tizer in 1994. However, its indication for GI cancers was limited to superficial esophageal and early gastric cancer which was not indicated for surgical operation.

In almost the same period, endoscopic mucosal resection (EMR) has developed for curative treatment of intra-mucosal GI cancers (esophageal, gastric and colon)[4], and it is considered the first choice of treatment in Japan. Thus PDT has been considered as one of the alternative treatments for GI cancers not indicated EMR including recurrent cancer; however, its efficacy was relatively limited. Therefore, we have designed a new therapy called "Modified PDT" to treat GI cancers not indicated for EMR or surgery.

Procedures and Principles of PDT using Photofrin® in Japan

Photofrin® (2mg per kg) is injected intravenously to the patient suffering from superficial esophageal and/or early gastric cancer. After injection of Photofrin®, it is cleared from most tissues in 40 to 72 hours but retained for longer periods in cancer cells, skin, and the reticuloendothelial system. Hence light application is usually scheduled at 40 to 50 hours after injection[5]. At that time, low level laser light of EDL (630nm, 4mj output, 40Hz) is irradiated to the target lesion including cancer through bare quartz fibers endoscopically. Total light doses of 60 to 100 J per target lesion (cm^2) are used for superficial esophageal cancer and early gastric cancer. Upon light exposure, the production of singlet oxygen and other reactive chemical radicals cause local non-thermal cellular damage, vascular thrombosis, and necrosis, which evolve over hours to several days[6]. Even if there is damage to healthy tissues, that is healed by regeneration. Therefore, the cancer and its surrounding healthy tissue can be treated without surgery. And treated areas are safely healed without risk of perforation and intense bleeding. On the other hand, cutaneous photosensitivity occurs in the patient because Photofrin® is retained for longer periods in skin. Thus avoidance of exposure to bright light or direct sunlight is needed for the patient for at least 30 days and often up to 90 days[5].

Materials and Methods

Patients

Between November 2002 and September 2005, Modified PDT was carried out on 20 patients (mean age 73 years, range 55 to 87) suffering from GI cancers (6 superficial esophageal, 10 early gastric, 3 advanced gastric and 1 rectal) who were not indicated for surgical operation or EMR. Written informed consent was obtained from all patients.

Methods of Modified PDT

The major points of Modified PDT are as follows.

1. Irradiation of EDL (630nm, 4mj output, 60-80Hz) is applied to the cancerous lesion and its surrounding mucosa not only 48 (Day 1) but also 72 hours (Day 2) after Photofrin® (2mg per kg) injection. Target light dose is 60-100 J/cm^2.
2. When the cancer is polypoid type, partial resection of the cancer is performed before irradiation.
3. Before the second irradiation on Day 2, necrotic tissue covering the surface of the cancerous lesion is removed by biopsy forceps. Target light dose of the second irradiation is less than 60 J/cm^2.

According to the shape and/or location of the cancerous lesion, cylindrical type of quartz fiber was applied for contact laser irradiation. For the treatment of superficial esophageal cancer, transparent food was used to obtain precise laser irradiation[7].

Admission period of Modified PDT patient was set at 2 weeks and avoidance of exposure to bright light or direct sunlight was demanded for the patient for at least 4 weeks after discharge.

Evaluation of Efficacy

Follow-up endoscopic examinations were carried out at 1 week, 3 months (M) and 6M after irradiations of EDL. Evaluation of the efficacy of Modified PDT was performed at the 3M follow-up period. Complete response (CR) was defined as: there was no evidence of residual and/or recurrent cancer cells by endoscopic observation and biopsy. Partial response (PR) was defined as: there was some evidence of residual and/or recurrent cancer. No change (NC) was defined as: there was no response for cancers by Modified PDT or rapid growth of recurrent cancer the same as the cancerous lesion before treatment.

Results

The efficacy results of Modified PDT for GI cancers are shown in **Table 1**.

In 6 esophageal cancer patients, 5 of them were squamous cell carcinoma histologically including two recurrent patients after chemoradiotherapy. There were 7 squamous cell carcinoma lesions and 6 of them (85.7%) disappeared completely by single course of Modified PDT. The other esophageal cancer patient

Table. 1: Efficacy results of Modified PDT for GI cacers

Tumor type	n	CR (%)	PR (%)
Esophageal	6	4 (66.7)	2 (33.3)
Gastric cancer	10	9 (90.0)	1 (10.0)
Gastric cancer (advanced)	3	1 (33.3)	2 (66.7)
Rectal cancer*	1	1 (100)	–

* Not indicated for surgical operation or EMR.
(Follow-up period: 10 to 44 months.)

had 3 adenocarcinomas arising from Barrett's esophagus including 2 polypoid lesions. One flat lesion disappeared completely and 2 polypoid lesions decreased by single course of Modified PDT. Finally, 4 of 6 patients (66.7%) with superficial esophageal cancers were considered CR.

In 10 early gastric cancer patients, 3 were recurrent after EMR. There were 13 adenocarcinoma lesions including 4 poorly differentiated type and 11 of them (84.6%) disappeared completely by single course of Modified PDT. Repeated Modified PDT was carried out for 2 remnant cancerous lesions; one of them disappeared completely but the other lesion remained in the patient who had 3 poorly differentiated adenocarcinoma lesions. Finally 9 of 10 patients (90%) with early gastric cancers were considered CR.

In 3 advanced gastric cancer patients, 2 of them had single lesion (T2 (tumor invades muscularis propria), N0 (no metastasis)) and the other patient had 3 lesions including 2 early gastric cancers. By single course of Modified PDT, 2 early gastric cancer lesions and one advanced gastric cancer lesion in another patient disappeared completely; however, 2 advanced gastric cancer lesions remained histologically. Finally, one of 3 patients (33.3%) with advanced gastric cancers (T2 (tumor invades muscularis propria) , N0 (no metastasis)) were considered CR.

Concerning rectal cancer patient, there was a polypoid lesion recurrent after EMR in the lower portion of rectum. Several times of piecemeal polypectomy were performed before Modified PDT, and the cancerous lesion disappeared completely after 30 M follow-up period. This patient was considered CR.

No patient died of recurrent GI cancers during 10 to 44M follow-up period. Slight sunburn in the face and/or the limbs occurred in 4 patients (20%) but they recovered. No serious side effect occurred.

Case 1, 62 year-old man, recurrent esophageal squamous cell cancer after chemoradiotherapy

In August, 1999, endoscopic examination revealed squamous cell carcinoma in the middle portion of the esophagus **(Fig. 1)**. Chemoradiotherapy was carried out because he was not indicated for surgery by liver cirrhosis. Squamous cell carcinoma recurred in the same portion of esophagus 3 years after chemoradiotherapy **(Fig. 2)**. EMR was not indicated for the recurrent cancer because endoscopic ultrasonography estimated it submucosal invasion. Thus Modified PDT was performed in May, 2003. Forty-eight hours after injection of Photofrin® (2mg per kg), EDL was irradiated at a dose of 100 J/cm^2 via endoscopy attached transparent food on its tip. Seventy-two hours after Photofrin injection, irradiation of EDL at a dose of 60 J/cm^2 was added. One week after Modified PDT, endoscopy

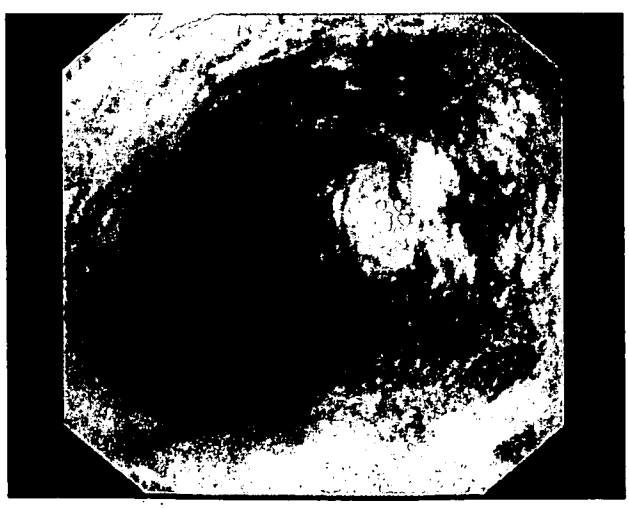

Fig. 1: Endoscopic image using iodine dye stain before chemoradiation in August, 1999
Polypoid and surrounding flat cancerous lesion not stained by iodine was located in the middle portion of esophagus.

Fig. 2: Endoscopic image using iodine dye stain before Modified PDT in February, 2003.
Flat extended cancerous lesion not stained by iodine was located in the same portion of esophagus as Fig. 1.

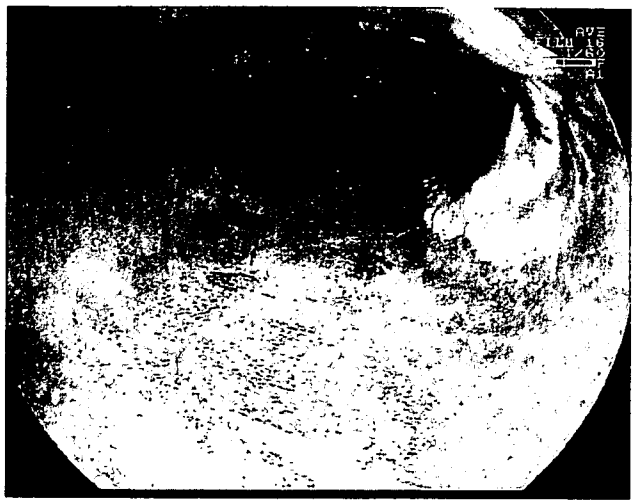

Fig. 3: Endoscopic image at 1 week after Modified PDT
A large laser ulcer coated with whitish necrotic tissue was seen but no cancerous lesion remained.

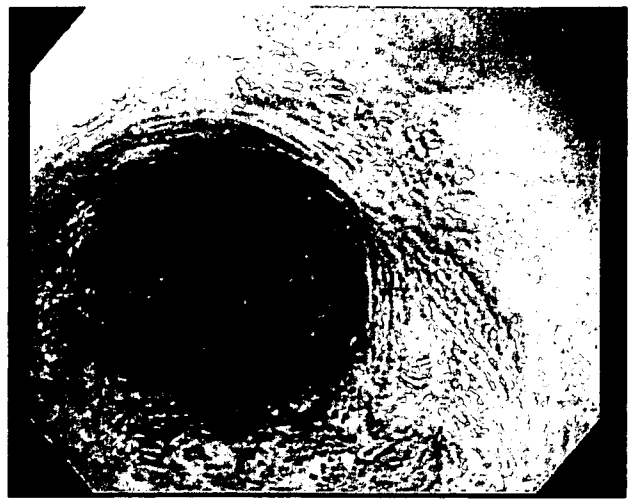

Fig. 4: Endoscopic image using iodine dye stain at 3 M after Modified PDT
Laser ulcer had healed completely and no cancerous lesion remained.

revealed a large laser ulcer coated with whitish necrotic tissue but no cancerous lesion remained by biopsy **(Fig. 3)**. Three months after Modified PDT, laser ulcer healed completely and no cancerous lesion remained by biopsy **(Fig. 4)**. There was no recurrence or metastasis until his death of cerebral hemorrhage 24 months after Modified PDT.

