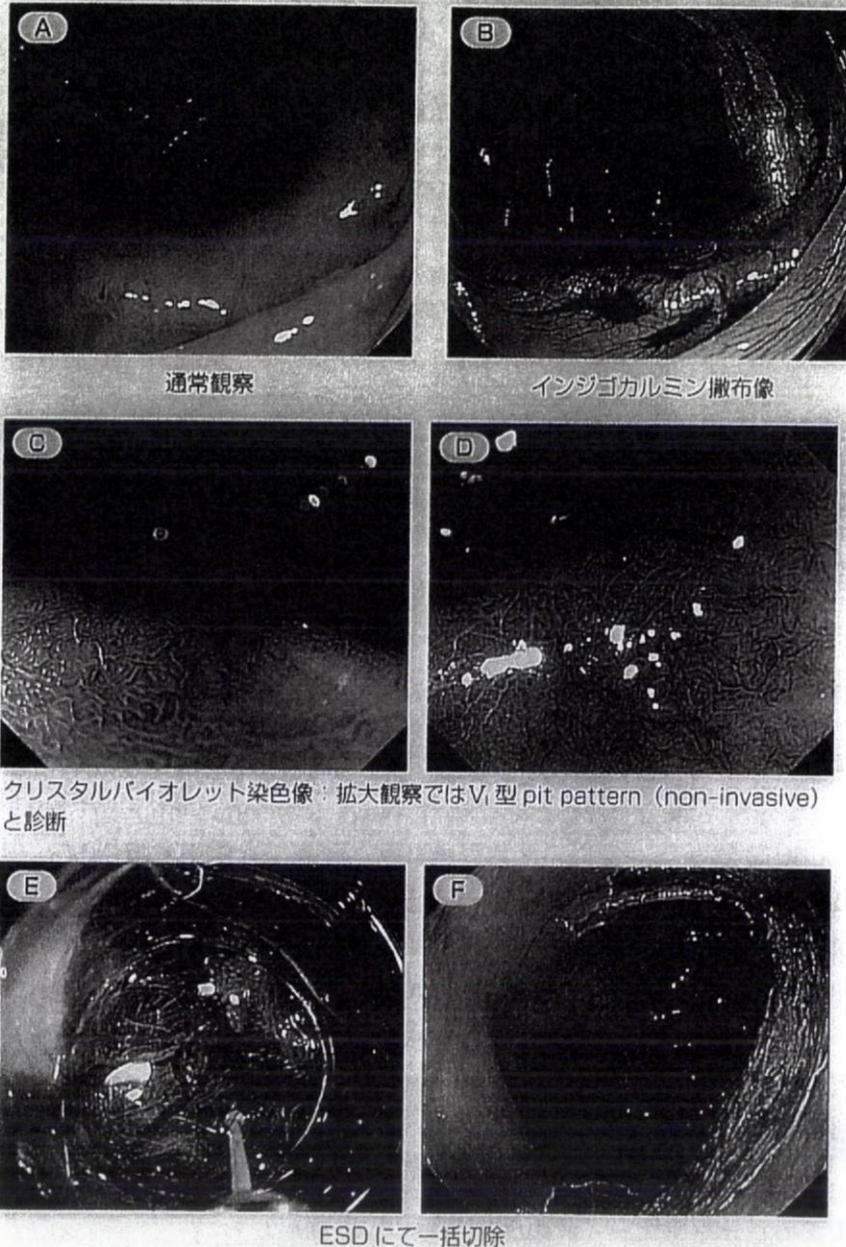


- **症例 1** 59歳，男性．上行結腸に55mm大のⅡa病変（LST-NG）を認める．通常観察では強くSM浸潤を示唆する所見はなく，拡大観察でも non-invasive pattern と判断し，ESDを施行した．病理組織学的には低異型ないし高異型度高分化腺癌よりなる病変で，大部分は粘膜内癌の組織構築が保たれていた．しかし，多巣性にSM浸潤がみられ，最大浸潤距離は1,300 $\mu$ m（粘膜筋板の状態はType A）であった．切除断端は陰性で，脈管侵襲や低分化腺癌，未分化癌はなかった．これもガイドラインからは，深達度の点のみで追加治療の適応ではあるが，粘膜筋板の状態や浸潤距離を考慮し，厳重な経過観察としている（図1）．



◆ 図1 参考症例1（ESD施行後の経過観察）

## ポイント

- 従来外科的切除されていた病変が内視鏡で切除可能となったが、適応の判断には拡大内視鏡診断の習得が不可欠である
- 20 mm を越える LST でも内視鏡治療の適応となりうるが、LST-NG は比較的高率に SM 浸潤があり、その部位の同定は困難なことがある
- 通常観察で SM 浸潤が疑われても、pit pattern 観察にて non-invasive であれば、一括切除を条件に診断的内視鏡治療を行うことも選択肢の 1 つである

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## 2. 切除手技の選択2

桐山真典, 斎藤 豊, 松田尚久

**Case** 肛門管にかかり痔核もある。出血も心配だが、範囲が広く経肛門的切除では一括切除も難しい。さて…?

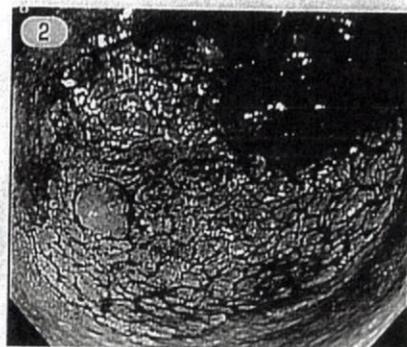
75歳女性。近医で下部直腸腫瘍を指摘された。直腸指診で、わずかに腫瘍を触知するも辺縁は不明瞭である。肛門鏡診察でも範囲は不明瞭であった。下部消化管内視鏡検査で、下部直腸に半周性で、大きさ70mmの軽度隆起性病変を認める(図A-①)。通常観察では境界不明瞭だが、インジゴカルミン撒布にて辺縁を明瞭に確認できる(図A-②)。口側にも約5cm進展している。腫瘍の一部は肛門管にかかり、痔核を取り囲んでいる(図A-③)。肛門近傍の軽度発赤した結節の拡大観察(クリスタルバイオレット染色)を示す(図A-④)。

