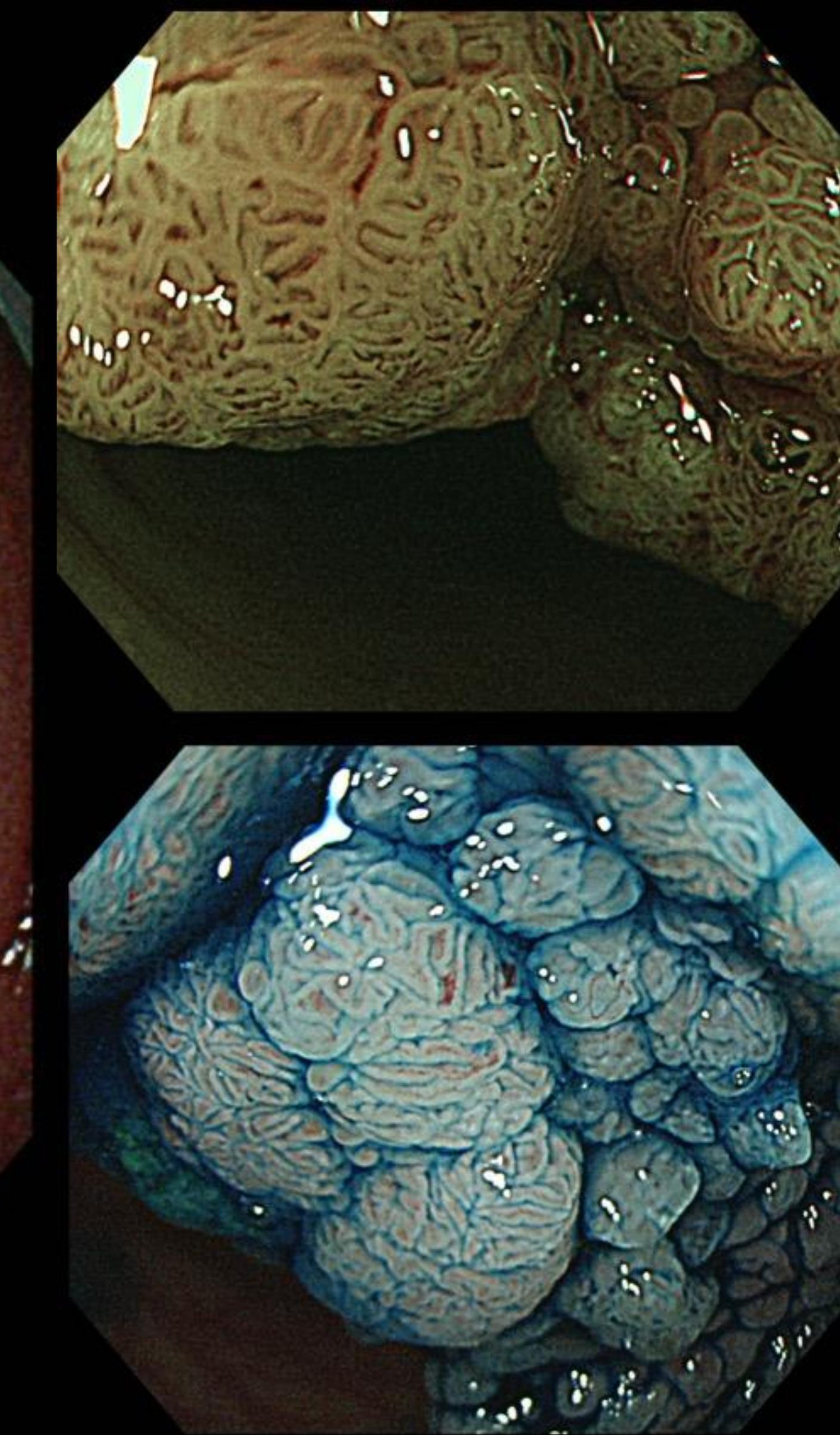
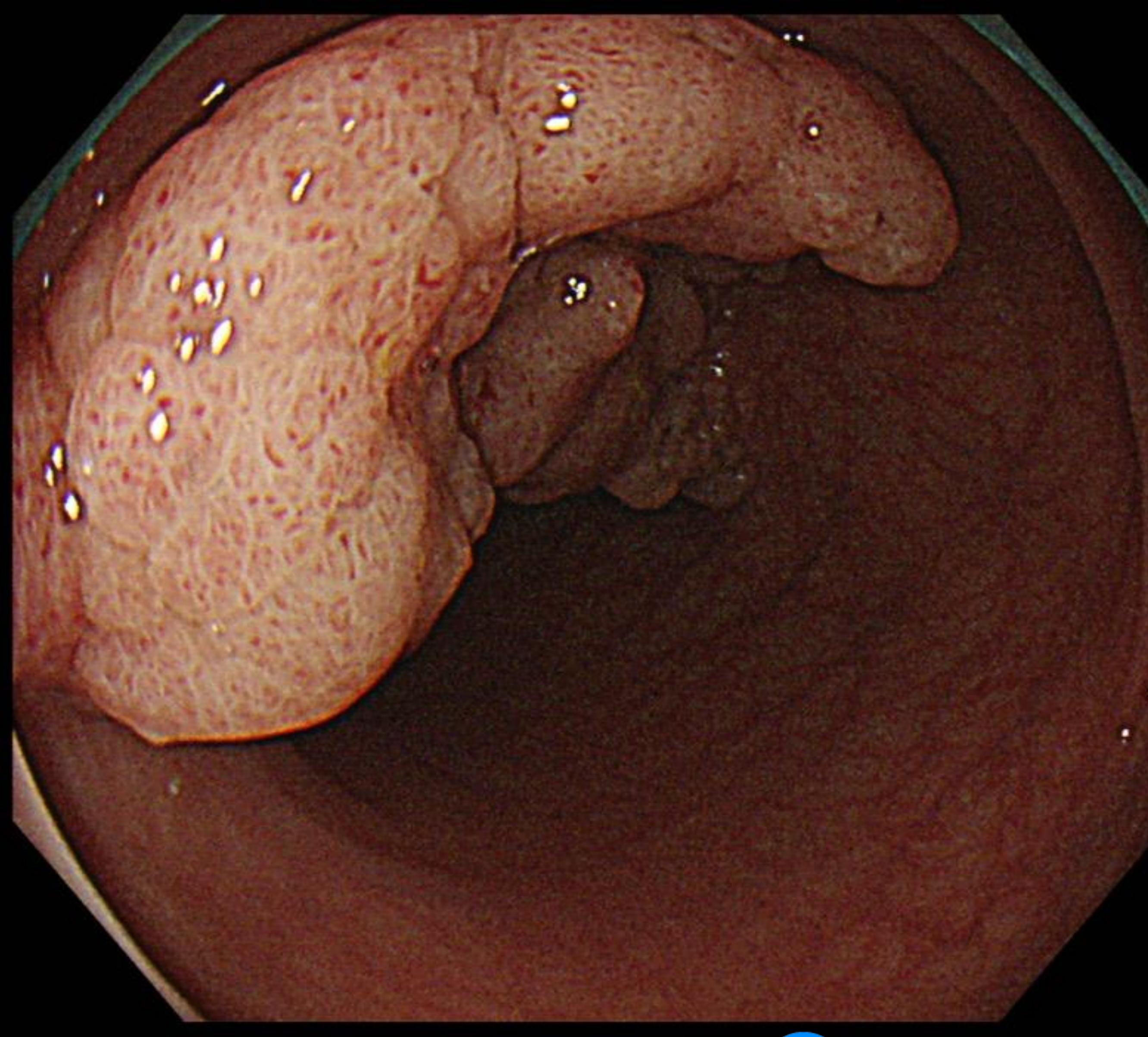
# CONCLUSIONS

In this multicenter cohort study,

- ✓ Favorable long-term outcomes after C-ESD  $\geq 20$  mm ; the 5-year DSS and OS rates were 99.6% & 93.5%, respectively.
- ✓ To note, the 5-year intestinal preservation rate was 98.1% when CR was achieved in the initial ESD procedure.
- ✓ ESD can be a potential first-line therapy for superficial colorectal neoplasms  $\geq 20$  mm.



# Endoscopic findings



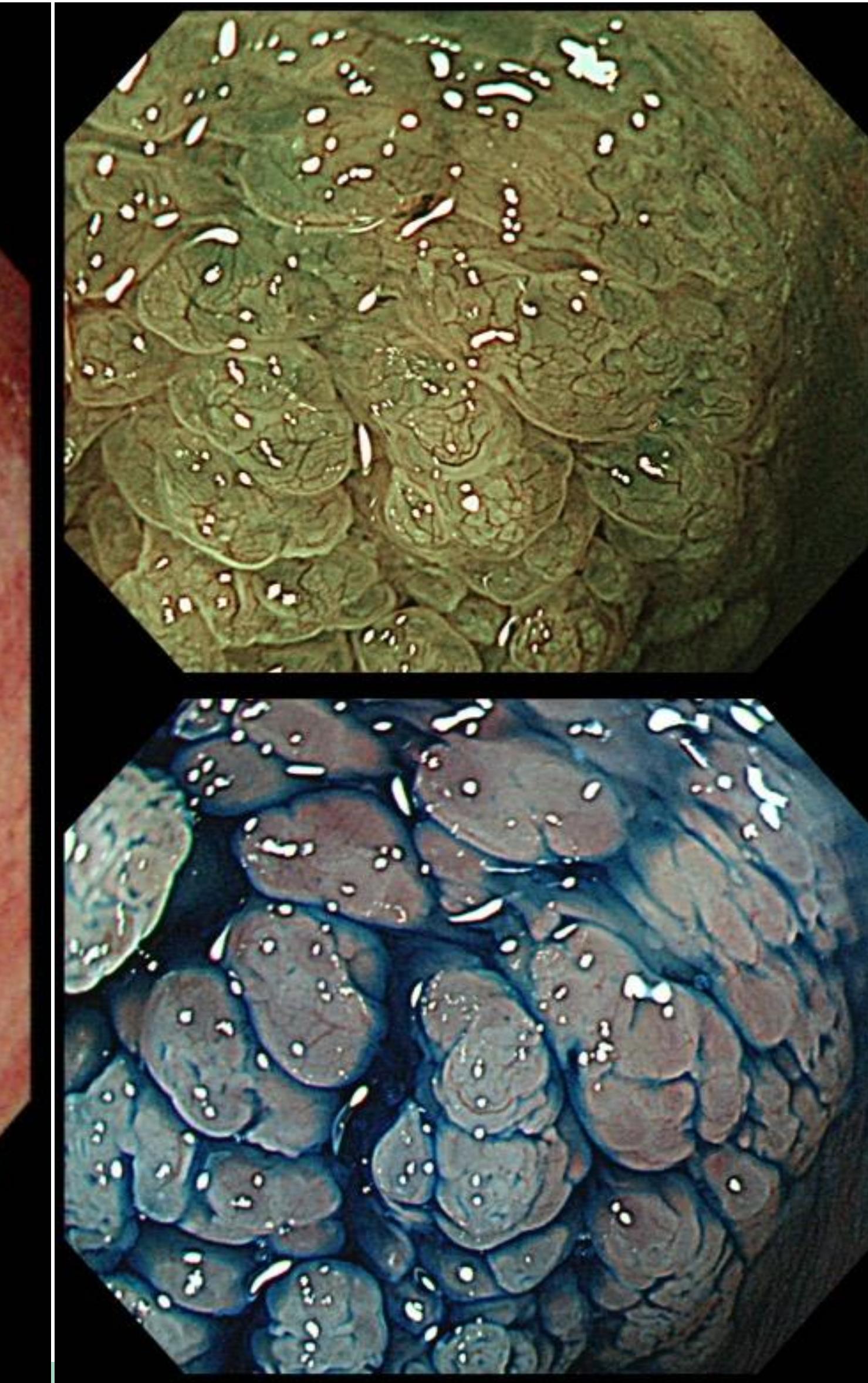
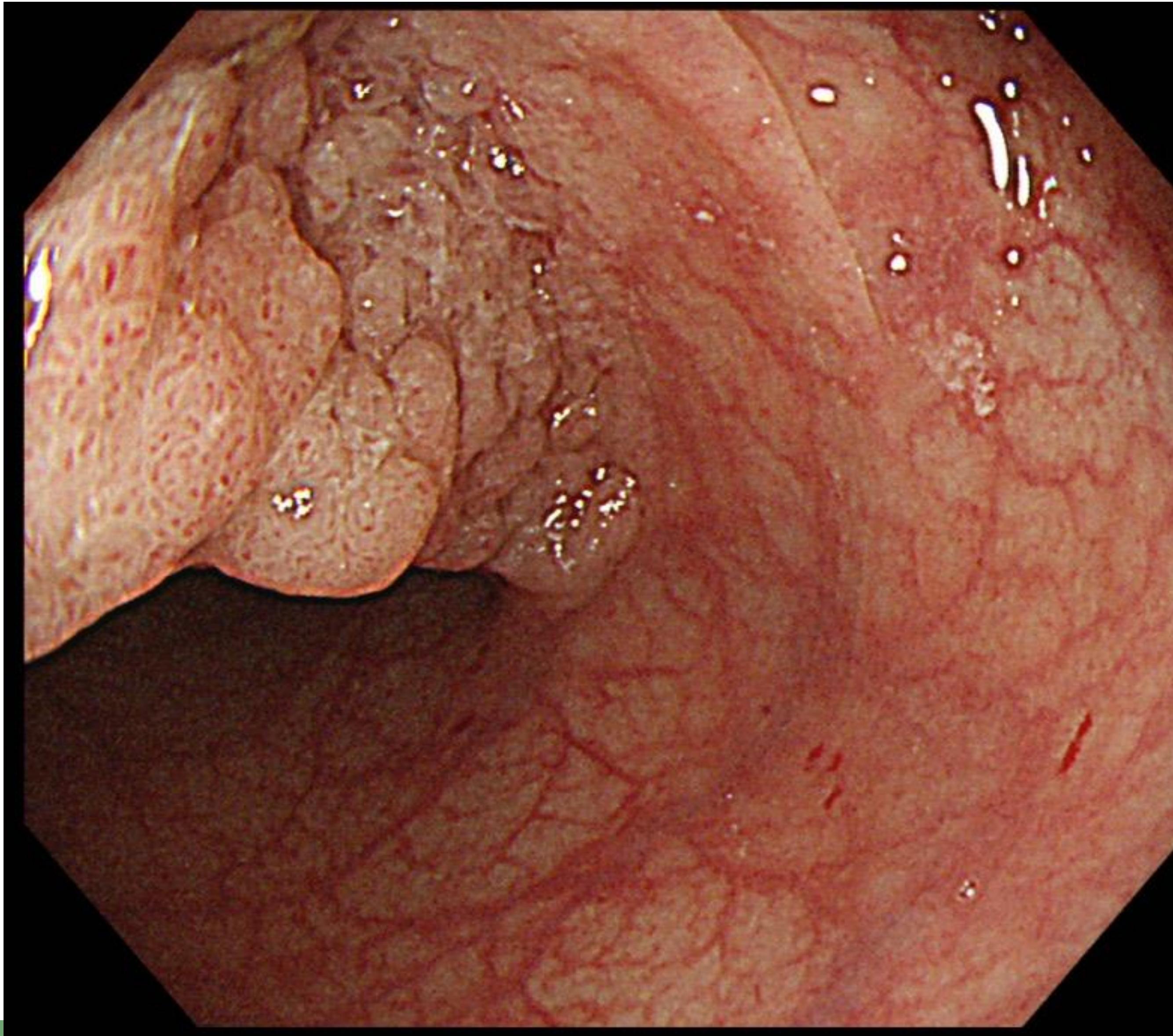
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*Endoscopy Division, National Cancer Center Hospital*