Case 2, 88 year-old woman, recurrent gastric cancer after EMR

In 2000, EMR was carried out for early gastric cancer; however it resulted in incomplete resection and the cancer recurred. She was followed up by endoscopy because she was not indicated for surgery by cerebral infarction and her advanced age. However, the recurrent cancerous lesion gradually enlarged and her anemia was progressive, therefore Modified PDT was carried out in January, 2003. Endoscopic examination before Modified PDT revealed superficial elevated cancerous lesion located in the anterior side of the middle portion of stomach **(Fig. 5)**. The lesion was estimated submucosal invasion by endoscopic ultrasonography. Forty-eight hours after injection of Photofrin® (2mg per kg), EDL was irradiated at a dose of 80 J/cm^2 via endoscopy using cylindrical type of quartz fiber for contact laser irradiation. Seventy-two hours after Photofrin injection, irradiation of EDL at a dose of 80 J/cm^2 was added after removal of necrotic tissue **(Fig.**

Fig. 5: Endoscopic image before Modified PDT in November, 2002
Superficial elevated cancerous lesion was located in the anterior side of the middle portion of stomach.

Fig. 6: Endoscopic image during irradiation of EDL on Day 2.

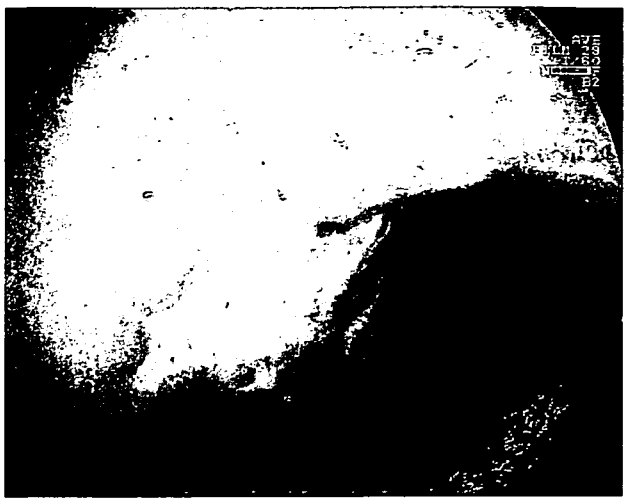

Fig. 7: Endoscopic image at 1 week after Modified PDT
A large laser ulcer coated with whitish necrotic tissue was seen but no cancerous lesion remained.

Fig. 8: Endoscopic image at 3M after Modified PDT
Laser ulcer had healed completely and no cancerous l esion remained.

6). One week after Modified PDT, endoscopy revealed a large laser ulcer coated with whitish necrotic tissue but no cancerous lesion remained by biopsy **(Fig. 7)**. Three months after Modified PDT, laser ulcer healed completely and no cancerous lesion remained by biopsy **(Fig. 8)**. There was no recurrence or metastasis 36 months after Modified PDT.

Discussion

PDT, a treatment now being used in patients with various types of cancers including GI tract, uses a combination of photosensitizer (a drug that is activated by light) and non-thermal low power laser light. Neither the photosensitizer nor the laser light alone can destroy the cancer cells; they must be used in combination.

The first endoscopic application of PDT for upper GI cancers was started in Japan[2]. At that time, HpD as a photosensitizer and an argon-dye laser were used for patients with superficial and non-superficial esophageal cancer and with early gastric cancer. Hayata et. al concluded that PDT using HpD should be employed primarily in inoperable early-stage cancer, to reduce the extent of resection, or to make previously inoperable cases to operable because of the difficulty in early stage diagnosis and in determining all cases of lymph node involvement[2].

According to the recent remarkable development of endoscopic and other imaging technologies, gastroenterologists have regarded that superficial esophageal and early gastric cancers were not rare cases especially in Japan. The majority of esophageal cancer is squamous cell carcinoma and gastric cancer is very common in Japanese people. On the other hand, more than half of esophageal cancer is adenocarcinoma arising from Barrett's esophagus and gastric cancer is extremely rare in Western white people. Under these circumstances, development of endoscopic PDT for GI cancers has been quite different in Japan and Western countries.

In 1995, Food and Drug Administration (FDA) of USA approved PDT using Photofrin® with diode laser (Diomed PDT laser system) for palliation of patients with completely or partially obstructing esophageal cancer (not only squamous cell carcinoma but aso adenocarcinoma) after multicenter randomized trial[8]. In 2003, FDA approved PDT using Photofrin® for the ablation of high-grade dysplasia associated with Barrett's esophagus in patients who do not undergo esophagostomy, Canada and Europe also approved it in 2004. The other indication of PDT using Photofrin® approved by FDA is reduction of endo-bronchial obstruction in patients with nonsmall cell lung cancer who are not candidates for surgery or radiotherapy[5].

In Japan, Ministy of Health and Welfare approved PDT using Photofrin® for the patients with early-stage cancers of proximal lung (bronchial), esophageal, gastric, uterine cervix and with dysplasia of uterine cervix who are not indicated for surgery or other curative treatment including EMR. For the purpose of curative treatment for early stage cancers, EDL was developed. EDL enables irradiation of a pulsed laser with extremely high peak power in comparison with argon dye laser. Mimura et al. reported the cooperative clinical trial of PDT using Photofrin® with EDL on 27 patients

with early gastric cancer. Complete responses (CR) were obtained in 88% of 24 assessable patients and the response rate was 100%. CR was observed in all cases of lesions of superficial depressed type without ulceration and/or with tumor diameter less than 2 cm. Regarding complications, mild cutaneous reaction and photosensitivity were seen and lasted several weeks[3]. The efficacy of PDT using Photofrin® with EDL is satisfying; however, superficial depressed type gastric cancers without ulceration and/or with tumor diameter less than 2 cm are considered the indication for EMR. In 2004, PDT using a new photosensitizer named Laserphyrin® (mono-L-aspartyl chlorin e6, Meiji Seika, Tokyo, Japan) with a new designed diode laser (PD laser, Panasonic, Tokyo, Japan)[9] was approved only for early lung cancer.

Under these conditions, we have designed a new therapy called "Modified PDT" to treat GI cancers not indicated for EMR or surgery. In spite of small number of patients, Modified PDT was remarkably effective for early stage of esophageal and gastric cancer in this study. This new method may be considered as curative therapy for early stage of GI cancers when the patients are not candidates for surgery or other curative therapy including EMR. Recently, Modified PDT was evaluated as salvage treatment for local failures after definitive chemoradiotherapy for esophageal cancer[10]. In combination with other treatment modalities, Modified PDT might be more valuable not only for early but also for advanced stages of GI cancers.

Conclusion

Modified PDT is remarkably effective and useful in the treatment of GI cancers which are not indicated for EMR or surgical operation. This technique may be considered an alternative therapy for not only esophageal but also gastric cancer, and even rectal cancer.

Acknowlegement

The authors wish to express their thanks to Dr. Michimaro Ejiri and Dr. Yoji Ishii (Nozatomon Clinic, Himeji, Japan) for their help and advice.

References

1: Dougherty TJ, Kaufman JE, Goldfarb A, Weishaupt KR, Boyle D and Mittleman A. (1978): Photoradiation therapy for the treatment of malignant tumors. *Cancer Research*, 38: 2628-2635.

2: Hayata Y, Kato H, Okitsu H, Kawaguchi M and Konaka C. (1985). Photodynamic therapy with hematoporphyrin derivative in cancer of the upper gastrointestinal tract. *Seminars in surgical oncology*.1: 1-11.

3: Mimura S, Ito Y, Nagayo T, Ichii M, Kato H, Sakai H, Goto K, Noguchi Y, Tanimura H, Nagai Y, Suzuki S, Hiki Y and Hayata Y. (1996): Cooperative clinical trial of photodynamic therapy with photofrin II and excimer dye laser for early gastric cancer. *Lasers in surgery and medicine*. 19: 168-172.

4: Tada M, Murakami A, Karita M, Yanai H, and Okita K. (1993): Endoscopic resection of early gastric cancer. *Endoscopy*. 25: 445-450.

5: Petersen BT, Chuttani R, Croffie J, DiSario J, Liu J, Mishkin D, Shah R, Somogyi L, Tierney W and Wong Kee Song LM. (2006): Photodynamic therapy for gastrointestinal disease. *Gastrointestinal Endoscopy*. 63: 927-932.

6: Bown SG, Lovat LB. (2000): The biology of photodynamic therapy in the gastrointestinal tract. *Gastrointestinal Endoscopy Clinical North America*. 10: 533-550.

7: Nakamura T, Fukui H, Shirakawa K, Fujii Y, Fujimori T and Terano A. (2004): Photodynamic therapy of superficial esophageal cancer with a transparent hood.. *Gastrointestinal Endoscopy*. 60: 120-124.

8: Lightdale CJ, Heier SK, Marcon NE, McCaughan JS Jr, Gerdes H, Overholt BF, Sivak MV Jr, Stiegmann GV and Nava HR. (1995): Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointestinal Endoscopy*. 42: 507-512.

9: Kato H, Furukawa K, Sato M, Okunaka T, Kusunoki Y, Kawahara M, Fukuoka M, Miyazawa T, Yana T, Matsui K, Shiraishi T and Horinouchi H. (2003): Phase II clinical study of photodynamic therapy using mono-L-aspartyl chlorin e6 and diode laser for early superficial squamous cell carcinoma of the lung. *Lung Cancer*. 42: 103-111.

10: Yano T, Muto M, Minashi K, Ohtsu A and Yoshida S. (2005): Photodynamic therapy as salvage treatment for local failures after definitive chemoradiotherapy for esophageal cancer. *Gastrointestinal Endoscopy*. 62: 31-36.

S1455

Gastric Lymphoma: Endoscopy Role and Epidemiologic Analysis in 73 Cases

Spencer Vaiciunas, Leomar C. Machado, Jose C. Ardengh, José Luis P. Módena

Background: Primary gastric lymphoma is still relatively uncommon, accounting for less than 15% of gastric malignancies, however is the most common extra nodal site of lymphomas, representing about 4-20% of these lymphomas. The incidence of this malignant illness is gradually increasing. Most of the lymphomas usually arise from submucosal and mucosa (mucosa-associated lymphoid tissue -MALT). Aim: To evaluate the epidemiology and the endoscopy role in gastric lymphoma. Patients and Methods: Retrospective analysis of patient's recorders performed at the Clinics Hospital of the Medical School of the University of São Paulo that had the diagnosis of gastric lymphoma. Results: In this study, 73 patients were evaluated, 47 (64.4%) males and 26 (35.6%) females with a mean age of 52.7 years. Abdominal pain in "burn type" occurred in 25 (34.2%) patients. Only 30% presented digestive hemorrhage, and hematemis was the main manifestation. Ulcerated lesions were found during upper gastrointestinal endoscopy in a half of the cases. The site of gastric lymphoma in stomach was in the region of (body + antrum) in 22 (30%) patients. The biopsy specimens obtained during endoscopy was positive in 17 cases of lymphoma. The rapid urease test for Helicobacter pylori infection was positive in 30 (41%) and negative in 29 (40%) cases. The surgical treatment was necessary in only 12 (17%) patients and the subtotal gastrectomy, Billroth II, was the most used. Lymph nodes infiltration by tumor cells occurred in 8 (20%) patients. In the clinical treatment, 74% were treated with chemotherapy and 4% with chemotherapy and radiation therapy. The follow-up was in 3% of the cases for a period up to 29 years and the average was 7 years. Currently, there are 24 (39%) patients alive and in follow-up. Conclusions: Endoscopy plays an important role in the diagnosis of gastric lymphoma. In addition to providing the specific area of location and extent of the tumor, it may provide a visual diagnosis in the majority of the patients, as well as in assessing associated lesions, such as H. pylori-related gastritis. Lymphomas are more common in men. Many patients are now being treated with chemotherapy alone or plus radiation therapy.

