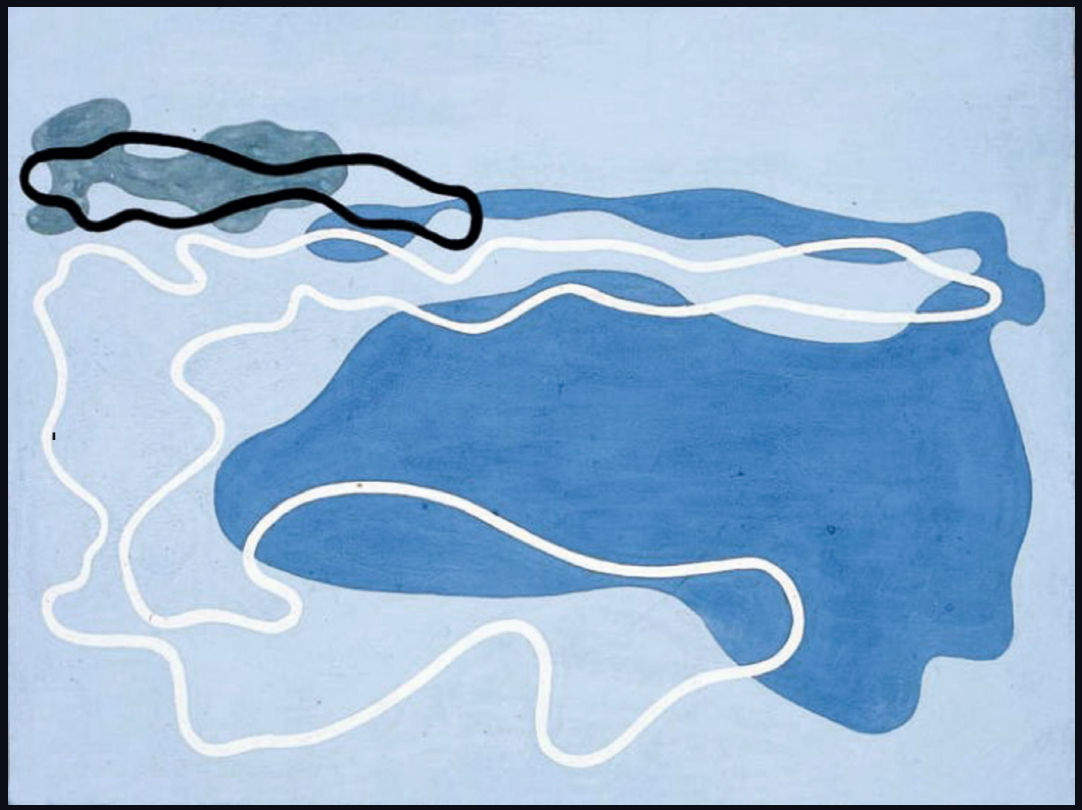


ENDOSCOPIC SEMIOLOGY OF THE STOMACH AND THE DUODENUM

Revisited concepts

Emmanuel Coron, Gabriel Rahmi & Xavier Dray, eds.

ENDOSCOPIC SEMIOLOGY OF THE STOMACH AND THE DUODENUM

Concepts revisited

Coordinated by Emmanuel Coron, Gabriel Rahmi and Xavier Dray

Initially published in French by Le Grand Métier (France) in 2020
Finished printed to mars 2020 by Corlet Imprimeur - 14110 Condé-en-Normandie
Legal deposit : mars 2020 - printer number : 206571 - *Printed in France*

The following authors contributed to this book

Einas ABOU ALI, CHU Cochin Paris
Maximilien BARRET, CHU Cochin Paris
Jérôme BELLANGER, CHU St Antoine, Paris
Céline BOSSARD, CHU Nantes
Chloé BROUDIN, HEGP, Paris
Marine CAMUS, CHU St Antoine, Paris
Nicolas CHAPELLE, CHU Nantes
Emmanuel CORON, CHU Nantes
Xavier DRAY, CHU St Antoine, Paris
Jean Paul GALMICHE, LGM, Rouen
Yuzo KODAMA, Kobe, Japan
Yoshinori MORITA, Kobe, Japan
Jean François MOSNIER, CHU Nantes
Yoshiko NAKANO, Kobe, Japan
Saskia PAPA, Fujifilm Europe
Guillaume PERROD, HEGP, Paris
Matthieu PIOCHE, CHU Lyon
Gabriel RAHMI, HEGP, Paris
Alexandre ROUQUETTE, CHU Cochin, Paris
Flore TESIOROWSKI, Fujifilm, Asnières
Takashi TOYONAGA, Kobe, Japan
Eiji UMEGAKI, Kobe, Japan
Geoffroy VANBIERVLIET, CHU Nice

General summary

Foreword

This work is the third opus in this collection devoted to endoscopic digestive semiology. This volume deals with the semiology of precancerous lesions and superficial cancers of the stomach and the duodenum. It is part of a larger educational project carried out with the support of Fujifilm France and Fujifilm Europe. We have kept the same model for this essay as for the previous ones: the first part is devoted to recent developments and the second part describes some common clinical cases, illustrated using endoscopic and histological images.

Gastric cancers are less common than colon and oesophageal cancers in France. However, they constitute a major problem for the gastroenterologist at the diagnostic level (especially because of their diversity), as well as the therapeutic level. In this regard, it is important to pay tribute to the remarkable work and expertise of Japanese authors who have revisited many concepts in this field, with a less pessimistic and more active approach in the management of these patients. However, progress cannot be made therapeutically without a better semiological characterisation of precancerous lesions and superficial stomach cancers. In this book, we are pleased to present Professor Takashi Toyonaga and his team, who give us both their expertise and their vision of future developments in endoscopy. We warmly thank Professor Takashi Toyonaga for accepting our invitation to contribute to this book in such a short time. The future of digestive endoscopy is certainly bright!

The duodenum is often the forgotten part of this type of work. Certainly the duodenal bulb is not affected by cancer, however the rest of this organ can be the site of cancer, especially in the context of more systemic diseases, such as digestive polyposes or lymphomas. We would therefore like to thank Professor Xavier Dray for joining the "historical" team of editors of this collection. We would also like to thank the authors of the clinical cases listed in this book whose composition is very similar to that of the previous book.

Finally, in order to maintain the link between 20th century art and Science that we have launched from the beginning of this series, we have chosen a work by Wladislaw Strzeminski for the cover of this book. Wladislaw Strzeminski was a Polish painter whose paintings try to capture the harmony of the Baltic sea; in this painting we find the notion of landscape and unity in diversity, which we believe are relevant to the subject discussed in this book[1].

1. Wladislaw Strzeminski who was born on the 21st of November 1893 in Minsk and died on the 26th of December 1952 in Lodz, was a painter and theorist of Polish art. A pioneer of the constructivist avant-garde of the 1920s and 1930s, he theorised unism.

How to explore the stomach? Where and how to perform biopsies?

Emmanuel Coron, Institut des Maladies de l'Appareil Digestif, CHU Nantes

Introduction

Endoscopic exploration of the stomach, combined with that of the oesophagus and the duodenum (oesogastroduodenal endoscopy – OGDE) is probably the most commonly performed procedure by gastroenterologists. It is estimated that in France, around one million OGDEs are performed every year. While common, the OGDE is also one of the most difficult examinations to perform when trying to detect "subtle" or early abnormalities, which involves the precise characterisation of mucosal abnormalities using advanced endoscopic imaging. This difficulty is due to the variety and complexity of pathologies that can be encountered (Table 1) and by the size and anatomy of the stomach, which are the source of a few common pitfalls that should be carefully avoided.

Table 1: A non-exhaustive list of gastric diseases likely to be detected by OGDE.

Ulcers and erosions (whatever the nature (mild or malignant) and etiology)
Gastric polyps (whatever the nature (mild or malignant) and etiology)
Acute gastritis (whatever the nature and etiology)
Chronic gastritis with or without gastric atrophy (including in the context of pernicious anemia)
Intestinal metaplasia with or without dysplasia at different stages
Menetrier's disease
MALT lymphoma
Primary or secondary carcinomas

The first chapter of this book, devoted to precancerous lesions of the stomach and the duodenum, is not intended to describe the entire endoscopic semiology of the stomach. On the contrary, it is focused on the detection of dysplastic lesions that develop in the context of atrophic gastritis and/or intestinal metaplasia. Specific recommendations exist regarding these lesions, which is not the case for other precancerous lesions, such as Menetrier's disease, partial gastrectomies or Biermer's disease. To begin with, it is important to mention the recommendations of good clinical practice. Compliance with these recommendations is essential to ensure a quality endoscopic examination. These recommendations were published by the European Society for Digestive Endoscopy (ESGE) in 2017 (1).

Conditions for conducting the examination

The OGDE is performed in a fasting patient, with no intake of solids for at least 6 hours, and liquids for at least 2 hours. Tobacco is also prohibited in the 6 hours preceding the procedure. We have thus observed a transition from "nile per os" for at least 6 hours (or even 8 hours for the oldest studies) to a strategy of "clear liquids authorised until 2 hours (sometimes 1 hour) before endoscopy". Indeed, it has been shown that the patient's intake of water leads to less general discomfort, and it does not impede the visualisation of the stomach, nor does it increase the risk of inhalation (2). Unlike colonoscopy, no score has been developed to characterise the "cleanness" of the stomach during endoscopy. It is however preferable to describe the gastric contents (bubbles, bile, liquid or food residues) and whether or not this has hampered the exploration of the gastric cavity. The use of a washing pump is highly recommended to optimise the detection of lesions. In some countries like Japan, the use of mucolytics is frequent, either per os before the procedure or by direct application in the working channel of the endoscope. Whether the examination is carried out under sedation or under general anesthesia largely depends on the country, the current recommendations, local habits and the patient's wishes.

In addition to the quality of the medical environment, one of the major points that improve the detection of at risk lesions is the time spent examining the stomach. It has indeed been shown (3) that "slow" endoscopists (i.e. whose average examination time is 8.6 minutes) detected three times more dysplastic lesions and cancers than "rapid" endoscopists (whose average examination time is 5.5 minutes) and this was regardless of their level of experience in endoscopy. Therefore, the ESGE has fixed the minimum time necessary to carry out an OGDE (from intubation to extubation of the endoscope) to 7 minutes in 2 precise situations: (i) patient with a 1st oesogastroduodenal endoscopy and (ii) the follow-up of gastritis with intestinal metaplasia. Likewise, the ESGE recommends that the areas examined should be photographed, at least the antrum, the fundus (in direct vision and in retrovision) and the angulus. Since today most systems are digital and storage of a large number of images is feasible, it seems possible to go further and adopt a "Japanese style" strategy. This strategy recommends a standardised exploration of the stomach, taking 22 images, in particular in patients with an at-risk mucosa[1]. This would have the advantage of helping European endoscopists to self-train by allowing them to precisely review the areas explored upon receipt of the histological results of the biopsies.

1. See page 21.

WHERE AND HOW TO PERFORM STOMACH BIOPSIES?

Before performing biopsies, it is important to precisely describe the lesions observed with white light using standardised and adapted terminology (1). Visible lesions should be at least biopsied and, if possible, specifically resected and placed in separate pots. Systematic biopsies (at least 2 in the fundus and 2 in the antrum) should also be performed. Many studies have compared the diagnostic efficacy of gastroscopy as a function of the number of gastric biopsies performed. The interest of a 5th biopsy of the angulus has been demonstrated, leading to a sensitivity of 100% for the diagnosis of H. pylori infection, 96% for the diagnosis of atrophy and 95% for the diagnosis of metaplasia and dysplasia (4). In addition, this latter strategy allows pathologists to use the OLGIM and OLGA systems, which assess the extent of bowel metaplasia and atrophy, respectively (Figure 1). The use of these classifications is recommended by the ESGE (5) because they make it possible to assess the risk of degeneration according to the degree of severity and the extent of gastric lesions, and thus to determine the optimal monitoring interval. In patients with intestinal metaplasia and/or minimal to moderate atrophy, limited to the antrum, no monitoring is recommended. Conversely, patients with diffuse lesions or severe atrophy should be monitored endoscopically every 3 years (Figure 2). It is essential to eradicate H. pylori when it is present. The effectiveness of eradication is associated with a regression of histological lesions of chronic gastritis, as well as atrophy. On the other hand, eradication of H.pylori does not lead to the regression of metaplastic and dysplastic lesions, which are irreversible.

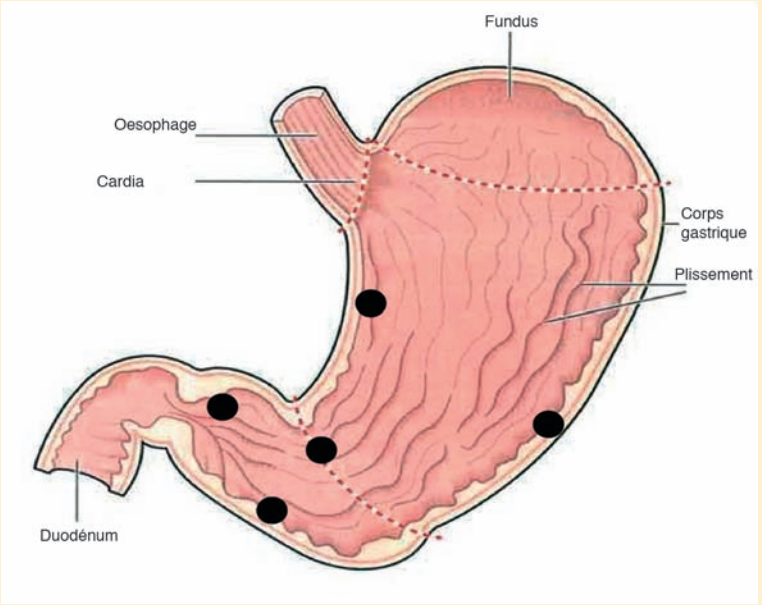


Figure 1: Biopsy sites. At least 4 biopsies should be performed in 2 separate pots (antrum, body).

The evolution of metaplasia-dysplasia-cancer was described more than 30 years ago by Correa (6). Endoscopic monitoring of patients at risk of degeneration is therefore

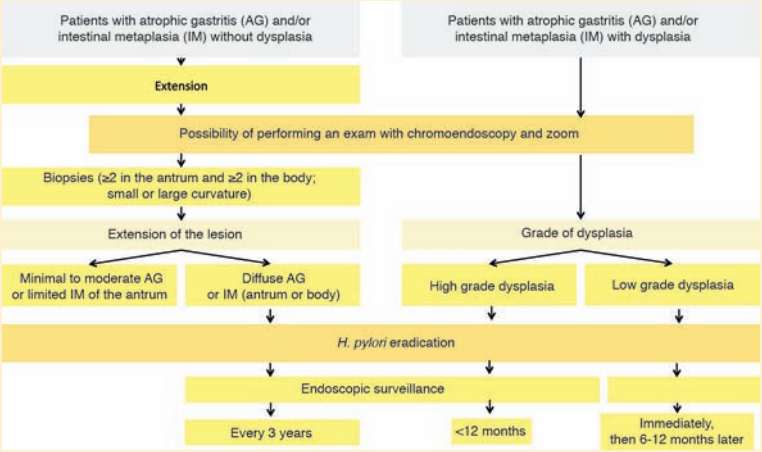


Figure 2: Decision algorithm for monitoring precancerous gastric lesions. Adapted from ESGE recommendations.

based on the premise that the detection of lesions at an early stage of carcinogenesis would improve the prognosis of patients, eventually curing them using minimally invasive methods and with a high success rate. However, this assumption has long been controversial because of the risk of biopsy sampling error, and the very relative efficacy of white light endoscopy in detecting macroscopic lesions at an early stage.

What imaging techniques should be used? At what intervals should patients be monitored?

Advances in endoscopic imaging have revolutionised the monitoring process, facilitating the identification of "subtle" lesions that were previously inaccessible to the eye of the endoscopist. Thus, intestinal metaplasia and the different stages of dysplasia have become identifiable using chromoendoscopy and magnification techniques, making it possible to perform targeted biopsies with high diagnostic efficacy, as well as endoscopic resection gestures. In its recommendations on the management of precancerous diseases of the stomach (MAPS guidelines), the ESGE recommends performing surveillance endoscopy every 3 years in patients with diffuse intestinal metaplasia of the stomach. This presupposes that the presence of intestinal metaplasia was confirmed on systematic or targeted biopsies. Given the poor sensitivity of the white light examination (of the order of 30%), the ESGE now suggests that this examination should be performed using chromoendoscopy by Narrow Band Imaging (NBI) or other staining, combined with optical magnification (5). Since the year 2003, Dinis-Ribeiro *et al.* had shown the feasibility of identifying anomalies of the gastric mucosal microarchitecture associated

with histological anomalies. For example, the presence of intestinal metaplasia or dysplasia can be identified by endoscopic examination, combining staining with methylene blue and zoom (7).

Despite the external validation of these results and the obtention of similar results using other dyes, such as indigo carmine (8), in some cases coupled to magnification techniques involving acetic acid (9), few teams in Europe are using vital dyes. In addition to the level of expertise required, one of the obstacles is the time and material necessary for the preparation and instillation of the products.