# ENDOSCOPIC FINDINGS



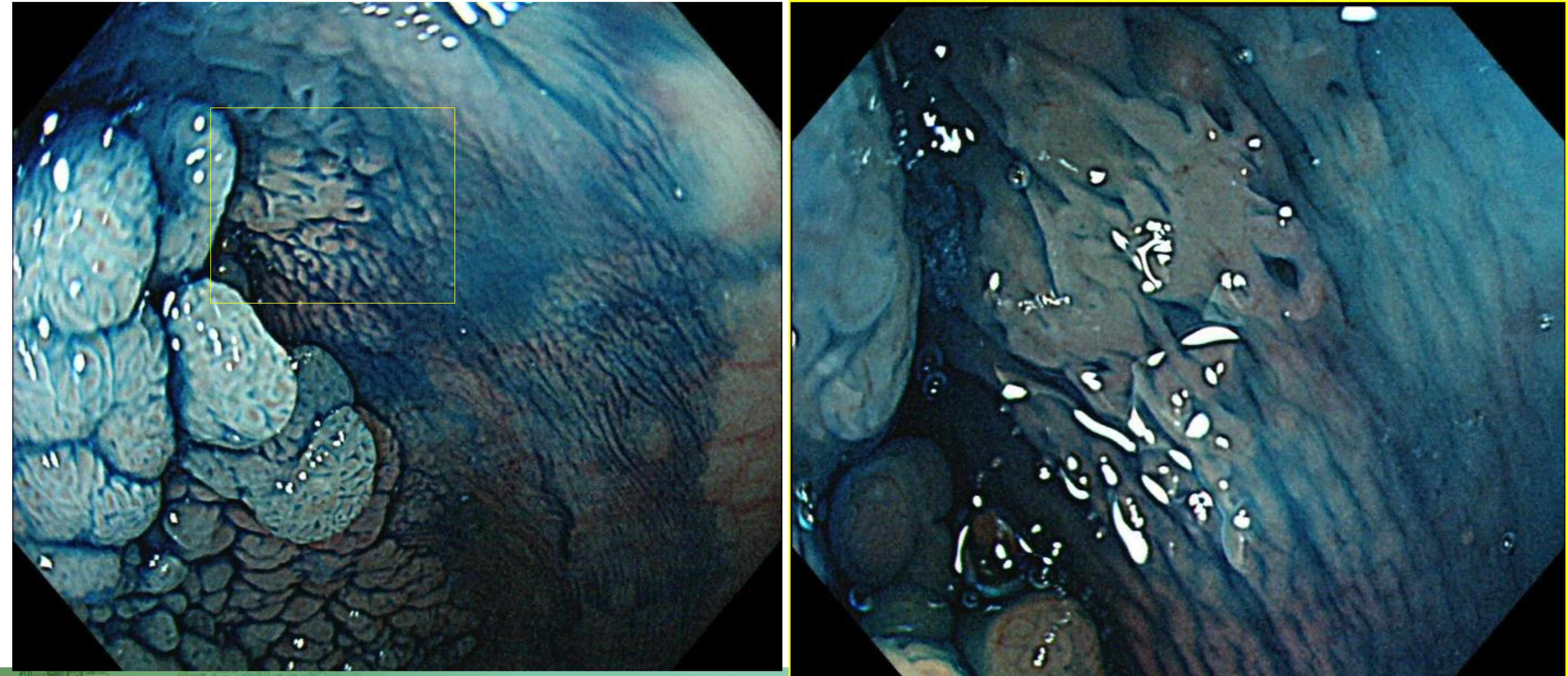
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# Indigo carmine dye image



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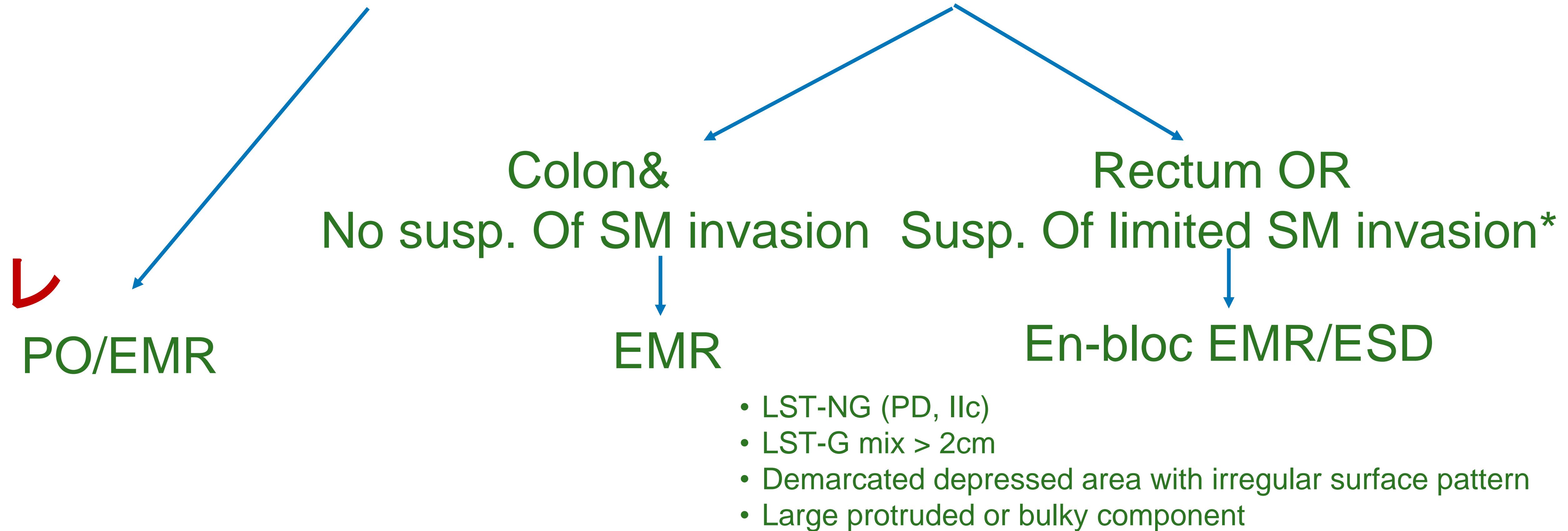
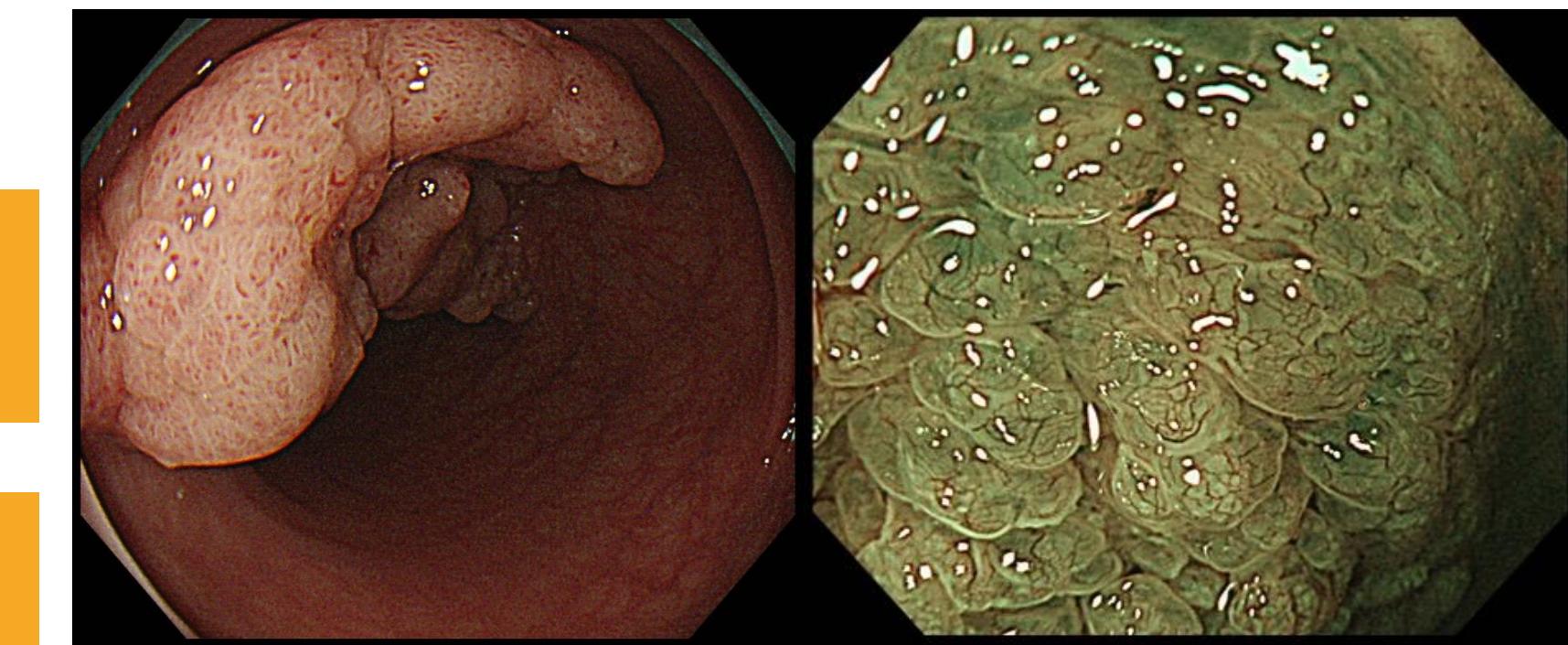


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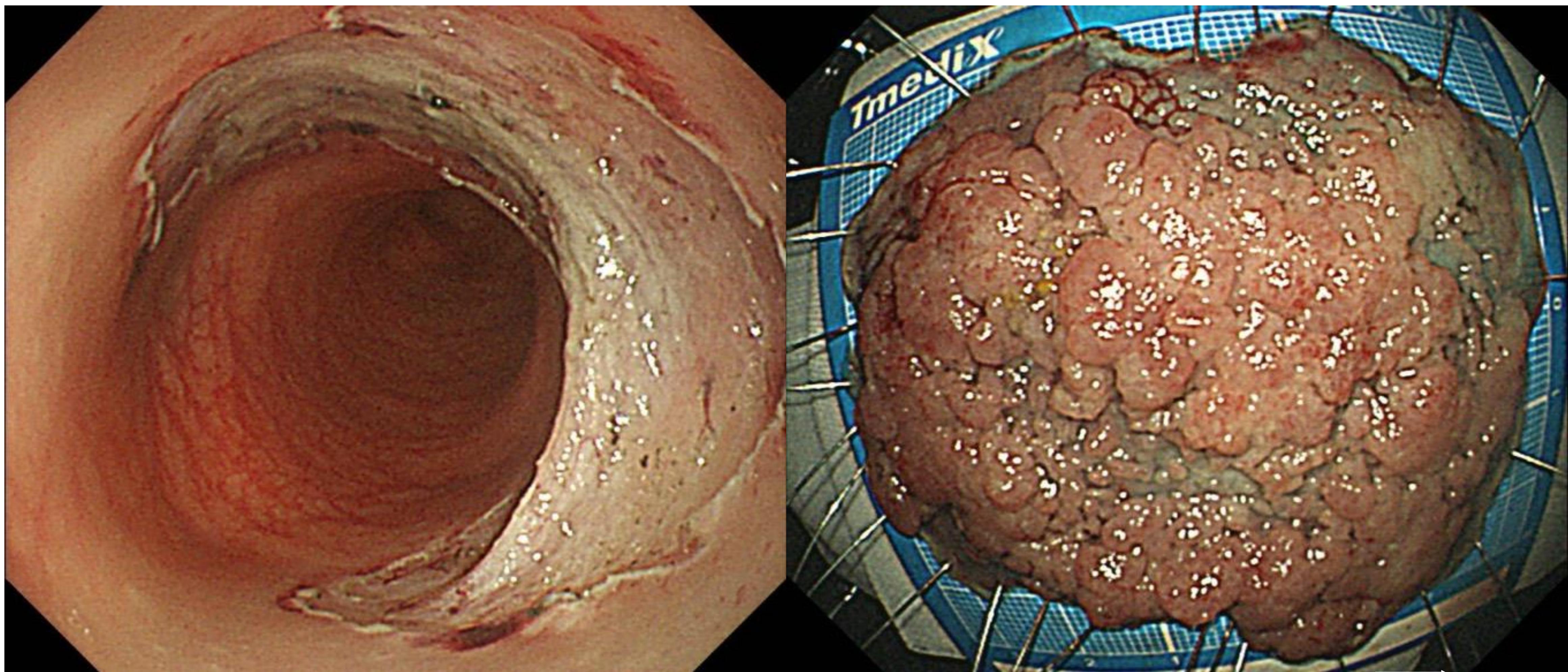
LGD

JNET 2B

HGD/Tis/sm1



# ESD was conducted according to JGES guidelines

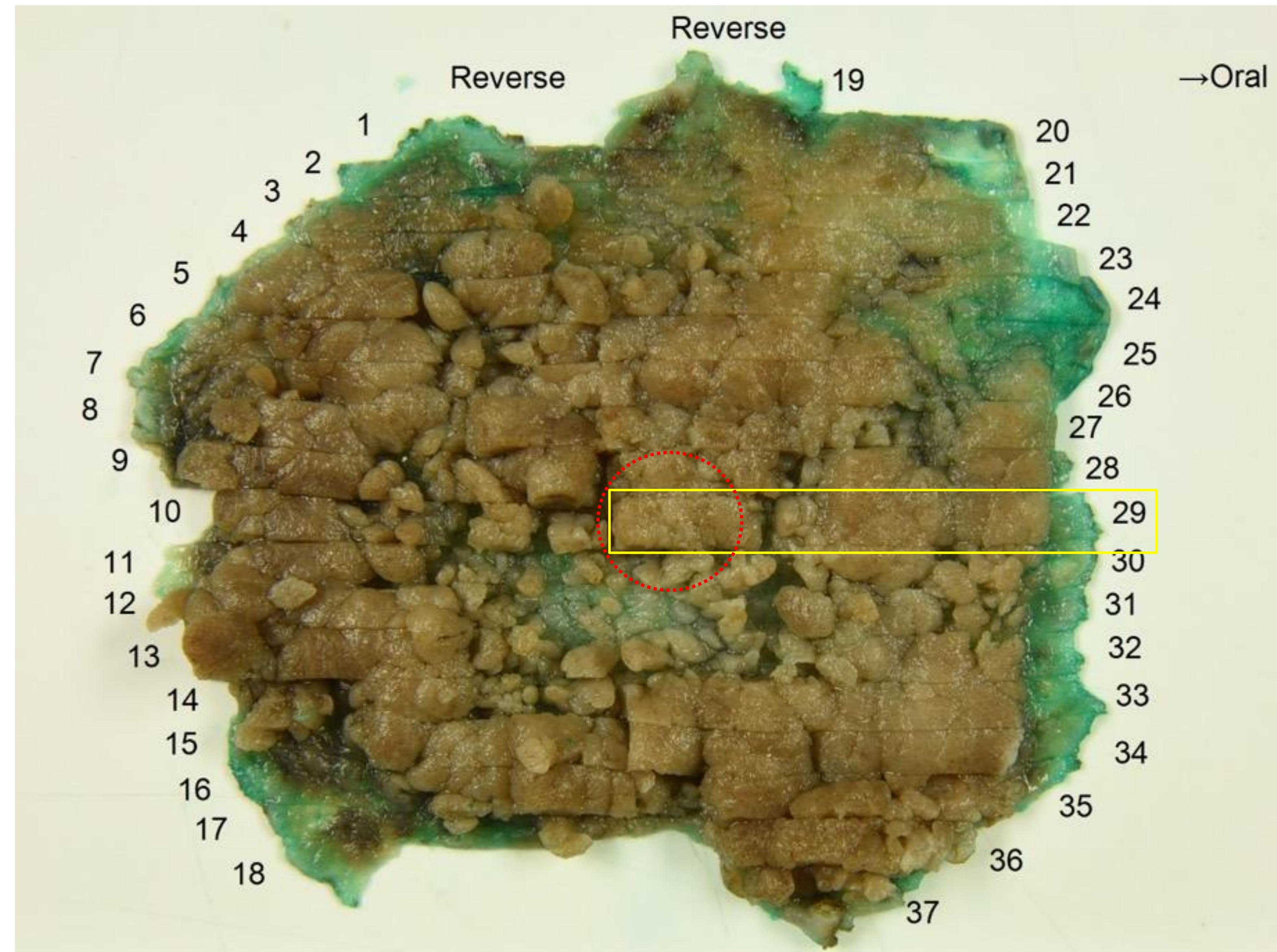


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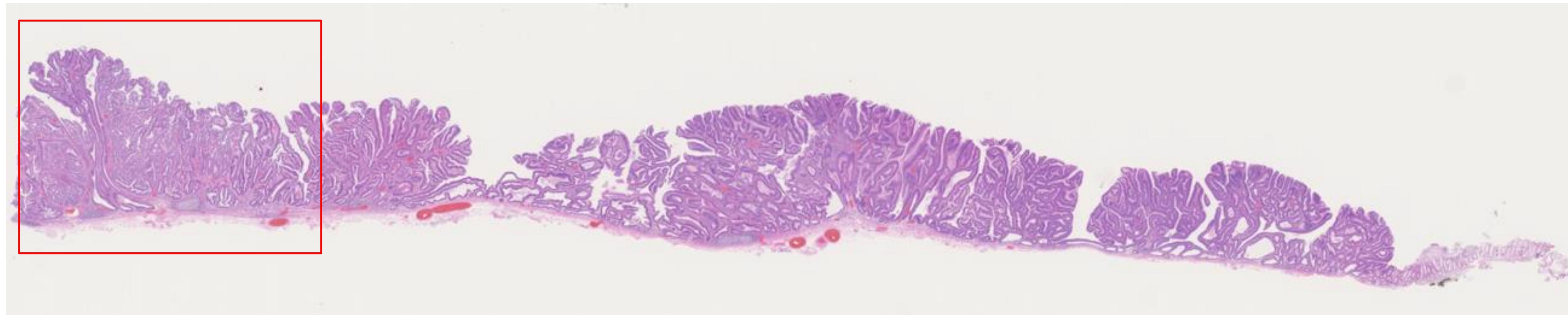