治療方法と、使用する局注液・デバイスの選択は？

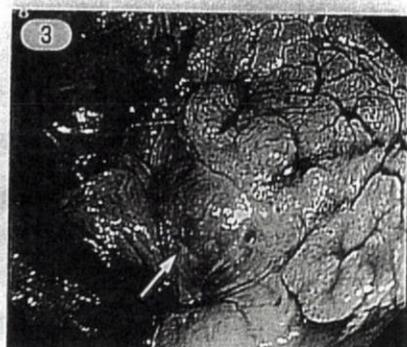
Case ◆ 図A 下部直腸腫瘍



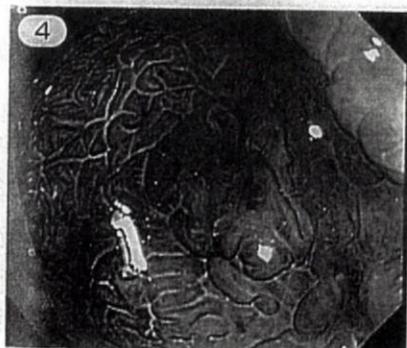
通常観察像



インジゴカルミン撒布

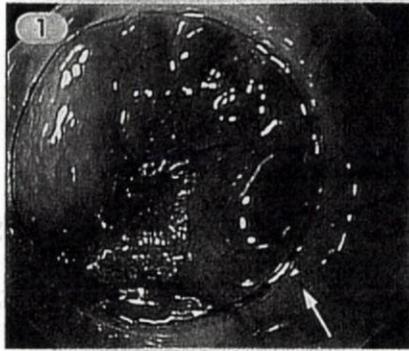


病変の一部が痔核(⇔)を取り囲む

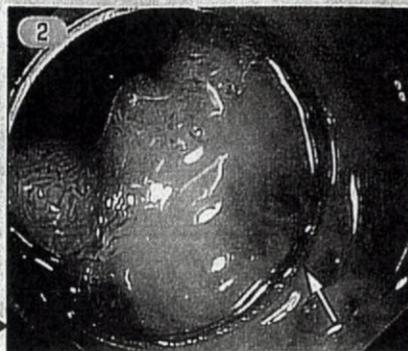


拡大観察(クリスタルバイオレット染色)

Case ◆ 図B 肛門管にかかるESD



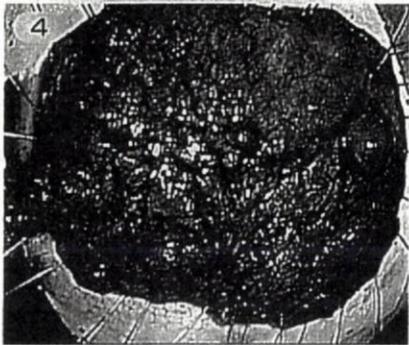
1 腫瘍肛門側辺縁：拡張した痔静脈（⇔）を認める



2 剥離時：痔静脈（⇔）を止血していきコントロールする



3 一括切除後の病変部：出血は認められない



4 切除標本

### Strategy

● 肛門管・下部直腸 ESD は怖くない！！そのコツと対策！！

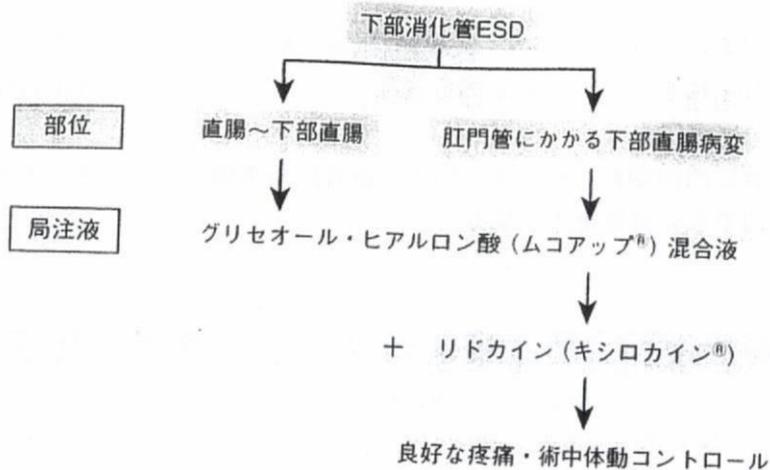
本症例においては、腫瘍サイズ・肉眼型・部位・通常観察での辺縁不明瞭なことより内視鏡治療が推奨される。内視鏡治療では

- ① 一括切除が可能である
- ② 歯状線近傍および口側まで切除可能である
- ③ 境界の判断のため拡大観察を瞬時に行うことができる

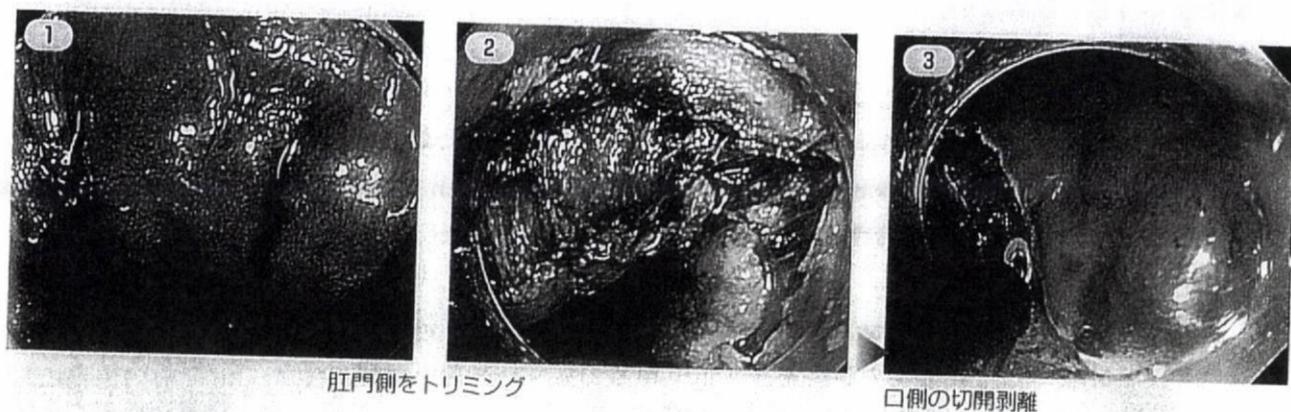
といったメリットがある。しかし内視鏡での観察下であるため、少量であっても断続的な出血がある場合、視野がとりづらく治療に支障をきたす。

先端アタッチメント装着後の観察では腫瘍肛門側辺縁に拡張した痔静脈を認める(図B-①)。痔核は治療の支障になりうるが、切除前から確実に認識し、剥離時に痔静脈を止血していくことでコントロール可能である(図B-②)。この際、デバイスに従来のモノポーラータイプだけでなく、バイポーラータイプのBナイフ®を使用することが推奨される。肛門括約筋が近傍に存在するため、モノポーラータイプでは強い筋収縮をきたし、思いがけない部分を凝固・切開しかねない。一方、Bナイフ®のようなバイポーラータイプを使用することで安全かつ確実な止血を行うことができる。

経肛門的切除は肛門近傍の腫瘍が適応で、術野展開によっては腫瘍辺縁の認識が難しいことがある。また側方発育型腫瘍(LST)で一部に結節を有する腫瘍では、SM浸潤をきたしている可能性があり、切除後の詳細な組織学検討には同部を確実に一括で切除するか、全体を一括



◆ 図1 局注液の選択



◆ 図2 剥離の手順

切除する必要がある (図 B-③, ④). 以上のような問題点を解決し確実な切除をめざすには ESD が望ましい.

● 疼痛管理

肛門管は結腸や直腸と比べ痛覚がしっかり存在し, 肛門管にかかる病変では治療中・後に疼痛を訴える症例が多い. そのため当院では ESD 施行時, 通常使用しているグリセオール・ヒアルロン酸 (ムコアップ®) 混合の局注液に局所麻酔薬 [リドカイン (キシロカイン®)] を混合した局注液を肛門管粘膜下層に注入し, 疼痛コントロールに努めている (図1).

● 剥離のコツ

また剥離手順を誤ると, 剥離を進めるうちに病変が捲かれてしまい剥離しづらくなる. 直腸 ESD の手順としては, 基本的には, 反転操作時に近位側となる口側から ESD を開始しているが, 肛門縁にかかる病変のみは, 肛門側を先にトリミングした後, 口側の切開剥離を行っている (図2).