S1456

Rebleeding Predictive Factors in OGIB After Capsule Endoscopy. Impact of Double-Baloon Enteroscopy

Begoña Gonzalez, Sara Galter, Candid Villanueva, Jordi Ortiz, David Monfort, Ingrid Ordas, Adolfo Gallego, Meritxell Casas, Joaquin Balanzo

Introduction: Obscure Gastrointestinal Bleeding (OGIB) is a pathology difficult to diagnose that implies several diagnostic procedures with a high cost and morbi-mortality. Aims: 1. To evaluate the rebleeding rate in the patients who underwent a capsule endoscopy (CE) and look for possible predictive factors of the rebleeding. 2. To analize the impact of the double-balloon enteroscopy (DBE) in the follow-up of these patients. Patients and methods: Since 5/2001 until 9/2006 we have performed 292 capsules in 279 patients (130 men, 149 women, mean age 61.7± 17.7 years) with the following indications: OGIB (n = 231, 122 with occult OGIB, 109 visible OGIB), inflammatory bowel disease (n = 32), abdominal pain (n = 11) and other indications in 18 patients. Firstly, we evaluate the rebleeding rate in the patients with OGIB (n = 231) and secondly we analize a subgroup of patients (n = 57 patients) with OGIB with a follow-up of 24 months. We divided these patients in 2 groups, depending on they have underwent a DBE (group I, n = 25) or a mesenteric arteriography (group II, n = 32). Results: 1. The rebleeding rate in patients with OGIB was 20.7% (48/231), being angiodisplasias the most frequent lesions detected (43%), followed by active bleeding (18%) and intestinal ulcers (14.5%). After a multivariate analysis we observed that anticoagulant or NSAID treatment were predictive factors of rebleeding ($p < 0.05$). 2. The rebleeding rate in group I was 28% and 34.4% in group II (pNS). In this case, the predictive factors were the anticoagulant treatment and the transfusion requirement ($p < 0.04$). Conclusions: 1. Patients with OGIB have a rebleeding rate of 20%. 2. Patients with anticoagulant treatment or with a higher transfusion requirement after a bleeding episode have a superior risk of rebleeding.

S1457

Comparison of Capsule Endoscopy and Combination of Capsule and Double Balloon Endoscopy in Obscure Gastrointestinal Bleeding

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Background and Aim: Capsule endoscopy (CE) and double balloon endoscopy (DBE) are new diagnostic tools especially for obscure gastrointestinal bleeding (OGIB). CE is noninvasive and physiological endoscopy; however, it lacks interventional capability. On the other hand, DBE is relatively technical and invasive endoscopy; however, it enables scrutiny and endoscopic treatment. To obtain good outcomes of OGIB, adequate combination of CE and DBE is needed. We evaluated the outcomes (final diagnosis or treatment) of OGIB by CE compared with combination of CE and DBE. Methods: A retrospective analysis of outcomes was carried out for 80 patients suffering from OGIB who underwent CE (PillCam SB, Given Imaging, Yoqneam, Israel) between July 2003 and October 2006. Patients were divided into two groups as follows. CE group: 42 patients (20 males, 22 females, 53.6 years in average) who underwent CE only or with other method except DBE. Combination group: 38 patients (21 males, 17 females, 58.0 years in average) who underwent not only CE but also DBE. Informed consent was obtained from every patient. Results: Among CE group, the outcomes were obtained in 28 of 42 patients (66.7%). The outcomes included 9 lesions not in the small bowel (gastric bleeding etc.), 7 ulcers and erosions (including 3 iatrogenic injuries), 7 portal hypertensive enteropathy, 2 small bowel adhesions (post traumatic and operative), lipoma, Behcet disease and ulcerative colitis. Among combination group, the outcomes were obtained in 34 of 38 patients (89.5%). The outcomes included 10 tumors (4 gastrointestinal stromal tumors, 2 capillary hemanigioma, cavernous hemanigioma, carcinoid, hamartoma, polyposis), 8 angiodysplasias, 6 lesions not in the small bowel (gastric ulcer etc.), 5 ulcers and erosions (including 2 iatrogenic injuries), 3 no abnormal findings, portal hypertensive enteropathy and eosinophilic enteropathy. Four of 10 tumors and all the angiodysplasia cases were successfully treated by DBE. Compared with CE group and combination group, the rates of outcomes showed statistical difference ($p < 0.05$). Conclusions: CE and DBE seem to be complementary methods to obtain good outcomes of OGIB. Especially in small bowel tumor and angiodysplasia cases, interventional capability of DBE is apparently effective.

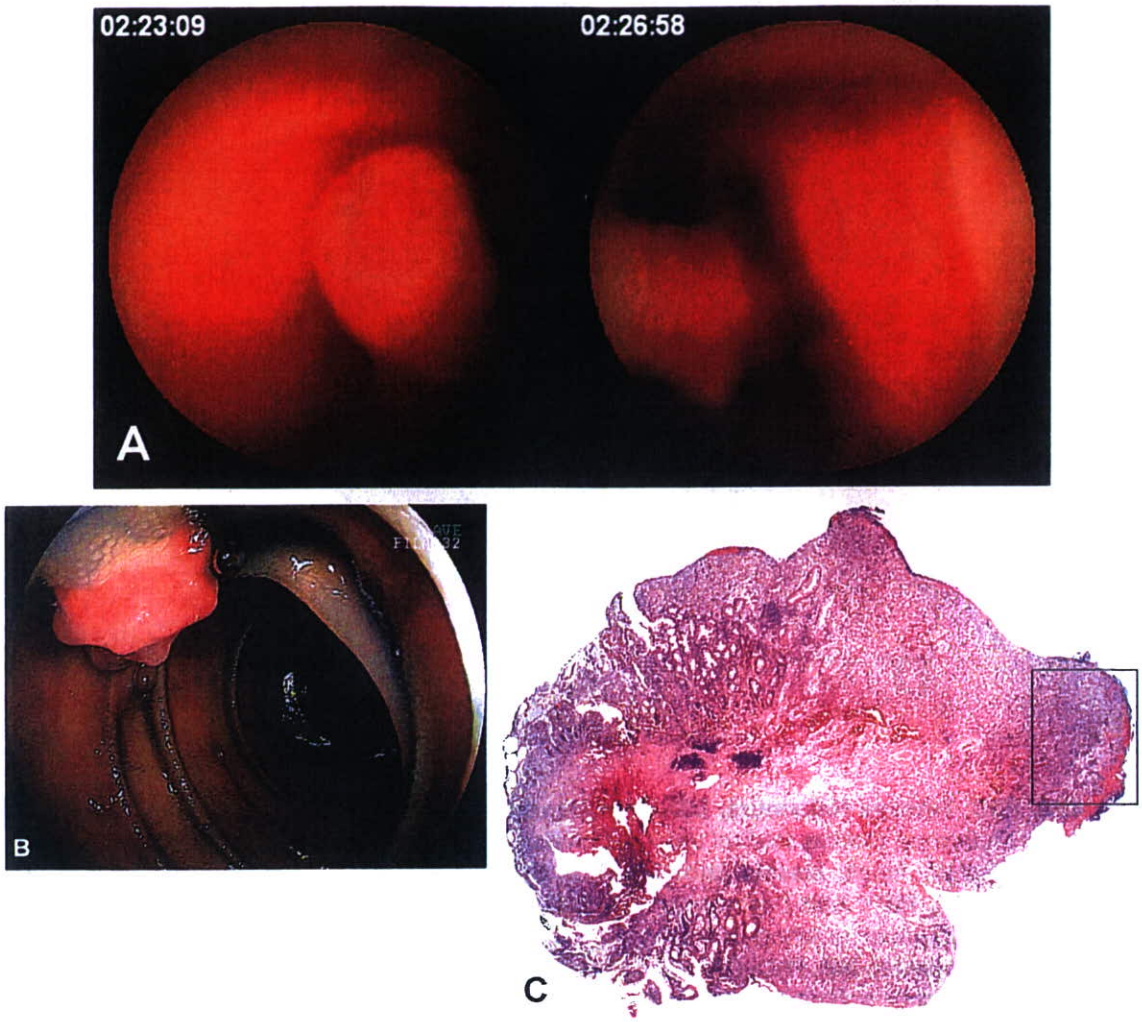
S1458

Effects of Alendronate Chronic Consume on Intestinal Mucosa Assessed By Capsule Endoscopy: A Prospective Controlled Trial (Preliminary Data)

Antonio Benitez Roldan, Angel Caunedo-Alvarez, Blas J. Gomez-Rodriguez, Javier Romero Vazquez, Andres Sanchez Yague, Francisco J. Pellicer Bautista, Lucia Orbea, Juan M. Herrerias Gutierrez

Background and Aim: There is increasing use of Bisphosphonates to prevent and to treat osteoporosis. Esophageal, and colonic injury caused by alendronate had been described, but there are no reports of injury to the small bowel. The aim of our study was to compare the presence of intestinal damage, assessed by capsule endoscopy, between patients with chronic consume of alendronate and a control group. Material and Methods: Twenty participants were included and underwent a capsule endoscopy to assess small bowel mucosa. Ten patients (10F/0M; age: 74.1 ± 8.5 yrs) with known osteoporosis and treated with alendronate (10 mg once per day) for 3 months or more were compared with ten healthy volunteers (8F/2M; age: 40.8 ± 10.93 yrs), considered as control group. None of the included patients was taking NSAIDs or other enterolesive drugs. A semi-quantitative scale ranging from 0 to 2 (0 = No lesions, 1-mild = only erytema or <5 erosive lesions; 2-moderate/severe ≧5 erosive lesions and/or bleeding ulcers and or strictures) was used to assess the severity of the findings. The investigator who reviewed the procedure was blind to the subject group. Results: The capsule endoscopy found intestinal injury in 1 out of 10 patients (10%) in the study group. Four erytematous and denudated areas, without erosions (mild damage) were found in this patient. Non-related findings (small angiectasias without bleeding) were reported in 3 patients (30%) in the study group. Small erosions (<5 erosions) in gastric mucosa were also found in two patients (20%) of the study group, none of them with intestinal damage. In the control group, 1 out of 10 subjects (10%) presented four small ileal aphtas (mild damage), and the other 9 individuals had no abnormal findings. Capsule endoscopy presented no complications in none of the patients. Conclusions: These preliminary data do not indicate that the chronic consume of alendronate is associated to an injury of intestinal mucosa.