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# Histological finding (Panoramic view:#29)



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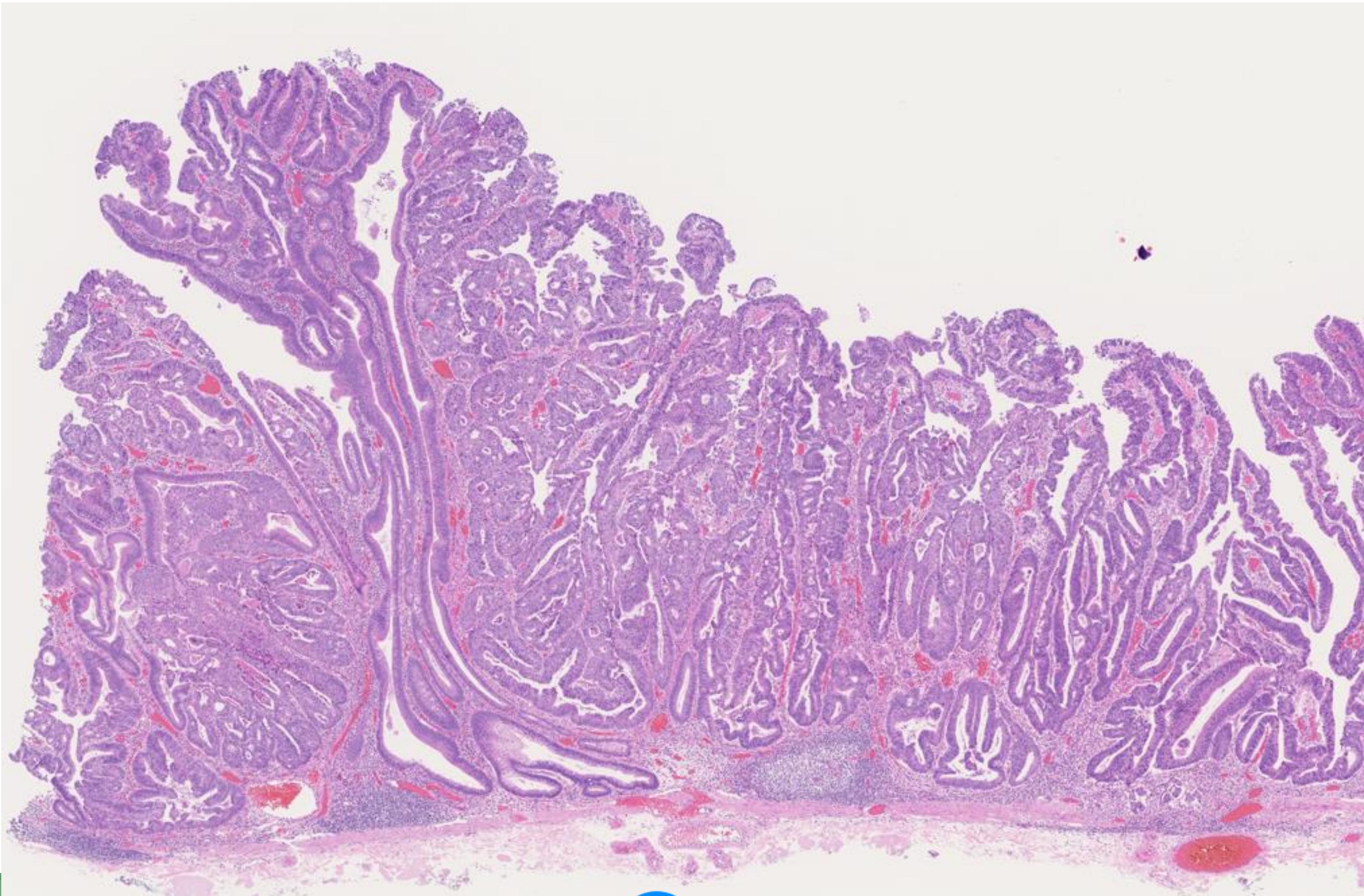


*Endoscopy Division, National Cancer Center Hospital*

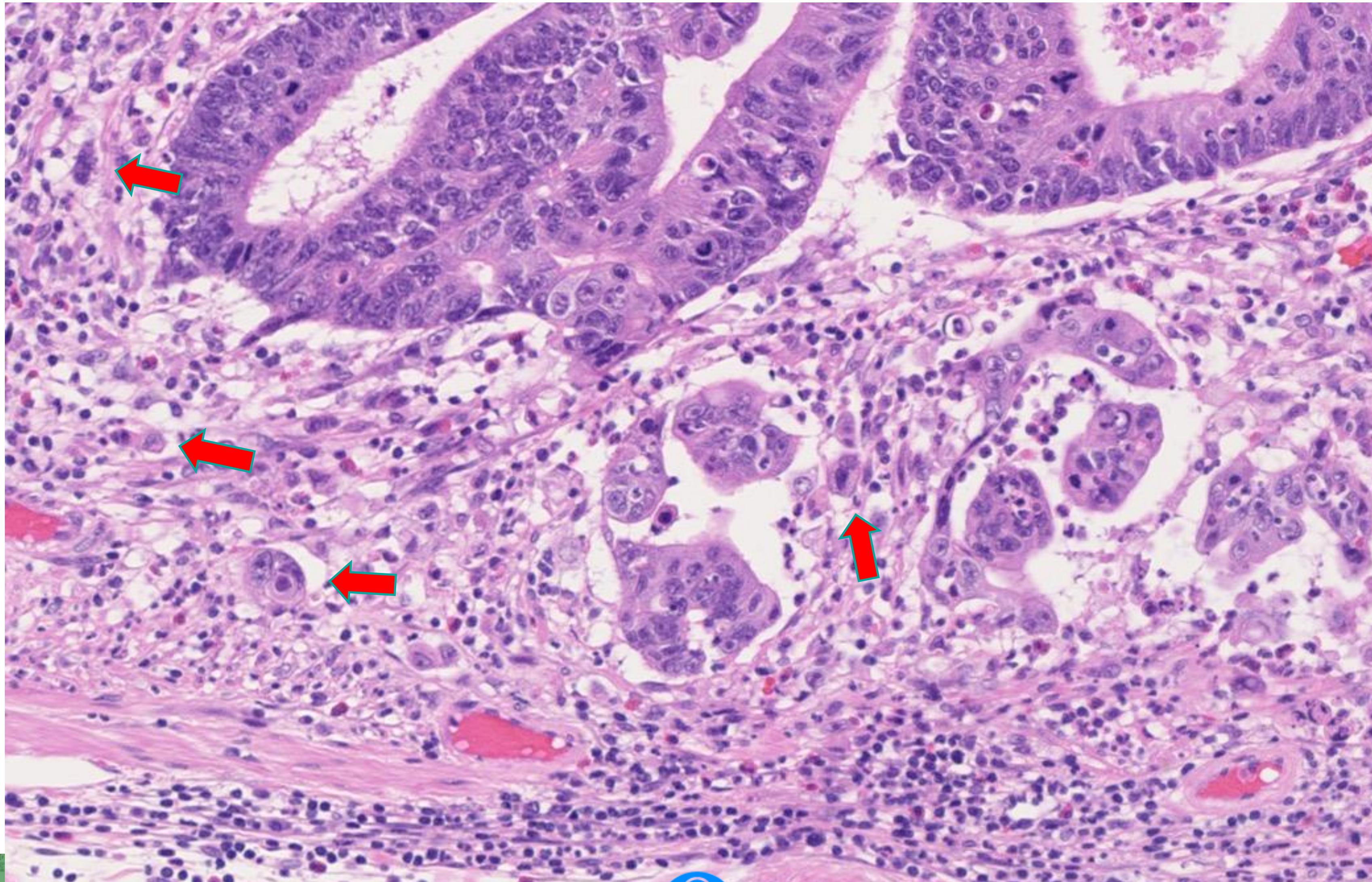


# Histological finding (#29)

## Mod. Dif. adenoca

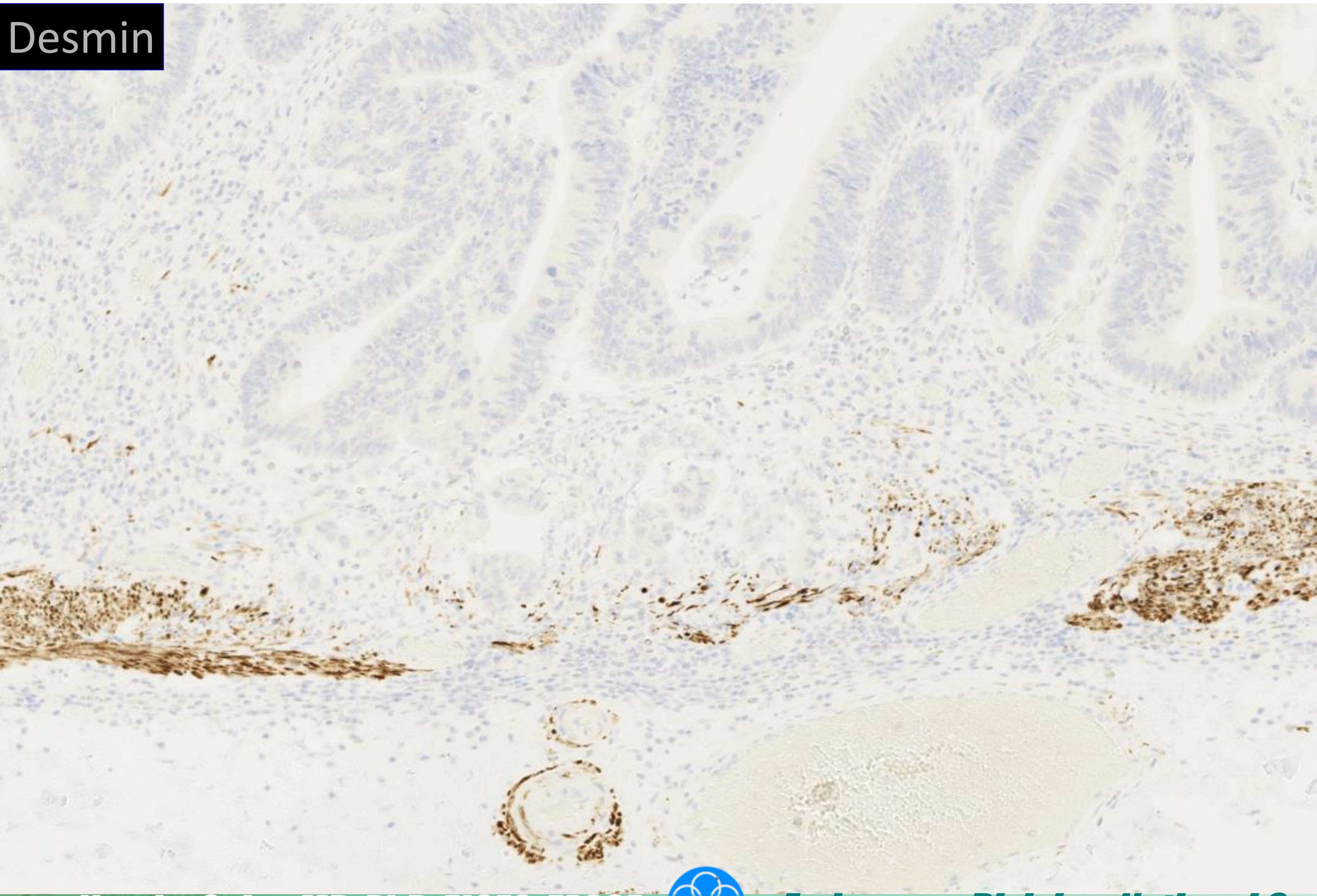


# Histological finding (#29) budding grade 2



# Histological finding (#28)

Desmin

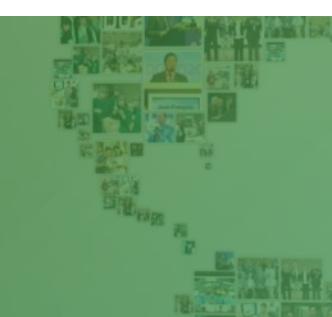


# Immunohistochemical staining

D2-40



ly (+)

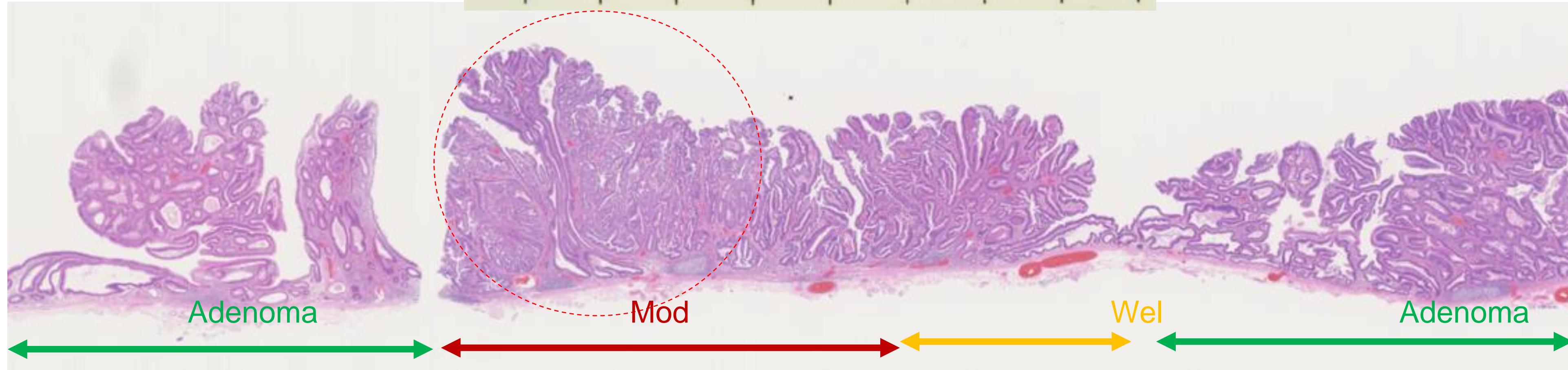
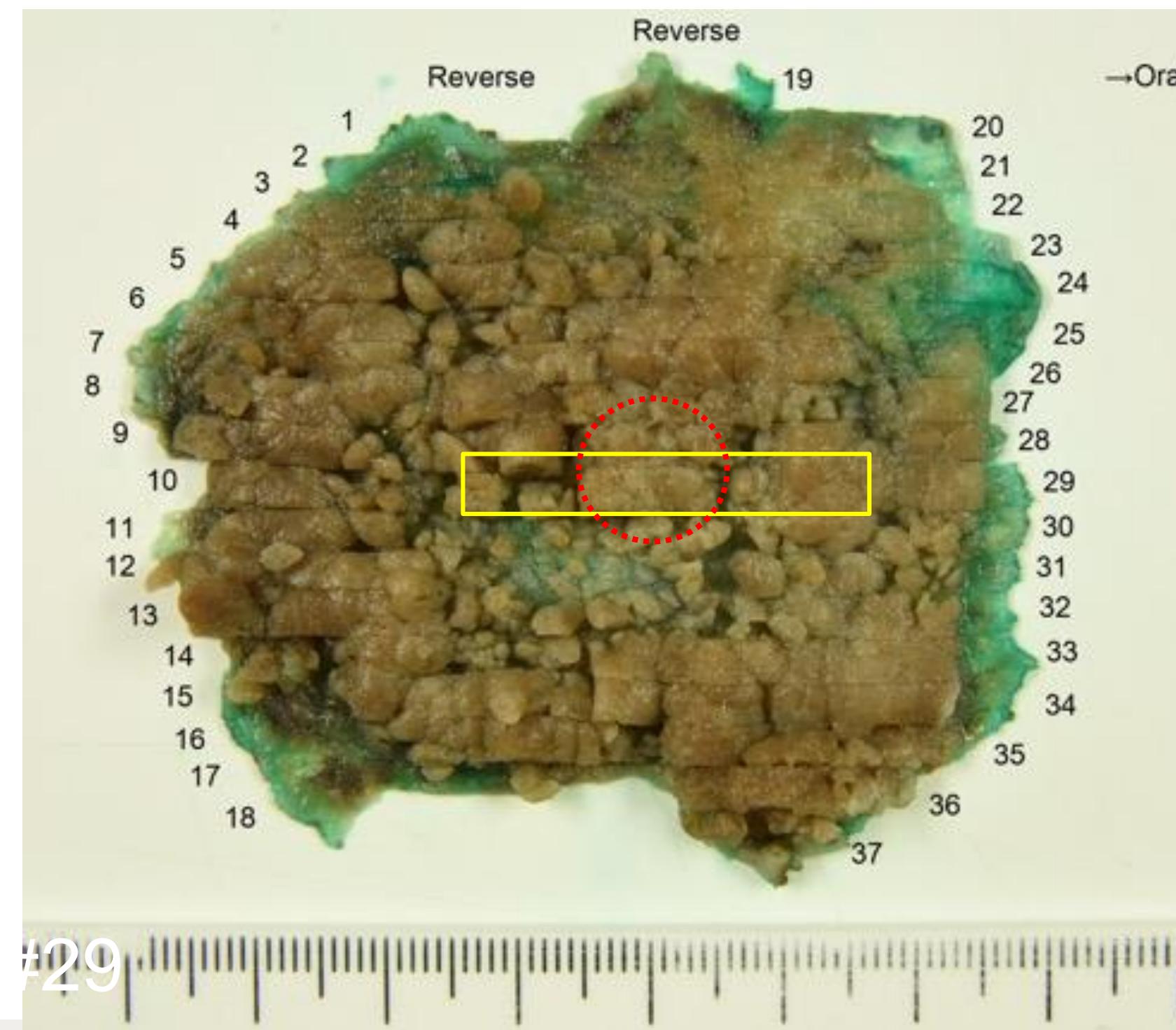