● ESD の適応

肛門管にかかる直腸腫瘍は, その解剖学的特徴から, 従来から経肛門的切除や経肛門的内視鏡下顕微鏡手術 (TEM) が施行されてきた. 近年, 内視鏡的粘膜下層剥離術 (ESD) が大腸病変にも施行されており, 当院では 1998 年 2 月から大腸腫瘍性病変に対し ESD を施行してい

る。このような肛門管にかかる病変は通常 EMR では切除が非常に困難であり、再発をくり返し、外科手術を必要とする症例も経験している。このように肛門管にかかる病変は ESD の非常により適応である。

また経肛門的切除を行う場合には、術前に内視鏡下にマーキングを行うことで病変範囲を正確に認識でき、再発予防となる。

## 回答：局所麻酔薬配合局注液と B ナイフ<sup>®</sup> を用いた ESD

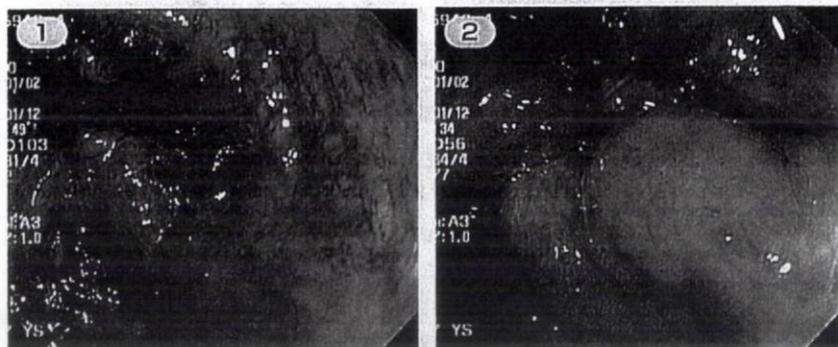
内視鏡観察では、一部に結節を有し、肉眼型は 0-I s + II a (LST-MIX) である。拡大内視鏡診断では M ~ SM1 までの深達度の腫瘍と診断できる。肛門側には 7 ~ 8 mm 大の内痔核を認める。腫瘍の大きさ・口側進展・肉眼型から、内視鏡的治療（内視鏡的粘膜下層剥離術：ESD）による一括切除が望ましいと判断できる。局所麻酔剤配合局注液を粘膜下層に注入して使用した。剥離操作の大部分で B ナイフ<sup>®</sup> を使用した。穿孔なし、合併症なし。組織学的に低異型度高分化腺癌の粘膜内増殖を認めた。経過中にも下血など術後出血を認めなかった。術後 6 日目に軽快退院した。約 6 カ月後の内視鏡検査で再発を認めない。

## Reference

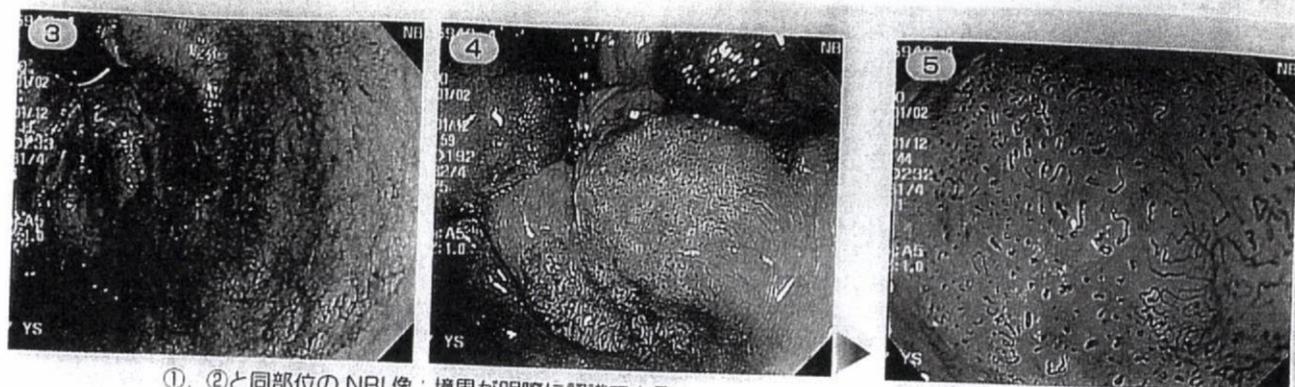
症例は少ないものの肛門管という解剖学的位置により、扁平上皮癌や経肛門的切除後遺残再発例が存在する。参考にそれらの症例を提示する。

- **症例 1** 70 歳，女性。検診で便潜血陽性を指摘され，精査のため施行された下部消化管内視鏡検査で肛門管近傍の腫瘍を認めた。生検で扁平上皮癌と診断された。治療前の内視鏡診断では一部に結節を有し，大きさ 40 mm の 0-I s + II a と診断した。通常観察やインジゴカルミン撒布では比較的境界不明瞭である（図 3 - ①，②）が，NBI 観察にて境界が明瞭に認識された（図 3 - ③，④）。さらに食道扁平上皮癌の拡張・蛇行した乳頭内血管ループ（intra-epithelial papillary capillary loop：IPCL）に似た異常血管も確認された（図 3 - ⑤）。ルゴール染色にて境界明瞭な淡染領域として捕らえられる（図 3 - ⑥）。内視鏡診断で SM1 までの腫瘍と診断し，ESD にて肛門管を一部切開し，一括切除した。

病理組織学的診断では扁平上皮癌，40 × 10 mm，深達度は SM1（400 μm），ly0，v0 であった。補助化学放射線療法（5FU + CDDP，RT）を施行した。術後経過は良好で，切除後 24 カ月現在，再発は認めていない。

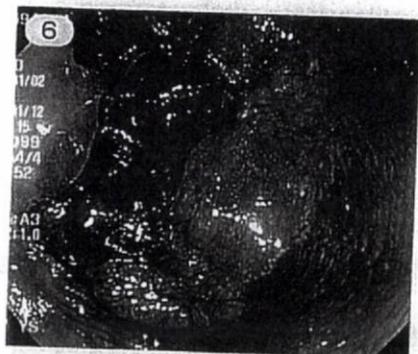


通常観察 (①) とその拡大像 (②)：境界不明瞭である



①, ②と同部位のNBI像：境界が明瞭に認識できる

NBI強拡大像：食道扁平上皮癌の拡張・蛇行した乳頭内血管ループ（IPCL）に似た異常血管が確認された



①, ③と同部位のルゴール染色：境界明瞭な淡染領域として捕らえられる

◆ 図3 参考症例1

肛門管近傍の扁平上皮癌に対するESD

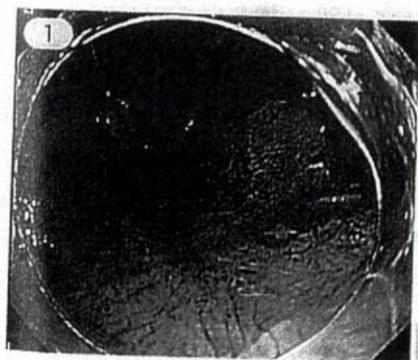
消化器

2. 切除手技の選択2

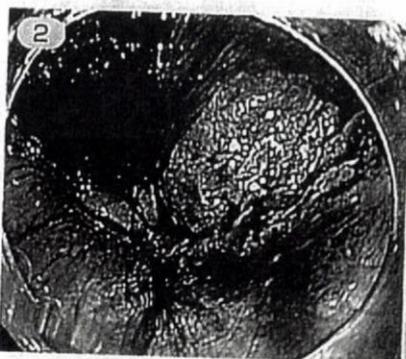
● 症例2

38歳，女性，直腸腫瘍に対し前医にて経肛門的切除術が施行された，切除検体の断端は切除時の焼灼のため判定困難であった，経過フォロー中に同部位に腫瘍を認め，術後再発と診断した。