Contribution of new dyes to the detection of pre-cancerous lesions

Since the year 2006, Japanese authors have shown (10) the possibility of replacing chromoendoscopy using vital dyes with virtual chromoendoscopy using narrow band imaging (NBI). Numerous studies have confirmed the ability of NBI to detect intestinal metaplasia and dysplasia with a diagnostic performance superior to that of white light. In addition, some specific signs described with NBI, such as the sign of the "light-blue crest" or the "white opaque substance" are typically associated with the presence of intestinal metaplasia. Dysplastic lesions are characterised by a disorganisation of the mucosal and vascular microarchitecture. Their characterisation is facilitated by performing the examination using NBI combined with magnification. Therefore, the ESGE recommends the use of these methods in patients with known low grade or high grade dysplasia, in order to facilitate the identification and removal of these lesions, and to detect metachronous lesions (5). It is important to emphasise that for any visible lesion with dysplasia (whatever the degree), endoscopic resection should be considered, ideally by dissection. The monitoring intervals for patients with dysplasia without visible lesions have also been specified: (i) in the case of low grade dysplasia, a check-up must be proposed no later than 1 year after the initial exam, (ii) in the case of high grade dysplasia, endoscopic control must be proposed immediately and then (in the absence of visible lesions) after 6 to 12 months (Figure 3).

By extrapolation, it is possible to think that chromoendoscopy by Blue Light Imaging (BLI) is at least equivalent to NBI since the same details of the mucosal and vascular microarchitecture are visible (Figure 3). However, not much data is available, even though the results regarding the detection of cancerous and pre-cancerous lesions seem to be encouraging (11, 12).

In conclusion, it is important to perform a quality evaluation by following simple recommendations. The use of chromoendoscopy and magnification should also be encouraged for better detection of precancerous gastric lesions. With the new generation endoscopes, the resolution and the level of detail with which one can now monitor gastric

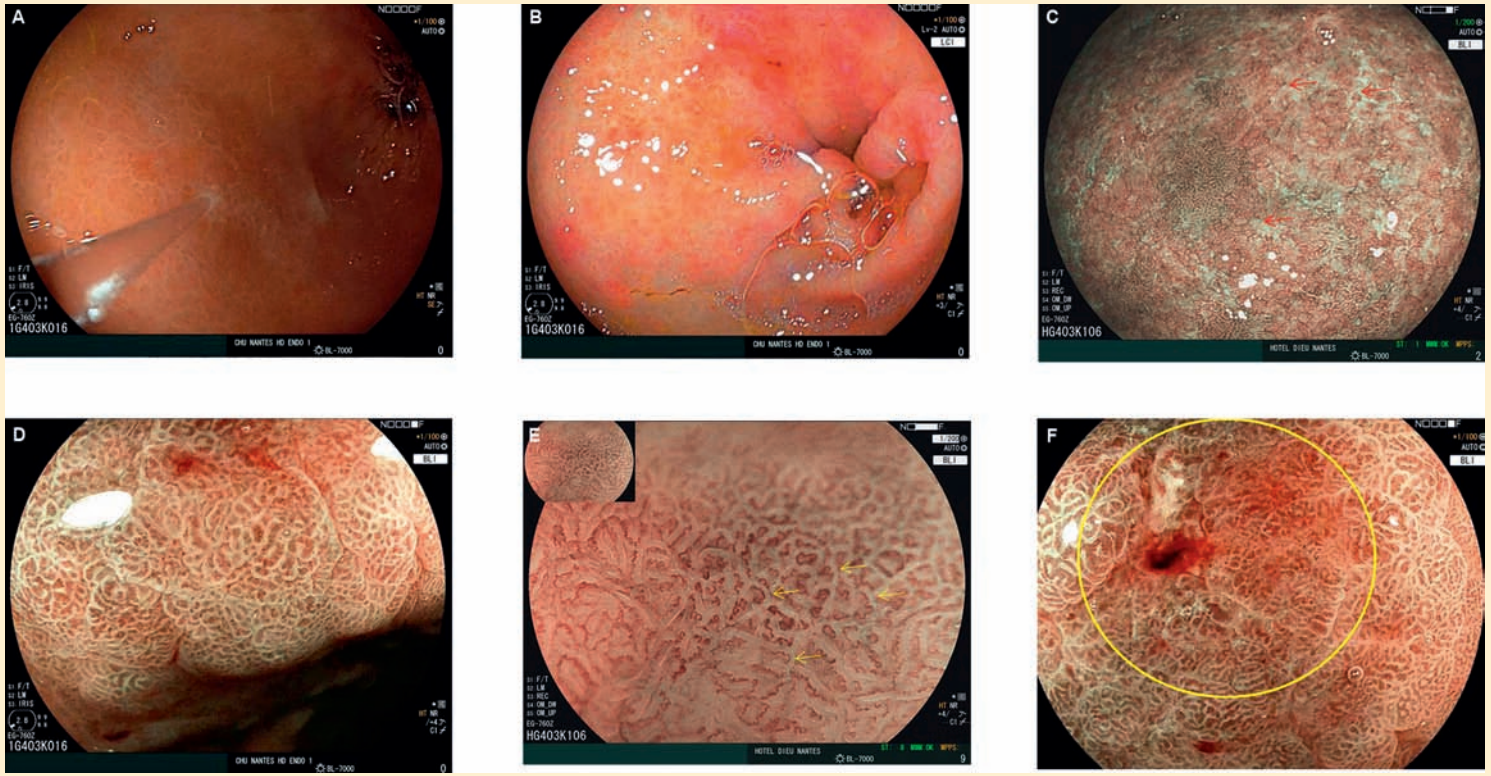


Figure 3: Semiology of precancerous lesions. (A) Normal appearance of the antrum using white light (WL), (B) Areas suspected for inflammation or dysplasia using the Linked Color Imaging mode (LCI), (C) Appearance of atrophic gastritis (red arrows indicate atrophic areas) using the Blue Light Imaging mode (BLI) at low magnification, (D) Mucosal and vascular irregularities using the BLI mode at low magnification, (E) Areas of intestinal metaplasia (yellow arrows indicate the light blue crest sign) in BLI mode with high magnification, (F) Intestinal metaplasia with foci of low grade dysplasia (yellow circle) in BLI mode with low magnification. In the absence of a clear demarcation line, this aspect is suggestive of dysplasia and not cancer.

mucosa greatly improves the endoscopic diagnostic capabilities compared to white light. While this is a great opportunity for improving the performance of endoscopic examination, it represents a real challenge in terms of personnel training.

References

1. Bisschops R, Areia M, Coron E, Dobru D, Kaskas B, Kuvaev R, *et al.* Performance measures for upper gastrointestinal endoscopy: A European Society of Gastrointestinal Endoscopy quality improvement initiative. *United European Gastroenterol J* 2016; 4: 629-656.
2. De Silva AP, Amarasiri L, Liyanage MN, Kottachchi D, Dassanayake AS, de Silva HJ. One-hour fast for water and six-hour fast for solids prior to endoscopy provides good endoscopic vision and results in minimum patient discomfort. *J Gastroenterol Hepatol* 2009; 24: 1095-1097.
3. Teh JL, Tan JR, Lau LJ, Saxena N, Salim A, Tay A, *et al.* Longer examination time improves detection of gastric cancer during diagnostic upper gastrointestinal endoscopy. *Clin Gastroenterol Hepatol* 2015; 13: 480-487.
4. Guarner J, Herrera-Goepfert R, Mohar A, Smith C, Schofield A, Halperin D, *et al.* Diagnostic yield of gastric biopsy specimens when screening for preneoplastic lesions. *Hum Pathol* 2003; 34: 28-31.
5. Dinis-Ribeiro M, Areia M, de Vries AC, Marcos-Pinto R, Monteiro-Soares M, O'Connor A, *et al.* Management of precancerous conditions and lesions in the stomach (MAPS): guideline from the European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter Study Group (EHSG), European Society of Pathology (ESP), and the Sociedade Portuguesa de Endoscopia Digestiva (SPED). *Endoscopy* 2012; 44: 74-94.
6. Correa P. A human model of gastric carcinogenesis. *Cancer Res* 1988; 48: 3554-3560.
7. Dinis-Ribeiro M, da Costa-Pereira A, Lopes C, Lara-Santos L, Guilherme M, Moreira-Dias L, *et al.* Magnification chromoendoscopy for the diagnosis of gastric intestinal metaplasia and dysplasia. *Gastrointest Endosc* 2003; 57: 498-504.
8. Fukuta N, Ida K, Kato T, Uedo N, Ando T, Watanabe H, *et al.* Endoscopic diagnosis of gastric intestinal metaplasia: a prospective multicenter study. *Dig Endosc* 2013; 25: 526-534.
9. Kono Y, Takenaka R, Kawahara Y, Okada H, Hori K, Kawano S, *et al.* Chromoendoscopy of gastric adenoma using an acetic acid indigocarmine mixture. *World J Gastroenterol* 2014; 20: 5092-5097.
10. Uedo N, Ishihara R, Iishi H, Yamamoto S, Yamamoto S, Yamada T, *et al.* A new method of diagnosing gastric intestinal metaplasia: narrow-band imaging with magnifying endoscopy. *Endoscopy* 2006; 38: 819-824.
11. Osawa H, Miura Y, Takezawa T, Ino Y, Khurelbaatar T, Sagara Y, *et al.* Linked Color Imaging and Blue Laser Imaging for Upper Gastrointestinal Screening. *Clin Endosc* 2018; 51: 513-526.
12. Dohi O, Yagi N, Naito Y, Fukui A, Gen Y, Iwai N, *et al.* Blue laser imaging-bright improves the real-time detection rate of early gastric cancer: a randomized controlled study. *Gastrointest Endosc* 2019; 89: 47-57.

Superficial gastric cancers: how macro- or microscopic mucosal analysis can guide endoscopic treatment

Gabriel Rahmi, HEGP, Paris

Introduction

Stomach cancer is the fourth most common cancer in men and the fifth most common cancer in women. It represents the 3rd cause of death from cancer. About 950,000 new cases are reported per year. The challenge is to diagnose this cancer at the earliest stages. Indeed, while the overall prognosis for gastric adenocarcinoma is very poor, with 25% survival at 5 years, the so-called early or superficial forms can be treated curatively and are associated with 95% survival at 5 years. Superficial cancers are defined by invasion that is limited to the mucosa or to the superficial part of the submucosa. They represent approximately 5 to 10% of gastric adenocarcinoma. Digestive endoscopy has a crucial role in the detection of these superficial forms. The use of new technologies such as high-definition imaging, electronic chromoendoscopy and optical zoom are powerful tools for the recognition and characterisation of superficial cancers, enabling better therapeutic management of these tumours.

How to optimise the detection of superficial cancers?

The latest generation endoscopes enable the acquisition of high definition images of the gastric cavity. The basic principles for optimal exploration of the stomach, detailed in the previous chapter, must be respected. A superficial cancer can be visible in the form of a sessile lesion (stage 0-Is of the Paris classification) or less commonly in the form of a pedunculated polyp (0-Ip). Flat lesions (0-IIa, 0-IIb or 0-IIc) are the most difficult to diagnose and should be looked for with minimal breathing. Mucosal inspection can be optimised by using a surface dye, such as indigo carmine. However, electronic chromoendoscopy is the procedure that helps in the detection of areas suspected of cancer. A prospective study carried out on 350 patients evaluated the performance of Blue Light Imaging (BLI- Eluxeo system, Fujifilm) for diagnosing superficial gastric cancer (1). The analysis was done using white light, followed by BLI before performing biopsies on areas suspected of cancer (irregularity of the vascular or glandular architecture and/or raised areas). A total of 127 lesions were analysed. Diagnostic accuracy (92% vs. 71%), sensitivity (93% vs. 46%) and specificity (91% vs. 80%) were significantly higher when the analysis was done using BLI compared to white light. These results are comparable to those obtained with the NBI (Olympus) (another electronic chromoendoscopy system).

The Linked Color Imaging mode (LCI- Eluxeo system, Fujifilm) plays a beneficial role in the detection of superficial cancers (2). A recent study compared the color intensity ratio between the visible lesion and the adjacent normal gastric mucosa. The analysis was performed on 43 lesions, first using white light then with BLI and LCI. The ratio was significantly higher (significant difference in color between the lesion and the adjacent mucosa) with LCI. Superficial

cancers appeared as redder areas surrounded by pale mucosa. The improvement in the visibility of gastric cancers using the LCI mode was also shown in another study based on the retrospective analysis of 82 images using white light, BLI or LCI (3). For each image, a number of improvement points (or negative points) were assigned by expert or non-expert endoscopists. Compared to white light and BLI, only the LCI mode significantly increased the visibility of the lesion, regardless of the reader's level of expertise. These results were independent of possible Helicobacter pylori infection.

Once the area suspected of cancer is detected, how should it be analysed?

When an area suspected of cancer is detected, it must firstly be characterised, that is to say its histological nature and its depth of invasion need to be predicted. Secondly, it needs to be precisely delimited. The latest generation endoscopes have the option of using high optical magnification (Multi Zoom 135x function, Fujifilm) by simply pressing a button on the handle. The two parameters that need to be analysed are glandular architecture and microvascularisation (Figure 1). Unlike normal gastric mucosa, where the glands are regular ("honeycomb-like" shape in the fundus or "springs" in the antrum), cancerous areas are the site of architectural disorganisation of various degree. The surface is irregular, sometimes smooth, suggestive of deep invasion.

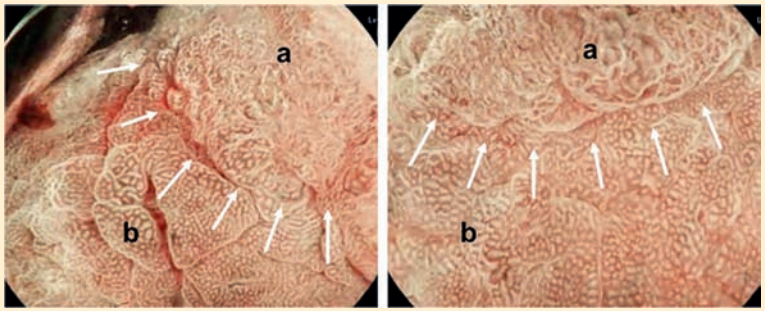


Figure 1: Demarcation line between an area suspected of cancer (a: irregular surface and irregular microvessels) and an area of normal gastric mucosa (b: regular appearance of the glands, rounded in a "honeycomb-like" pattern evocative of a fundic localisation, and regular microvessels).

Regarding microvascularisation, an irregularity of the vessels, dilation or complete disappearance in depressed areas should be looked for. These two parameters must be taken into account to demarcate the lesion for endoscopic resection (mucosectomy or submucosal dissection). The Japanese authors have described the "VS" classification, which combines three criteria: (i) the presence of a demarcation line between healthy mucosa and pathological mucosa, (ii) an irregular surface and (iii) irregular microvessels (Figure 2). In a study of 417 superficial gastric adenocarcinomas, expert endoscopists and beginners looked for these three criteria in images obtained using white light or BLI + zoom (4). The evaluation by the experts showed the

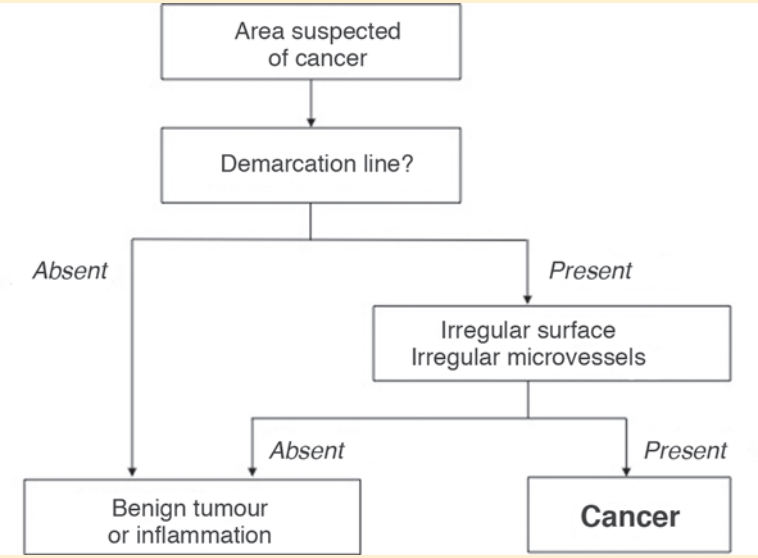


Figure 2: Algorithm for the diagnosis of superficial gastric cancers using electronic chromoendoscopy and high optical zoom. The three criteria (demarcation line, irregular surface and microvessels) must be present to support the diagnosis of cancer.

presence of a demarcation line in 99% of the cases, an irregular surface in 96% of the cases and an irregular microvascularisation in 96% of the cases with a good inter-observer agreement (the results were comparable in the beginners group).

Prior eradication of Helicobacter pylori made it more difficult to visualise this demarcation line. This could be explained by a change in the shape of the cancer, becoming flatter and being partially replaced with non-neoplastic epithelium. Moreover, the delimitation of poorly or undifferentiated cancers was more difficult because the transition zone between regular and irregular structures was less clear. These results are in agreement with those published on the NBI mode with zoom, when used to delimit cancers, which showed a sensitivity of 95%, a specificity of 97% and a diagnostic accuracy of 97% (5).

What is the optimal endoscopic treatment for superficial gastric cancers?

Thanks to the advances in endoscopic techniques, such as endoscopic submucosal dissection (ESD), resection of superficial gastric cancers now represents the first line treatment, without any size limit.