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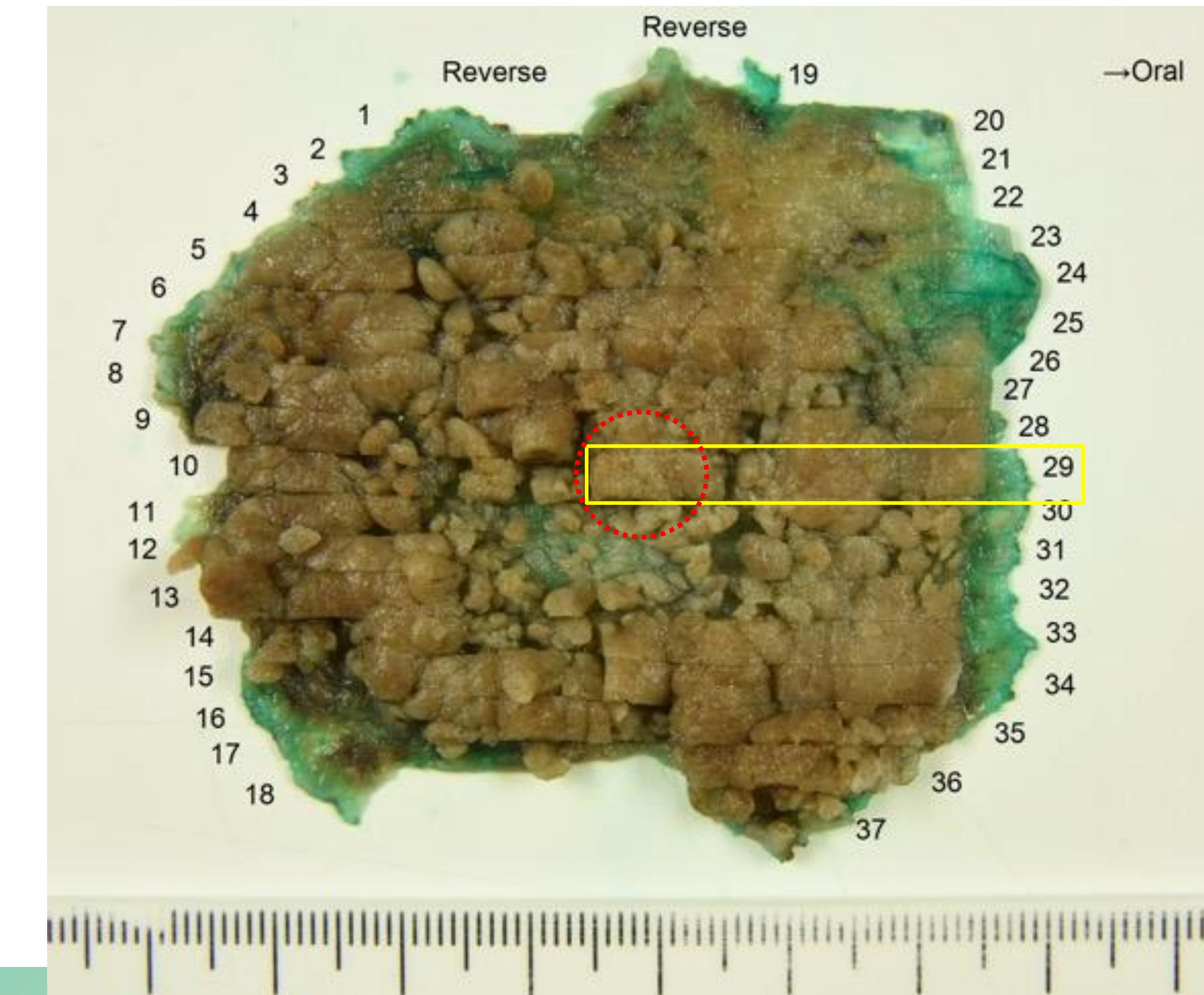


**Mod. Diff. adenoca~Well diff.adenoca (LG)~high-grade adenoma**

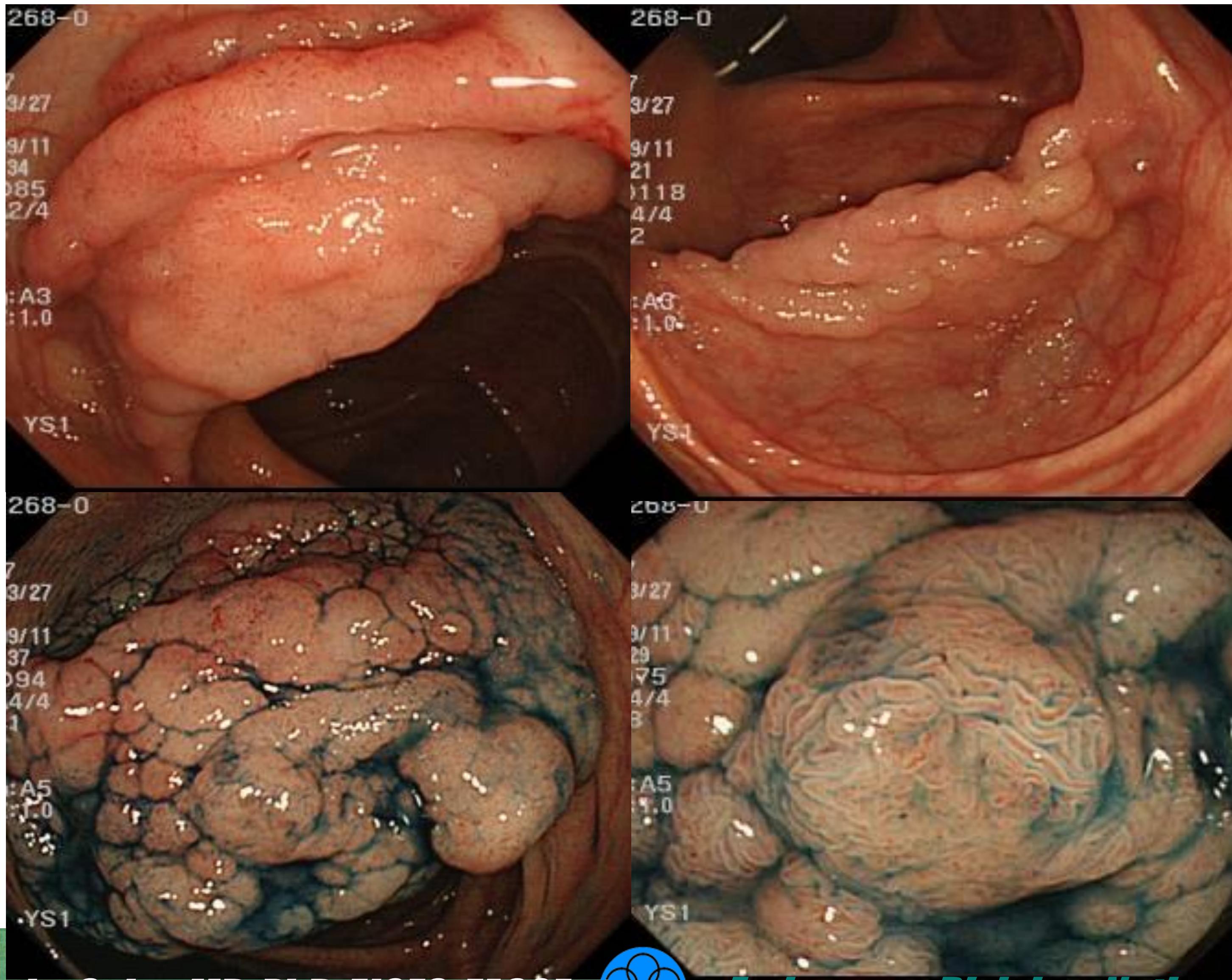
# Pathological Diagnosis

Well to moderately differentiated adenocarcinoma, in adenoma

- Category 5.1 Vienna classification
  - Location : sigmoid colon
  - Macroscopic type : 0-Is+IIa
  - Size of lesion : 63x62mm
  - Depth of invasion : pM(MM)
    - ly 1, v 0, BUD2
    - HM(-), VM(-)