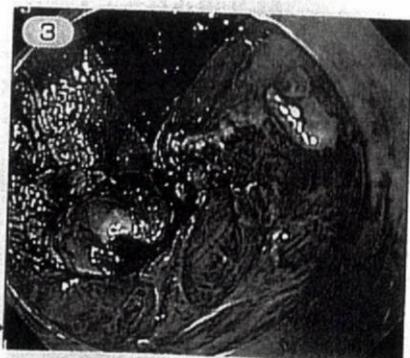
追加経肛門的切除術は困難と判断され，当院にてESDを施行した（図4），強い瘢痕線維化を認め，non-lifting sign陽性であった，粘膜下層の瘢痕線維化を少しずつ切離し，切除した，また，術中穿孔は認めなかった，切除後中心線維化部分にAPCを追加した，病理組織学的診断では大きさ25mmの管状腺腫であった，切除後2年2カ月再発を認めていない。



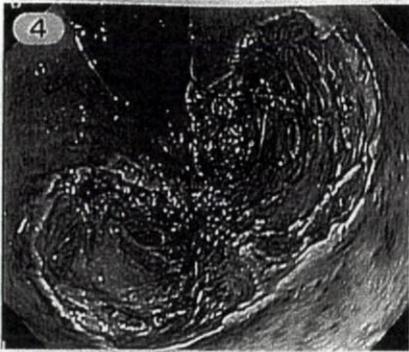
通常観察



インジゴカルミン撒布後，瘢痕の辺縁に再発病変を認める



瘢痕中心部は強い線維化を伴う



切除後

◆ 図4 参考症例2

経肛門的切除後遺残再発例に対するESD

ポイント

- 内視鏡治療 ESD では、拡大観察を用いて範囲診断をしながら口側まで広範囲に広がる腫瘍の一括切除が可能である
- 痔核を有する場合も、剥離時に B ナイフ<sup>®</sup> のようなバイポーラータイプを使用し、痔静脈を安全・確実に止血していくことでコントロール可能である
- 肛門管近傍病変では治療中・後に疼痛を訴える症例が多いため、局所麻酔薬配合局注液を使用し、疼痛コントロールすることが有用である
- 経肛門的切除を施行する場合、術前に内視鏡下マーキング（針状メスによる凝固マーキング）を行うことで、病変の範囲確認が可能となり、再発予防となる

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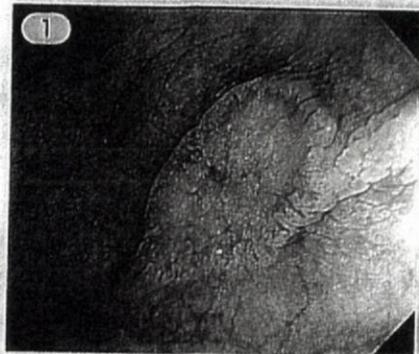
# 1. 微小穿孔

太田昭彦, 斎藤 豊

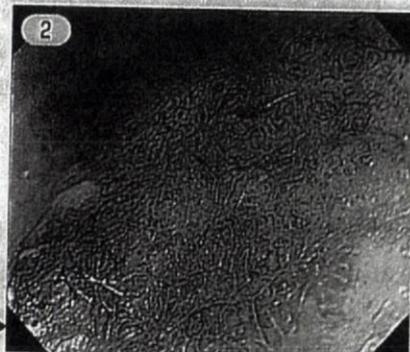
## Case 粘膜下層剥離中に微小穿孔が生じた症例

検診にて便潜血反応陽性であったため大腸内視鏡を施行, S 状結腸に 13mm 大の II c 病変を認めた。通常観察では, 陥凹中心部に軽度の隆起と凸凹があり, SM 浸潤も否定できなかった (図 A-①)。拡大観察では, 陥凹中心部の軽度隆起も含めて, 軽度不整の V<sub>I</sub> pit pattern と診断し, 浸潤度 M ~ SM-s (sm1) と診断した (図 A-②, ③)。以上陥凹型で, SM 浸潤も否定できないことより一括切除が望ましいと判断し, ESD を選択した。周囲粘膜切開, 粘膜下層剥離と順調に進んだが (図 A-④), 粘膜下層剥離の際に一瞬ブラインド操作となり微小穿孔を生じた (図 A-⑤)。このような穿孔を認めた場合どうするか?

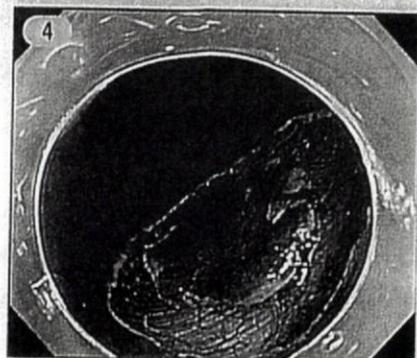
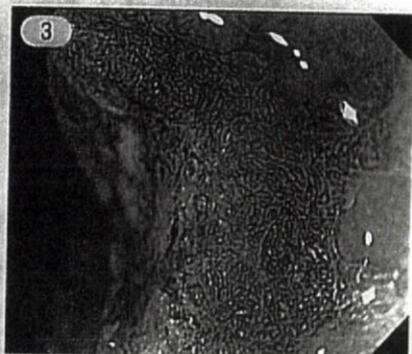
Case ◆ 図 A 13mm 大の II c 病変



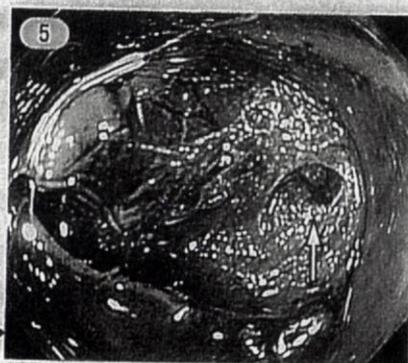
通常観察像 (インジゴカルミン撒布)



拡大観察像 (クリスタルバイオレット染色)



ESD による周辺粘膜切開および粘膜下層剥離



微小穿孔 (⇔)

## ● 内視鏡治療を行ううえでの留意点

内視鏡治療においては、病変の的確な診断のもと、術者の経験、技量をふまえたうえで治療方針を決定すべきである。そのうえで、患者および家族に治療法や治療により起こりうる偶発症（穿孔、出血など）の可能性、その頻度、起きた際にどのような事態が想定されるかを十分説明し、承諾を得ることが前提である。