ESD has many advantages compared to surgical treatment, notably the maintenance of organ integrity and function, lower morbidity and mortality, shorter hospital stay and lower cost. The objective of endoscopic treatment is to perform a curative R0 monobloc resection. This means obtaining histologically healthy lateral and deep margins, a well differentiated lesion, minimal depth of invasion, absence of tumour budding and absence of lymphovascular emboli (Figure 3). The depth of invasion should not go beyond the mucosa (risk of lymph node invasion < 1%), or if the submucosa is invaded (risk < 3%) the extent should

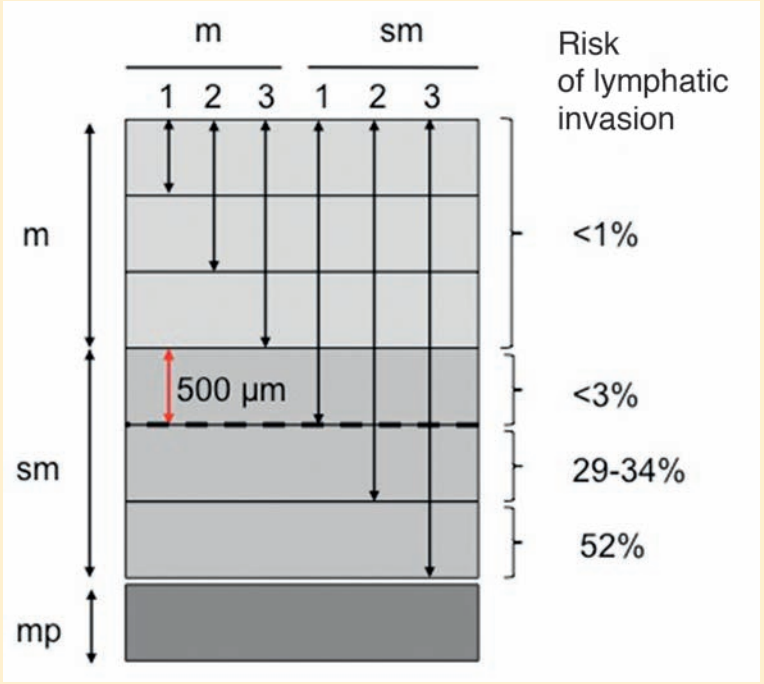


Figure 3: Risk of lymph node invasion depending on the depth of infiltration of the cancer. Resection is not curative when the invasion exceeds the dashed line, that is to say reaching the submucosa over more than 500 µm).

be as small as possible, of less than 500 µm. The two main techniques for endoscopic resection are endoscopic mucosal resection (EMR) and ESD. The advantages of EMR are its low cost and short procedure time. On the other hand, the arguments which will make ESD preferable are: (i) a monobloc resection rate of almost 100%, (ii) an optimal histological analysis and (iii) very low local recurrence rate (compared to about 30% for EMR). According to European recommendations, EMR is indicated for differentiated cancer of less than 10 mm in size. For all other non-ulcerated lesions and for any undifferentiated lesions, ESD should be selected (6). When a lesion is ulcerated, a resection by ESD can be considered if the lesion is less than 30 mm in size. When the resection is curative, long-term endoscopic monitoring should be proposed to the patient because the risk of metachronous gastric cancer is around 6% at 5 years. It is recommended that an endoscopy should be performed at 6 months, 12 months and then annually with systematic chromoendoscopy.

Conclusion

The use of new generation endoscopes combined with the development of minimally invasive endoscopic techniques provides optimal management of superficial gastric cancers. The indications for resection must be well defined and complex cases must be referred to expert centers. This management is done in collaboration with oncologists, surgeons and pathologists. Endoscopic follow-up of these patients is essential to diagnose possible recurrence or metachronous cancer.

References

1. Dohi O, Yagi N, Yoshida S, Ono S, Sanomura Y, Tanaka S, *et al.* Magnifying Blue Laser Imaging versus Magnifying Narrow-Band Imaging for the Diagnosis of Early Gastric Cancer: A Prospective, Multicenter, Comparative Study. *Digestion* 2017; 96 (3): 127-134.
2. Kanzaki H, Takenaka R, Kawahara Y, Kawai D, Obayashi Y, Baba Y, *et al.* Linked color imaging (LCI), a novel image-enhanced endoscopy technology, emphasizes the color of early gastric cancer. *Endosc Int Open* 2017 Oct; 5 (10): E1005-E1013.
3. Yoshifuku Y, Sanomura Y, Oka S, Kurihara M, Mizumoto T, Miwata T, *et al.* Evaluation of the visibility of early gastric cancer using linked color imaging and blue laser imaging. *BMC Gastroenterol* 2017 Dec 8; 17 (1): 150.
4. Yoshifuku Y, Sanomura Y, Oka S, Kuroki K, Kurihara M, Mizumoto T, *et al.* Clinical Usefulness of the VS Classification System Using Magnifying Endoscopy with Blue Laser Imaging for Early Gastric Cancer. *Gastroenterol Res Pract* 2017; 2017: 3649705.
5. Yamada S, Doyama H, Yao K, Uedo N, Ezoe Y, Oda I, *et al.* An efficient diagnostic strategy for small, depressed early gastric cancer with magnifying narrow-band imaging: a post-hoc analysis of a prospective randomized controlled trial. *Gastrointest Endosc* 2014 Jan; 79 (1): 55-63.
6. Pimentel-Nunes P, Dinis-Ribeiro M, Ponchon T, Repici A, Vieth M, De Ceglie A, *et al.* Endoscopic submucosal dissection: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2015 Sep; 47 (9): 829-854.

Towards a better endoscopic characterisation of gastric lesions: future perspectives

Yoshiko Nakano[1], Takashi Toyonaga[2], Yoshinori Morita[1], Eiji Umegaki[1], Yuzo Kodama[1], [1] Division of Gastroenterology, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan, [2] Department of Endoscopy, Kobe University Hospital, Kobe, Japan

Introduction

The stomach can be the site of numerous lesions, such as acute and chronic gastritis, ulcers, cancers, dysplasias (adenomas), non-neoplastic polyps, such as hyperplastic polyps and glandulocystic fundic polyps, tumour metastases, lymphomas (mucosa-associated lymphoid tissue – MALT – lymphoma), submucosal tumours, Menetrier's disease, gastric varices, angiodysplasias and vascular ectasias (gastric antral vascular ectasia – GAVE), viral infections... to name but a few examples.

For some of these lesions, Helicobacter pylori (H. pylori) infection plays a pathogenic role; this is the case for chronic gastritis, ulcer disease, adenocarcinomas, dysplasias, hyperplastic polyps and MALT lymphomas. These pathologies are mainly attributable to H. pylori infection. It is therefore important to know how to recognise the presence of an H. pylori infection in order to determine the risk of such lesions occurring.

Endoscopic appearance of the gastric mucosa with or without H. pylori infection

Certain endoscopic aspects of the gastric mucosa are fairly representative of H. pylori infection; this may include atrophic changes, hyperplasia with diffuse erythema, giving the mucous membrane a rough appearance, oedema, spotty appearance made of erythematous spots, exudate, and features suggestive of intestinal metaplasia or hyperplastic polyps [1] (Figure 1). Nodular gastritis, characterised by the presence of small protrusive lesions whose antral distribution is fairly uniform is mainly seen in young women; it is considered to be an indicator of H. pylori infection. This type of gastritis is associated with the risk of diffuse gastric cancer.

On the other hand, in the absence of H. pylori infection, the gastric mucosa does not have an atrophic appearance, the venous network is regularly arranged, erythematous streaks are sometimes present, as well as hemorrhagic zones, and glandular fundic polyps [1] (Figure 1).

Because the eradication of H. pylori decreases the risk of gastric cancer, the Kyoto global consensus on H. pylori-induced gastritis recommends the eradication of the bacteria in infected patients, apart from a few exceptions related to co-morbidities, or to significant risk of reinfection in the community where the patient lives, or because of public health priorities, especially financial ones. In Japan, the cost of eradication of H.pylori has been covered by health insurance since 2013. Meanwhile, the number of patients that have undergone H. pylori eradication has been increasing. After eradication, the endoscopic appearance changes with erythema images showing the presence of regular venous networks and glandular fundic polyps with mucosal atrophy.

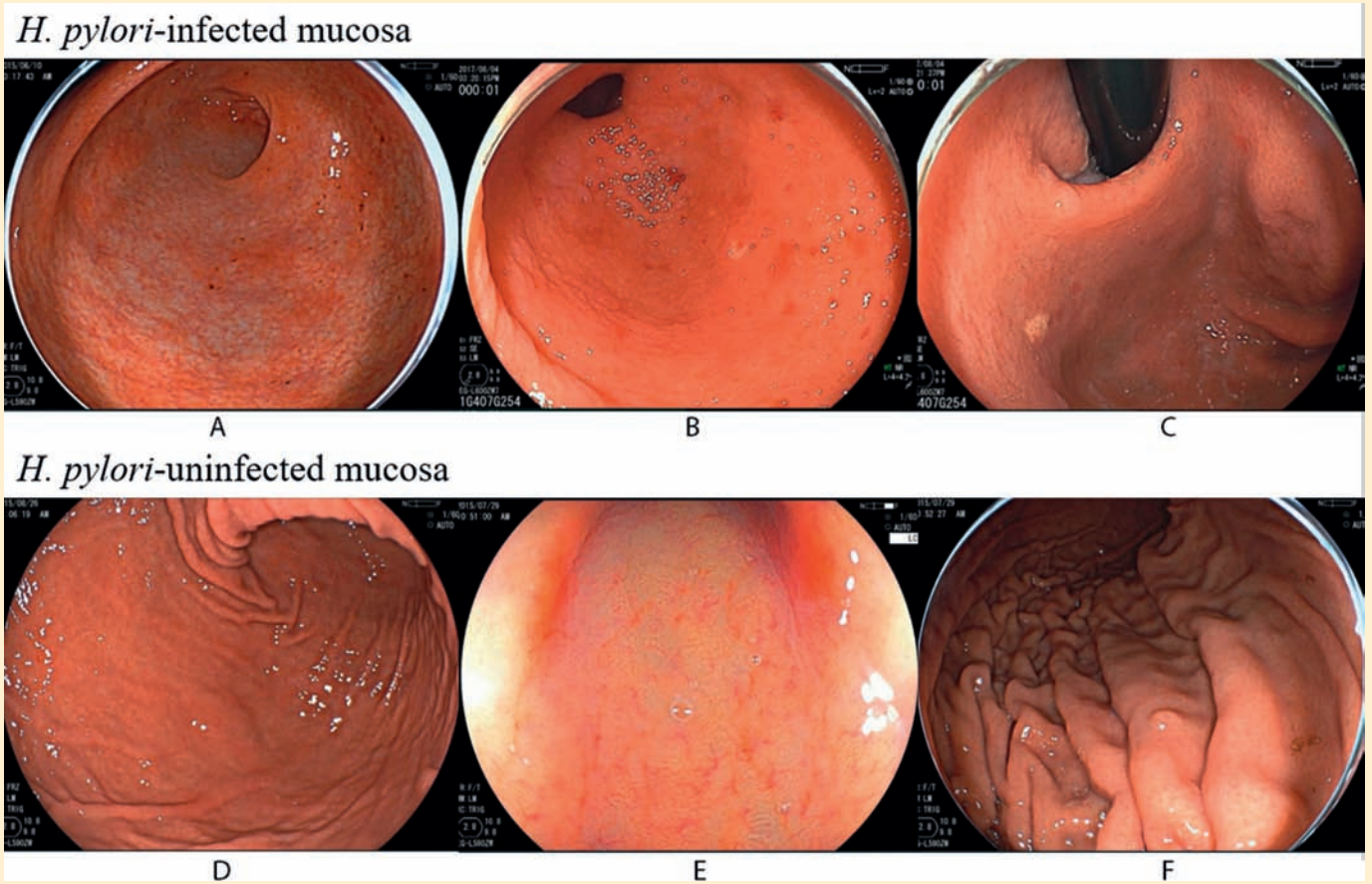


Figure 1: Endoscopic appearance of a mucosa with or without H. pylori infection. A) Atrophic antral mucosa. B) Reddish spotting and presence of a xanthoma. C) Atrophy and presence of a cardial xanthoma. D) Non-atrophic gastric mucosa. E) Regular arrangement of the venous network. F) Glandular fundic polyps.

Recent advances in techniques using high optical magnification have made it possible to analyse the vascular network of the mucosal surface. These techniques make it possible to reliably diagnose the presence of gastritis linked to H. pylori. In this analysis the venous networks can be regular, irregular or absent [2] (Figure 2). Regular appearance is associated with the absence of H. pylori infection, while irregular appearance or absence of venous network are histopathological markers of gastritis and H. pylori infection. In addition, irregular appearance suggests the existence of significant atrophy of the gastric mucosa.

Initial endoscopic detection and characterisation of gastric cancer

Gastric cancer is the fifth most common cancer type in the world. The detection of this cancer endoscopically at an early stage is important to assure better prognosis for the patient. This implies the early detection and characterisation of these cancers, often called "early gastric cancers" (EGC) in the English language literature. A standardised systematic screening protocol has been proposed by Yao *et al.*, which involves obtaining quadrant photographs either

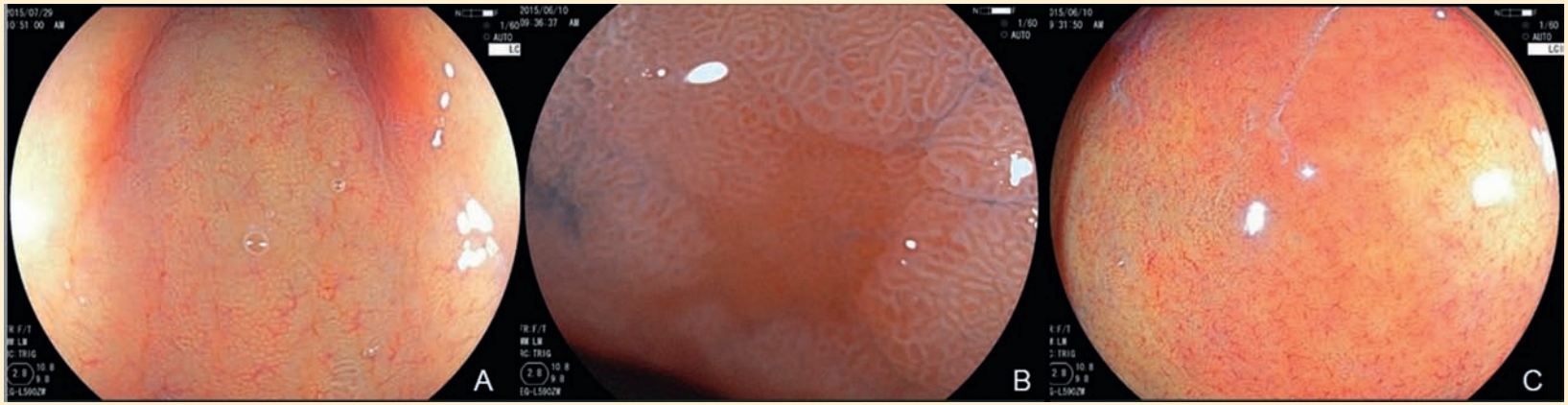


Figure 2: Endoscopic view with optical magnification showing: A) a regular venous network (regular pattern); B) the absence of visible venous network (obscured pattern); C) an irregular venous network (irregular pattern).

clockwise or counterclockwise depending on the order of the different stages of the procedure [3] (Figure 3).

Using this method, it is relatively easy to uncover the presence of sessile or pedunculated (0-I) or ulcerated (0-III) lesions by conventional white light endoscopy (C-WLI) and chromoendoscopy (CE). On the other hand, flat lesions (0-II) are sometimes more difficult to detect because they resemble foci of chronic gastritis. However, EGCs often have an irregular coloring and surface pattern, and well-defined edges which distinguish them from simple gastritis (Figure 4).

However, it is still difficult to diagnose small, depressed or flat cancerous lesions, and therefore the use of new imaging techniques is necessary to identify these "subtle" mucosal lesions. Blue Laser Imaging (BLI-Fujifilm)[1] is a system which enables illumination in a narrow field of the light spectrum thanks to two monochromatic lasers (410 and 450 nm); it enhances very small changes in the surface mucosa.

Both microvascular (MV) and microsurface (MS) architectural patterns can be analysed using BLI with high magnification. The MV pattern corresponds to the subepithelial capillary network and the MS pattern corresponds to the presence of glandular crypts on the surface (marginal crypt epithelium (MCE)) at their opening and the mucosal bridges connecting them. MV and MS patterns are classified into 3 types: regular, irregular and absent [3] (Figure 5). The regular MV pattern corresponds to mucosal capillaries of uniform size, shape, and morphology, distributed in a symmetrical and regular manner. The irregular MV pattern is characterised by tortuous, branched or oddly shaped vessels; their morphology is heterogeneous, their distribution asymmetrical and their organisation irregular. The absence of the MV pattern means that the subepithelial MV network is masked by a white opaque substance (WOS) present on the surface of the mucosa. In the regular MS pattern, the crypts are uniform (linear/curved/oval/circular), with homogeneous morphology, symmetrical distribution and regular organisation.

In the irregular MS pattern, the marginal crypt epithelium (MCE) is an irregular structure of heterogeneous morphology, asymmetric distribution and irregular organisation.