# *Another LST-G , A/C, 50mm, Is + IIa (LST-G)*

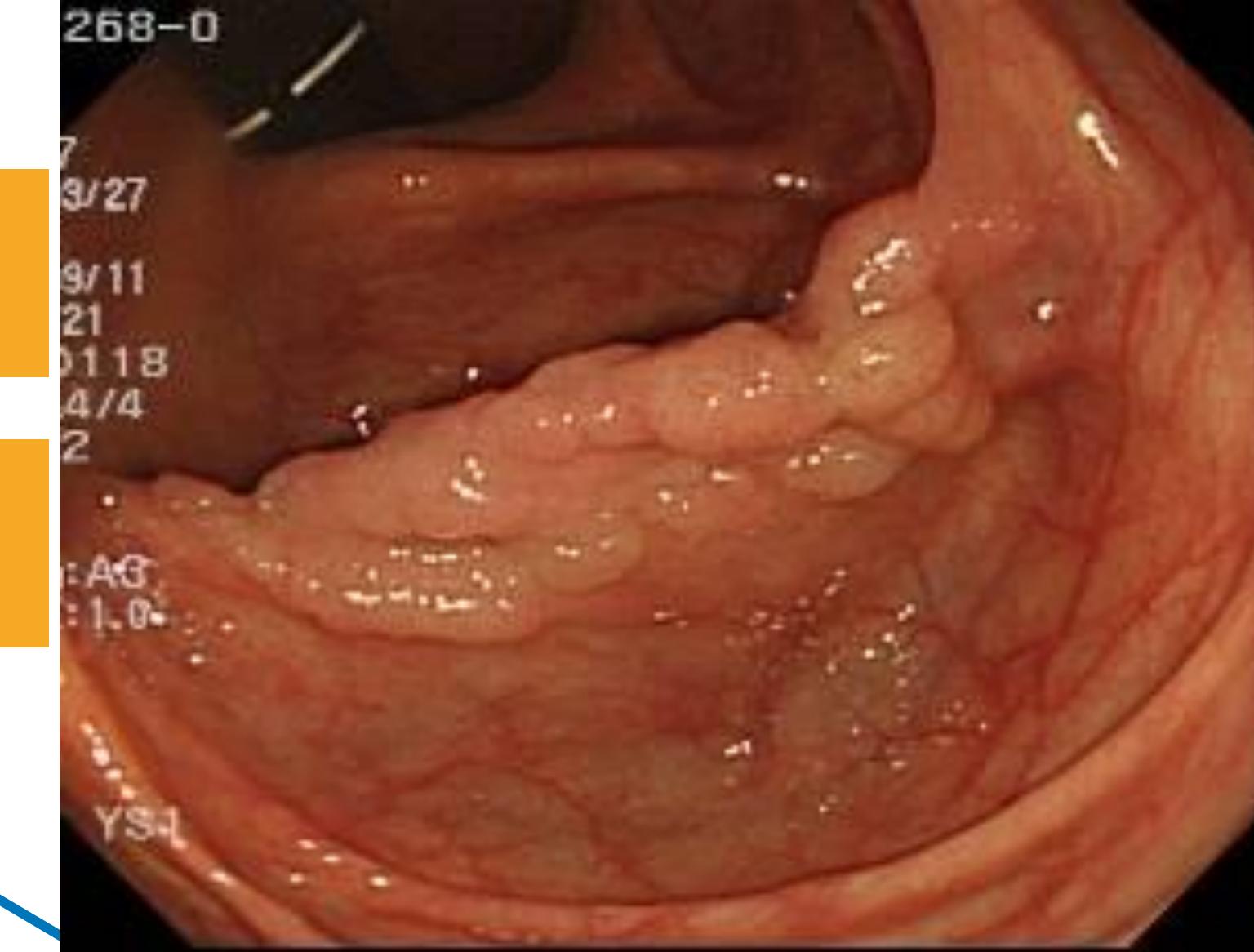


JNET 2A

LGD

JNET 2B

HGD/Tis/sm1



✓

PO/EMR

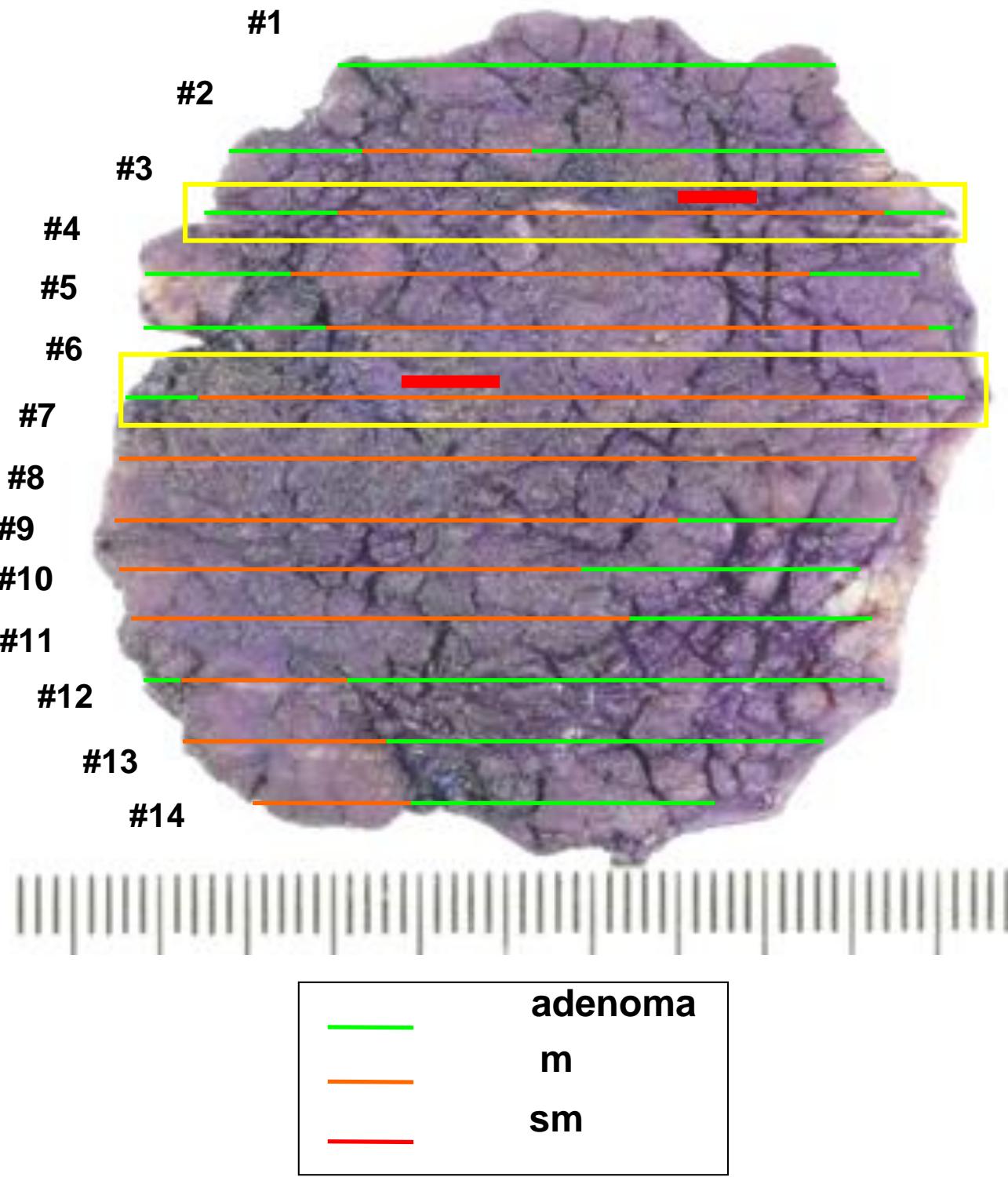
Colon&  
No susp. Of SM invasion

EMR

Rectum OR  
Susp. Of limited SM invasion\*

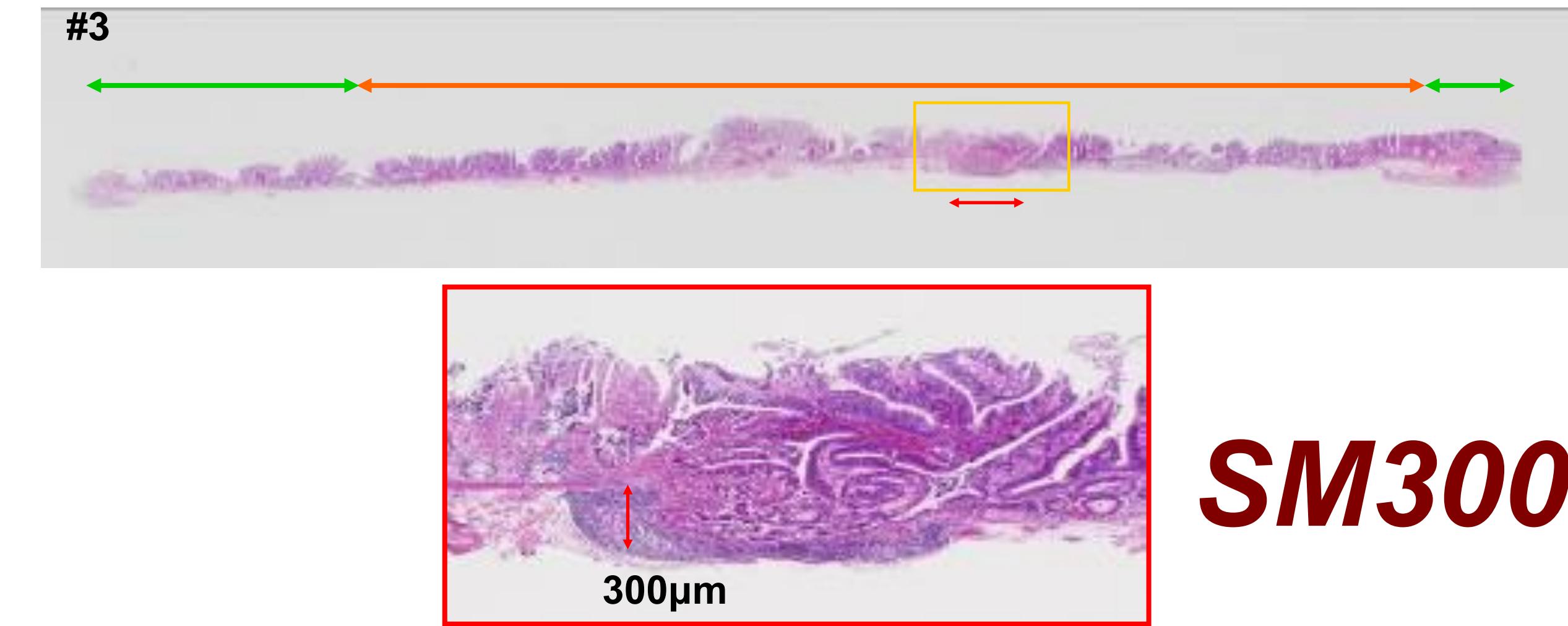
En-bloc EMR/ESD

- LST-NG (PD, IIc)
- LST-G mix > 2cm
- Demarcated depressed area with irregular surface pattern
- Large protruded or bulky component



**Well differentiated adenocarcinoma,  
low and high grade atypia, in  
adenoma.**

**Category 5.2 Vienna classification  
0-Is+IIa, PG, 50 × 50mm,  
pSM2 1100µm, ly0, v0,  
adenoma component (+), cut end (-)**



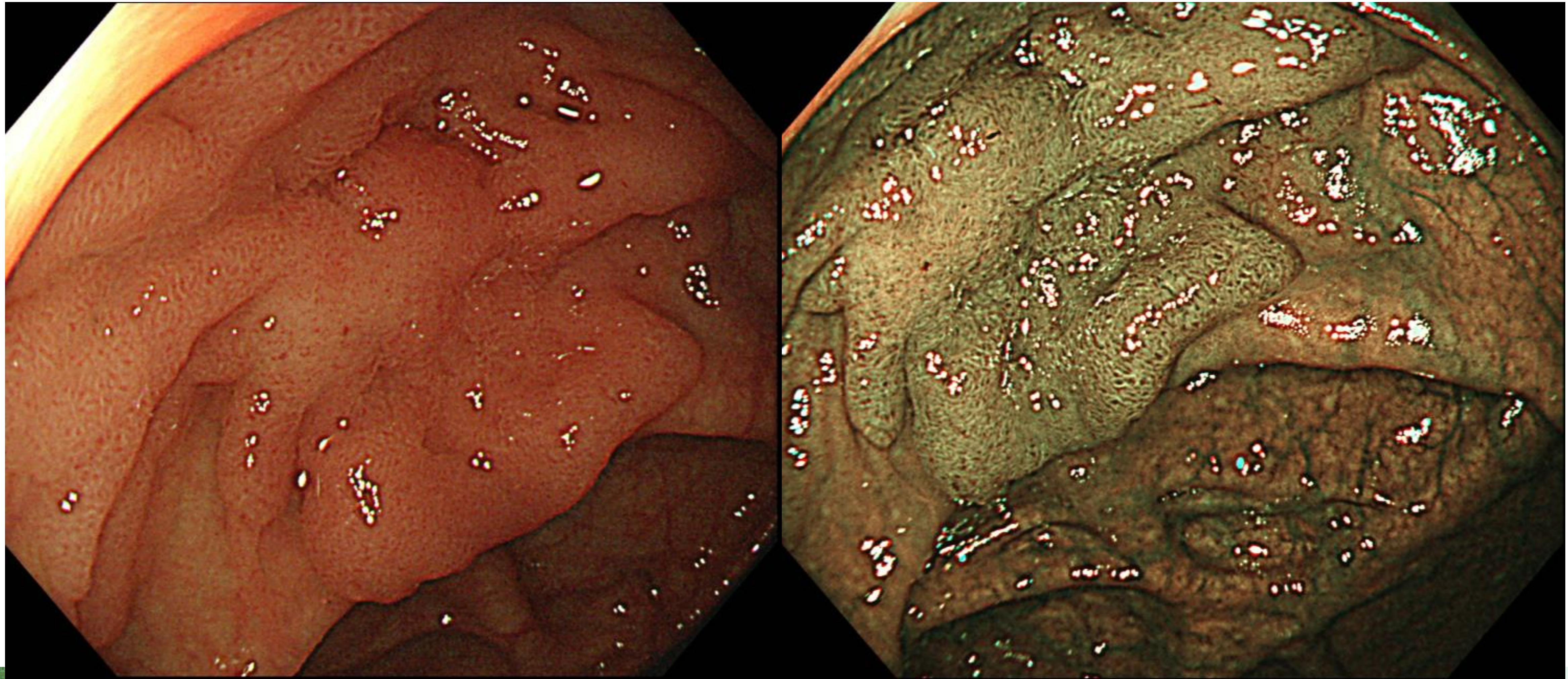
**SM300µm**



**SM1100µm**



# Cecum, 0-IIa+IIc (LST-NG, PD)



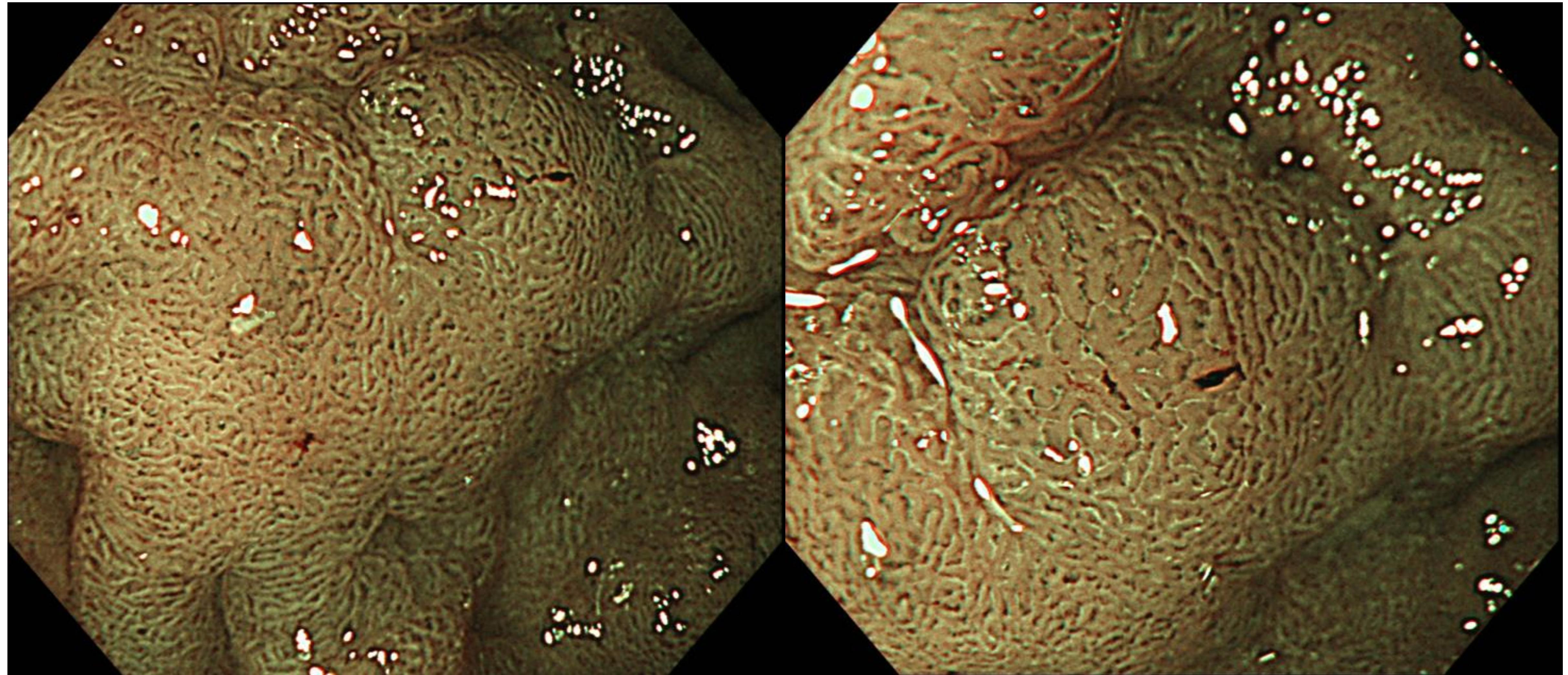
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# NBI



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# NBI

## Type 2B

Vessel pattern

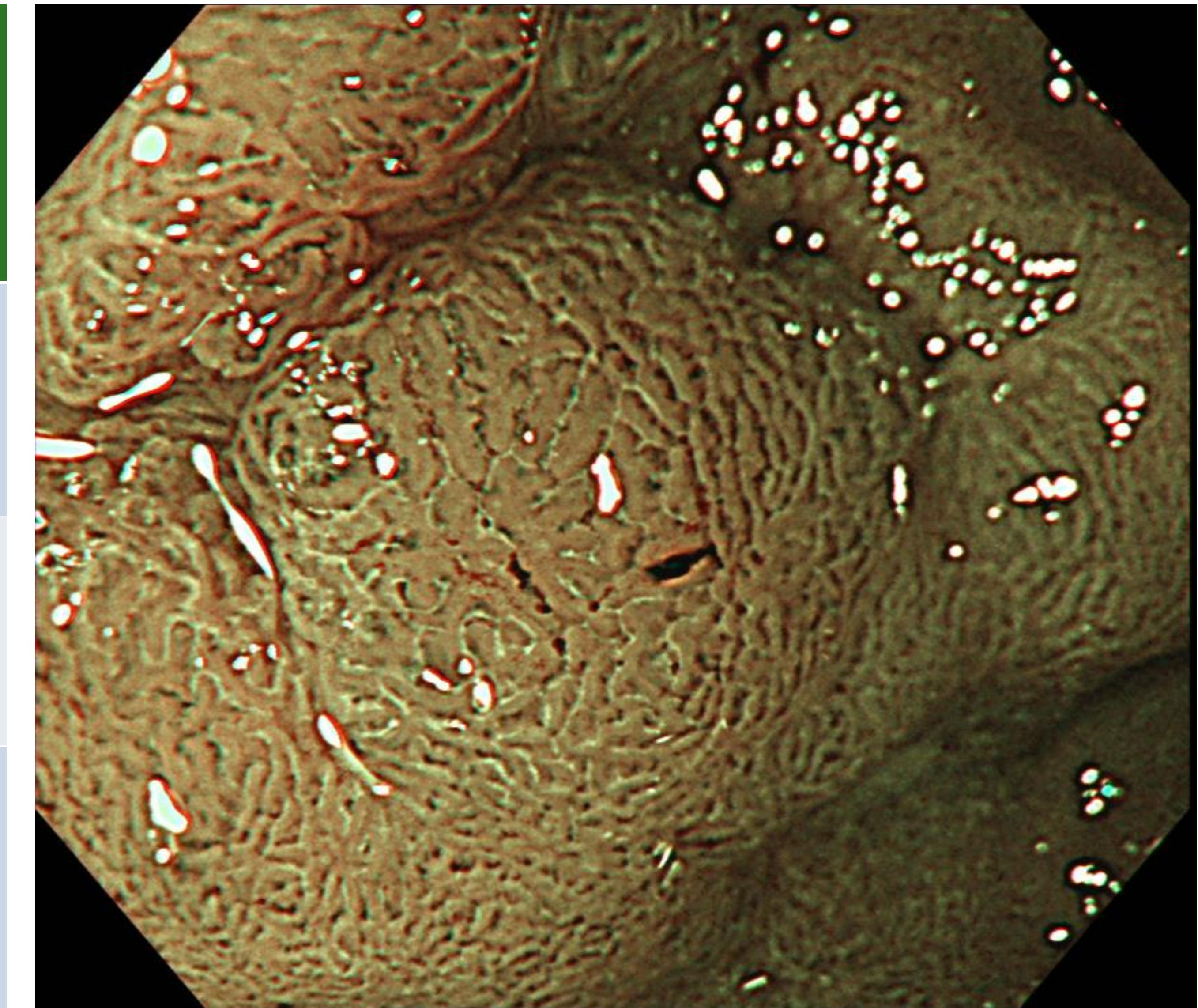
- Variable caliber
- Irregular distribution