大腸 ESD では、屈曲やひだの存在、壁が薄いことなど技術的に難易度が高いこと、かつ腸液が腹腔内に漏出した場合は腹膜炎を併発し重篤な状態になりうることもある。そのため、安全に行うための準備が必要で、局注液にヒアルロン酸製剤を<sup>1)</sup>、デバイスもより穿孔の危険が少ないものを使用する必要がある。送気においては通常送気に比較し吸収が早いことより、CO<sub>2</sub>送気の選択が患者腹部膨感の軽減、および穿孔後の気腹の予防に有用（p116, 基礎編第3章③-5）と報告されており<sup>2)</sup>、これらを最低限備えておくことが望ましい。

## ● 穿孔の対処

また穿孔が生じた場合は、前述のごとくバイタルサインの変化、腹痛など、まず患者の状況を確認することが第一である。

次に病変および穿孔部の処理をどうすべきかの判断が必要となる。バイタルサインの変化などがみられた場合には、状況により穿孔部の縫縮を優先し、治療を断念せざるをえない場合も想定される。しかし ESD における穿孔は、本症例のようにそのほとんどが微小穿孔であり、ある程度剥離を進めたうえで穿孔部を縫縮し、ESD を完遂することが可能である。その際、腸液が腹腔外に漏出するのを予防するため、余分な腸液はあらかじめ十分吸引しておくこと、体位変換を利用し病変が腸液の貯留する方向と反対側に位置するようにすることで、腸液の漏出を予防することができ、かつ病変に重力によるトラクションがかかり粘膜下層の剥離が容易となる。

## ● 術後管理

術後の管理は、外科医や放射線医とも綿密に連絡をとり、絶飲食および広域の抗生物質を使用し、発熱、腹痛、腹膜炎の有無、炎症反応の変化や単純 X 線写真による free air の確認をしていく。ときに単純 X 線写真のみではわからない微量の free air が CT にて判明することもあり、これらを併せ、経時的にみていくことが重要である。

また腹膜炎を生じた場合は、より慎重に、かつ外科手術のタイミングを逃さないように観察し、患者および家族へ十分な説明と、スタッフ間での検討が必要となる。

クリップによる縫縮も、必ずしも完全に縫縮できていない可能性や、腸管内圧上昇や排ガスなどによりクリップが外れることがありうることも念頭に置き、慎重な観察は必要である。

## ● 提示症例の場合

本例も局注液にはヒアルロン酸、デバイスはパイポーラナイフ（B ナイフ<sup>®</sup>）<sup>3)</sup>、送気には CO<sub>2</sub> を使用した。十分な局注のうえ、粘膜下層を慎重に剥離していったが、一瞬ブラインド操作となり穿孔をきたした。B ナイフ<sup>®</sup> は構造上穿孔の危険性がきわめて少ないとされるが、先端が鋭であることから、針先で機械的穿孔をきたす場合がある。そこで先端にボールチップを配し、さらに穿孔の危険性を減じたボールチップ型 B ナイフ<sup>®</sup> が現在市販化されている<sup>4)</sup>。

本例は幸い微小穿孔であり、粘膜下層剥離も進んでいたため、病変はスネアリングにて一括切除が可能であった（図 B-①）。

さらに穿孔部縫縮をしようとした際、腸管内の空気を十分に吸引したところ、穿孔部に腸管外の脂肪と思われる黄色の組織が吸引され、陥頓したため（図 B-②）、小野の omental patch<sup>5)</sup>

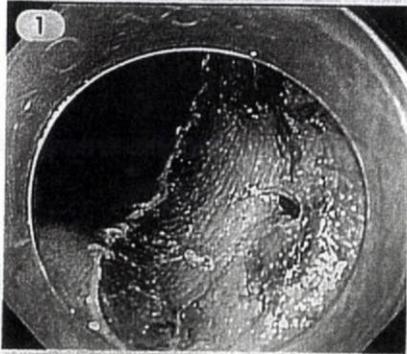
の要領でクリッピングした (図 B-③)。バイタルサインの変化, 腹痛, 炎症反応の亢進はなく経過し, 術後にわずかな free air を認めたが (図 B-④), 翌日には消失した。経過は良好で第 9 病日に退院した。

組織学的に, 中心の軽度隆起部で SM-s (sm1) (900  $\mu$ m) の浸潤を認めた。ly, v ともに陽性であったため腹腔鏡補助下結腸切除術が行われたが, 腫瘍遺残やリンパ節転移は認めなかった。

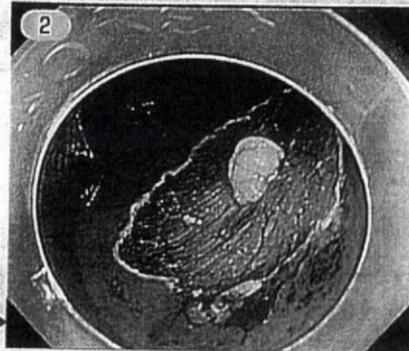
### ● ESD の注意点

大腸 ESD は, 十分慎重に行っても一瞬のブラインド操作で穿孔をきたすことがありうる治療であることを認識し, 十分な技量と経験を有してから行っていくことが必須である。後から振り返ってみれば本症例は通常 EMR でも一括切除が可能な病変であった。ESD の適応に関しては術者の技量を踏まえ慎重に検討する必要がある。

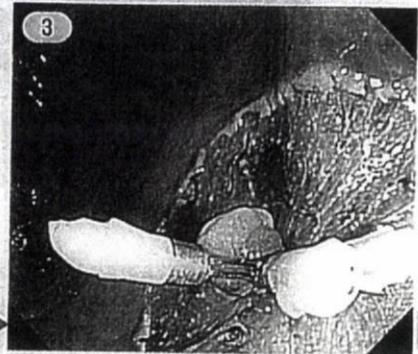
Case ◆ 図 B 穿孔後の対応



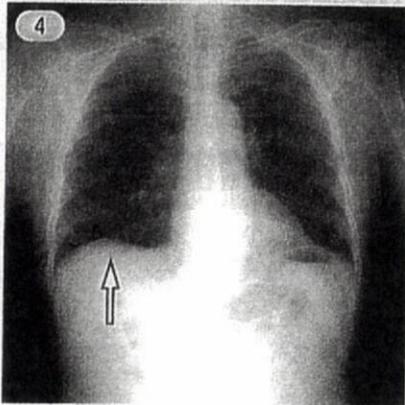
1 スネアリングによる一括切除



2 腸管内の空気の吸引により陥頓した腸管外の脂肪と思われる組織



3 穿孔部のクリッピング



4 術後単純 X 線写真: わずかに free air (⇒) を認める

## 回答：バイタルサインの変化，症状の有無の確認 → 穿孔部の処理，病変の対応を判断する

まずバイタルサインの変化，腹部膨満，腹痛の有無の確認を行い，これらをふまえて，どう対応するかをすみやかに判断する．穿孔部の縫縮をする場合には，ある程度粘膜下層の剥離を進めてからでないと，その後の剥離が困難となる．バイタルサインの変化がみられた場合には，穿孔部の処理を優先し，ときには病変の切除を中止することも必要であるが，ESDにおいては仮に穿孔しても，本症例のように微小穿孔である場合が多く，基本的にはESDを完遂することが可能である．