In the absent MS pattern, neither the MCE nor the WOS are visible. Yao *et al.* propose to use two criteria for the diagnosis of EGC: (i) the presence of an irregular MV pattern and clear delimitation and/or (ii) an irregular MS pattern and clear delimitation. If one of these two criteria is present, the endoscopic diagnosis of gastric cancer can be made [4] (Figures 4, 6). Of course, in clinical practice, the performance of a biopsy remains necessary to definitively ensure

1. This is the first generation of BLI systems. Currently the acronym BLI stands for Blue Light Imaging (without laser).

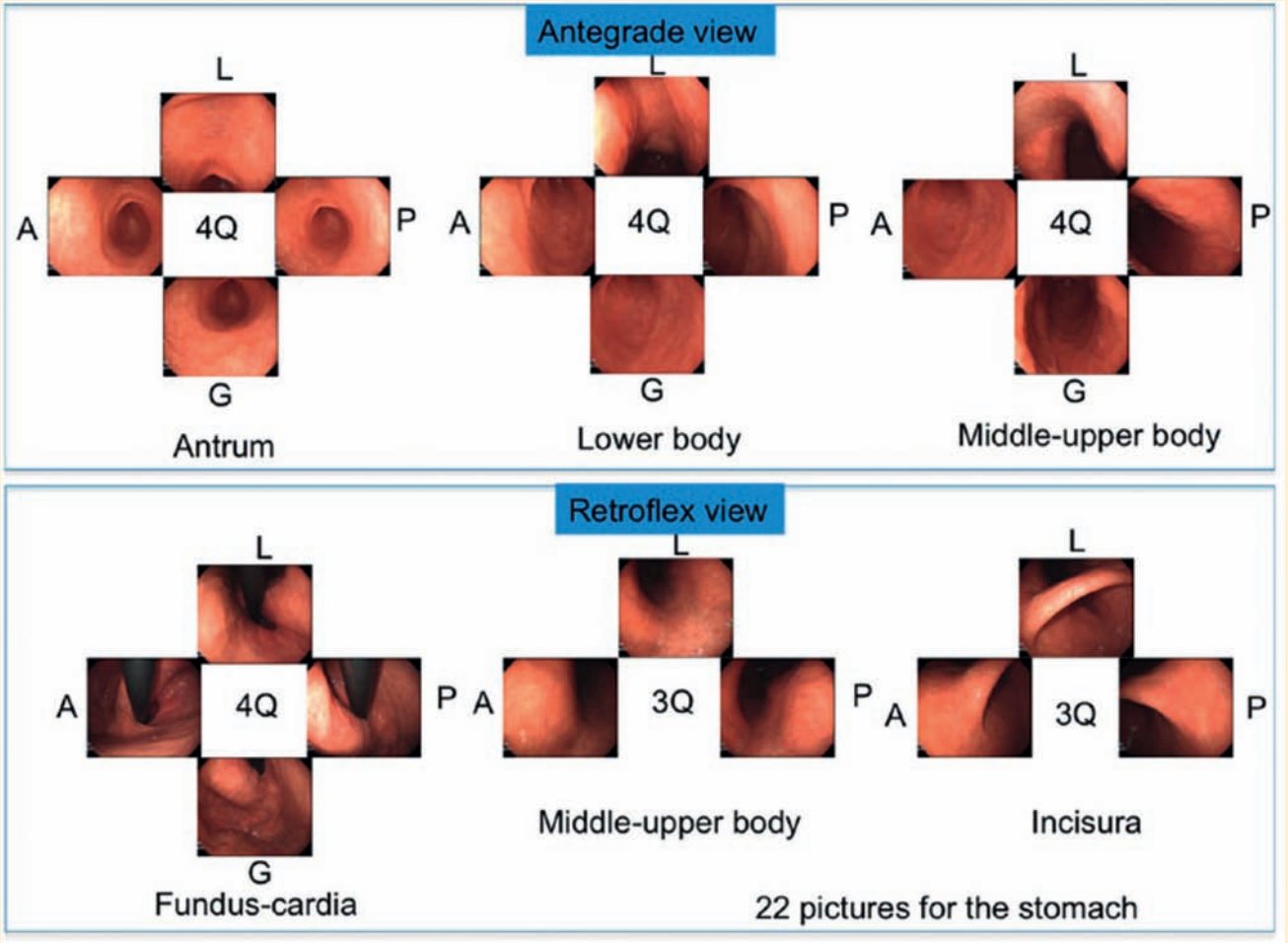


Figure 3: Screening of the stomach by systematic photodocumentation.

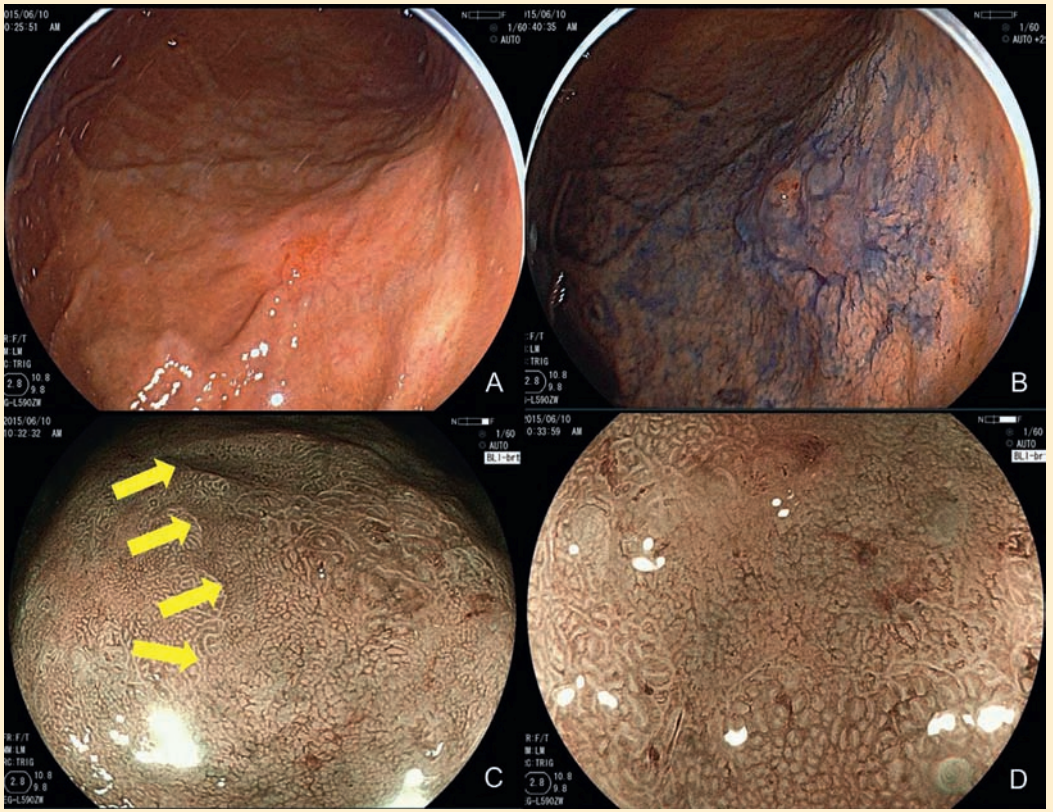


Figure 4: Type 0-IIc superficial cancer (early gastric cancer, EGC). A) Appearance using endoscopic white light (conventional white-light imaging or C-WLI) of an EGC 0-IIc of the middle part of the gastric body; note the reddish and depressed appearance of the lesion with irregular borders and convergence of the mucosal folds. B) Indigo carmine staining of the lesion, with sharper boundaries. C, D) Irregular MV pattern using the BLI mode. Note the visualisation of the fine vascular network using optical magnification and the BLI mode; the lesion boundaries are sharper (arrows).

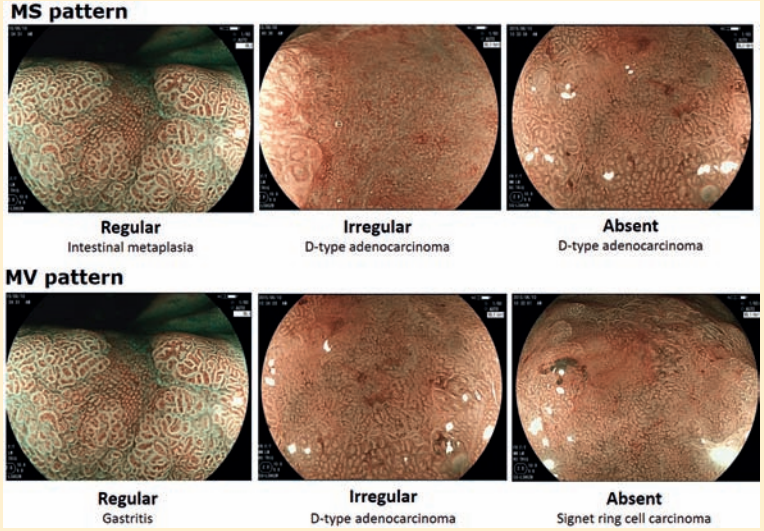


Figure 5: Classification of the different microvascular (MV) and microsurface (MS) patterns.

the diagnosis, document the histological type, and choose the appropriate therapeutic strategy.

Indications of endoscopic submucosal dissection (ESD)

According to the fifth version of the Japanese recommendations regarding the treatment of gastric cancers (JGCT)

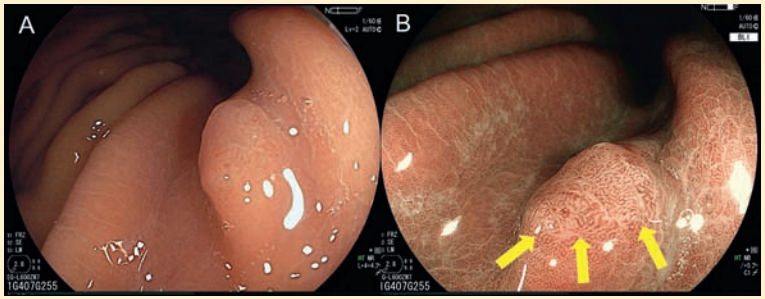


Figure 6: Superficial cancer (early gastric cancer, EGC) of the type 0-IIa A) Endoscopic appearance using conventional white light (C-WLI) of an EGC0-IIa in the middle part of the gastric body. B) Irregular MV pattern using the BLI mode and optical magnification. Note the clear delimitation of the lesion (arrows).

guidelines (2018), an ESD for EGC is indicated in the case of differentiated adenocarcinoma, detected at the intramucosal stage and in the absence of ulceration UL(-), or presence of ulceration UL(+) if the diameter of the lesion is less than 3 cm. The indication can be extended to undifferentiated adenocarcinomas, UL(-) of less than 2 cm in diameter. Thus, the choice between ESD and surgery requires a rigorous evaluation of the histological type, the depth of the tumour, the size of the lesion, and evaluation of whether ulceration is present or not.

Endoscopic appearance based on histological type (differentiated or undifferentiated)

Endoscopy alone is not sufficient to predict the histological type of an EGC. However, to some extent, endoscopic data may prove useful. Generally, differentiated cancers (D-type) develop on an atrophic mucosa of the gastric body and the antrum. They are often reddish and depressed/raised or, on the contrary, white, flat and raised. Conversely, undifferentiated cancers (UD-type) develop on a non-atrophic lining of the large curvature of the stomach body, and often have a "washed out" and depressed appearance. Yokoyama *et al.* have established a classification of MV patterns and irregularities of the superficial glandular structures into four categories; (i) fine-network pattern or (FNP) characterised by small glandular orifices opening on the mucosal surface and associated with an abnormal MV mesh structure surrounding each glandular well, (ii) corkscrew pattern (CSP), with the disappearance of almost all glandular structures and the presence of numerous abnormal corkscrew-like vessels, (iii) the "intra-lobular loop type 1" pattern (ILL-1) characterised by glandular structures with a villous appearance and containing "looped" microvessels, and (iv) the "intra-lobular loop type 2" pattern (ILL-2), with partial rupture of the villous structures [5] (Figure 7). These authors showed that in type D adenocarcinomas, the FNP, ILL-1, ILL-2 and CSP phenotypes were present in 15.7%, 59.6%, 24.2% and 0.5% of cases, respectively [5]. In addition, in UD-type adenocarcinomas, the ILL-2 and CSP phenotypes were present in 41.2% and 58.8% of cases, respectively. These markers could therefore be useful for assessing the histological type of these cancers.

Depth of tumour invasion

Yao *et al.* showed that a deep extension should be suspected when one of these two criteria is present: (i) significant tumour protrusion; or (ii) a convergence of the mucosal folds with an elevation. The sensitivity and specificity of this criterion for the diagnosis of submucosal invasion were 90.5% and 68.5%, respectively [6].

Abe *et al.* have shown that the presence of a tumour of more than 30 mm in size, reddish in appearance, with an irregular surface, with raised edges, was significantly associated with deep invasion of the submucosa [7]. These data are therefore useful for predicting tumour depth extension.

In a similar way to endosonography being useful for the evaluation of the degree of tumour invasion, widening the indications of ESD, Okada *et al.* showed that the diagnostic accuracy of endoscopy was 87.8% (259/295) in the case of D type adenocarcinoma with a diameter of less than or equal to 30 mm, and 43.5% (10/23) for D type tumours larger than 30 mm, and 75% (42/56) for UD type tumours with a diameter of less than or equal to 20 mm [8]. In a multivariate analysis, the diagnostic accuracy of endosonography, in terms of predicting the depth of invasion, was significantly

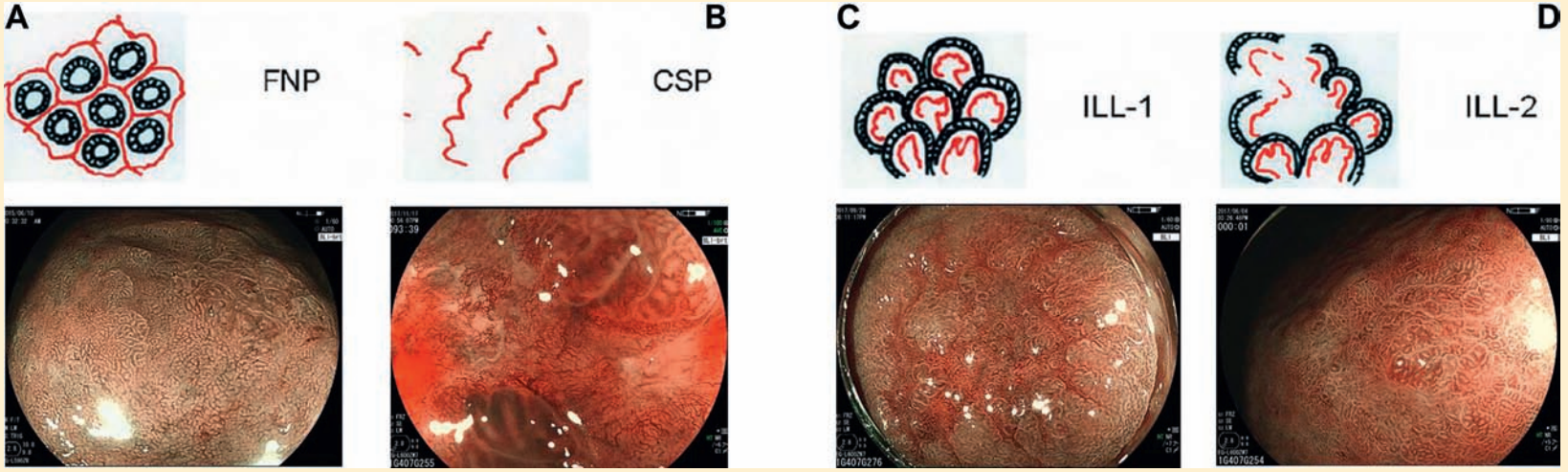


Figure 7: Classification of different types of abnormal microvascular patterns (MV) and irregularities in the glandular surface structures. A) Fine network pattern (FNP). B) Corkscrew pattern (CSP). C) Intralobular Loop Pattern 1 (ILL-1). D) Intralobular Loop Pattern 2 (ILL-2).

reduced in the presence of ulceration or when the tumour diameter was ≥ 30 mm.

Presence or absence of ulceration

The diagnosis of ulceration (UL) is made in the presence of an active ulceration covered with a thick whitish exudate in the active phase or in the case of a convergence of the mucous folds during the healing stage.

Lateral extension

To completely resect an EGC with ESD, it is essential to accurately determine the lesion boundaries. Although it is possible to define the edges of the tumour satisfactorily using white light or using chromoendoscopy, certain situations remain difficult in particular for 0-IIb type lesions after eradication of H. pylori. In these cases, the use of high optical magnification contributes to an improvement in the demarcation of the tumour margins as a whole.

In summary, better characterisation of EGCs requires careful consideration in order to detect minimal changes. Then, it is necessary to specify whether the lesion is malignant or not, and in the case of cancer it is necessary to determine the histological type, the size, the depth of invasion, the presence of ulceration. Finally it is also necessary to carefully identify the tumour boundaries.

The precise detection and characterisation of an EGC make it possible to propose an endoscopic resection to the patient for curative purposes, thus avoiding invasive surgery, leading to reduced mortality from gastric cancer.

Future perspectives

Endocytoscopy

Endocytoscopy is a new technology enabling very high magnification. It makes it possible to distinguish between gastritis, atrophy, intestinal metaplasia, and in general distinguish between normal and neoplastic tissue [9]. It is a promising tool for the performance of virtual biopsies.

Artificial intelligence (computer-aided diagnosis)

The term artificial intelligence designates a system based on neural computer networks, enabling in-depth self-learning; it can thus automatically detect gastric cancer from endoscopic images. It can process many endoscopic images in a very short period of time; its sensitivity for detecting EGC appears to be very high [10]. This technology, which is applicable to current practice, will in the future lead to a reduction in the workload of endoscopists.