Surface pattern

Irregular or obscure

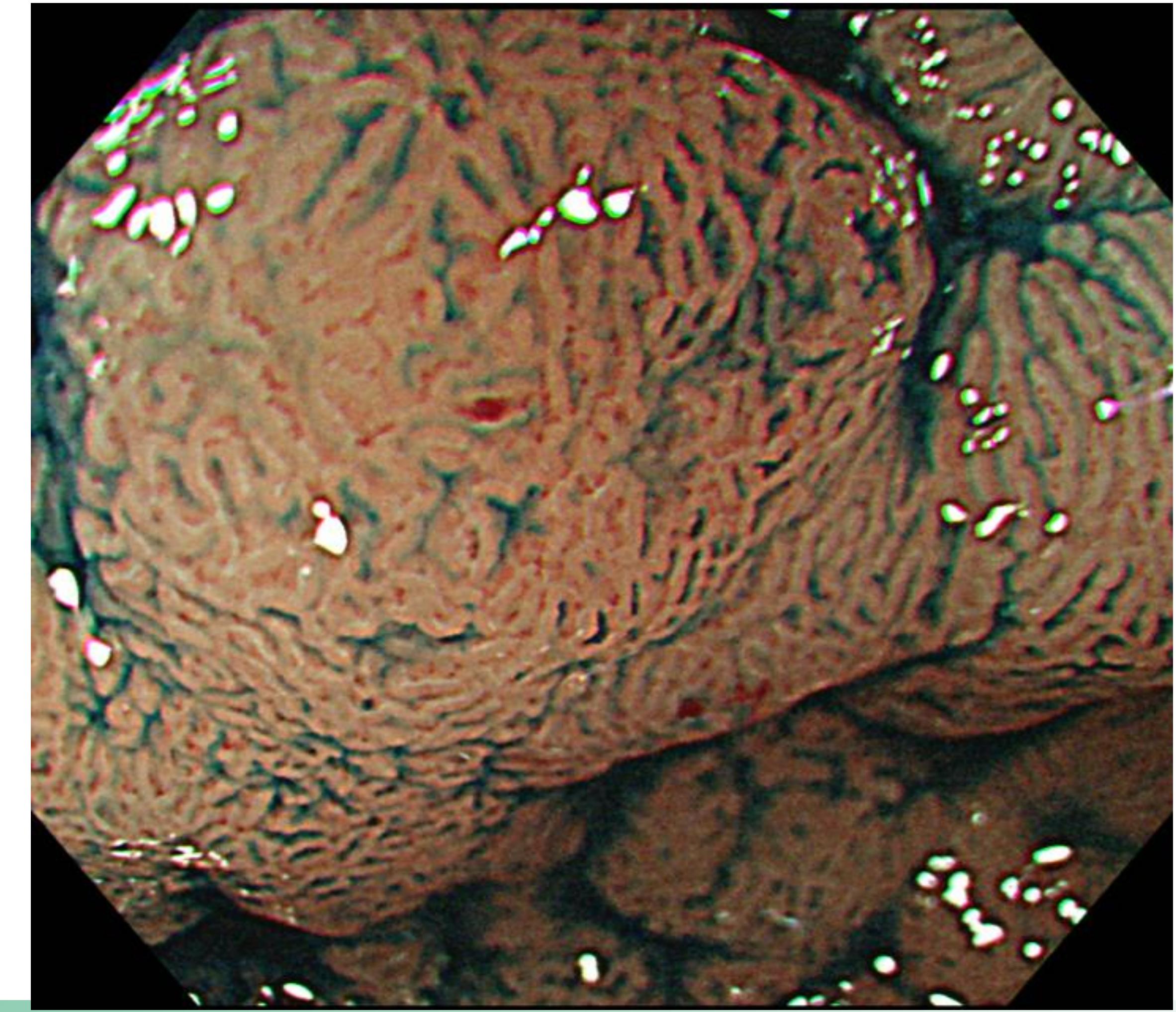
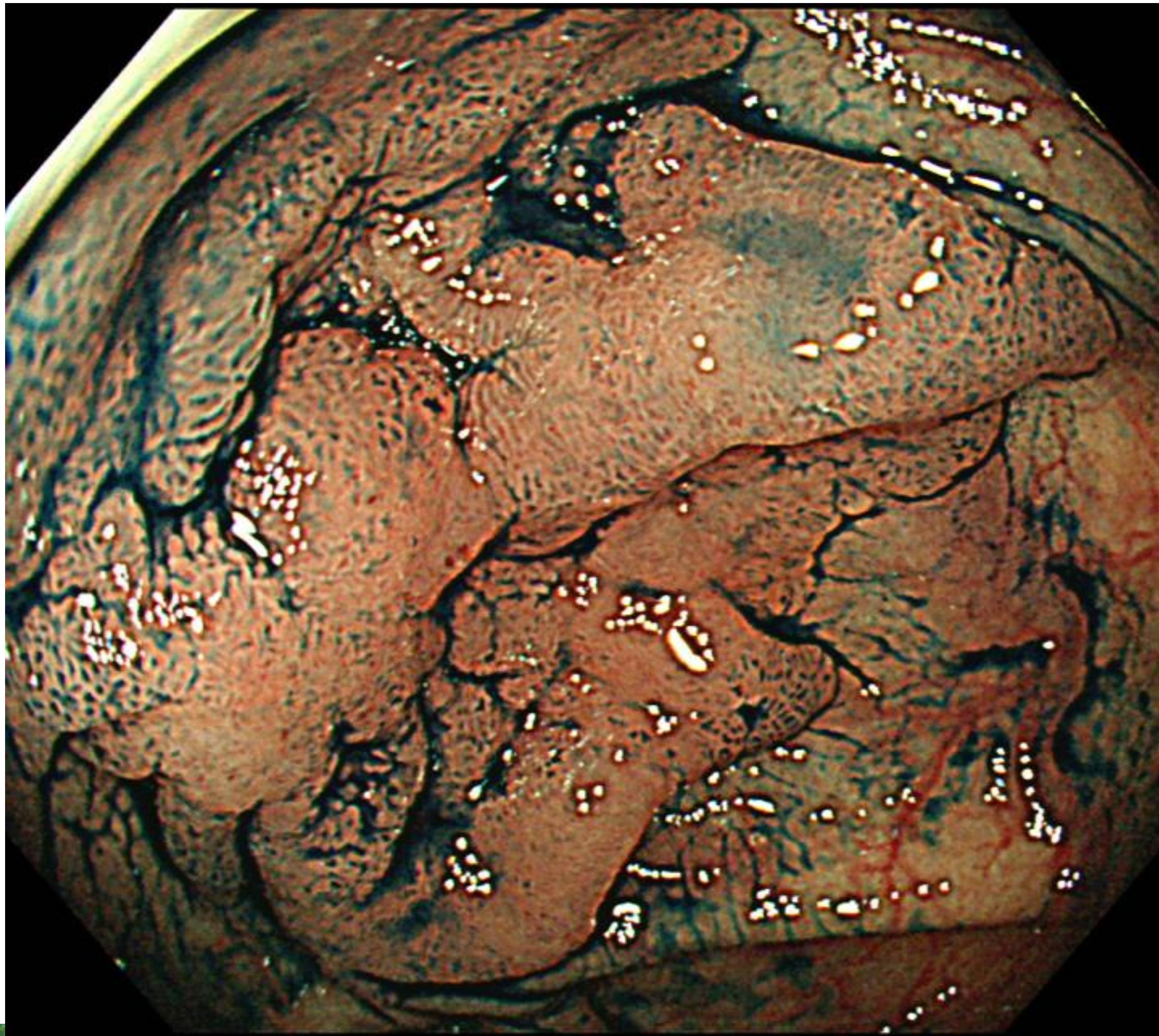
Most likely histology

Tis/T1a\*<sup>3</sup>  
High grade intramucosal  
neoplasia/Shallow  
submucosal invasive  
cancer



**\*3. Deep SM invasive cancer may be included.**

# *Indigo*



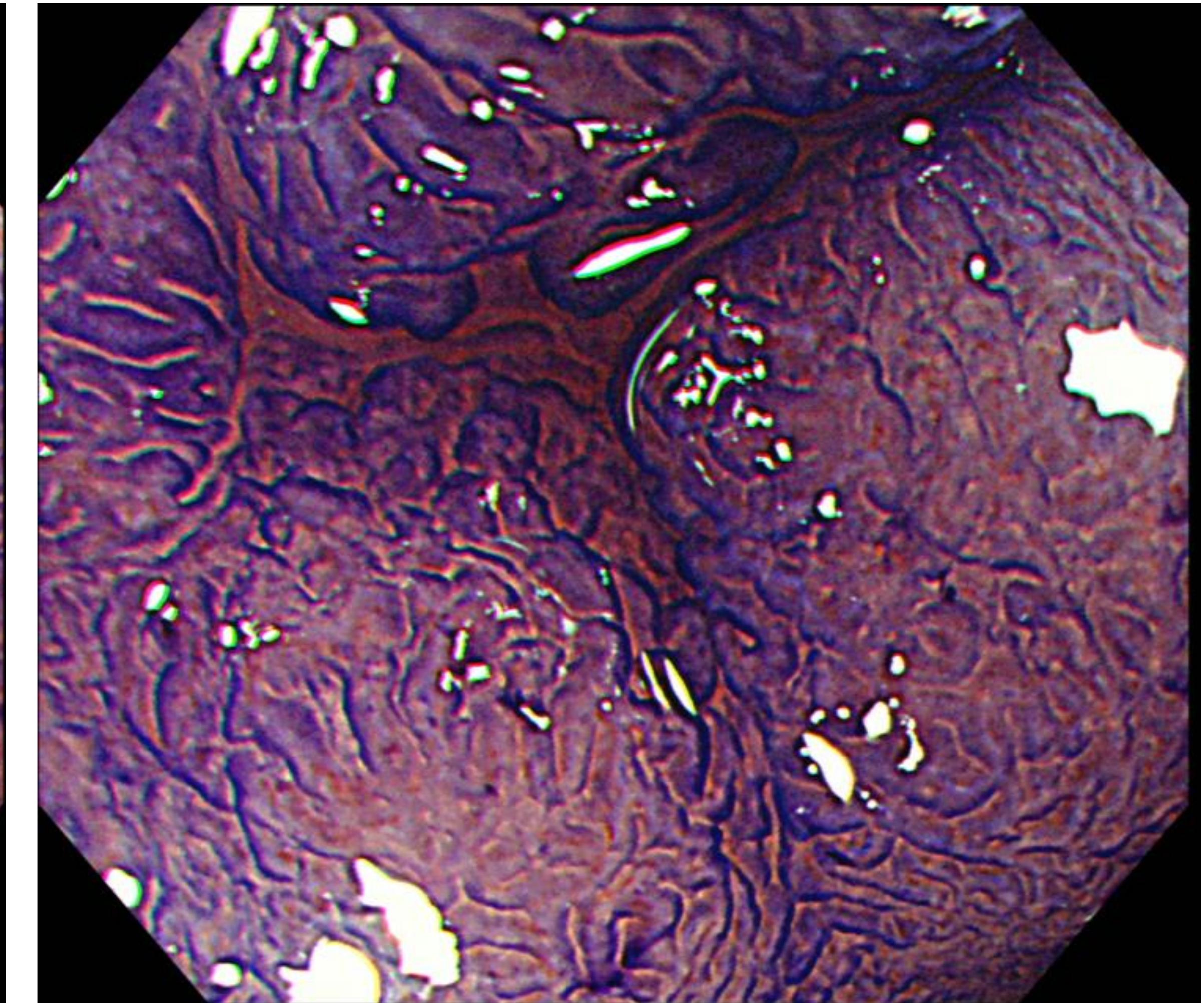
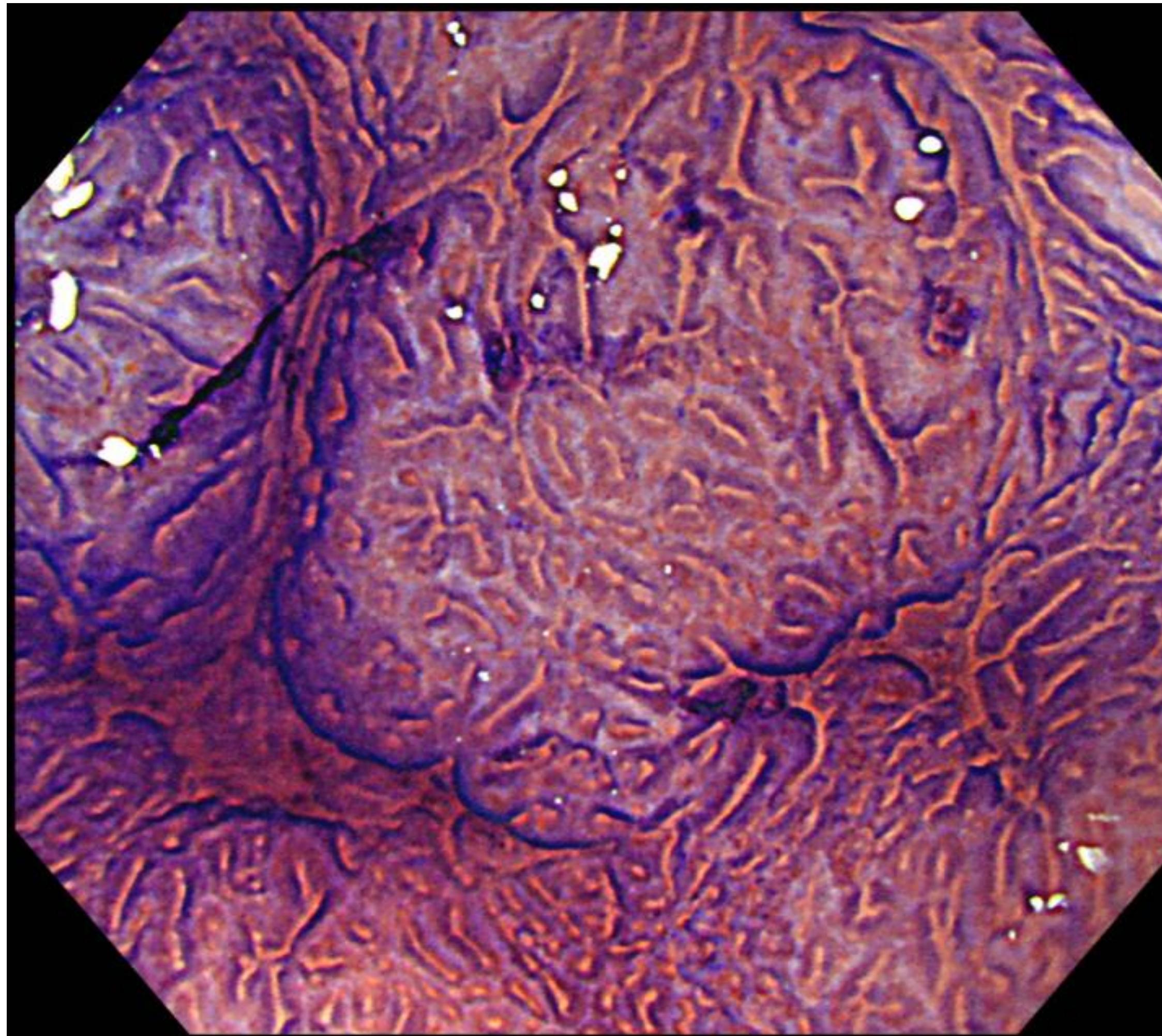
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# *CV stain*