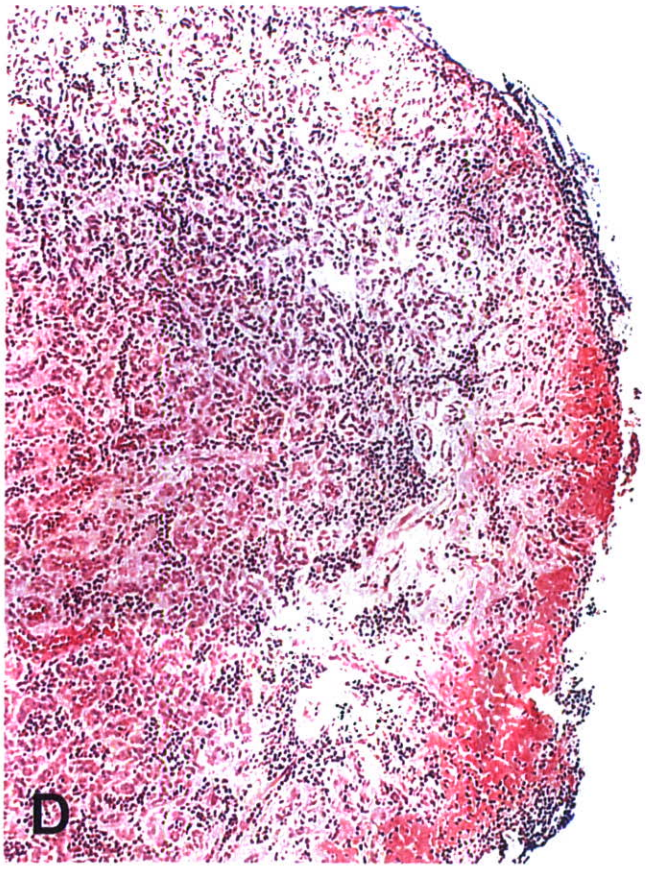
Pyogenic granuloma of the small intestine



A 72-year-old man underwent capsule endoscopy (CE) because of obscure GI bleeding over a 1-year period. CE showed a small polyp in the mid small intestine (**A,** *left*). Bleeding from the lesion was observed after prolonged contact with the capsule (**A,** *right*), thereby suggesting that it was the bleeding point. The patient underwent double balloon endoscopy (DBE), which confirmed an irregularly shaped polyp (**B**) and allowed an endoscopic resection to be performed successfully. Histologic examination revealed proliferation of capillary-sized vessels with a lobular arrangement (**C,** H&E, orig. mag. ×4). The stroma of the lesion was edematous with an acute and chronic inflammatory cell infiltration (**D** [*magnification of box in* **C**], H&E, orig. mag. ×40). These findings were consistent with pyogenic granuloma. There has been no recurrence of GI bleeding 13 months after the polypectomy.

DISCLOSURE

The authors have no disclosures to make.



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Commentary

Shakespeare asked, what's in a name? In the misnomer pyogenic granuloma (PG), the answer is, not much of value, because this lesion is not infectious, it does not form pus, and it is not granulomatous; it is a lobular capillary hemangioma, first described in 1897 by Poncet and Dor. PG usually occurs in the skin of young children or is found as a gingival lesion in 5% of pregnant women. The etiology of cutaneous PG usually is not apparent, although trauma has been implicated and pharmacologic causes include retinoids, the protease inhibitor indinavir, 5-fluorouracil, capecitabine, and some EGF receptor inhibitor therapies. An elderly man with PG is unusual, and GI involvement (esophagus, stomach, small bowel, and colon) is rare. PG is a glistening red nodule that is prone to ulcerate, and in the GI tract it must be distinguished from Kaposi sarcoma. PG is amenable to excision or ablation but can recur, so remember PG on your list of rare lesions that cause recurrent bleeding. Do I hear the hoof beats of zebras?

Lawrence J. Brandt, MD
Associate Editor for Focal Points

WED-E-331 THE NEW APPROACH FOR THE DIFFICULT CASES IN EARLY GASTRIC CANCER TREATMENT – DEVELOPMENT OF DOUBLE SCOPE-ESD METHOD

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INTRODUCTION: Endoscopic submucosal dissection (ESD) has enabled en-bloc resection for early gastric cancer (EGC) regardless of tumor size and ulcer findings. However, in case of quite a large lesion, difficult location such as greater curvature of corpus, and lesions with severe fibrosis, it is difficult to accomplish by conventional ESD methods.
AIMS & METHODS: In order to overcome these difficult cases in ESD, we developed double scope ESD (D-ESD) method, using newly developed flexible double-lumen overtube to prevent scopes from getting twisted each other. This study introduced our preliminary experience and evaluated the feasibility, efficacy and procedure time. 15 consecutive patients with differentiated mucosal EGC judged by biopsy and EUS were enrolled, whose lesions have some difficulties that cannot be conquered with conventional ESD due to the followings reasons: 1. Quite a large lesion (more than 50 mm), 2. Difficult location (more than 30 mm lesion at the greater curvature of corpus), 3. With severe fibrosis (due to ulcer scar). D-ESD was performed by two kinds of endoscope. One is a XP260N (Olympus) with small diameter which works such as a surgeon's left hand to keep a clear view by catching and lifting the targeted lesion. The other is a Q260J (Olympus) having the function of water-jet, which enables easy detection of bleeding point. VIO300D (ERBE) was used for an electrical surgical unit. Mucosal cutting and dissection was performed by IT knife-2 (Olympus) and Flush knife (FTS).
RESULTS: The mean procedure time was 65 min and D-ESD could shorten procedure time about 25% compared with conventional ESD. All the patients achieved complete en-bloc resection without complications such as massive bleeding or perforation. Injuries of the hypopharynx and the esophagus by the overtube were not observed.
CONCLUSION: D-ESD can provide a good feasibility and efficacy even in the difficult cases of EGC, which can expand the indication to lesions that are considered difficult to treat by conventional ESD. *Endoscopy 2007; 39 (Suppl I)* A355

WED-E-332 A PROSPECTIVE RANDOMIZED TRIAL OF EITHER ORAL LANSOPRAZOLE OR INTRAVENOUS OMEPRAZOLE SODIUM FOR THE PREVENTION OF BLEEDING AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION IN PATIENTS WITH GASTRIC CANCERS

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INTRODUCTION: Endoscopic submucosal dissection (ESD) is a new technique, which enables to remove large (over 2 cm) intramucosal gastric lesions in one-piece. Bleeding is major complication of ESD. Routinely, proton pump inhibitor (PPI) was given intravenously during and after ESD. However, it is not clear for the ESD whether intravenous PPI treatment in the perioperative period was essential for preventing the bleeding or not.
AIMS & METHODS: The aim of this study is to prospectively compare the frequency of bleeding following ESD between patients treated with oral lansoprazole and those with intravenous omeprazole sodium. Between July 2006 and May 2007, forty gastric cancers (larger than 20 mm as a resected specimen) were enrolled in this study. To equalize the PH condition in the stomach, all the patients were given 30 mg of lansoprazole orally after dinner on the day before ESD. Patients were randomized into two groups, PO group (30 mg of lansoprazole was given orally once a day) and IV group (10 mg of omeprazole sodium was given intravenously twice a day). ESD was performed by the experienced endoscopists using insulated-tip diathermic knife or hooking knife. On the second day after ESD, follow-up endoscopy was done to check the hemostasis condition. In case of sufficient hemostatic condition, oral-intake was started and IV treatment has changed to PO treatment. In case of insufficient hemostatic condition, additional endoscopic hemostasis was done and fasting was prolonged. In such a case, oral treatment has changed to IV treatment and it has continued till the hemostasis was confirmed endoscopically. Bleeding was defined by the endoscopic findings or laboratory data. Clinical data was collected and examined.
RESULTS: PO group consisted of 15 males and 5 females and IV group 17 males and 3 females. The median age of PO group was 73 (55–85) years old and 75 (47–84) years old in the IV group. No differences was seen in the size of the resected specimen between the two groups (32 (23–84) mm in the PO group and 32 (21–57) mm in the IV group). Frequency of bleeding was 20.0% (4/20) both in the PO and IV group. No differences was seen in the fasting period between the two groups (2 (2–9) days in the PO group and 2 (2–4) days in the IV group). In all eight bleeding cases, the lesions were located on the middle (3 cases) or lower (5 cases) third of the gastric body (anal side from the gastric angle).
CONCLUSION: Oral lansoprazole is as effective as intravenous omeprazole to prevent the bleeding after ESD. When the lesions were located on the anal side from the gastric angle, sufficient prophylactic endoscopic hemostasis was more important than acid-suppressing treatment. Oral drug is easy-to-use and low-cost than injection drug, therefore, oral PPI treatment in the perioperative period may be the standard therapy to prevent the bleeding after ESD. *Endoscopy 2007; 39 (Suppl I)* A355

WED-E-333 CHROMOENDOSCOPY WITH INDIGO CARMINE ON THE DETECTION OF DUODENOGASTRIC REFLUX

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INTRODUCTION: Duodenogastric reflux (DGR) is risk factor for intestinal metaplasia (IM) of the stomach. Repeated contact with duodenal contents may damage the gastric mucosa, resulting in atrophic changes and ultimately in IM. IM is generally considered to be an early stage in the multi-step process leading to the development of gastric cancer or to be associated with an increased risk of gastric cancer. Detection of patients with DGR may be significant for follow up patients, but endoscopist can not always see reflux of bile during examination.
AIMS & METHODS: The aim of this prospective study was determination of the effectiveness of dye spray (indigo carmine) on detection of DGR during routine upper endoscopy.
In one institution, 55 patients (F20, M35; mean age 43) entered into a prospective study. Duodenal stenoses, acute pancreatitis, ileus and gastrointestinal bleeding were excluded. All endoscopic procedures were performed with video endoscopes by a single endoscopist. All stainings were performed during routine upper endoscopy after obtaining permission. We used to spray 10 ml 0.2% solution indigo carmine onto the mucosa in the second part of duodenum. Immediately after that, endoscope was removed from duodenum to stomach. During one minute we determined grade of dye's reflux.
RESULTS: There was not reflux of indigo carmine in 43 patients, reflux until angle of stomach in 4, reflux to gastric body in 8 patients. In all patients, who had reflux until gastric body, there was abundance of bile in stomach. Pearson correlation coefficient between grade of dye's reflux and presence of bile in stomach was 0.94 ($p < 0.001$). There were no complications after chromoendoscopy. Limitations: Small patient number and uni-centric study.
CONCLUSION: Here we present a new method of chromoendoscopy with indigo carmine. This new method is fast, easy and not expensive and can be used for visual detection of DGR. *Endoscopy 2007; 39 (Suppl I)* A355

WED-E-334 NOVEL TECHNIQUE, PERCUTANEOUS TRANS-ESOPHAGEAL GASTROTUBING (PTEG) FOR THE PATIENTS WHO FAILED PERCUTANEOUS ENDOSCOPIC GASTROSTOMY (PEG) INSERTION