Conclusion

It is important to recognise the endoscopic appearance of the gastric mucosa in the presence or absence of an H. pylori infection, as well as the appearance of the mucosa that is suggestive of EGC. EGC can be treated curatively by ESD. Achieving this goal involves careful examination of the stomach in order to detect small lesions, thereby providing the patient with a treatment less invasive than surgery. The recent introduction of new endoscopic technologies, that combine high optical magnification and better image analysis, are improving the efficacy of the diagnosis of gastritis and EGC. These new endoscopic technologies will be useful for better detection of mucosal anomalies and for accurate characterisation of gastric lesions.

References

1. Sugano K, Tack J, Kuipers EJ, *et al.* Kyoto global consensus report on Helicobacter pylori gastritis. *Gut* 2015; 64: 1353-1367.
2. Nakagawa S, Kato M, Shimizu Y, *et al.* Relationship between histopathologic gastritis and mucosal microvascularity: observations with magnifying endoscopy. *Gastrointest Endosc* 2003; 58: 71-75.
3. Yao K, Nagahama T, Matsui T, *et al.* Detection and characterization of early gastric cancer for curative endoscopic submucosal dissection. *Dig Endosc* 2013; 25 Suppl 1: 44-54.
4. Yao K. The endoscopic diagnosis of early gastric cancer. *Ann Gastroenterol* 2013; 26: 11-22.
5. Yokoyama A, Inoue H, Minami H, *et al.* Novel narrow-band imaging magnifying endoscopic classification for early gastric cancer. *Dig Liver Dis* 2010; 42: 704-708.
6. Yao T, Tanabe. H, Nagahama. T, *et al.* Clinicopathological study for accurate endoscopic diagnosis of submucosal invasion by early cancer of depressed type. *Stom Intest (Tokyo)* 2008; 43: 1109-1125.
7. Abe S, Oda I, Shimazu T, *et al.* Depth-predicting score for differentiated early gastric cancer. *Gastric Cancer* 2011; 14: 35-40.
8. Okada K, Fujisaki J, Kasuga A, *et al.* Endoscopic ultrasonography is valuable for identifying early gastric cancers meeting expandedindication criteria for endoscopic submucosal dissection. *Surg Endosc* 2011; 25: 841-848.
9. SatoH, InoueH, HayeeB, *et al.* In vivo histopathology using endocytoscopy for non-neoplastic changes in the gastric mucosa: a prospective pilot study (with video). *Gastrointest Endosc* 2015; 81: 875-881.
10. Hirasawa T, Aoyama K, Tanimoto T, *et al.* Application of artificial intelligence using a convolutional neural network for detecting gastric cancer in endoscopic images. *Gastric Cancer* 2018; 21: 653-660.

Duodenal tumours do exist: we have encountered them!

Xavier Dray, Jérôme Bellanger, Centre d'endoscopie digestive, Sorbonne Université & Hôpital Saint-Antoine, Paris

Introduction

The probability of finding a duodenal tumour (benign or malignant) during an oesogastroduodenal endoscopy (OGDE) is not negligible (of the order of 5%). These lesions are often discovered unexpectedly during an examination carried out for another reason. These tumours are in fact sporadic adenomas in 0.5% of the OGDE, located at the ampulla in 0.05 to 0.12% of OGDE. In other words, non-adenomatous lesions (mucosal or submucosal) are not uncommon and immediately raise the question of a differential diagnosis, which is of great importance in the decision of whether or not to abstain from treatment, endoscopic or otherwise.

Less frequently, the discovery of a tumour is made in a guided context. For example in the presence of symptoms, such as dyspepsia, abdominal pain, exteriorised digestive hemorrhage or anemia, nausea or vomiting. This can take place during screening, in a context of identified polyposis.

In this update, we describe the semiology of the polyps and duodenal cancers most often encountered. The therapeutic approach to these lesions is briefly discussed. For more detail we refer the reader to recent reviews of the literature (1-4).

How to handle a duodenal tumour?

Certain anatomical features of the duodenum can make it difficult to detect, characterise and treat the tumours found there: narrow lumen, the presence of bile and bubbles, intestinal contractions, a natural tendency to form a loop along the large gastric curvature, the frequent hyperplastic appearance of the Brunner's glands in the bulb, a thin muscularis (which increases the risk of perforation), great vascular supply (which increases the risk of haemorrhage), proximity to the duodenal papilla (which increases the risk for pancreatitis), the high frequency of diverticula on the inner side of the second duodenum. These difficulties can lead to the referral of the patient to an expert center, sometimes soon after the discovery of the lesion.

In these circumstances, the use of high definition systems (endoscopes, processors, screens, cables, etc.) cannot be over-recommended. In addition to the gastroscope, the joint use of a side-viewing duodenoscope, a colonoscope (possibly with variable stiffness) or even an enteroscope may prove useful. The magnification (zoom) and chromoendoscopy options, real staining (indigo carmine in particular) or virtual staining (depending on the system used), are essential, in particular at the characterisation stage.

These staining techniques, real or virtual, are all the more important in the duodenum since the contours of a villous or tubulo-villous adenoma (with a villous surface appearance) are less distinct within a duodenal mucosa that itself contains villi, compared to a colonic surface that does not contain villi. Other devices must be available and are often used: anti-bubble (Simethicone for example), antispasmodics,

short and transparent cap. The tattooing of a tumour should only be considered in the event of difficult identification, and always at a distance from the lesion so as not to promote the development of submucosal fibrosis which would significantly complicate its resection. Echoendoscopic evaluation of the submucosa and its connection to the bile ducts and pancreas is sometimes essential before considering attempting endoluminal treatment.

The description of a duodenal tumour should include its size, its precise location and in particular its relationship to the major and minor papillae, as well as its mucosal or submucosal character. Superficial mucosal tumours should be described according to the Paris classification, which provides decision-making information on possible endoscopic resectability. The Kudo and Sano classifications, that have to date been better assessed for colonic lesions, facilitate the description of the surface of the crypts (pit pattern) and vessels (vascular pattern) in a standardised way in order to predict the invasive (and therefore possibly resectable) character of the mucosal tumours. Overall, indented (Paris0-IIc) or ulcerated (0-III) tumours, pulling in or retracting the mucosal folds and/or those with clear disorganisation, or even the loss of the pit/vascular pattern have a high probability of having a deep sub-mucosal extension, and possibly lymph node extension. These features contraindicate endoscopic resection. The challenges of a possible endoscopic or surgical resection must of course be compared with the clinical context and the patient's comorbidities.

Different types of sporadic duodenal tumours can be identified. The most frequent ones are presented in Table 1. They are roughly divided into submucosal tumours and mucosal tumours. Rare duodenal lymphomas will not be detailed here.

Submucosal tumours

1. Lipomas

Duodenal lipomas are rare. However, they represent 3 to 15% of benign small bowel tumours. Within the small intestine, it is estimated that a quarter are located in the duodenum, another quarter in the jejunum, and the other half in the ileum. They are often asymptomatic (especially when they are of less than 20 mm in size) and are therefore discovered incidentally.

Their characteristic appearance is that of a round, soft tumour of yellowish tinge, isolated, and very slow growing. They are typically sessile, but can be pedunculated. They are also recognised by a "pillow sign", i.e. the formation of a depression when palpating the top of the lesion with a closed biopsy forceps or any other non-traumatic instrument. When in doubt, the fatty components of the lipoma are easily recognisable by endosonography and sectional imaging (CT scan). These lesions are benign. They do not

Table 1: Most common sporadic duodenal tumours.

Type of tumour	Malignant potential	Indication for treatment
Submucosal tumours		
Lipoma	No	Presence of symptoms (rare) : fenestration
Hemangioma	No	Presence of symptoms (common): destruction
Lymphangioma	No	Presence of symptoms or diagnostic doubt : surgery
Leiomyoma	No	Presence of symptoms or diagnostic doubt : surgery
Stromal tumour (GIST)*	Yes	Yes, often surgical resection, sometimes endoscopic for small lesions
Neuroendocrine tumour	Yes	Yes, often surgical resection, sometimes endoscopic for small isolated lesions
Mucosal tumours		
Brunner's hamartoma	No	Presence of symptoms (rare) : endoscopic resection
Peutz-Jeghers polyp (isolated)	Yes	Yes : endoscopic resection
Adenoma	Yes	Yes : endoscopic resection

* Gastrointestinal stromal tumor.

require any treatment when they are asymptomatic. The rare symptomatic lipomas (intestinal obstruction, bleeding by ulceration) can be treated by fenestration using pure cutting current. Indeed, endocut currents are designed for tissues that are high in water (and not high in fat). In fatty tissues, endocut currents are ineffective, requiring prolonged use, thus exposing the tissues to significant overheating and to a high risk of perforation (immediate or delayed). The main differential diagnosis is the rare liposarcoma.

2. Hemangiomas

Hemangiomas are benign tumours made of blood vessels. They are often found in the middle jejunum or the

ileum. They represent up to 0.05% of benign small bowel tumours. They include phlebectasias, cavernous hemangiomas (appearing as polyps, with dilated venules and venous sinuses protruding beneath the mucosa), capillary hemangiomas (small isolated submucosal tumours) or angiomatosis (as in Rendu-Osler disease, with angiodysplasias on the surface, or bluish tumours seen in Bean syndrome or blue rubber nevus syndrome and Klippel-Trenaunay-Weber syndrome). These lesions require treatment only when they are symptomatic (bleeding most often, rarely intussusception or obstruction).

3. Lymphangiomas

Lymphangiomas represent 3% of tumours of the small intestine. They are slow growing benign tumours, very often asymptomatic. For large lesions, hemorrhagic or obstructive complications have been reported in rare cases.

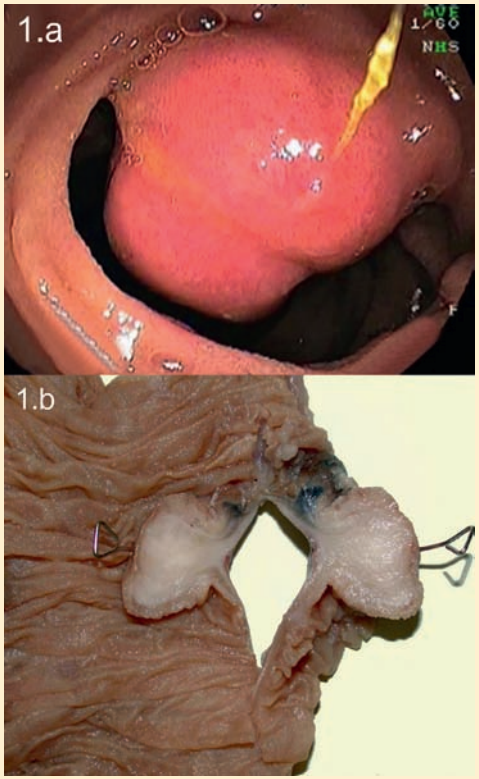
They are classified into 3 anatomopathological categories: (i) capillaries: small, fine, superficial lymphatic dilations; (ii) cavernous: dilated mucosal and submucosal lymphatic vessels, communicating with normal lymphatic vessels; (iii) cystic: lymphatic vessels of variable size, containing a chylous, serous or bloody liquid, without communication with normal lymphatic vessels. The endoscopic distinction between the last two categories is of modest importance, since they both require complete surgical resection allowing formal diagnosis.

4. Leiomyomas

These tumours are benign, typically submucosal, isolated, firm and not very mobile under the forceps, sometimes umbilicated at the top (Figure 1). They are most frequently located in the jejunum, sometimes the ileum, rarely the duodenum. They are uncommon, but relatively more symptomatic than other benign small bowel tumours, due to a higher propensity for ulceration and hemorrhage. They are rarely the cause of obstruction. The main and difficult differential diagnosis is leiomyosarcoma. The submucosal nature of the lesion increases the risk of perforation during endoscopic treatment: a symptomatic or doubtful lesion is most often an indication for surgical resection.

5. Stromal tumours (GIST)

Stromal tumours (or gastrointestinal stromal tumours, GIST) are mesenchymal tumours of the digestive tract and they have the potential for malignant transformation. They are often diagnosed in symptomatic patients. GISTs are derived from Cajal cells, in the muscularis: GIST are classified as submucosal tumours for the purpose of nosological simplification. They can hardly be distinguished from benign leiomyomas by their endoscopic and echoendoscopic location and appearance. Echoendoscopic puncture is therefore often required to achieve a formal diagnosis. Treatment is then most often surgical even if, for small tumours, endoscopic submucosal approaches have been proposed by some experts.



Figures 1a and 1b: Leiomyoma of the 4th duodenum in a 69-year-old woman. Discovery by upper endoscopy of a large polypoid lesion with a wide base. Tattooing. Non-contributory biopsies (non-specific inflammatory changes). Small bowel resection with lymph node dissection by laparoscopic route enabling diagnosis.

6. Neuroendocrine tumours

The current nomenclature no longer recognises the term "carcinoid tumour" for these lesions. Duodenal neuroendocrine tumours form whitish or yellowish nodules, rather immobile and firm during endoscopic palpation, sometimes with an indentation or ulceration of the top. These lesions are often multiple in the duodenal setting, and downstream. A seemingly isolated lesion should be investigated with special attention, in order to check for poorly visible associated lesions, for example by performing a side viewing duodenoscopy and enteroscopy. The diagnostic approach is based on endosonography and repeated biopsies in the same orifice, eventually combined with endosonographic aspiration. The pre-therapeutic exam also requires a sectional examination (CT or MRI), and functional imaging (scintigraphy of somatostatin receptors). The submucosal nature of the lesion limits the possibility of endoscopic resection to isolated and small lesions in an expert center. Most lesions are indications for surgical resection (a fortiori when they are multifocal).

Mucosal tumours

1. Brunner's hamartomas

Brunner's hamartomas represent 1% of duodenal tumours. These lesions are most often asymptomatic. Infracentimetric lesions are often called "Brunner's gland hyperplasia" while supracentimetric lesions are called

"hamartomas" (and sometimes inappropriately "adenomas"). These hamartomas are typically pedunculated, rarely measure more than 2 cm, and are located in the bulb (often on the posterior surface) or the duodenojejunal flexure (Figure 2). The vast majority of these tumours are benign (exceptional malignant degenerations have been reported). Their resection is considered when they are symptomatic (hemorrhage by ulceration, obstruction) or when there is a differential diagnosis (especially when they exceed 2 cm in size). The frequently pedunculated nature of the lesion makes its resection relatively easy and safe.

2. Peutz-Jeghers polyps

The solitary duodenal polyp of Peutz-Jeghers is uncommon. It can be found in patients without any family history of Peutz-Jeghers hereditary polyposis and without the perioriflex lentiginosis, that is characteristic of this syndrome. This polyp has an irregular, lobular or nodular surface. While it is sessile when small, as it grows it often develops a pedunculated appearance (Figure 3). Resection is recommended, because of the risk of malignant transformation. The discovery of these polyps in the duodenum should lead to the consideration of a broader assessment (colonoscopy, and exploration of the small intestine by scanner or MRI or videocapsule endoscopy) so as not to miss an unclear clinical presentation.

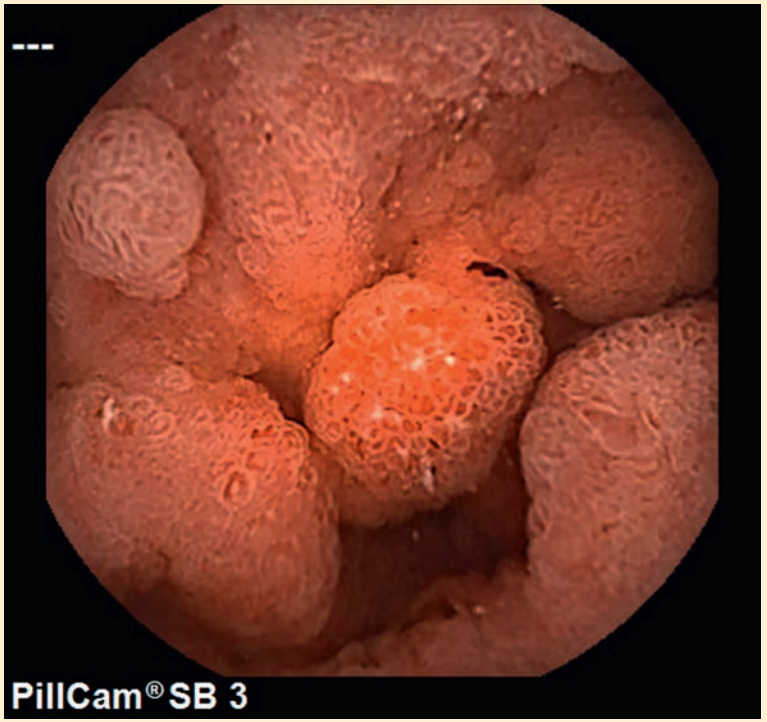


Figure 2: Brunner's gland hyperplasia in a 77-year-old man. Unexplained and occult digestive bleeding. Videocapsule endoscopy view. No specific treatment.