### ポイント

- 穿孔した場合，まずバイタルサインの変化，腹痛などの症状の有無を確認し，冷静に病変・穿孔部の処理を行う
- 術後は本人，家族に現状および今後起こりうる可能性を十分説明し，外科医・放射線医とも綿密な連絡をとり，経過をみていく
- 絶飲食，広域の抗生物質の使用，ならびに腹部所見，画像検査による慎重な観察が必要である
- 特に腹膜炎が生じた際は，外科手術のタイミングを逃さないよう冷静に判断していく

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## Review

# Capsule endoscopy: past, present, and future

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A capsule endoscope is a swallowable wireless miniature camera for getting images of the gastrointestinal (GI) mucosa. The initial capsule endoscope model was developed by Given Imaging and approved in Western countries in 2001. Before the introduction of capsule endoscopy (CE) and double-balloon endoscopy (DBE), there was no effective modality for the evaluation and management of patients with obscure GI bleeding. Obscure GI bleeding is defined as bleeding of unknown origin that persists or recurs after a negative initial or primary endoscopy (colonoscopy or upper endoscopy) result. The first capsule endoscope model, which is now regarded as a first-line tool for the detection of abnormalities of the small bowel, was the PillCam SB. It was approved in Japan in April 2007. The main indication for use of the PillCam SB is obscure GI bleeding. Almost the only complication of CE is capsule retention, which is the capsule remaining in the digestive tract for a minimum of 2 weeks. A retained capsule can be retrieved by DBE. There are some limitations of CE in that it cannot be used to obtain a biopsy specimen or for endoscopic treatment. However, the combination of a PillCam SB and DBE seems to be the best strategy for management of obscure GI bleeding. Recently, several new types of capsule endoscope have been developed, such as Olympus CE for the small bowel, PillCam ESO for investigation of esophageal diseases, and PillCam COLON for detection of colonic neoplasias. In the near future, CE is expected to have a positive impact on many aspects of GI disease evaluation and management.

**Key words:** capsule endoscopy, obscure gastrointestinal bleeding, double-balloon endoscopy

## Introduction

A capsule endoscope is a swallowable wireless miniature camera for getting images of the gastrointestinal (GI) mucosa. The initial capsule endoscope model was developed by Given Imaging (Yoqneam, Israel)<sup>1</sup> and approved in Europe and the United States in 2001.<sup>2,3</sup> Almost at the same time, Yamamoto et al.<sup>4,5</sup> developed double-balloon endoscopy (DBE), which is based on a new insertion technique that makes it possible to insert an endoscope into the distal portion of the small bowel. Since the introduction of capsule endoscopy (CE) and DBE into clinical use, dramatic changes have occurred in the evaluation and management of patients with GI bleeding and obscure GI bleeding. Obscure GI bleeding is defined as bleeding of unknown origin that persists or recurs after a negative initial or primary endoscopy (colonoscopy or upper endoscopy) result.<sup>6</sup> As a result of the capability of both CE and DBE to easily visualize the small bowel, GI bleeding has been reclassified into three categories (upper, mid, and lower GI bleeding) instead of the traditional classification into upper and lower GI bleeding.<sup>7</sup> Bleeding above the ampulla of Vater, within the reach of an esophagogastroduodenoscopy (EGD), is defined as upper GI bleeding. Small-bowel bleeding from the ampulla of Vater to the terminal ileum, best investigated by CE and DBE, is defined as mid GI bleeding, and colonic bleeding is defined as lower GI bleeding, which can be evaluated by colonoscopy.<sup>7</sup>

In this article, we review previous reports, including the latest reports, focusing on CE and management of obscure GI bleeding, which is the most important indication for CE of the small bowel. In addition, we briefly discuss other types of capsule endoscope and the future of CE.

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## Capsule endoscopy of the small bowel

### Brief history

The first capsule endoscope model in the world, called M2A (meaning "mouth to anus"), was manufactured by Given Imaging.<sup>1</sup> After clinical use and evaluation,<sup>2,3,8</sup> M2A was approved for general clinical use in Europe in May 2001, and by the U.S. Food and Drug Administration (FDA) in August 2001.

The FDA initially approved M2A as an adjunctive tool for visualization of abnormalities of the small bowel. Afterward, in July 2003, it approved M2A as a first-line tool for the detection of abnormalities of the small bowel, based on evidence provided by a meta-analysis.<sup>9</sup> M2A was renamed PillCam SB (meaning "small bowel"; Fig. 1) after the advent of esophageal CE (PillCam ESO; Fig. 2),<sup>10</sup> also developed by Given Imaging.

In Japan, the first clinical CE trial for small-bowel disease, including Crohn's disease, was carried out at Dokkyo Medical University (Tochigi) and Social Insurance Central Hospital (Tokyo) in 2003.<sup>11,12</sup> PillCam SB was approved by the Ministry of Health, Labour and Welfare of Japan in April 2007, and finally reimbursement for CE costs was approved by Social Insurance Agency of Japan in October 2007.

Another type of CE for the small bowel has been developed by Olympus (EndoCapsule EC type 1)<sup>13</sup> and is already approved in Europe but not yet in Japan. More than 600 000 PillCam SB capsules have been used worldwide since 2001.

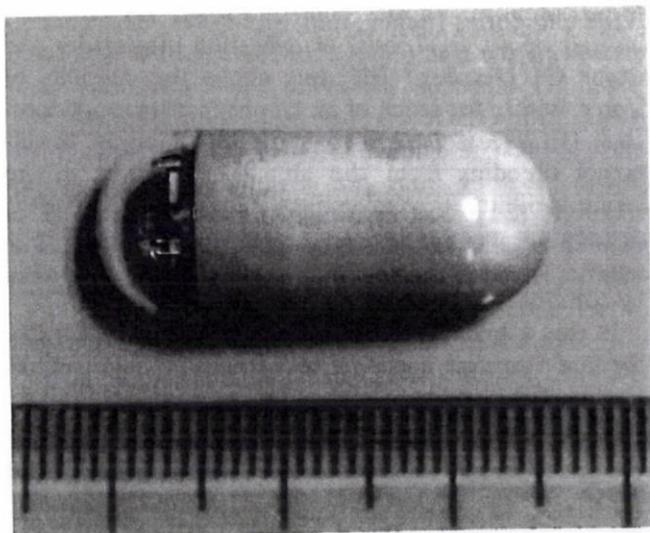


Fig. 1. PillCam SB (11 mm × 26 mm): a first-line tool for the detection of abnormalities of the small bowel

### PillCam SB system

The PillCam SB system has three components: a capsule endoscope body, an external receiving antenna (consisting of eight sensor arrays) with attached portable hard disc drive (data recorder), and a customized PC workstation (RAPID: reading and processing images and data) with dedicated software for review and interpretation of images.<sup>14</sup> The PillCam SB capsule (11 mm × 26 mm, 3.64 g) consists of a metal oxide silicon (CMOS) chip imager, a short focal lens, six white light-emitting diode illumination sources, two watch batteries, and a UHF band radio telemetry transmitter. Image features include a 140° field of view, 1:8 magnification, 1- to 30-mm depth of view, and a minimum size of detection of about 0.1 mm.