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INTRODUCTION: Percutaneous Endoscopic Gastrostomy (PEG) is the established procedure for long-term enteral nutrition and/or decompression. However, PEG has been contraindications in the patient who had gastrectomy, gastric anterior wall malignancies, massive ascites and so forth. Percutaneous Trans-Esophageal Gastrotubing (PTEG) has been developed as an alternative route to access into the gastrointestinal tract.
AIMS & METHODS: The aim of this study is to evaluate the clinical usefulness of PTEG as an alternative entral access to PEG. We performed in total of 62 PTEG (41 males and 21 females; mean age 74.1 y/o) for whom PEG could not be performed. There were 26 peritoneal carcinoma, 24 post gastrectomy, 4 severe gastric herniation into the thoracic cavity, and 2 post ventricle-peritoneal shunt. Concerning about the purpose, 32 patients had PTEG for nutrition and 30 were for decompression. PTEG procedure is as follows; (1) Rupture free balloon (RFB) catheter is inserted from the nose or mouth to lower esophagus. (2) RFB is inflated and pulled towards the proximal side of esophagus. (3) Percutaneous balloon puncture with the exclusive needle is then performed from the left side of patient's neck under ultrasonographic control. (4) Remove the inner cylinder of needle and insert a guide wire into RFB. (5) Deflate and push down RFB towards the distal side of esophagus to release the guide wire from RFB. (6) A dilator with peel-away sheath is inserted into the esophagus over the guide wire. (7) A placement tube is then inserted through the sheath and the sheath is peeled off. As the assistance to confirm the procedure, 30 patients were performed under fluoroscopy and 32 were performed by endoscopic assistance.
RESULTS: Satisfactory results were achieved in all 62 patients with a follow up period of 92.5 days for drainage group and 267.5 days for nutrition group (median). Nine of 30 patients who used fluoroscopy need endoscopic assistance to accomplish the procedure. None of 32 patients who used endoscopy needs fluoroscopy. One patient had right neck puncture due to the left side metastatic lymph nodes swelling. As the complication, there was 1 postoperative bleeding that required blood transfusion in fluoroscopy group, 1 subcutaneous emphysema that was managed conservatively in endoscopy group, 4 self tube removals, 2 fever and 3 skin infection.
CONCLUSION: Our study showed that PTEG is a feasible, safe and useful technique. PTEG could be an optimal procedure for long-term nutrition and/or decompression even for the patients who failed PEG insertion. Endoscopic assistance is safer and better confirmation to accomplish the procedure.
REFERENCE(S): Oishi H. et al. A nonsurgical technique to create an esophagostomy for difficult cases of percutaneous endoscopic gastrostomy. Surg Endosc 2003; 17: 1224–1227 *Endoscopy 2007; 39 (Suppl I)* A355

WED-E-335 MODIFIED PHOTODYNAMIC THERAPY FOR ESOPHAGEAL AND GASTRIC CANCERS NOT INDICATED FOR ENDOSCOPIC MUCOSAL RESECTION

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INTRODUCTION: Photodynamic therapy (PDT) is based on the theoretical principle: the specific low level laser light irradiation activates a photosensitizer which is selectively concentrated in rapidly proliferating tissues including malignant tumor cells, resulting in selective necrosis by the intracellular singlet oxygen from photochemical reaction. PDT using Photofrin?(porfimer sodium) with excimer-dye laser (EDL) was approved in Japan. Its indication for gastrointestinal (GI) cancers was limited to superficial esophageal and early gastric cancer not indicated for other curative treatments. Meanwhile, endoscopic mucosal resection (EMR) is considered the first choice of treatment for intra-mucosal GI cancers. Thus PDT has been considered as one of the alternative treatments for GI cancers including recurrent cancer; however, its efficacy was relatively limited.
AIMS & METHODS: To improve efficacy for esophageal and gastric cancers not indicated for EMR, we have designed a new therapy called "Modified PDT". The major points of Modified PDT are as follows. 1. Irradiation of EDL is applied to the lesion not only 48 but also 72 hours after Photofrin? (2 mg/kg) injection. 2. When the cancer is polypoid type, partial resection of the cancer is performed before irradiation. 3. Before the second irradiation, necrotic tissue covering the surface of the lesion is removed. Between November 2002 and March 2006, Modified PDT was carried out for 30 cancerous lesions of 20 patients (mean age 71.6 years, range 55 to 87) suffering from GI (7 superficial esophageal, 12 early gastric, 3 advanced gastric) cancers who were not indicated for surgical operation or EMR. Written informed consent was obtained from all patients. Complete response (CR) was defined as disappearance of all signs of cancer for 12 months. Partial response (PR) was defined as disappearance of over 50% of cancer for 12 months.
RESULTS: CR was achieved in 6 of 9 (66.7%) lesions' and 5 of 7 (71.4%) patients of superficial esophageal cancers. CR was achieved in 15 of 16 (93.8%) lesions and 10 of 12 (83.3%) patients of early gastric cancers. PR was achieved 3 of 3 (100%) lesions of advanced gastric cancers patients. Temporal fever in 2 patients and slight sunburn in 5 patients was occurred; however, there were no serious complication.
CONCLUSION: Modified PDT is extremely effective for especially early gastric cancers. It may be considered one of curative treatments for early esophageal and gastric cancers not indicated for EMR or surgery.
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Early diagnosis and successful treatment of small-intestinal carcinoid tumor: useful combination of capsule endoscopy and double-balloon endoscopy

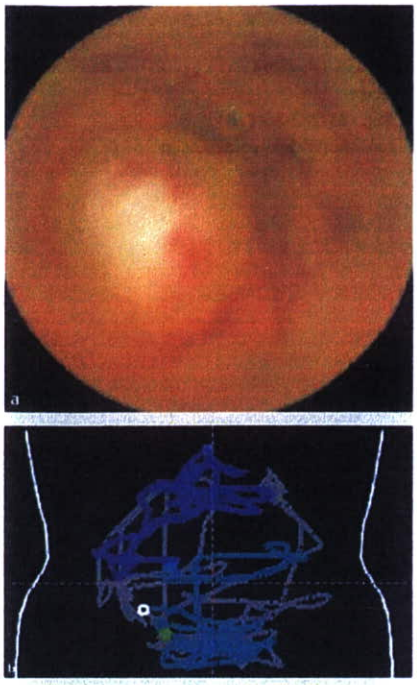

Fig. 1 Capsule endoscopy. **a** A tumor rising gradually from the mucosa was seen in the proximal ileum. **b** RAPID software (Given Imaging Ltd., Yoqneam, Israel) showing capsule endoscopy site (white circle).

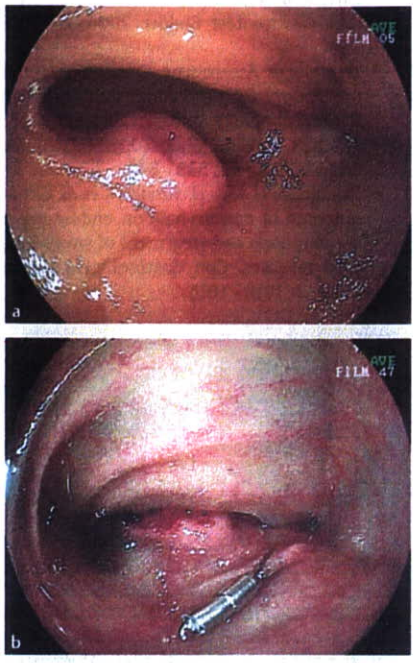

Fig. 2 Double-balloon endoscopy. **a** A tumor 6 mm in diameter has a navel-like depression in its center. **b** Clips are placed near the tumor after biopsies.

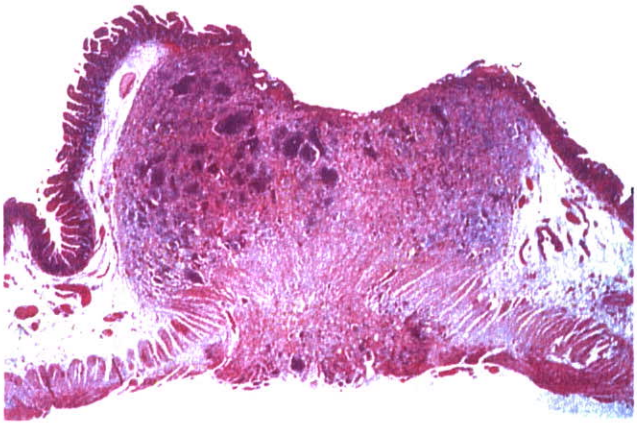

Fig. 3 Histological section of the resected carcinoid tumor. The tumor was growing mainly in the submucosa but had also invaded the subserosa.

A 38-year-old man with bloody stools underwent esophagogastroduodenoscopy and colonoscopy. However, no bleeding point was detected and therefore, bleeding in the small intestine was considered likely.

We carried out capsule endoscopy and detected a tumor in the proximal ileum (**Fig. 1**). Double-balloon endoscopy (DBE) was then carried out transanally and reconfirmed the presence of the tumor in the expected part of the ileum (**Fig. 2a**). On the basis of its appearance, the lesion was suspected to be a submucosal tumor such as a carcinoid. We obtained biopsy samples from the tumor and marked it for surgery by placing clips close to it (**Fig. 2b**).

The patient showed no metastases in a series of imaging examinations and subsequently underwent partial ileectomy. The tumor was completely resected and diagnosed histologically as a carcinoid tumor (**Fig. 3**). During the follow-up period, the patient showed no recurrence or metastasis.

The main merit of DBE is that it allows biopsy or transendoscopic procedures [1]. However, DBE requires a very high level of skill and a considerable degree of patient tolerance [2]. It is therefore important to avoid using DBE unnecessarily or inappropriately. In this case, we first screened for the bleeding point by capsule endoscopy and found a tumor in the proximal ileum, for which DBE was subsequently employed transanally and not orally. Thus, screening by capsule endoscopy was useful for deciding the most suitable approach for DBE.

Image resolution in capsule endoscopy has recently improved [3]. Interestingly, in our patient capsule endoscopy detected a small lesion 6 mm in diameter in the small intestine, suggesting that this procedure is sufficiently useful for screening diseases of the small intestine. On the other hand, DBE has extensive potential for the treatment of hemostasis or dilation of strictures in the small intestine [4]. Thus, capsule endoscopy has certain merits for screening, while DBE seems better suited to final diagnosis or treatment.