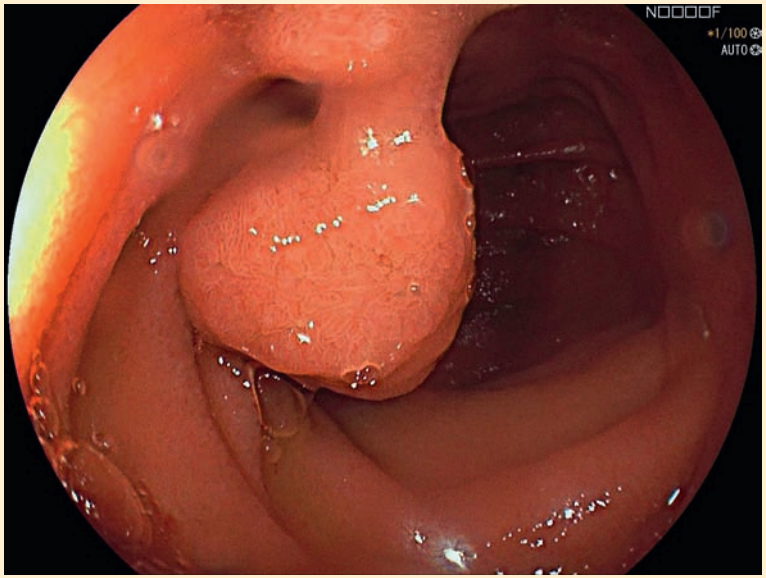


Figure 3: Sporadic hamartomas of Peutz-Jeghers in a 47-year-old woman. Epigastric pain. Upper endoscopy. Discovery of a 15 mm polypediculate tumour. Complete excision (no indication of a syndromic presentation).

3. Adenomas and adenocarcinomas

Duodenal adenomas represent a quarter of duodenal tumours. They are classified according to their syndromic nature (familial adenomatous polyposis (FAP), Lynch syndrome, or other), and according to their ampullary anatomy or its absence. Indeed, these classifications have a direct impact on therapeutic decision making. Adenomas represent around 7% of duodenal tumours. They are often asymptomatic and found incidentally in patients over 60 years of age.

The sporadic duodenal adenomas are often isolated and sessile, and typically occur in the D2 duodenum, on the posterior or lateral sides. The villi in the adenoma are sometimes whiter than those in the surrounding mucosa in white light. Although the classification of the motifs of crypts and vessels are mainly proposed to distinguish adenomas and adenocarcinomas in the colon (in particular those with deep submucosal invasion which require surgery), their criteria can be used analogously in the duodenum.

In an adenoma, the villi often have a conical or fringed shape, while in an adenocarcinoma they are more irregular, destructured or even absent (opaque, aglandular, avascular appearance, possibly depressed or ulcerated). Other criteria that are suggestive of the presence of deep submucosal invasion are the size, the circumferential character (Figure 4), the involvement of the papilla and the absence of surface elevation after submucosal injection. Endoscopic characterisation is all the more important since the sensitivity of the biopsies is often poor due to insufficient sampling. Conversely performing too many biopsies can complicate an already risky duodenal resection, by creating submucosal fibrosis. The malignant progression of a sporadic duodenal adenoma (15 to 20 years) is considered slower than that of a colonic

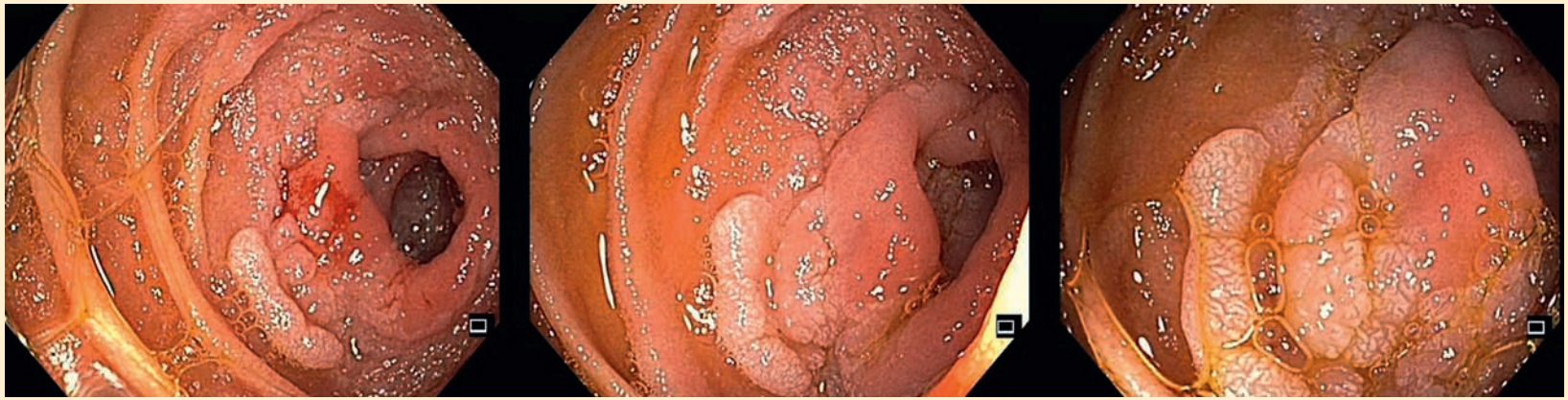


Figure 4: Tubulo-villous adenoma with low grade dysplasia and areas of high grade dysplasia, and a 2 mm focal point of adenocarcinoma in a 73 year old woman. Upper endoscopy (performed with a colonoscope) showed the presence of a tumour with lateral extension, with macronodules, circumferential, stenosing (impassable) over the length of about 5 cm. Histological examination of the surgical sample (surgical excision with lymph node dissection) revealed an invasion of the upper third of the submucosa (500 µm). There was no vascular embolism or perineural invasion, no budding or lymph node involvement (pT1b N0 M0). At a pluridisciplinary meeting, simple surveillance was decided on. No recurrence at 2 years.

adenoma. However, lesions larger than 20 mm, or with high grade dysplasia, can harbor degenerate foci from the beginning.

Patients with sporadic duodenal adenoma carry a higher risk of a colonic adenoma than expected in other patients, by around 50%. There are no recommendations for patient monitoring after resection of a sporadic duodenal adenoma, but it is probably good practice to have an endoscopic check-up once in a while. The benefit of doing an assessment of the downstream small intestine (by capsule or entero-CT or entero-MRI) is debatable.

Unlike sporadic adenomas, which are uncommon, duodenal adenomas occur in more than 90% of FAP patients. These adenomas may involve the bulb or the distal duodenum. The risk of duodenal adenocarcinoma in patients with FAP is estimated to be between 3 and 5% during their lifetime, and this pathology is the leading cause of death in

colectomised patients with FAP. Thus, during FAP progression, the risk of developing duodenal adenocarcinoma is about 300 times that of the general population, where the prevalence is around 0.01 to 0.04%. Duodenal cancer occurs in this context at around the age of 35 (compared to 60 in sporadic patients). In FAP patients, monitoring of the duodenum begins at around the age of 25 to 35 years old. If there are no lesions, the exam is performed every 3 years (Table 2). If a lesion is found (Figure 5), the Spigelman classification is used to assess the severity of duodenal involvement and the risk of occurrence of an adenocarcinoma in FAP, in order to better select patients for endoscopic or surgical treatment. These guidelines have recently been revised.

Adenomas involving the papilla (major or minor) can be sporadic or syndromic (FAP) (Figure 6). In the case of sporadic adenomas, a differential diagnosis that should not be overlooked is inflammatory papilla after lithiasis migration. The endoscopic diagnosis of ampulloma can be difficult if the lesion integrates into a florid location during the development of familial polyposis. The ampullary lesion can be confused with periampullary polyps, which can sometimes be numerous and large. When confirmed, these adenomas are considered to be at higher risk of degeneration into carcinoma (26% to 65%) compared to other sporadic duodenal adenomas. Ampullary adenoma can be specifically responsible for jaundice, pancreatitis and hemorrhage.

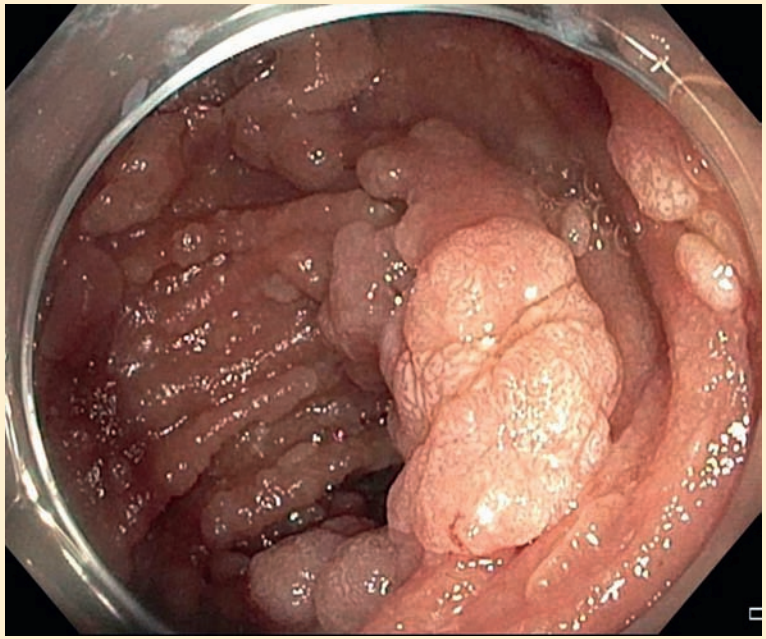


Figure 5: Severe duodenal involvement (Spigelman 11) of familial adenomatous polyposis (tubullo-villous adenomas with low and high grade dysplasia) in a 57-year-old man. Multistep endoscopic treatment.

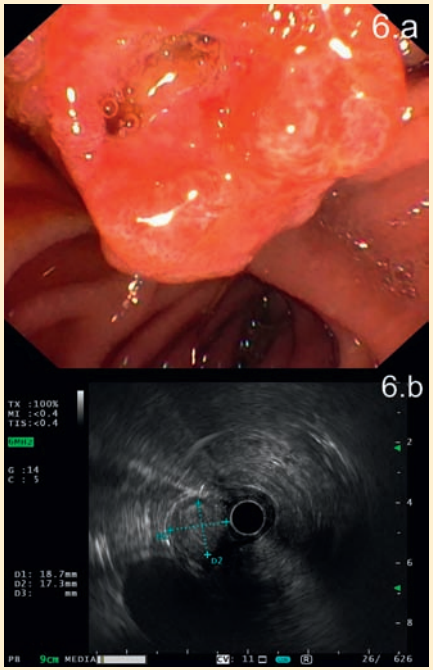
Differential diagnoses (neuroendocrine tumour or gangliocytic paraganglioma of the ampulla) are difficult endoscopically, hence the need to obtain a histological diagnosis before any attempt at endoscopic resection of an ampulloma. As is the case with non-ampullary adenoma, any

Table 2: Spigelman score and proposed surveillance in familial adenomatous polyposis.

Polyps	0 points	1 point	2 points	3 points
Number	0	< 4	5-20	> 20
Size	/	0-4 mm	5-10 mm	> 10 mm
Histology	/	Tubular	Tubulo-villous	Villous
Degree of dysplasia	/	Mild	Moderate	Severe

Spigelman score	Total number of points	Frequency of exams
0	0	Every 4 years
I	≤ 4	Every 2 to 3 years
II	5-6	Every 1 to 3 years
III	7-8	Every 6 to 12 months
IV	9-12	Every 3 to 6 months by a specialised doctor + surgical evaluation + mucosectomy or duodenectomy or Whipple procedure if the papilla is affected

ulceration, indentation or aglandular/avascular areas should arouse suspicion of a deep submucosal invasion. The mobile nature of the lesion is on the other hand a favourable element. Carrying out biopsies with a side viewing endoscope can be repeated, but must be done carefully (pediatric forceps, upper right external quadrant of the papilla as much as possible) in order to limit the risk of acute pancreatitis. Pathology diagnosis is however sometimes only obtained after the endoscopic treatment (papillectomy) has been carried out. Lateral extension is an element that should be evaluated with particular attention, especially since in the therapeutic phase, it is often advisable to start by treating these areas, in order to "isolate" the papilla before its resection. Endosonography has a major role in local (deep extension beyond the submucosa) and regional assessment (especially the invasion of the bile ducts and pancreatic



Figures 6a and 6b: Papillary adenocarcinoma, likely infiltrating (ulceration at the level of its pancreatic orifice) in a 52-year-old man. Papilla about 30 mm in length, with loss of glandular surface in some places, with a tumour-like appearance. Lack of locoregional extension shown using section imaging. Ultrasound endoscopy showing a usT1 N0 lesion. Pluridisciplinary meeting: Contraindication to cephalic duodenopancreatectomy due to non-weaned alcohol cirrhosis Child B9. Endoscopic papillectomy discussed.

ducts), before any therapeutic treatment. Papillectomy is typically indicated for supracentimetric ampullomas with high grade dysplasia, as well as for intramucosal adenocarcinomas (usT1N0), without biliary or pancreatic invasion. Morbidity is high (10 to 30%) with early complications (pancreatitis, hemorrhage and perforation) or late complications (pancreatitis, biliary stenosis, recurrence).

While the objective is to cure patients with sporadic duodenal adenoma, in FAP the objective is the early detection and treatment of lesions that are at risk of dysplasia (more than 10 mm in size) or dysplastic high grade lesions, with a reduction of the Spigelman score (thus a reduction of the risk of duodenal adenocarcinoma). In the latter situation, the current trend is to favour endoscopic treatment. Surgery (most often cephalic duodenopancreatectomy, more rarely duodenectomy with pancreatic preservation) is reserved for stages IV Spigelman and in case of failure of endoscopic treatment.

The diagnosis of duodenal cancer with deep invasion is often evident from the endoscopic appearance. The lesion is often supracentimetric in size, with ulcerative presentation, sometimes obstructive with upstream stasis and a difficult access, spontaneously hemorrhagic or very fragile on contact. In the more subtle forms that are not ulcerated, but nodular or indented, many surface irregularities and irregular vascularisation can be seen, even opaque areas (no

visible glands or vessels, in the absence of ulcers). The diagnosis must nevertheless be confirmed by the results of the biopsies. It can be either of a sporadic or syndromic form, typically a degenerate duodenal localisation of FAP. More uncommonly, the diagnosis is made in the context of hamartomatous polyposis (especially Peutz Jeghers). The degeneration of a duodenal lesion in the context of Lynch syndrome is rare (the MSH2 mutation being in these cases often involved).

Regarding therapy, we can recapitulate the following principles for superficial lesions:

– Adenomas in the millimetric size range can reasonably be resected with a mixed current with a low coagulation effect (or even with a cold loop);

– Adenomas in the centimetric size range can be treated by mucosectomy;

– Papillary adenomas require a papillectomy (often wrongly called "ampullectomy") and the installation of a pancreatic prosthesis;

– Submucosal duodenal dissection is relatively contraindicated given the high risk of delayed perforation. Fragmented mucosectomy is often preferred in the case of a tumour with lateral extension without any signs of deep submucosal invasion.

– Endoscopic monitoring is essential after resection of a duodenal adenoma.

Conclusion

The spectrum of duodenal tumours is wide, ranging from benign polyps discovered serendipitously, to advanced precancerous lesions at high risk for adenocarcinoma. In a syndromic context (especially FAP), close monitoring is required. Advances in endoscopic tumorectomy will likely lead to a reduction in the need for surgery, including for ampullary lesions. To date, however, only a few teams have attempted to address dysplastic duodenal lesions by submucosal dissection.

References

1. Ma MX, Bourke MJ. Management of duodenal polyps. *Best Pract Res Clin Gastroenterol* 2017; 31 (4): 389-399.
2. de Latour RA, Kilaru SM, Gross SA. Management of small bowel polyps: A literature review. *Best Pract Res Clin Gastroenterol* 2017; 31 (4): 401-408.
3. Gaspar JP, Stelow EB, Wang AY. Approach to the endoscopic resection of duodenal lesions. *World J Gastroenterol* 2016; 22 (2): 600-617.
4. Syngal S, Brand RE, Church JM, *et al.* ACG clinical guideline: Genetic testing and management of hereditary gastrointestinal cancer syndromes. *Am J Gastroenterol* 2015; 110 (2): 223-262.

List of clinical cases[1]

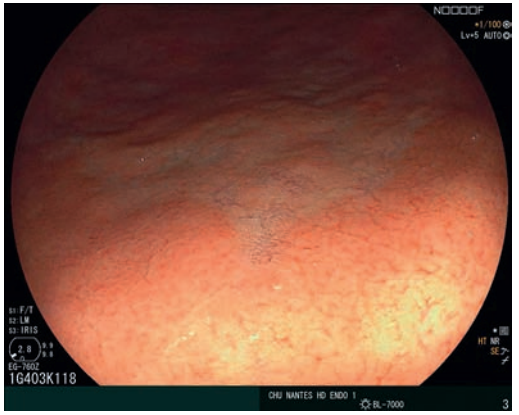
CC1: Atrophic gastritis with intestinal metaplasia without dysplasia
CC2 Low grade dysplastic adenoma associated with pernicious anemia
CC3: High grade dysplasia in a cirrhotic patient
CC4: Hyperplastic stomach polyp
CC5: Submucosal dissection of an intramucosal adenocarcinoma of the stomach
CC6: Curative resection of a superficial adenocarcinoma of the stomach
CC7: Anastomotic recurrence of a superficial adenocarcinoma of the stomach
CC8: Resection of an antro-duodenal adenoma by transpyloric excision
CC9: Low and high grade dysplastic adenoma of the duodenum. Complete excision by monobloc mucosectomy
CC10: Duodenal adenoma with high grade dysplasia
CC11: Juvenile gastrointestinal polyposis: a separate entity

Main abbreviations used in the text

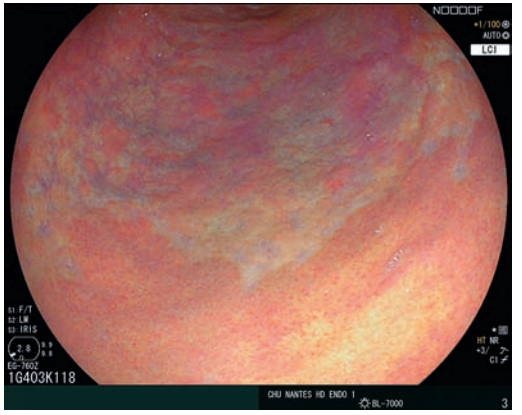
BLI: Blue Light Imaging
LCI: Linked Color Imaging

1. The editors would like to thank Nicolas Chapelle and Guillaume Perrod for their contribution to the collection of clinical cases and the creation of the endoscopic image database.