The activated PillCam SB capsule provides images at a frequency of 2 frames per second until the battery expires, after about 8 h, which enables the device to take up to 55 000 still images (JPEG format).<sup>14,15</sup>

### Indication (obscure GI bleeding)

In Japan, the only indication for PillCam SB is GI bleeding of unknown origin after negative upper and lower GI examination (including endoscopy). This is almost the same as "obscure GI bleeding," previously mentioned. Indeed, obscure GI bleeding is the main clinical indication for PillCam SB use: about 70%–80% of patients undergoing CE suffer from obscure GI bleeding.<sup>16,17</sup> The American Society for Gastrointestinal Endoscopy (ASGE) Technology Assessment Commit-



Fig. 2. PillCam ESO (11 mm × 26 mm): capsule endoscope for investigating esophageal diseases

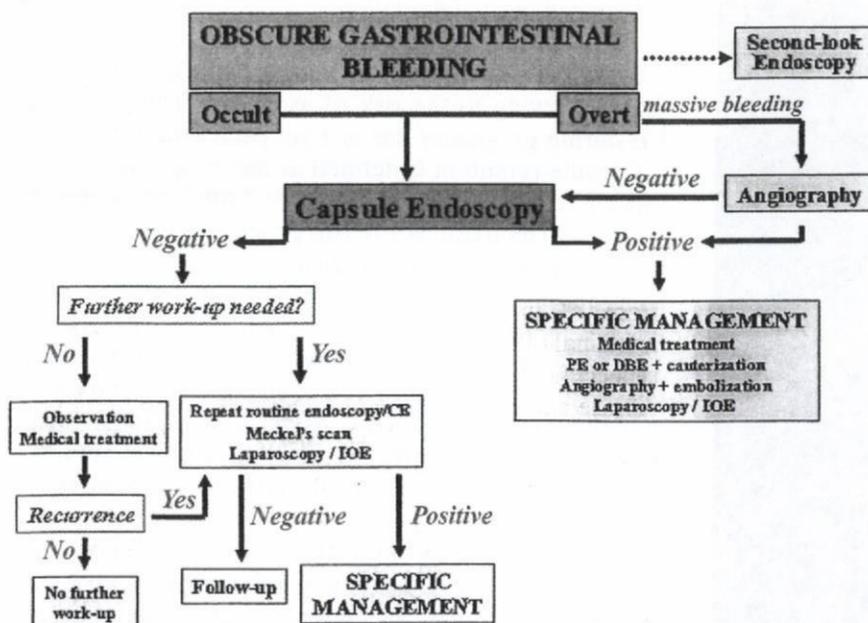


Fig. 3. Algorithm for capsule endoscopy in cases of obscure gastrointestinal bleeding. PE, push enteroscopy; DBE, double-balloon endoscopy; CE, capsule endoscopy; IOE, intraoperative endoscopy. Second-look endoscopy: upper and lower gastrointestinal endoscopy should be repeated before investigation of the small bowel and will frequently identify lesions overlooked at the initial endoscopy. Massive bleeding: patients with significant active bleeding are unsuitable candidates for endoscopy

tee concluded that PillCam SB shows superior yield compared with both radiographic contrast studies and push enteroscopy.<sup>18</sup> Two published meta-analyses support the utility of PillCam SB in obscure GI bleeding.<sup>19,20</sup> The ASGE Technology Assessment Committee also concluded that PillCam SB is indicated not only for evaluating obscure GI bleeding but also for unexplained iron deficiency anemia.<sup>18</sup>

DBE has also been used to evaluate patients with obscure GI bleeding.<sup>5</sup> The comparative diagnostic value of DBE and PillCam SB has been shown to be similar by a recent meta-analysis.<sup>21</sup>

Two meta-analyses<sup>19,20</sup> and the ASGE status report<sup>17</sup> suggest that CE for small bowel should be performed third (after upper and lower GI endoscopy). The proposed algorithm for CE in cases of obscure GI bleeding is shown in Fig. 3.<sup>22</sup>

A case of angiectasia and one of carcinoid,<sup>23</sup> both detected by PillCam SB, are shown in Figs. 4 and 5, respectively.

#### Other indications

Crohn's disease has been discovered in patients with obscure GI bleeding undergoing PillCam SB.<sup>24</sup> Therefore, PillCam SB has also been proposed in Western countries for evaluation of the small-bowel mucosa of patients with Crohn's disease. In patients undergoing PillCam SB for suspected Crohn's disease, the frequency of capsule retention is low (approximately 1.5%).<sup>16</sup> On the other hand, capsule retention occurs in 5%–13% of patients with diagnosed Crohn's disease.<sup>16,25</sup> Therefore, diagnosed Crohn's disease is a contraindication



Fig. 4. Angiectasia of the proximal jejunum in a patient undergoing capsule endoscopy for obscure gastrointestinal bleeding

for PillCam SB use in Japan because of the possible presence of asymptomatic stenosis, which causes retention.

Small-bowel tumors such as gastrointestinal stromal tumors, carcinoid, lymphoma, and cancer have been discovered by PillCam SB, mostly as polyps, masses, or stenosis. The presence of tumors leads to capsule retention in about 10%–25% of cases.<sup>26,27</sup> The most frequent



**Fig. 5.** Submucosal tumor (carcinoid) of the proximal ileum in a patient undergoing capsule endoscopy for obscure gastrointestinal bleeding

treatment in patients with small-bowel tumors is surgical intervention, which allows the retrieval of the retained capsule at the same time. Therefore, capsule retention in patients with small-bowel tumors is now considered a minor complication, except in Japan.<sup>28</sup>

Celiac disease is rare in Japan but an important problem in Western countries. At the present time, traditional gastroscopy with duodenal biopsies remains the method of choice to assess mucosal atrophy in patients with suspected celiac disease. However, PillCam SB may be a suitable tool in patients in whom celiac disease is highly suspected clinically and who are unable or unwilling to undergo traditional endoscopy.<sup>29,30</sup>

PillCam SB has also been used in other clinical conditions as follows.

1. Nonsteroidal anti-inflammatory drug (NSAID)-induced mucosal damage.<sup>31,32</sup>
2. Diagnosis and surveillance of patients with hereditary polyposis syndrome.<sup>33-35</sup>
3. Indeterminate colitis.<sup>36</sup>
4. Irritable bowel syndrome with clinically suspected celiac disease.<sup>37</sup>
5. Protein-losing enteropathy.<sup>38</sup>
6. Whipple disease.<sup>39</sup>
7. Small-bowel transplantation.<sup>40</sup>
8. Graft-versus-host disease.<sup>41,42</sup>
9. Primitive lymphangiectasia (mostly in pediatric patients).<sup>43</sup>

### Complications and limitations

CE should not be used in patients with a swallowing disorder owing to the risk of aspiration. The safety of CE during pregnancy has not yet been established.