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References

1 *Hadithi M, Heine GD, Jacobs MA et al.* A prospective study comparing video capsule endoscopy with double-balloon enteroscopy in patients with obscure gastrointestinal bleeding. Am J Gastroenterol 2006; 101: 52–57

2 *Mehdizadeh S, Ross A, Gerson L et al.* What is the learning curve associated with double-balloon enteroscopy? Technical details and early experience in 6 US tertiary care centers. Gastrointest Endosc 2006; 64: 740–750

3 *Technology Assessment Committee, American Society for Gastrointestinal Endoscopy.* ASGE Technology Status Evaluation Report: wireless capsule endoscopy. Gastrointest Endosc 2006; 63: 539–545

4 *Yamamoto H, Kita H, Sunada K et al.* Clinical outcome of double balloon endoscopy for the diagnosis and treatment of small-intestinal diseases. Clin Gastroenterol Hepatol 2004; 2: 1010–1016

Bibliography

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小腸用カプセル内視鏡の実際

——日本の多施設共同研究を中心に

Present state of capsule endoscopy for small intestine in Japan

中村哲也(写真)　**寺野　彰**

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◎カプセル内視鏡は，被検者が自ら飲み込むだけで検査ができる従来のものとはまったくメカニズムの異なる内視鏡で，イスラエルの Given Imaging 社が開発した小腸用カプセル内視鏡 PillCam™SB が世界でもっとも普及している．日本では，2004 年以来カプセル内視鏡研究会において施設限定で医師主体の自主研究を行っている．このたび，第一次多施設共同研究の結果がまとまり，これまで病変が少ないと考えられてきた小腸にも腫瘍を含むさまざまな病変が存在することが判明した．カプセル内視鏡の画期的なところは，生理的に近い状態の消化管内腔を被検者の苦痛なしに診断することができることである．小腸用カプセル内視鏡は臨床応用されてから比較的日が浅いが，IT 技術の進歩に伴い，機器や解析ソフトの開発や改良が急速に進んでおり，小腸病変の内視鏡診断や治療が劇的に変化しているのが現状である．

Key word：小腸用カプセル内視鏡，カプセル内視鏡研究会，多施設共同研究，原因不明消化管出血

カプセル内視鏡は，被検者が自ら飲み込むだけで検査ができる従来のものとはまったくメカニズムが異なる内視鏡で，イスラエルの Given Imaging 社が世界ではじめて開発した[1)]．それは被検者にとってほとんど苦痛がないうえに，生理的な状態に近い消化管，とくに小腸を比較的容易に観察することができる，新しい内視鏡診断法である．

本稿では代表的な小腸用カプセル内視鏡である PillCam™SB(図 1)について，その実際と日本における現況について，多施設共同研究の結果を交えて紹介する．

小腸用カプセル内視鏡(PillCam™SB)の実際

1. カプセル内視鏡システムの概略

システムは以下の 3 つから構成される[2)]．

① カプセル内視鏡本体(図 1，図 2-A)．

② カプセル内視鏡本体から送信された画像データを受信するセンサアレイ(図 2-B)と外部記憶装置であるデータレコーダ(図 2-C)．

③ 患者のデータや撮影された画像を処理し解

サイドメモ

小腸用以外のカプセル内視鏡

小腸用カプセル内視鏡 PillCam™SB 以外に，両方向で写真撮影が可能な食道用カプセル内視鏡 PillCam™ESO と，消化管狭窄の有無を事前に調べる目的で開発された，小腸用カプセル内視鏡とまったく同じ形・大きさをした patency capsule(いわばダミーのカプセル)とがある．これらは CE-Mark(ヨーロッパ連合域内で販売される，安全や健康を保護する安全規格に合致した製品に付与されるマーク)を取得し，アメリカの FDA(Food and Drug Administration)にも認可されている．最近，あらたに大腸用カプセル内視鏡 PillCam™COLON も開発され，2006 年 10 月に CE-Mark を取得した．これらのカプセル内視鏡はいずれも Given Imaging 社で開発された．

図 1　小腸用カプセル内視鏡(11×26 mm, PillCam™SB, Given Imaging, イスラエル)

析する専用ソフトウェア RAPID® (Reporting and Processing of Images and Data；図 3)がインストールされたワークステーション.

2. カプセル内視鏡検査の実際

患者は 8 時間以上 12 時間程度絶食した後，腹部に 8 個のセンサアレイを貼りつけ，データレコーダをセットした専用ベルトを装着する．機器の動作を確認してからカプセル内視鏡本体を適量の水とともに飲み込む．カプセル内視鏡を飲み込んだ 2 時間後には水分が飲め，4 時間後には軽い食事もとれる．強い磁気にさらされたり激しい運動をしたりさえしなければ，患者は自由に行動し仕事をすることもでき，外来での検査が可能である.

現在の小腸用カプセル内視鏡は，稼働開始後 1 秒に 2 回発光すると同時に写真撮影を開始し，1 回の検査で 55,000～60,000 枚程度の静止画像(JPEG 画像)が撮影できる．カプセル内視鏡本体内の発信器から送信されたすべての画像データは，腰に装着したデータレコーダに保存される．カプセル内視鏡本体は排便とともに患者の体外に排出され，使い捨てである．カプセル内視鏡を飲み込んだ 8 時間以降にデータレコーダなどの機器をはずし，撮影された画像データを RAPID® ワークステーションに転送する．そこで静止画像は特殊な形式のビデオ画像に変換され，それを医師が読影して診断する．RAPID® ソフトウェアにはコンピュータによる診断支援機能がついているので，若干のトレーニングにより画像診断は比較的容易にできる．小腸用カプセル内視鏡による検査の詳細については文献[3]を参照されたい.

小腸用カプセル内視鏡の多施設共同研究の概要

2003 年に，獨協医科大学病院と社会保険中央総合病院においてカプセル内視鏡の日本最初の臨床治験が終了した．カプセル内視鏡の臨床応用が欧米より遅れたこと，日本にも原因不明の消化管出血など小腸疾患に苦しむ患者が数多く存在することなどから，2004 年に獨協医科大学を中心にカプセル内視鏡研究会を立ちあげ，施設限定で医師主体の自主研究を行っている．2004 年 2～10 月にかけてカプセル内視鏡検査を行った 185 症例を対象として，日本最初の多施設共同研究が行われた[4]．その結果の一部を以下に紹介する.

1. カプセル内視鏡の消化管通過時間

全国 9 施設(表 1)において，185 症例に対し 197 件のカプセル内視鏡検査を行った．撮影不良 3 件を除いた 194 件の平均撮影時間は 8 時間 5 分 18 秒であった．カプセル稼働開始から胃に到達するまでの時間に関しては 194 件の平均は 6 分 33 秒であったが，食道内に 30 分以上とどまった 7 件を除いた 187 件の平均は 17 秒であった．胃を通過した 189 件の平均通過時間は 39 分 20 秒で，小腸通過時間の平均は 5 時間 4 分 44 秒(146 件)であった(表 2)．1 回のカプセル内視鏡検査により全小腸が観察できる割合は 74.1%(146/197)であったが，これは下剤投与などの前処置を行っていない症例についての検討結果である．最近は全小腸の観察率を上げるために，前処置を行ったうえで検査を施行することが多くなってきている[5]．したがって，表 2 に示したカプセル内視鏡の通過時間の平均は日本人における平均通過時間の基準と考えられる.

2. カプセル内視鏡により確定診断された症例の内訳

小腸用カプセル内視鏡の第 1 の適応は，上部消化管・下部消化管内視鏡検査など従来の検査法で出血源が不明の“原因不明消化管出血(obscure gastrointestinal bleeding)”である[4,6,7]．今回の多施設共同研究でも，185 症例のうち原因不明消化管出血は 135 例ともっとも多かった．現在のカプセル内視鏡は画像撮影専用のため，小腸内の出血などが明瞭に映しだされるが，それがどのような病変からの出血なのかがわからないことも多い．そ

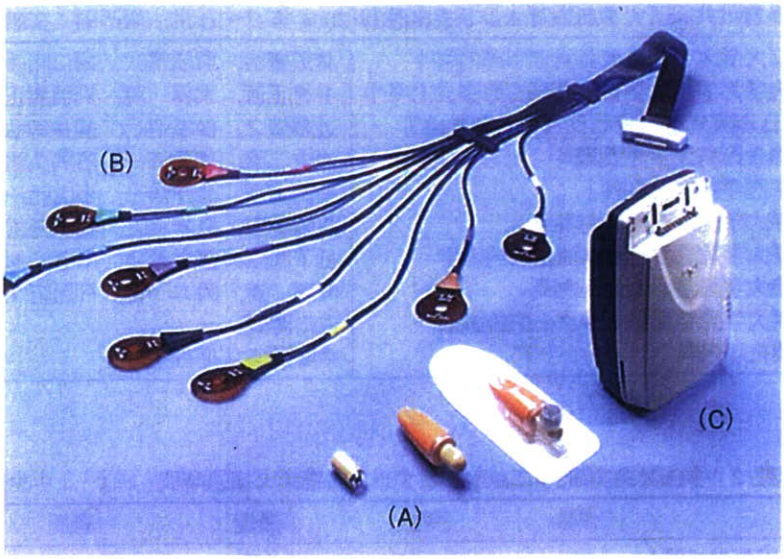

図 2　小腸用カプセル内視鏡システム(Given Imaging 社, イスラエル)
A：カプセル内視鏡本体(PillCam™SB), B：センサアレイ, C：データレコーダ.

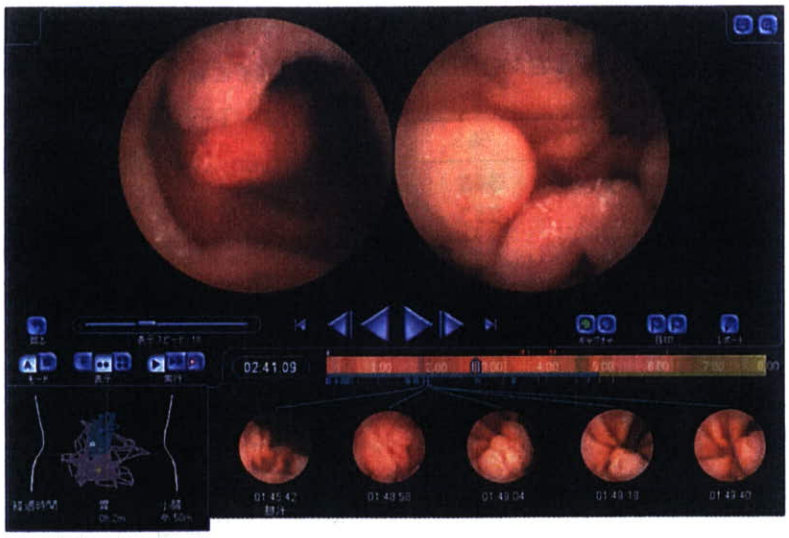

図 3　画像解析用ソフトRAPID® (Given Imaging社, イスラエル)の2画面表示

こで，原因不明消化管出血 135 例について追跡調査を行い，カプセル内視鏡で得られた所見あるいはそれが契機となって確定診断がついたと報告のあった 70 例について，その内訳を検討した(表 3).