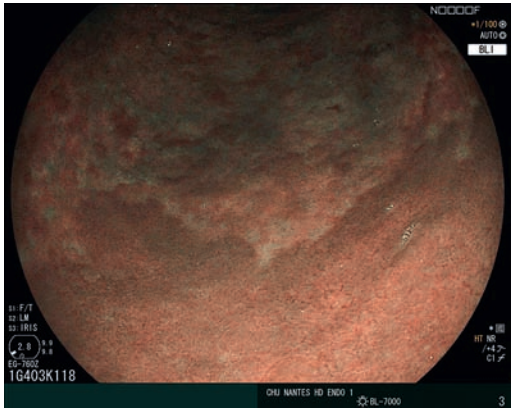
CC1 Atrophic gastritis with intestinal metaplasia without dysplasia



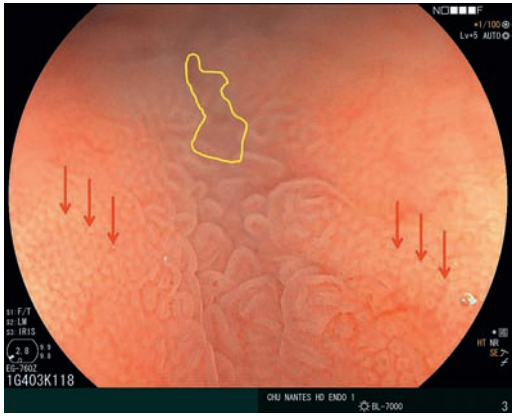
- 1 -



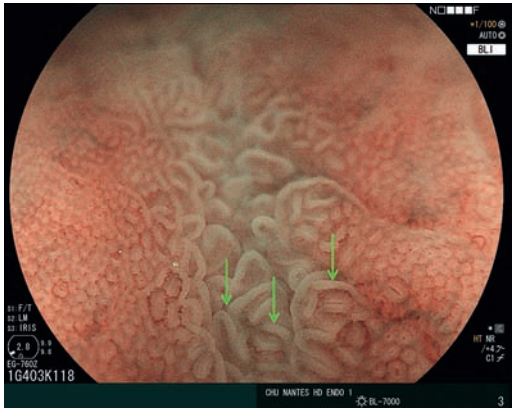
- 2 -



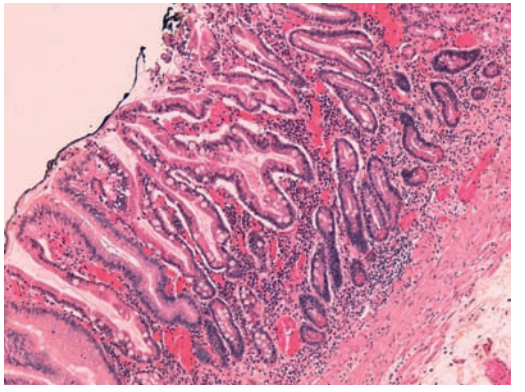
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

A 68-year-old patient was followed for chronic gastritis of undetermined etiology: areas of low-grade dysplasia in the fundus were noted during the initial endoscopy. During follow-up, no dysplastic lesions were detected, but antral atrophic gastritis was noted.

Endoscopic description

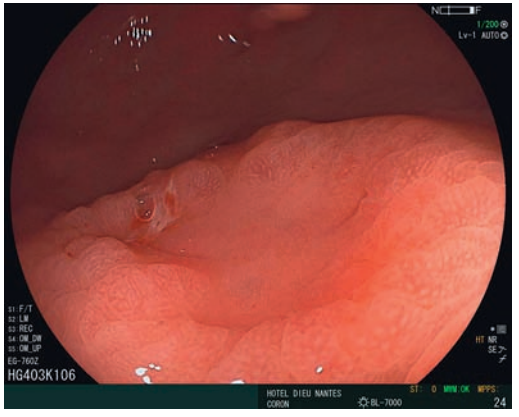
▶ **Images 1, 2 and 3:** White light endoscopic exploration without zoom showed a clear delineation between the normal mucosa on the proximal side of the antral floor, that was regular and pink in color, and the atrophic pathological area on the distal side, irregular and whitish in appearance (Image 1).
LCI made it possible to accentuate this delineation, with the atrophic mucosa looking bluish in the most atrophic areas (Image 2). LCI also enabled the visualisation of other pathological areas. BLI increased the contrast between the healthy zone that looked brown, and atrophic areas, that looked lighter in color (Image 3).

▶ **Images 4 and 5:** Examination using zoom made it possible to analyse the mucosal microarchitecture in white light and to differentiate the normal mucosa (consisting of rounded glands, on the right and left of the image, red arrows) from the pathological area in the center circled in yellow (Image 4). The proximal part of this area was the site of an intestinal metaplasia consisting of elongated and regular glands. This aspect was particularly visible using the BLI mode, the central zone appearing bluish with elongated and regular intramucosal glands and capillaries, resembling intestinal villi (green arrows, Image 5).

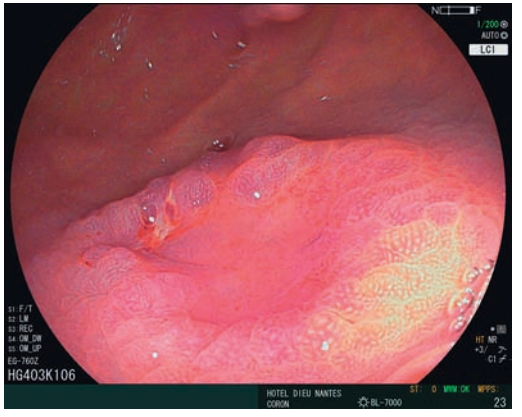
Histological description

▶ **Image 6:** Using samples obtained from the pathological zone, light intensity lesions due to chronic gastritis were apparent. They were complicated by plurifocal lesions of intestinal metaplasia without epithelial dysplasia, associated with areas of glandular atrophy. No H. pylori infection was present. Biopsies from the healthy area did not show any histological abnormality.

CC2 Low grade dysplastic adenoma associated with pernicious anemia



- 1 -

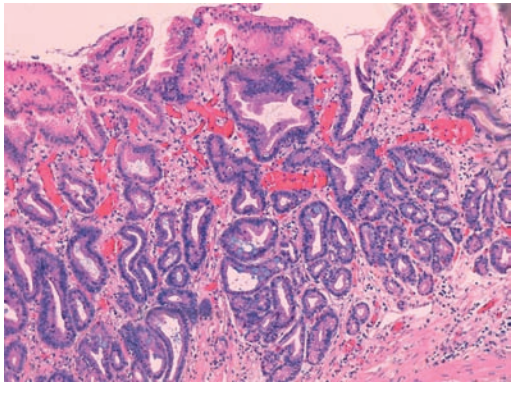


- 2 -

- 3 -

- 4 -

- 5 -



- 6 -

Clinical description

A 77-year-old patient was followed regularly for pernicious anemia. He was referred for endoscopic resection of a lesion of the antral floor that developed during the endoscopic follow-up period performed every 3 years.

Endoscopic description

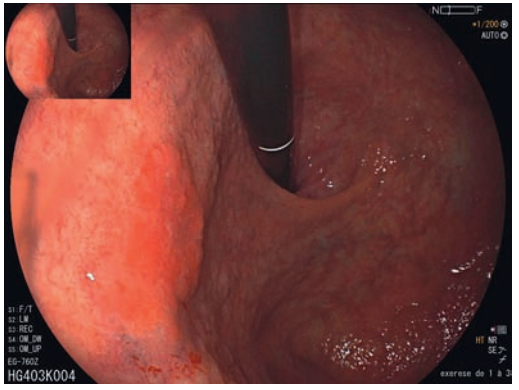
▶ **Images 1, 2 and 3:** A lesion of about 20 mm in diameter, spanning the floor of the antrum, classified as 0-IIa+c, was easily identifiable using a weak zoom with white light (Image 1). The center of the lesion did not appear darker (therefore not highly suspicious) with the LCI mode (Image 2). In BLI mode, the center was characterised by a clear demarcation between the edges, that were congestive and hyperemic, and the center of the lesion whose mucosal microarchitecture looked regular and atrophic (Image 3).

▶ **Images 4 and 5:** Using zoom and the BLI mode, the mucosal and vascular microarchitecture was easier to analyse. In particular, this mode showed a higher density of intramucosal capillaries in the center of the lesion, that were regular and of small caliber (Image 4). On the other hand, on the periphery of the lesion, capillaries of larger caliber were present, responsible for hemorrhagic spread (Image 5), as well as hypertrophic and regular glands. There were no other suspicious lesions in the stomach. A submucosal dissection was performed.

Histological description

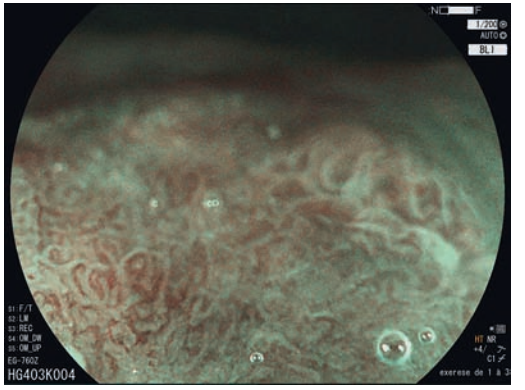
▶ **Image 6:** The anatomopathological examination of the specimen (50 x 30 mm), dissected from the resected lesion identified a tubular adenoma with intestinal differentiation and low grade dysplasia. The lesion consisted of tubes bordered by a base of tall, basophilic cylindrical cells, with ovoid nuclei, located at the basal pole of the cells. No focal carcinomatous transformation was seen. The lesion was completely resected, both laterally and depth-wise.

CC3 High grade dysplasia in a cirrhotic patient

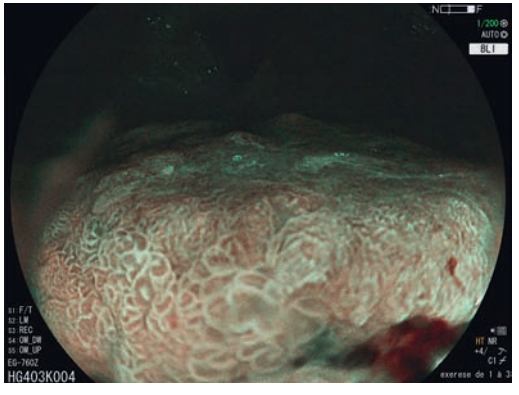


- 1 -

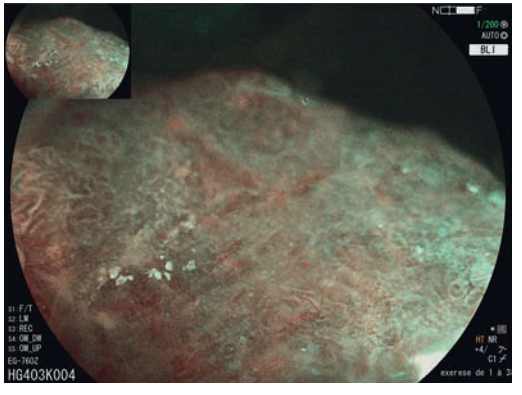
- 2 -



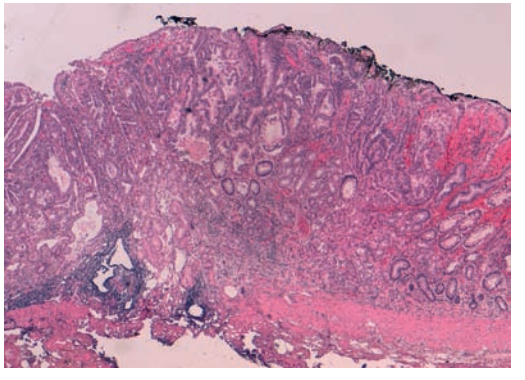
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

A 71-year-old patient was followed for compensated alcoholic and hemochromatotic cirrhosis. A portal hypertension surveillance endoscopy showed a subcardial lesion, and the corresponding tissue specimen analyses revealed high-grade dysplastic lesions. Endosonography showed the presence of a usT1N0 lesion, validating the indication for endoscopic resection.

Endoscopic description

▶ **Images 1 and 2:** The examination carried out in retrovision using white light showed a lesion of approximately 2 cm, on the slope of the small curvature, classified as 0-IIa+IIc according to the Paris classification. This lesion looked more coloured than the adjacent, irregular mucosa and did not show any clear demarcation (Image 2). There were also no signs of portal hypertension.
▶ **Images 3, 4 and 5:** Analysis carried out using the BLI and zoom mode, made it possible to precisely analyse the mucosal and vascular microarchitecture, and showed significant anomalies. In some places, there were totally dystrophic glands (Image 3), within which large, irregular and deep neo-capillaries circulated, responsible for spontaneous hemorrhagic spread or intramucosal hematomas (Image 4). In some places the examination showed a complete disappearance of the glandular and vascular architecture (Image 5), and suggested the presence of intraepithelial neoplasia. The lesion was resected by mucosectomy, without complications during or after the procedure.

Histological description

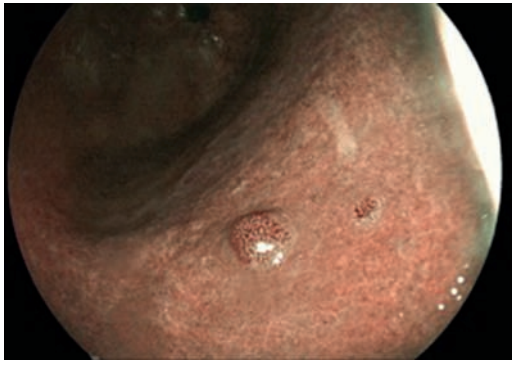
▶ **Image 6:** The histological evaluation showed an adenomatous lesion consisting of tubular structures eventually ectatic and forming microcysts. These structures were bordered by cylindrical or cubical cells with a clear cytoplasm, with rounded or ovoid nuclei that were irregular in size. While in some areas the cytonuclear anomalies were more striking, there was no clear infiltration center: the lesion was identified as a tubular gastric adenoma with high grade dysplasia. Depth-wise, exeresis was in the healthy zone. Laterally, adenomatous lesions were present.

CC4 Hyperplastic stomach polyp

- 1 -

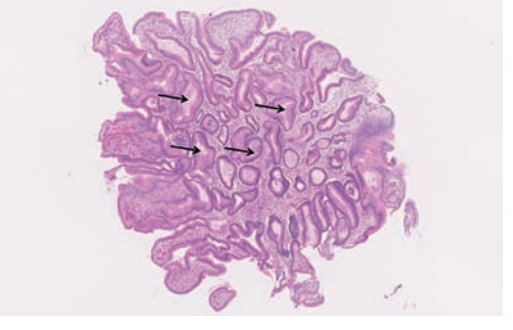
- 2 -

- 3 -



- 4 -

- 5 -



- 6 -

Clinical description

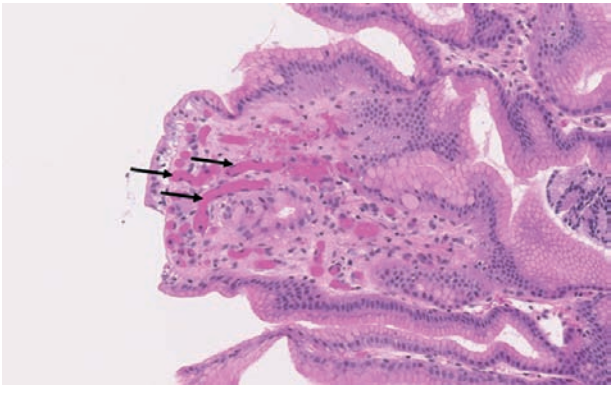
A 73-year-old female patient underwent oesogastroduodenal endoscopy as part of a post-endoscopic resection follow-up for superficial squamous cell cancer of the oesophagus. The examination showed a small gastric polyp.

Endoscopic description

▶ **Images 1 and 2:** White light and zoom showed the presence of two polypoid formations located by the antrum. One was of about 6 mm in size classified as stage 0-Is of the Paris classification. The other, smaller one was 2 mm long classified as stage 0-IIa. The pit pattern was regular with a branched structure of the crypts.
▶ **Image 3:** Using LCI, the presence of an inflammatory halo (arrow) surrounding these two polypoid formations was shown.
▶ **Images 4 and 5:** Using BLI with zoom, we confirmed the regular and branched character of the pit pattern. There were no vessels on the surface of the polyp.