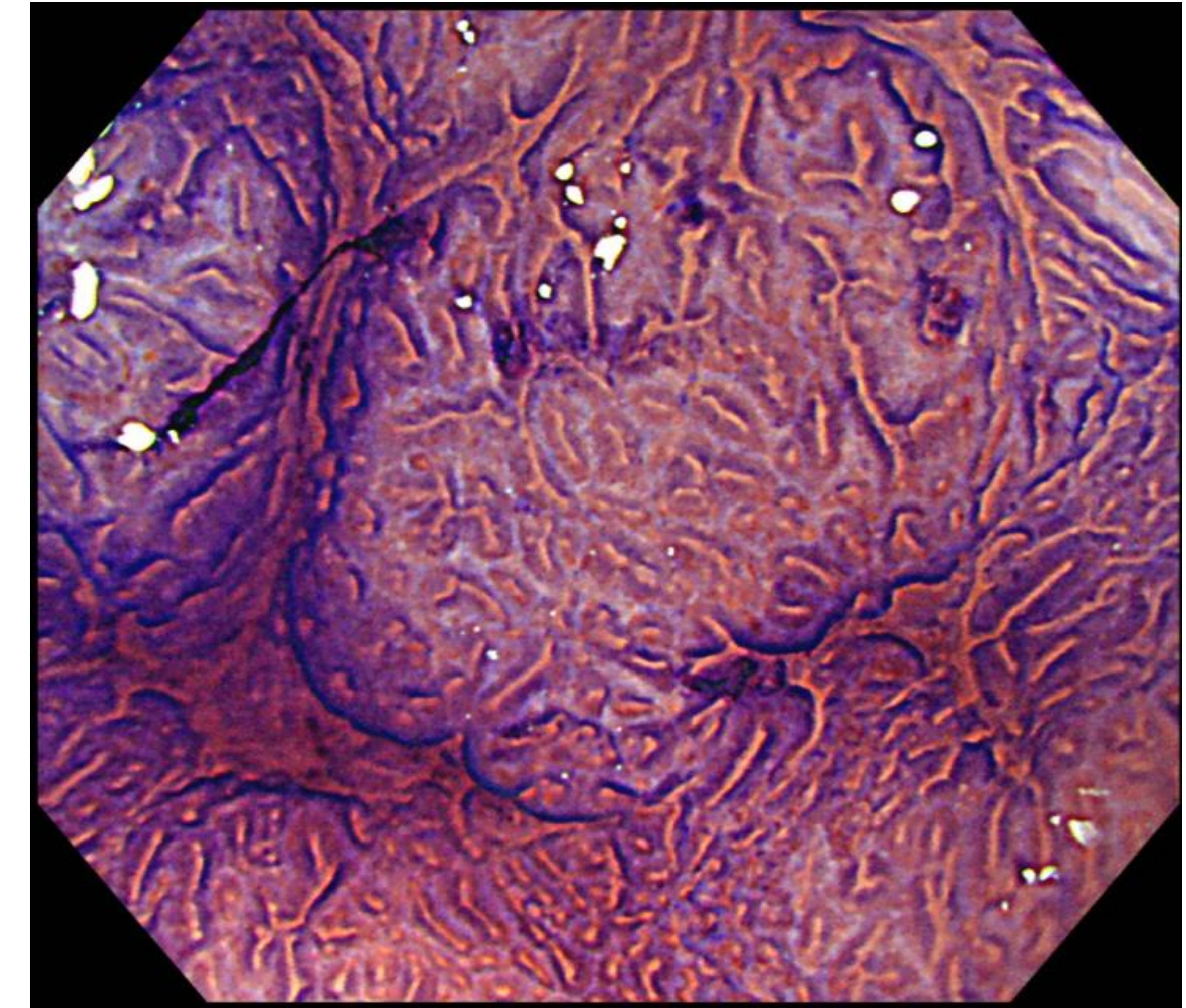


# Answer; pit?

1. III L/III s

2. VI (non-inv)

3. VI (inv)

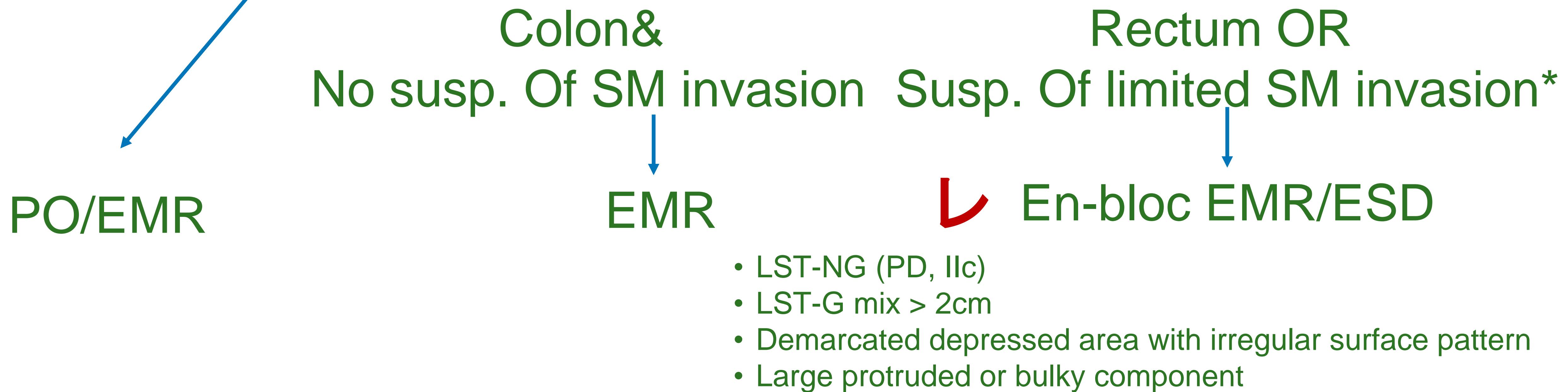
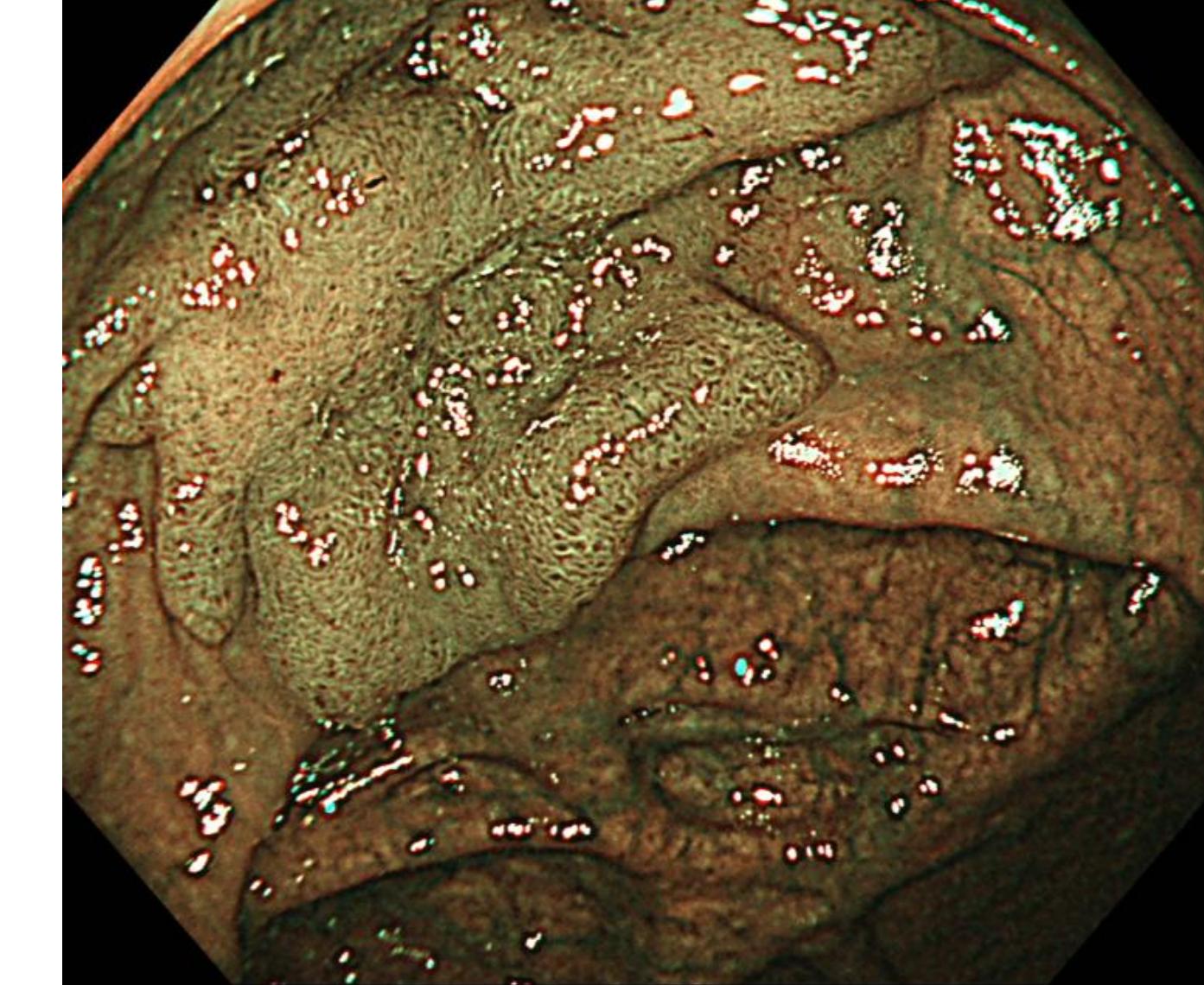


JNET 2A

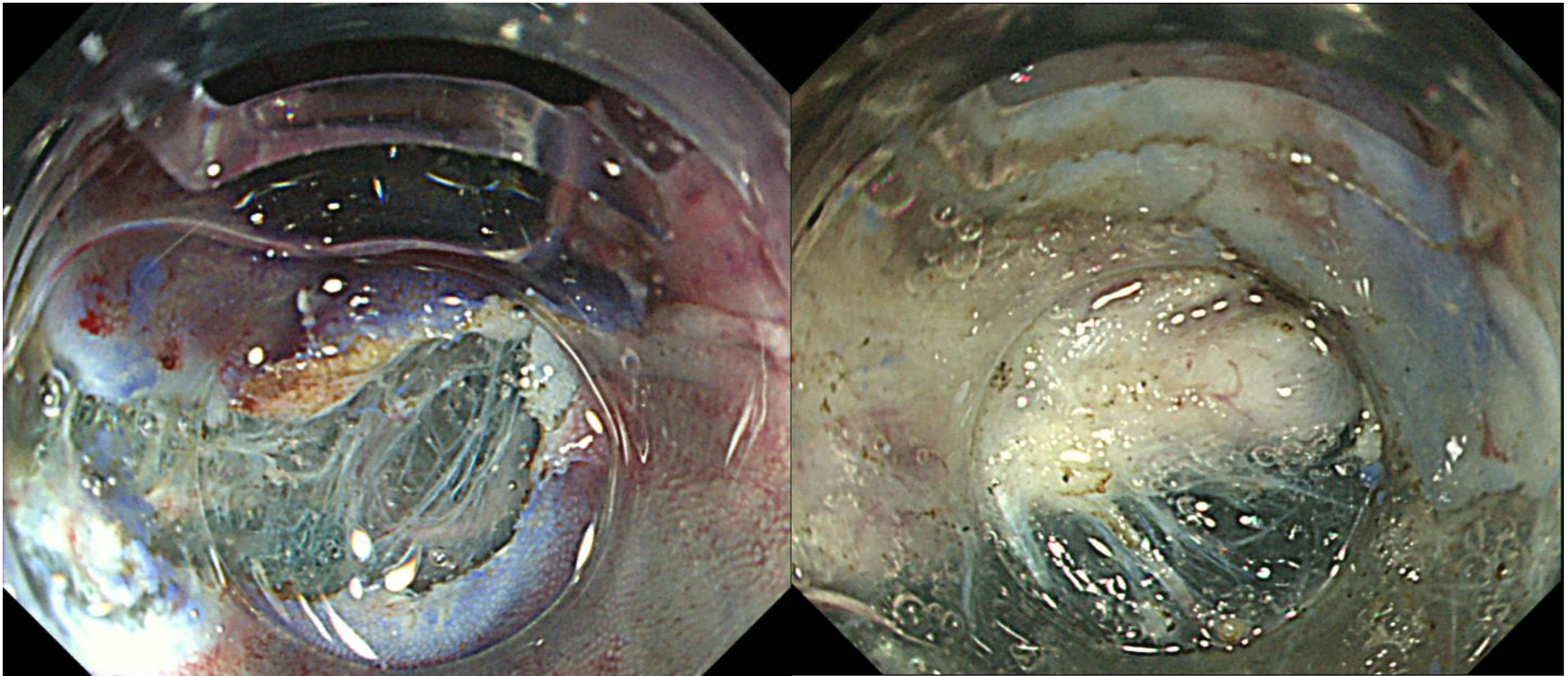
LGD

JNET 2B

HGD/Tis/sm1



# *ESD; Intraoperative dx; T1b*



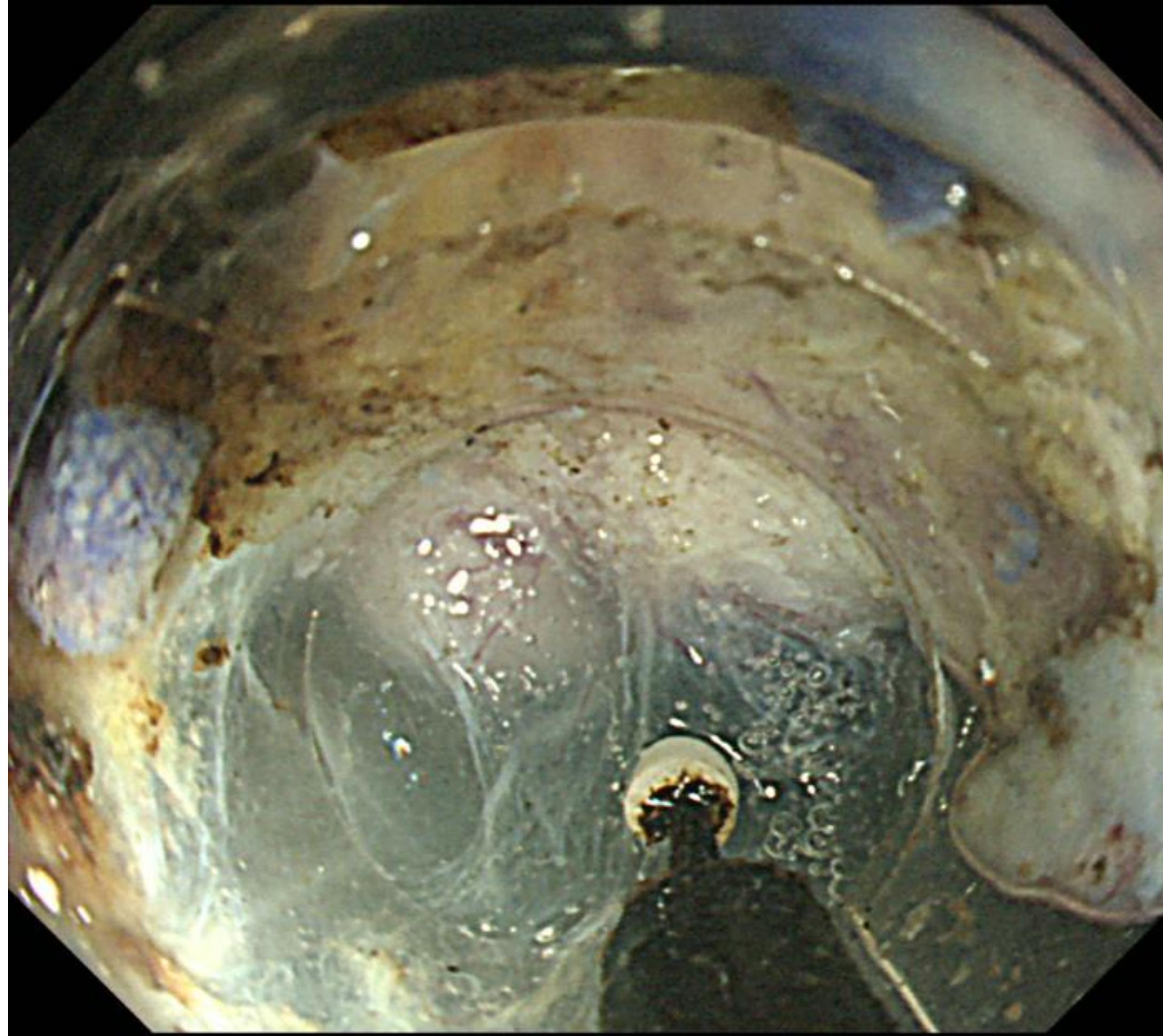
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# ESD