潰瘍あるいはびらんが 24 症例(34.3%)ともっとも多く，angiodysplasia などの血管性病変が 18 例(25.7%)，小腸癌を含む腫瘍性病変が 12 例(17.1%)，Crohn 病が 7 例(10%)で，小腸外病変と判明した症例も 6 例(8.6%)あった．ほかにも多数の小腸病変が発見され，従来病変が少ないと考えられてきた小腸の診断学に関する認識を大きく変える必要がある．海外では angiodysplasia などの血管性病変がもっとも多いという報告[8]が多いが，今回の検討では血管性病変は 18 例(25.7%)にとどまり，潰瘍あるいはびらんが 24 症例(34.3%)ともっとも多かった．これはダブルバルーン内視鏡で日本人の小腸を検討した Yamamoto らの結果[9]と合致しており，欧米人と日本人とにおける小腸病変の相違点のひとつと考えられる．ただし，潰瘍あるいはびらんと診断がついてもその真の原因が不明で，非特異的小腸潰瘍とされている症例があり，小腸の潰瘍性病変の成因については今後さ

表 1　多施設共同研究参加施設および担当医師(2004 年 2〜10 月，順不同；文献[4]より改変)

大阪市立大学大学院消化器器官制御内科学	渡辺憲治，斯波将次，樋口和秀，荒川哲男
名古屋大学大学院医学系研究科病態修復内科学	中村正直，大橋　暁，丹羽康正，後藤秀実
NTT 東日本関東病院消化器内科・内視鏡部	近藤靖之，松橋信行，櫻井幸弘
東京慈恵会医科大学内視鏡科	仲吉　隆，斉藤彰一，田尻久雄
杏林大学医学部第三内科	平田真理，池井洋子，小山元一，高橋信一
九州大学大学院病態機能内科学	江崎幹宏，松本主之，飯田三雄
京都大学大学院医学研究科消化器内科学	日下利広，西尾彰功，千葉　勉
慶應義塾大学医学部消化器内科	桜庭　篤，岡本　晋，日比紀文
獨協医科大学光学医療センター内視鏡部門	白川勝朗
同　消化器内科	中野道子，平石秀幸

表 2　多施設共同研究におけるカプセル内視鏡の通過時間(文献[4]より改変)

	件数	平均	最短	最長
胃到達時間*A	194	6 分 33 秒	2 秒	4 時間 27 分 29 秒
胃到達時間*B	187	17 秒(注：30 分以上の症例を除外)		
胃通過時間	189	39 分 20 秒	5 秒	6 時間 52 分 41 秒
小腸通過時間	146	5 時間 4 分 44 秒	17 分 53 秒	8 時間 28 分 46 秒

*：カプセル稼働開始時から胃に到達するまでの時間.

表 3　確定診断がついた原因不明消化管出血70症例の内訳(文献[4]より改変)

病変およびその詳細	症例数	%
1．潰瘍・びらん*	24	34.3
潰瘍*	17	24.3
びらん	7	10.0
2．血管性病変*	18	25.7
angiodysplasia*	14	20.0
小腸静脈瘤	3	4.3
PHE	1	1.4
3．腫瘍性病変	12	17.1
GIST	3	4.3
良性ポリープ	3	4.3
小腸腺癌	2	2.9
悪性リンパ腫	1	1.4
転移性腫瘍(腺癌)	1	1.4
カルチノイド	1	1.4
粘膜下腫瘍(脂肪腫)	1	1.4
4．Crohn病	7	10.0
5．小腸外病変	6	8.6
大腸癌	2	2.9
GAVE	2	2.9
胃潰瘍	1	1.4
慢性膵炎	1	1.4
6．Behçet病	2	2.9
7．その他	2	2.9
小腸憩室	1	1.4
異常所見なし	1	1.4

*：潰瘍と angiodysplasia が重複した症例を 1 例含む.
PHE：portal hypertensive enteropathy.
GIST：gastrointestinal stromal tumor.
GAVE：gastric antral vascular ectasia.

らに検討を続けていく必要がある.

なお，185 症例中 3 例(1.62%)において滞留(retention；消化管内の狭窄部の口側に，2 週間以上カプセルがとどまること)を認め，内視鏡的あるいは外科的処置によりカプセルは回収された．それらの患者に健康被害はなく，他に偶発症の報告はなかった.

おわりに

日本初の多施設共同研究の結果を含め，小腸用カプセル内視鏡の実際とその現況について紹介した．カプセル内視鏡は臨床応用されてから比較的日が浅いが，IT 技術の進歩に伴い，機器や解析ソフトの開発や改良が日々行われている．本稿で紹介したように，症例の蓄積とともに小腸病変の診断・治療も急速に変化している．小腸以外の消化管を対象としたカプセル内視鏡もつぎつぎと開発されており，消化器内視鏡検査は今後劇的に変化していくものと期待される.

文献

1) Iddan, G. et al.：Wireless capsule endoscopy. *Nature*, **405**：417, 2000.
2) 榊　信廣：カプセル内視鏡とは．カプセル内視鏡診療ガイド(寺野　彰監)．南江堂，2006, pp.2-7.
3) 中村哲也・他：検査の実際．カプセル内視鏡診療

ガイド(寺野　彰監). 南江堂, 2006, pp.8-24.
4) 中村哲也・他：小腸用カプセル内視鏡の日本人における多施設共同研究報告―原因不明消化管出血症例を中心に. *Gastroenterological Endoscopy.*(in press)
5) Selby, W.：Complete small-bowel transit in patients undergoing capsule endoscopy：determining factors and improvement with metoclopramide. *Gastrointest. Endosc.*, **61**：80-85, 2005.
6) Zuckerman, G. R. et al.：AGA technical review on the evaluation and management of occult and obscure gastrointestinal bleeding. *Gastroenterology*, **118**：201-221, 2000.
7) Rey, J. F. et al.：European society of gastrointestinal endoscopy guideline for video capsule endoscopy. *Endoscopy*, **36**：656-658, 2004.
8) Pennazio, M. et al.：Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy：Report of 100 consecutive cases. *Gastroenterology*, **126**：643-653, 2004.
9) Yamamoto, H. et al.：Clinical outcomes of double-balloon endoscopy for the diagnosis and treatment of small-intestinal disease. *Clin. Gastroenterol. Hepatol.*, **2**：1010-1016, 2004.

*　　*　　*

原 著

小腸用カプセル内視鏡の日本人における多施設共同研究報告 ―原因不明消化管出血症例を中心に―

カプセル内視鏡研究会

中村哲也[1]，荒川哲男[2]，後藤秀実[3]，櫻井幸弘[4]，
田尻久雄[5]，高橋信一[6]，飯田三雄[7]，千葉　勉[8]，
日比紀文[9]，寺野　彰[10]

要旨：【背景・目的】小腸用カプセル内視鏡（PillCam™ SB，Given Imaging Ltd.）の日本人における有用性を調べるため，多施設共同による医師主体の自主研究を行った．【方法】197件，185例を対象に，検査理由，通過時間，偶発症の有無を調べた．原因不明消化管出血135例の追跡調査を行い，確定診断を得た70例を抽出して，診断の内訳，それまでの医療行為等を調べ，有用性を検討した．【結果】検査理由のうち73%が原因不明消化管出血で，胃の平均通過時間は39分20秒，小腸は5時間4分44秒であった．滞留により内視鏡・外科的処置が行われたのは3例（1.62%）であった．確定診断された70例の内訳は，潰瘍・びらん34.3%，血管性病変25.7%，腫瘍性病変17.1%，クローン病10%の順であった．カプセル内視鏡の導入により，早期診断が可能であることから，入院費用軽減の可能性が示唆された．【結論】カプセル内視鏡は，安全かつ有用な検査法である．

Key words　カプセル内視鏡／原因不明消化管出血／多施設共同研究

I　はじめに

カプセル内視鏡は，イスラエルのGiven Imaging Ltd.が世界で初めて開発した，従来のものとは全くメカニズムの異なる内視鏡で，2000年にNature誌上で発表された[1]．翌2001年にはヨーロッパやアメリカで認可され，臨床応用が始まった．当初はM2A™（Mouth to Anus）という名称がつけられ，口から肛門までの全消化管の診断

Figure 1　小腸用カプセル内視鏡（PillCam™ SB，Given Imaging Ltd.，11 mm×26 mm）．

Gastroenterol Endosc 2007；49：324-34.
Tetsuya NAKAMURA
The First Multicenter Study of Capsule Endoscopy in Japan：Clinical Outocome of Obscure Gastrointestinal Bleeding.

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別刷請求先：〒321-0293 栃木県下都賀郡壬生町北小林880 獨協医科大学 光学医療センター内視鏡部門 中村哲也

Table 1　CESG多施設共同研究参加施設および担当医師（2004年2～10月，順不同）.

大阪市立大学大学院消化器器官制御内科学	(41)	渡辺憲治，斯波将次，樋口和秀
名古屋大学大学院医学系研究科病態修復内科学	(31)	中村正直，大橋　暁，丹羽康正
NTT東日本関東病院消化器内科		近藤靖之
同　内視鏡部	(23)	松橋信行
東京慈恵会医科大学内視鏡部	(19)	仲吉　隆，斉藤彰一
杏林大学医学部第3内科	(18)	平田真理，池井洋子，小山元一
九州大学大学院病態機能内科学	(16)	江崎幹宏，松本主之
京都大学大学院医学研究科消化器内科学	(9)	日下利広，西尾彰功
慶応義塾大学医学部消化器内科	(2)	桜庭　篤，岡本　晋
獨協医科大学光学医療センター内視鏡部門		白川勝朗
同　消化器内科	(38)	中野道子，平石秀幸

（　）内の数字は施設毎のカプセル内視鏡実施件数

Table 2　CESG多施設共同研究の目的と対象.

[目的]
主要目的：日本人におけるカプセル内視鏡による小腸病変の診断能についての検討
副次目的：小腸以外の消化管病変の診断能についての検討
[対象]
小腸疾患および原因不明の消化管出血など小腸疾患が疑われる患者
[選択基準]
1）満16歳以上の患者（未成年者の場合は，本人以外に法定代理人の同意が必要）
2）書面によるインフォームドコンセントが得られた患者
[除外基準]
1）嚥下障害のある患者
2）妊婦
3）臨床画像，あるいは過去の検査および既往歴や病歴に基づいて，腸閉塞，狭窄，または瘻とわかる，あるいはその疑いが否定できない患者
4）心臓ペースメーカーまたは他の医療用電子機器を体内に埋込んでいる患者
5）本研究の結果に直接または間接的に影響するような他の研究または治験に参加している患者
6）研究および／または装置に関する指示を遵守できない患者
7）高度の食道裂孔ヘルニアを有する患者
8）生命を脅かす疾患に罹患している患者
9）腹部に放射線治療を行ったことのある患者
10）膠原病などのNSAIDsを長期使用する基礎疾患があり，NSAIDsを長期使用しているか，あるいはしていた患者
11）カプセル滞留時における内視鏡または外科的手術による摘出に対しての同意が得られない患者
12）研究責任医師または研究分担医師が対象として不適当と判断した患者
[除外基準の特例]
滞留の可能性がある患者において，当該疾患の内視鏡的治療または外科的手術が事前に決定しており，患者からの検査希望があり，その治療に関して主治医の協力が得られる場合は，除外基準3），7），10)に当てはまってもカプセル内視鏡検査を行っても良いこととする.