Capsule retention is defined as having an endoscopy capsule remain in the digestive tract for a minimum of 2 weeks.<sup>44</sup> The frequency of this problem varies, depending mostly on the clinical indication for CE, and ranges from 0% in healthy subjects to 21% in patients with intestinal obstruction.<sup>16</sup> This problem has been reported especially among patients with diagnosed Crohn's disease and among those at a high risk for stricture formation, such as NSAID users and patients with ischemic colitis (associated with small-bowel tumors, radiation enteritis, and surgical anastomotic strictures).<sup>45</sup> Capsule retention may occur with any type of capsule endoscope, not only with the PillCam SB. For this reason, if CE is indicated, careful consideration is necessary in the case of high-risk patients before performing CE. CE should be preceded by imaging tests to exclude stenosis in patients with suspected Crohn's disease. Patients with a history of abdominal obstruction, abdominal surgery, or abdominal or pelvic area radiation exposure should be excluded.<sup>45</sup> Capsule retention must be considered a serious and major complication in patients in whom surgical intervention must be avoided as long as possible.<sup>28</sup> On the other hand, a retained capsule can be retrieved by DBE.<sup>46,47</sup>

Electromagnetic interference with thoracic pacemakers or implanted defibrillators can occur; however, several recent studies have reported CE to be safe in patients with such implanted devices.<sup>48-50</sup>

The possibility of a false-negative CE result is a clinical limitation of PillCam SB. The global miss rate of PillCam SB is about 11%, ranging from 0.5% for ulcerative disease to 18.9% for neoplastic disease, according to a master database provided by Given Imaging.<sup>51</sup> At present, there are no conclusive explanations for false-negative CE results.

Small-bowel cleanness is thought to be key to ensuring a complete and accurate CE examination. Several studies about small-bowel cleaning with laxatives, prokinetic drugs, and so on have been published; however, no recommendations have been made.<sup>28</sup>

CE has some technical limitations; it cannot be used to obtain biopsy specimens or for endoscopic treatment, and it cannot be controlled remotely. On the other hand, DBE can be used for biopsies and endoscopic treatments.<sup>5</sup> Therefore, at the present time, the combination of PillCam SB and DBE seems to be the best strategy for the management of obscure GI bleeding.

## Other types of capsule endoscope and the future of capsule endoscopy

### *EndoCapsule EC type 1*

EndoCapsule EC type 1 is another type of small-bowel capsule endoscope, developed by Olympus. There are two differences between the Olympus CE and PillCam SB systems. The Olympus capsule has a high-resolution CCD and an external real-time image viewer (External Viewer) monitor.<sup>13</sup> However, a recent randomized study comparing these two types of capsule endoscope reported a statistically nonsignificant trend for the EndoCapsule to detect more bleeding sources in patients with suspected small-bowel bleeding than the PillCam SB.<sup>52</sup>

### *PillCam ESO*

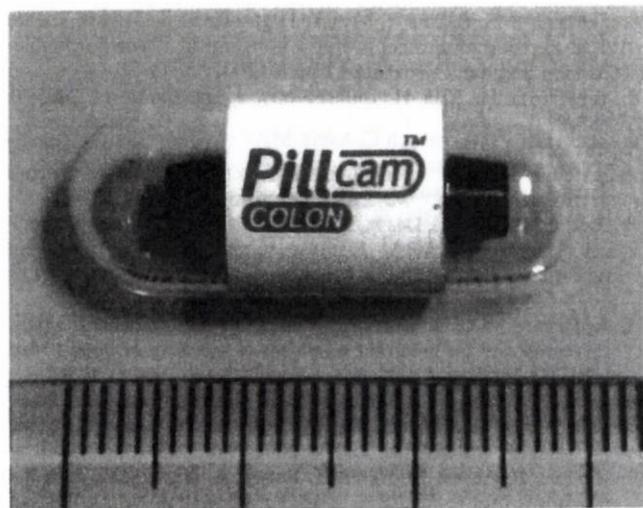
PillCam ESO (Fig. 2), the same size and shape as PillCam SB (Fig. 1), was specifically designed by Given Imaging to investigate esophageal diseases.<sup>10</sup> The main potential indication for PillCam ESO is in patients with gastroesophageal reflux disease or Barrett's esophagus. It was approved by the FDA following a study by Eliakim et al.,<sup>53</sup> which has been published in abstract form. PillCam ESO may be an accurate noninvasive alternative to EGD for the detection of esophageal varices and portal hypertensive gastropathy.<sup>54</sup> On the other hand, a recent multicenter study reported that PillCam ESO in its present form is not suitable as a primary screening tool for Barrett's esophagus, although it may be useful in patients unwilling to undergo EGD.<sup>55</sup>

### *PillCam COLON*

PillCam COLON (Fig. 6, 11 mm × 31 mm) was recently developed by Given Imaging to detect colonic neoplasia. Two pilot trials with PillCam COLON have been conducted,<sup>56,57</sup> and a large prospective multicenter trial is now underway.<sup>58</sup> Interestingly, some polyps can be detected by PillCam COLON that are missed by a traditional colonoscopy, according to this interim analysis.<sup>58</sup>

### *Patency capsule*

A patency capsule, which similar in size to PillCam ESO and PillCam SB and dissolves spontaneously because it is composed of lactose, has been developed by Given Imaging to assess bowel patency and degree of stenosis. If passage of the patency capsule is blocked, the capsule dissolves in 40–100 h. The safety and efficacy of the initial model has been questioned.<sup>59</sup> Recently, a new



**Fig. 6.** PillCam COLON (11 mm × 31 mm): capsule endoscope for detecting colonic neoplasias

patency capsule model with a biodegradable body has been developed. The new patency capsule is a reliable indicator of functional patency in suspected or even known cases of intestinal stricture, and it can be used prior to conventional CE to predict and minimize the risk of retention and impaction.<sup>60</sup>

### *The future of capsule endoscopy*

Therapeutic interventions using a capsule endoscope, such as delivery of medication to specific disease sites and the possibility of using lasers, are also being discussed, according to updated CE guidelines of the European Society of Gastrointestinal Endoscopy.<sup>45</sup>

## Conclusion

CE is an important new diagnostic modality for the GI tract. It is a safe, noninvasive, epoch-making method of endoscopy. In the near future, CE will certainly have an impact on many aspects of GI disease evaluation and management.

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# SAFETY GUIDELINES FOR PERFORMING PHOTODYNAMIC THERAPY (PDT) ON DIGESTIVE TRACT

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## 1. Purpose

The purpose of these Guidelines is to ensure and secure the safety of all those concerned (the patient, medical and paramedical personnel) in PDT procedures PDT for digestive tract lesions (superficial esophageal cancers, early stage superficial gastric cancers, and so on) by listing rules and stipulations that need to be observed.

As of July, 2005 the only PDT for digestive tract insured by the Japanese health system is PDT with Photofrin injection and irradiation with the excimer laser or the YAG-OPO laser. The procedure is restricted to superficial esophageal cancers and early stage superficial gastric cancers. PDT for any other digestive tract lesion is still in its investigative stage and will be noted at the of these Guidelines for reference purposes.

## 2. Qualification and requirements of the doctor performing PDT, and the facility where PDT is to be performed

### 1) Qualifications and requirements of the facility

The facility must have a complete set of all hardware including endoscopes and other laser light managing devices and employ personnel with ample knowledge on handling of the devices along with the knowledge of PDT and appropriate photosensitizers. The facility is required to have qualified medical doctors fulfilling the qualifications and requirements for medical doctors, listed below.

It is better that the facility has a CT scanning device and ultrasonographic devices for assisting diagnosis.

Facilities maintaining the status of Board Certified Facility or Board Certified Instructional Facility from the Japan Society of Laser Surgery<sup>(1)</sup> and Medicine or the status of Board Certified Facility from the Japan Gastroenterological Endoscopy Society<sup>(2)</sup> are adequate.

### 2) Qualifications and requirements of the medical doctor

It is better that the attending surgeon performing the PDT procedure be a member of the Japan

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