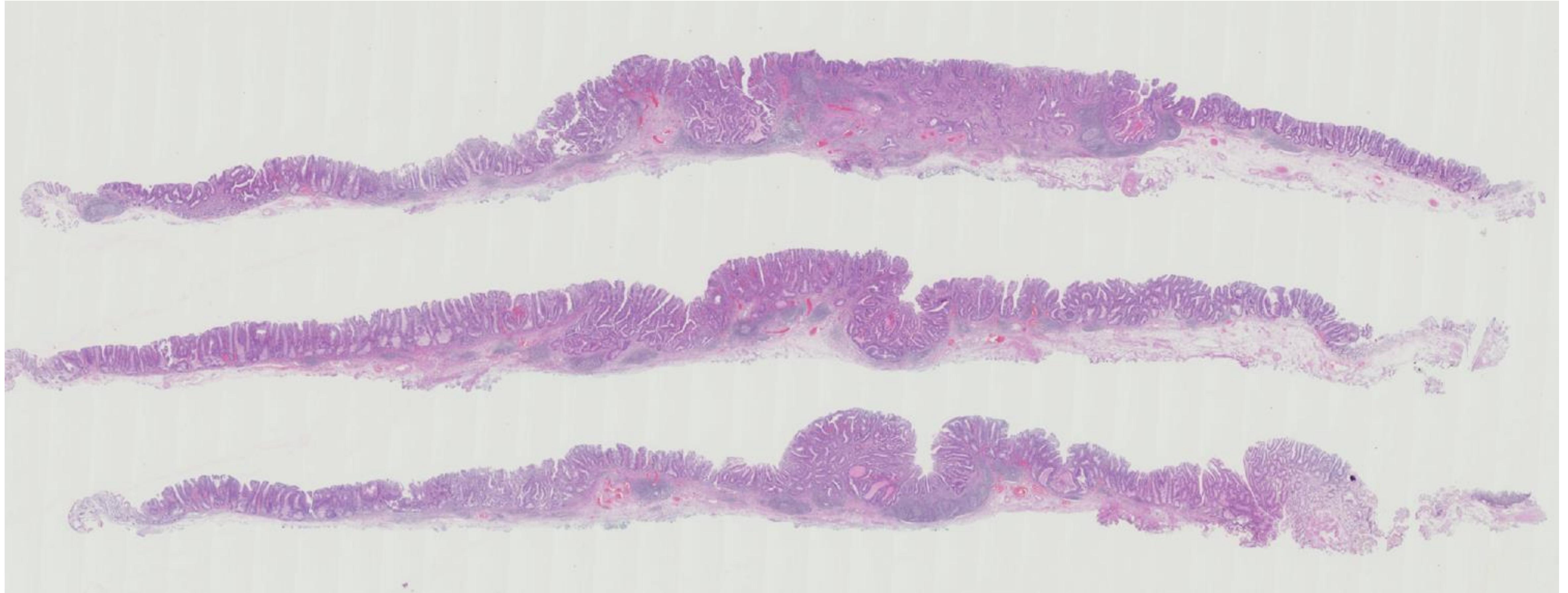
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# *Pathology*



*Pathology by Dr. Sekine S, Taniguchi H, et al.*



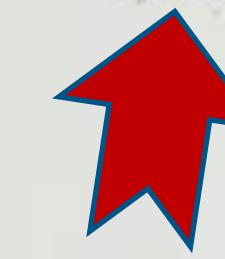
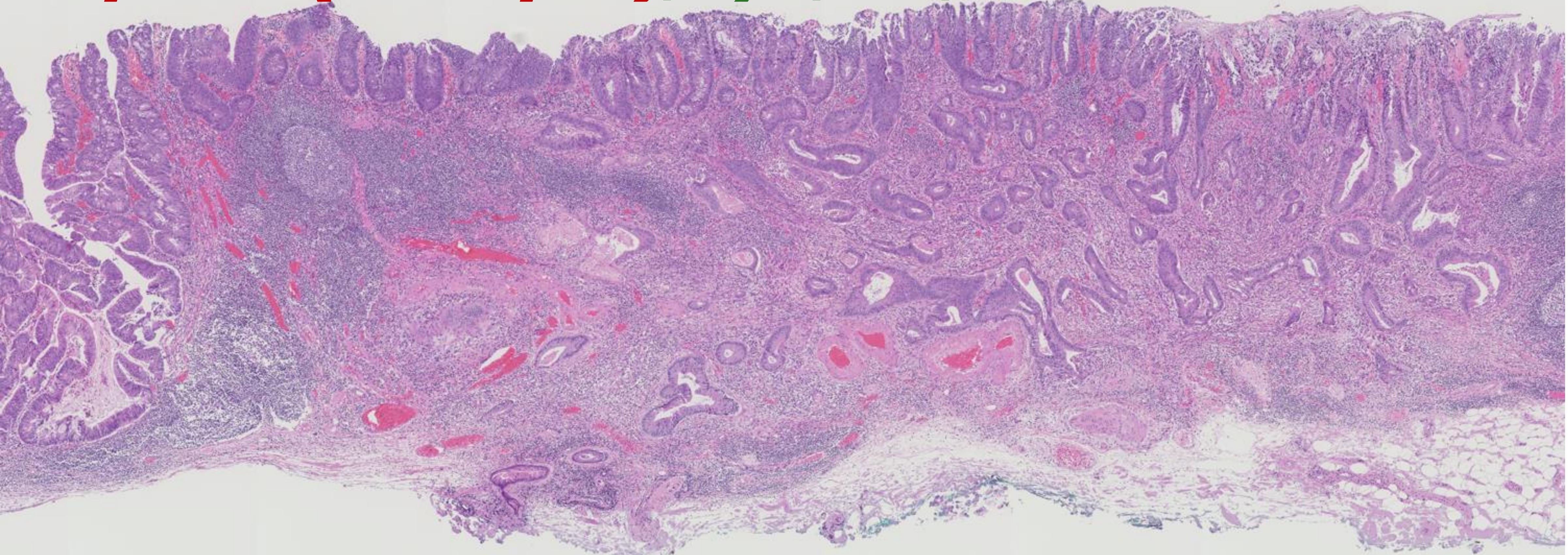
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*Well, low and high grade  
pSM2(2500 $\mu$ m), ly0, v1, VM+/-*



***→Recommended Surgery***

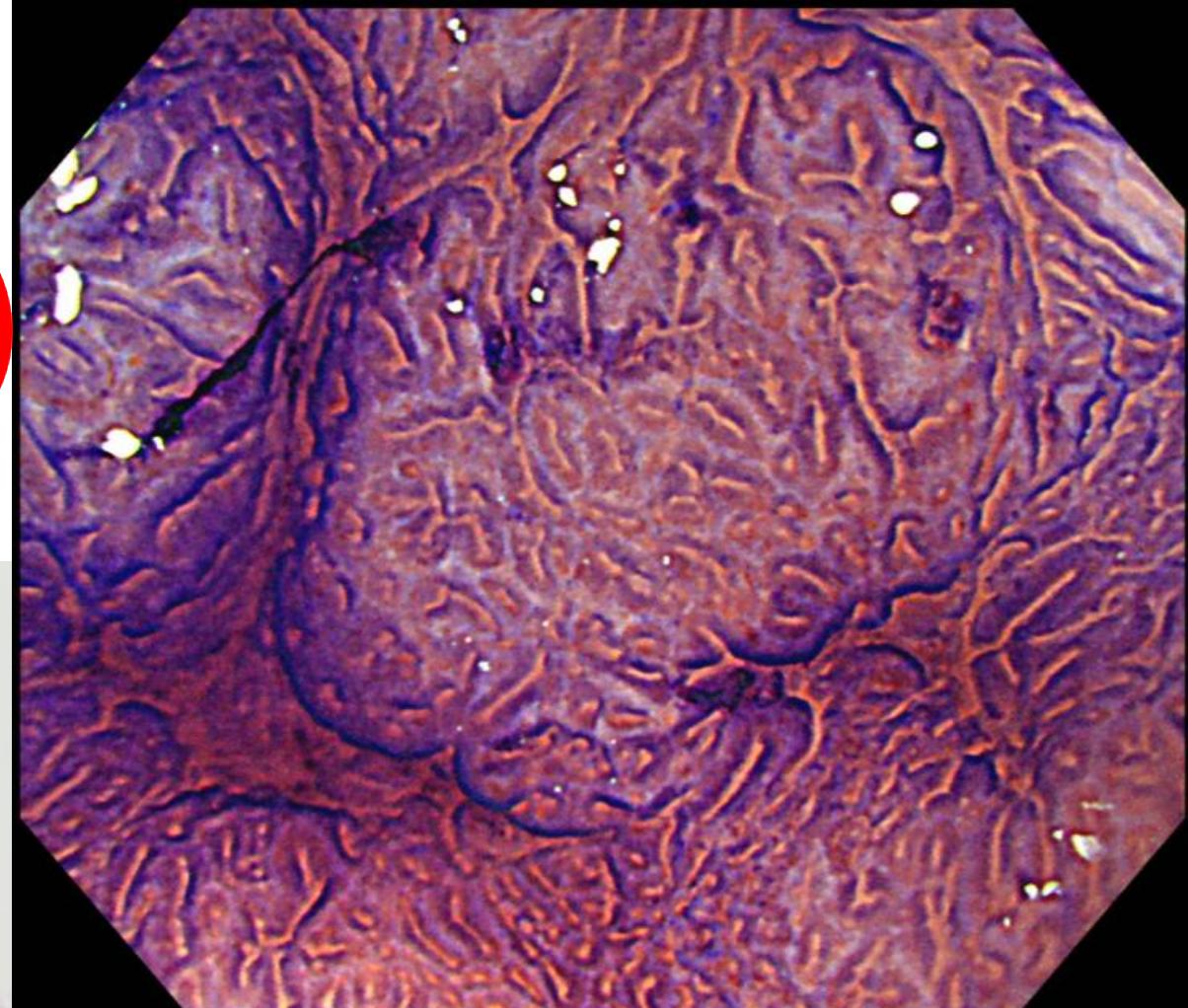
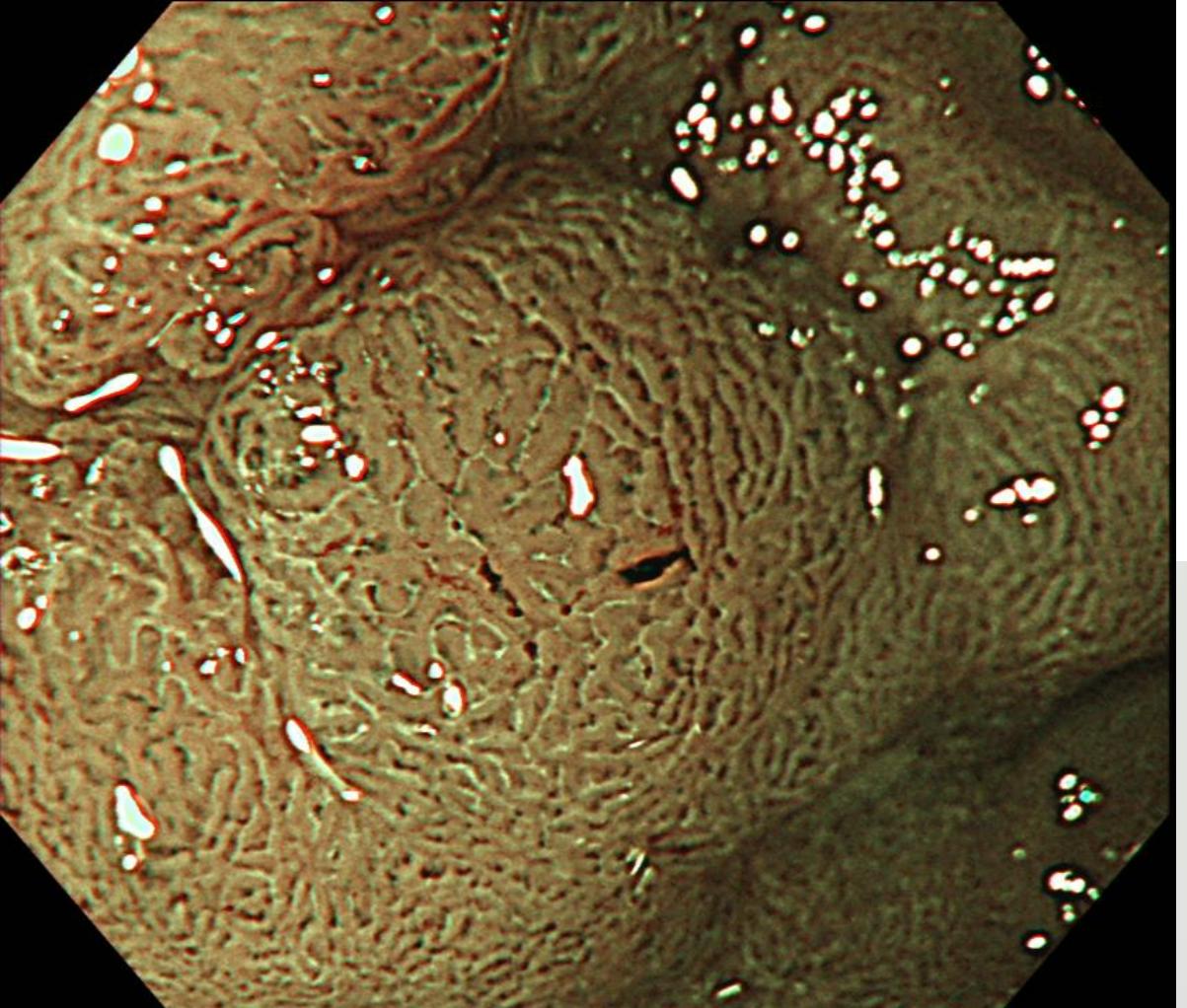
Pathology by Dr. Sekine S, Taniguchi H, et al.

*Yutaka Saito, MD, PhD, FJGES, FASGE*

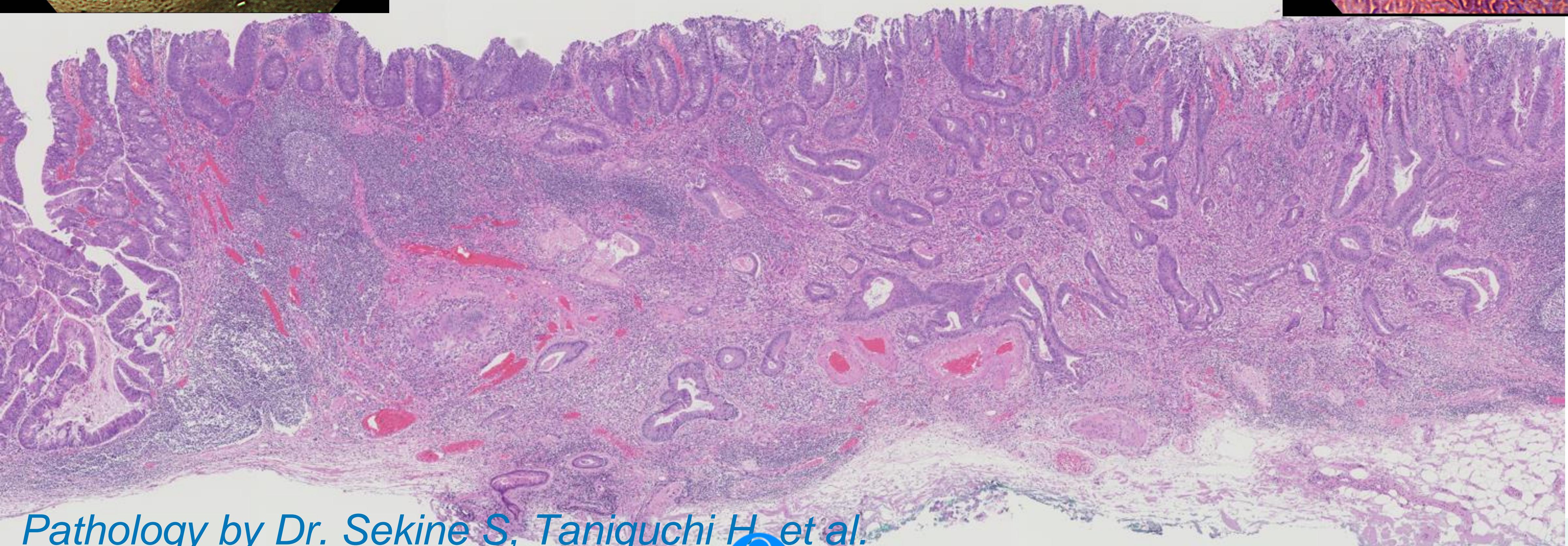


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# Need to understand the limitation of IEE



Pathology by Dr. Sekine S, Taniguchi H et al.

Yutaka Saito, MD, PhD, FJGES, FASGE



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# Agenda

Indication for ESD

JGES guidelines

ESGE guidelines

Proposal for WEO guidelines CQ



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*Indication for ESD*  
*JNET 2B & Non-invasive pattern*  
*Any Location including proximal colon*

LST-subtypes & Tumor size	20mm-	30-	40-
0-IIa (LST-G, homogenous)		EMR	ESD
0-Is+IIa (LST-G, nodular mixed)	EMR		ESD
0-IIa(+IIc), 0-IIc (LST-NG)			ESD

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# Diskussion Points

**CQ1 Does Tis (HGD) require en bloc resection?**

**CQ2 Does Tis of the right -colon also require en bloc resection?**

**CQ3 Must Histology define intramucosal carcinoma instead of HGD?**

Statement;

This could be high-grade dysplasia.

If all agree that intramucosal cancer is equal to HGD.

**CQ4 Must Histology conduct I-H staining such as Desmin, D2-40, etc for ESD specimens?**



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