を意図していた．2001年から2006年9月末までに，このカプセル内視鏡を用いた検査は世界でのべ40万件以上行われ，小腸疾患や消化管出血，特に小腸出血の診断に有用であることが多数報告されている[2)~7)]．2004年，新たに食道用のカプセル内視鏡PillCam™ ESO（Pill Camera for Esophagus）が開発され[8)]，従来のカプセル内視鏡は小腸用と位置づけられて，PillCam™ SB（Pill Camera for Small Bowel，Figure 1）と呼ばれるようになった[9)]．

日本では，2003年に獨協医科大学病院と社会保険中央総合病院において，クローン病などの小腸疾患を対象としたカプセル内視鏡の最初の臨床治験が行われた[9)]．その結果をもとに認可を申請中であるが，未だに認可および保険収載には至っていない．しかし，診断困難な小腸疾患や，上部・下部消化管内視鏡でも原因が不明の消化管出血（原因不明消化管出血：obscure gastrointestinal bleeding[10)]）に苦しむ患者が数多く存在する．そこ

Table 3 カプセル内視鏡の検査準備.

1．問診：症状の有無，最近の排便回数，便の性状，前日の夕食終了時間
2．血圧，脈拍，体温などの測定
3．機器装着ベルトの調整
4．消泡剤（dimeticon，40～80 mg）の内服
5．センサアレイの貼付（Figure 2）
6．体外バッテリーおよびデータレコーダを装着（Figure 3-a，b）
7．カプセル内視鏡およびデータレコーダの動作確認

で，獨協医科大学を中心としてカプセル内視鏡研究会（CESG-Japan：Capsule Endoscopy Study Group, Japan）を立ちあげ，会員施設の責任医師が小腸用カプセル内視鏡を個人輸入して検査を行う多施設共同の自主研究を行っている[9]．この日本で初めての多施設共同研究について，2004年2月から2004年10月までに行った検査の概要を述べる．また，原因不明消化管出血のうち2005年6月末までに確定診断がついたと報告があった症例に関して，小腸用カプセル内視鏡の有用性を検討した．

II 対象と方法

1．目的と対象

カプセル内視鏡研究会（以下CESG）所属施設のうち9施設11科（部）（Table 1）において，小腸用カプセル内視鏡（PillCam™ SB，旧名M2A™）を各施設の責任医師が個人輸入して，多施設共同の自主研究を行った．海外の文献や資料を参考にして定めたその目的と対象を，Table 2に示す．本研究は，CESGが中心となって作成した研究計画書が，各施設の倫理委員会の承認を得たのちに開始された．なお，以下「カプセル内視鏡」とは，すべて小腸用カプセル内視鏡（PillCam™ SB）を指す．

今回，2004年2月から10月にかけてカプセル内視鏡検査を行った197件，185症例を対象に，以下について検討した．

1）185症例の検査施行理由
2）カプセル内視鏡の画像記録時間および各臓器の通過時間
3）偶発症の有無

185症例のうち原因不明消化管出血135例について追跡調査を行い，2005年6月末までに確定診断がついたと報告のあった70例を対象として，以下について検討した．

4）確定診断がついた原因不明消化管出血の内訳
5）カプセル内視鏡検査施行前の医療行為および検査の内訳

2005年6月末時点で診断が未確定であった65例について，さらに2006年6月末まで追跡調査を追加し，以下について検討した．

6）診断未確定であった原因不明消化管出血65例の経過・転帰

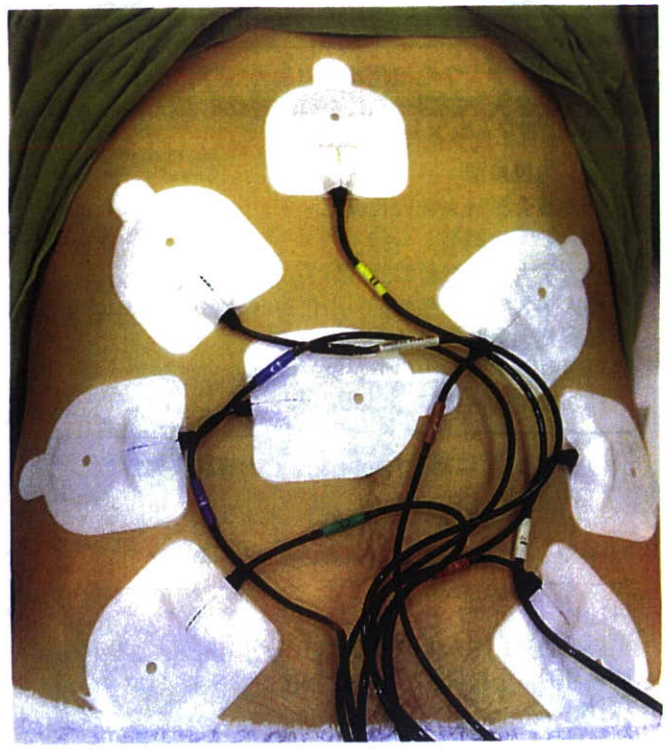


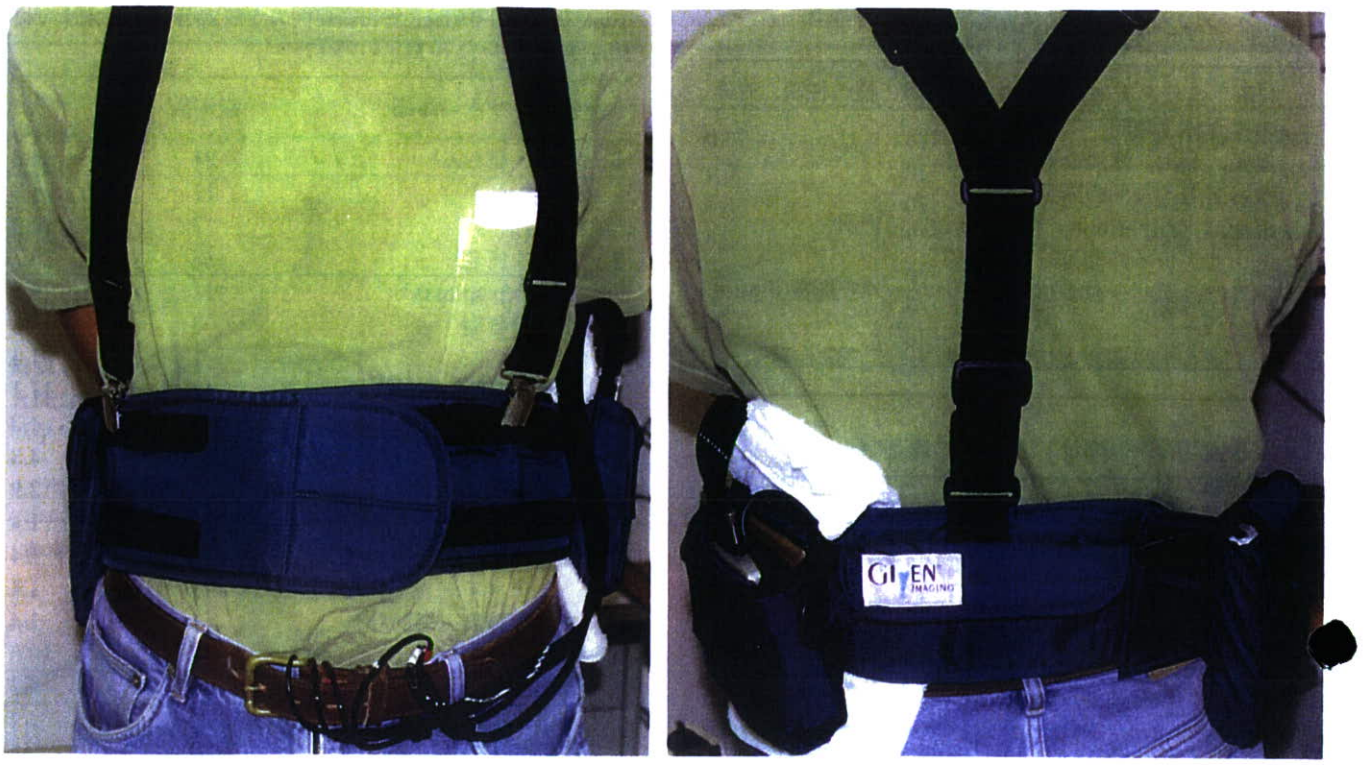
Figure 2 センサアレイの貼付位置.

2．方法

1）カプセル内視鏡の検査法

検査準備をTable 3およびFigure 2，3に，検査の概略をTable 4に示す．カプセル内視鏡検査を初めて行う医師は，CESG事務局が主催した講習会に参加して，予め機器の取り扱いや読影方法および診断法についてトレーニングを受けた．カプセル内視鏡の読影や診断には，画像解析用の専用ソフトであるRAPID®（Reporting and Processing of Images and Data）を用いた．

各施設でカプセル内視鏡検査を行う予定の患者については，事前に検査理由と選択基準（Table 2）に該当するか否かについて記載した症例登録票を，CESG事務局に送って登録した．検査終了後は各施設において読影・診断し，検査毎に記録された画像および所見・診断はCD-Rおよびハー



a　b

Figure 3　体外バッテリーとデータレコーダの装着図.
a. 正面図（ベルトの上から出たセンサアレイのコードをデータレコーダに接続）
b. 背面図（向かって左がデータレコーダ）

Table 4　検査の概略.

[外来初診時]
説明と同意の上，検査日を決定
[検査前日]
12 時間程度の絶食（通常，前日の夕食終了以降）
[検査当日]
検査準備（約 20 分）*後，水と共にカプセル嚥下
嚥下 2 時間後，飲水可
嚥下 4 時間後，食事可
嚥下 8 時間後，レコーダー回収・読影
[検査後日]
カプセル排泄が不明で大腸の画像が写っていない時
→検査から 1 週間以内に腹部 X 線撮影（背臥位）

＊：Table 3 参照

ドディスクに記録され，各施設で保管するとともに CESG 事務局においても全症例を一括保管した．カプセル内視鏡による偶発症が生じた場合には，その詳細と対応およびその後の経緯・結末とを，ただちに CESG 事務局に届け出た．

また研究開始後に生じた問題や診断困難症例については，CESG 事務局主催の症例検討会等において会員医師間で討議し，それ以外にも会員医師相互間で適宜情報交換を行った．

2）追跡調査

2004 年 2 月から 10 月にかけてカプセル内視鏡検査を行った 185 症例のうち，検査理由が原因不明消化管出血であった 135 例について，追跡調査を行った．まず，2005 年 6 月末までに，カプセル内視鏡の所見またはその後に行った検査によって確定診断がついた症例を，各施設からの報告に基づいて抽出した．抽出した 70 例について，カプセル内視鏡施行前の罹病期間，他の検査内容および検査回数，入院の有無およびその日数，輸血の有無およびその単位数と，追加検査の有無およびその内容，病理所見の有無およびその詳細，最終的な診断名について，専用の調査用紙で調査した．調査内容が不十分な場合には，CESG 事務局員が直接検査施行医と連絡をとって確認した．転院などの理由により不明であった罹病期間，入院日数などは欠損値として扱い，それらは平均値算出の際に除外した．

2005 年 6 月末時点で確定診断がつかなかった 65 症例については，2006 年 6 月末までのカプセル内視鏡施行後の検査状況および経過・転帰について追跡調査を追加した．