Histological description

▶ **Images 6 and 7:** Gastric mucosa of the antrum and the antro-fundic junction. Presence of mild chronic gastritis with two hyperplastic polyps characterised by significant epithelial indentation, cystic foveal dilations (Image 6, arrows). The chorion is not affected, and vascular congestion is associated with mild inflammation (Image 7, arrows showing congestive vessels). Absence of acute inflammation, intestinal metaplasia or dysplasia.



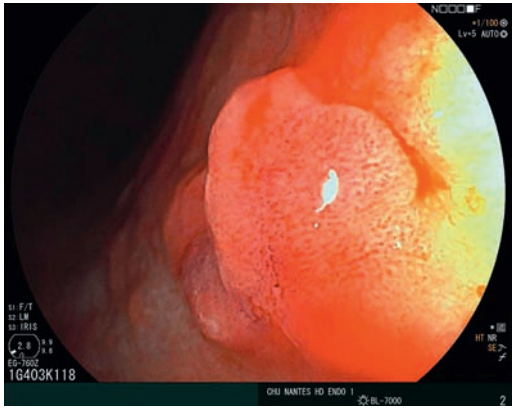
- 7 -

CC5 Submucosal dissection of an intramucosal adenocarcinoma of the stomach

- 1 -

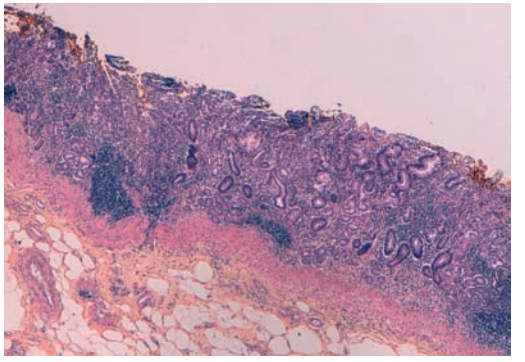
- 2 -

- 3 -



- 4 -

- 5 -



- 6 -

Clinical description

An emergency hospitalisation of a 69-year old man for melena and acute anemia of 8.3 g/dL. He had a medical history of ischemic heart disease treated by stenting and an anti-aggregant platelet treatment introduced 4 months earlier. The initial endoscopy showed an ulcer of Forrest III type that was 1 centimeter in size and that was bleeding when the endoscope was passed. Biopsies revealed chronic atrophic gastritis with antral intestinal metaplasia, the presence of Helicobacter pylori (H. pylori) and high-grade dysplastic lesions on the boarders of the ulcer. A control endoscopy was scheduled.

Endoscopic description

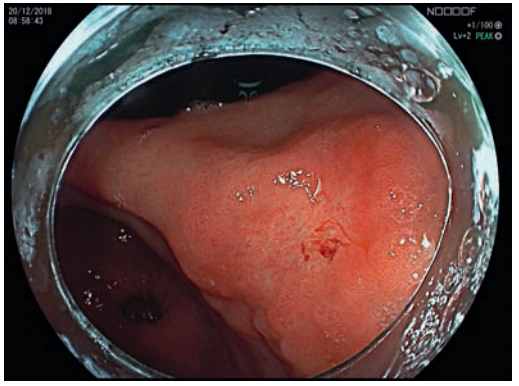
▶ **Images 1, 2 and 3:** This control endoscopy showed the persistence of the angulus lesion of approximately 15 mm in size, classified as Paris 0-IIa+Is, spontaneously bleeding (Image 1). In LCI mode, the lesion boundaries, in pink, were clearly visible, distinct from those of the adjacent, atrophic and pale mucosa (Image 2). In BLI mode, the mucosal and vascular microarchitecture became visible but could not be clearly specified without zoom.

▶ **Images 4 and 5:** Using a zoom, the irregular and aberrant arrangement (sometimes even absent) of the mucous and vascular microarchitecture of the lesion was clearly distinguishable (Image 4). This appearance was particularly identifiable using the BLI mode (Image 5) with multiple irregular capillaries, responsible for hemorrhagic spread, suggestive of carcinomatous transformation. A decision to performed submucosal dissection was taken and the procedure was carried out without complication.

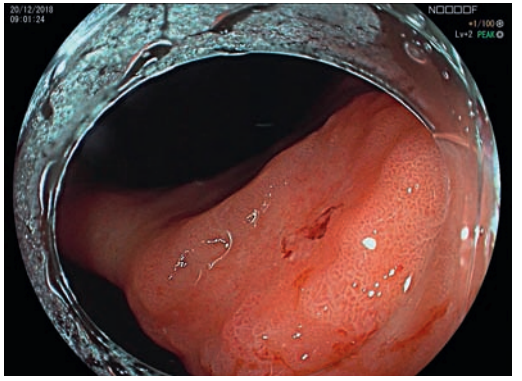
Histological description

▶ **Image 6:** The histological analysis suggested the presence of a lesion containing a focal point of intramucosal carcinoma of 11 mm in length. This carcinoma consisted of ill-defined glandular formations, with moderate cytonuclear atypia. The stroma was poorly developed. The lesion reached the muscularis mucosae in some places without invading it. There was no budding, lymphatic or vascular embolism, and H. pylori was absent on immunohistochemical examination. The resection margins were healthy.

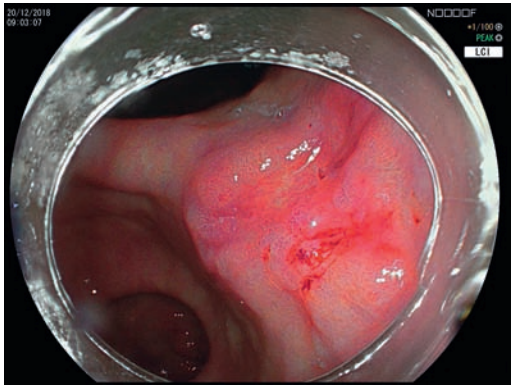
CC6 Curative resection of a superficial adenocarcinoma of the stomach



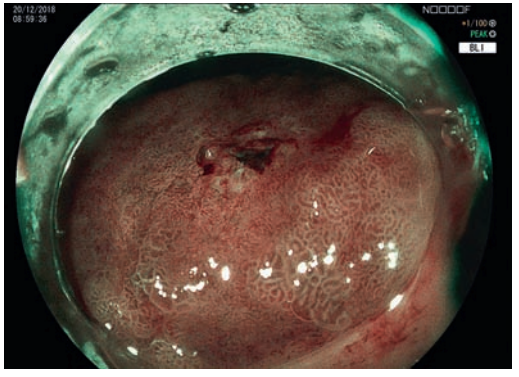
- 1 -



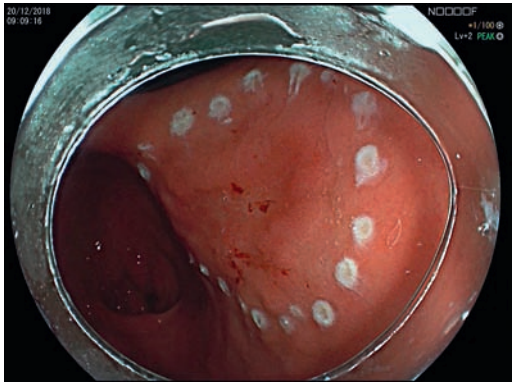
- 2 -



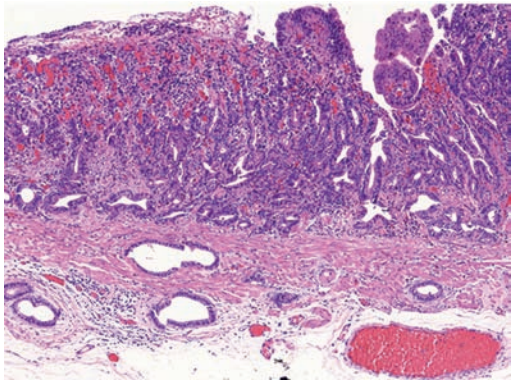
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

A 74-year-old Portuguese patient with chronic atrophic pangastritis secondary to Helicobacter pylori infection that was eradicated in 2001. The patient was monitored by gastroscopy according to current European recommendations.

Endoscopic description

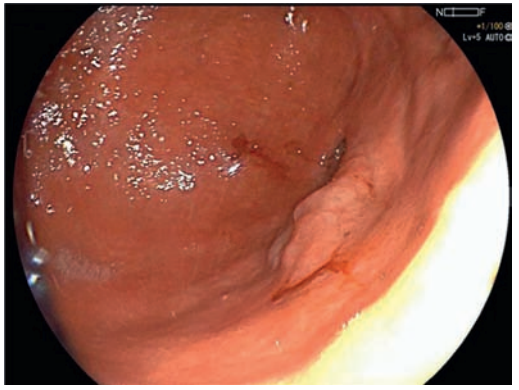
▶ **Images 1 and 2:** The gastric exploration using white light revealed a flat lesion, depressed in its center, measuring approximately 20 mm in size, located on the angulus. Initially, there was a doubt about a central ulceration, but after washing the lesion, it was classified as 0-IIa-IIc according to the Paris classification.
▶ **Images 3 and 4:** Using LCI and BLI modes highlighted the disappearance of the mucous gland surface, and the rarefaction of the vascularisation, which was irregular, indicating the presence of a carcinomatous lesion very probably invading the gastric submucosa.
▶ **Image 5:** A submucosal dissection was performed.

Histological description

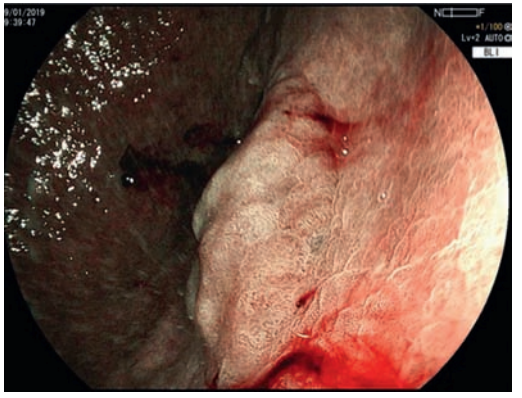
Histological examination revealed the presence of adenocarcinomatous proliferation, mostly intra-mucosal, with glands with a narrow, irregular, slightly contoured lumen. In some parts, the glands dissociated the muscularis mucosae, surpassing it and reaching the most superficial part of the submucosa over very limited distance of 200 µm. There were no tumour emboli, no budding. The mucosal excision margins were healthy. The resection was complete and curative.
▶ **Images 6 and 7:** After HES staining, the diagnosis of well-differentiated adenocarcinoma, infiltrating the submucosa was confirmed.

- 7 -

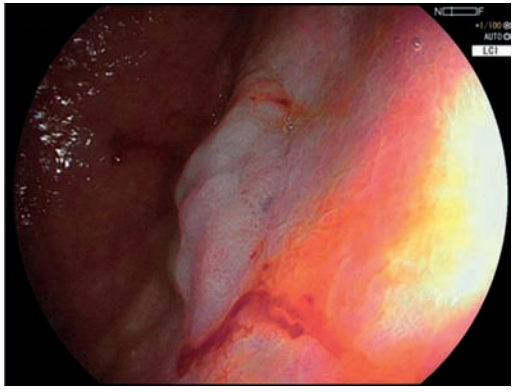
CC7 Anastomotic recurrence of a superficial adenocarcinoma of the stomach



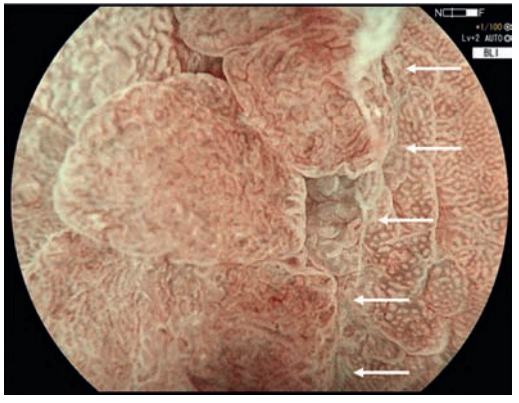
- 1 -



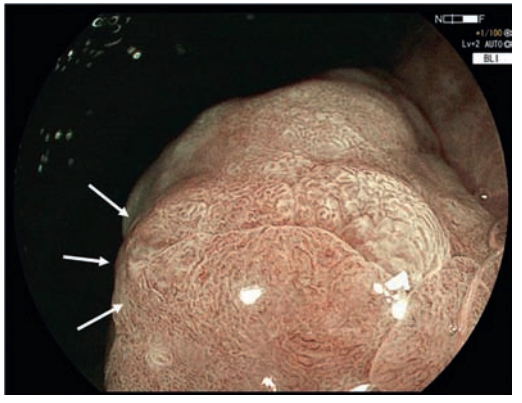
- 2 -



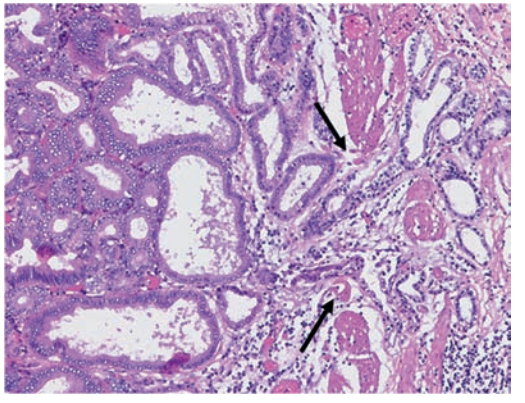
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

A 76-year-old patient who had had a partial gastrectomy in 1992 for superficial gastric adenocarcinoma. A follow-up gastroscopy revealed the presence of a 40 mm sessile lesion that developed from the residual fundus, at the level of the gastro-jejunal anastomosis. A first series of biopsies enabled the diagnosis of tubular adenoma with high grade dysplasia. The patient was referred for endoscopic resection by submucosal dissection.

Endoscopic description

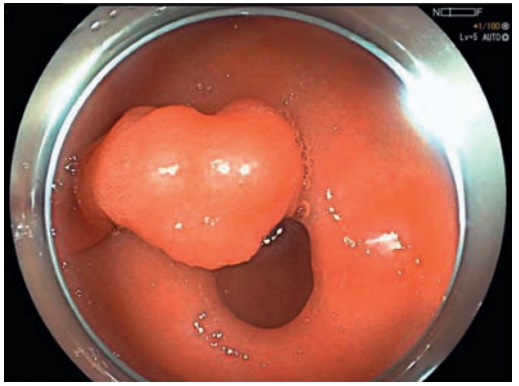
▶ **Images 1, 2 and 3:** On the right lateral side of the residual fundus there was an elevated lesion classified as 0-Is according to the Paris classification. This non-ulcerated lesion seemed well delineated after analysis by virtual chromoendoscopy using BLI (Image 2) and LCI (Image 3).

▶ **Images 4 and 5:** BLI with zoom made it possible to clearly identify the limits of the lesion (Image 4). At several levels areas characterised by the disappearance of glandular patterns and branched vascularisation were noted, especially on the upper lesion (Image 5). These areas were suggestive of carcinomatous degeneration.

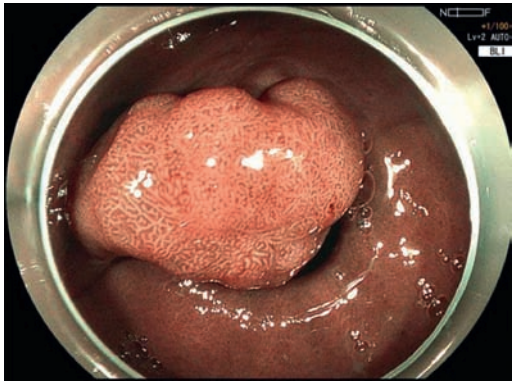
Histological description

The lesion was a well-differentiated adenocarcinoma that developed on atrophic gastritis without metaplasia. In some places, it infiltrated the submucosa (black arrows) at a maximum depth of 100 µm (Image 6). The lateral and deep resection margins were healthy, with no lymphatic or vascular emboli. This monobloc R0 resection was therefore curative, and the tumour was classified as pT1b with a submucosal invasion of less than 500 µm.

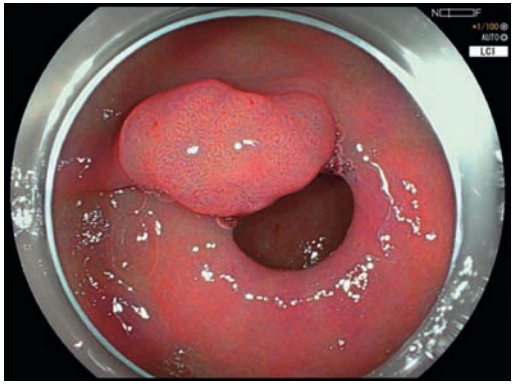
CC8 Resection of an antro-duodenal adenoma by transpyloric excision



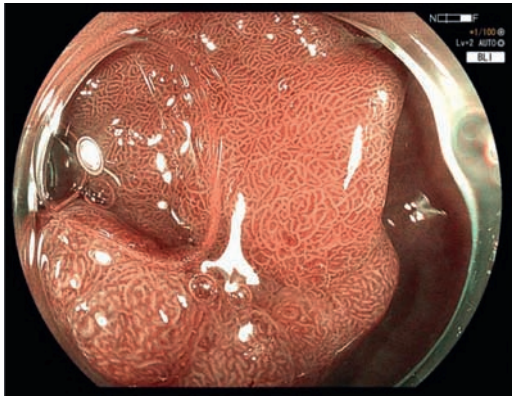
- 1 -



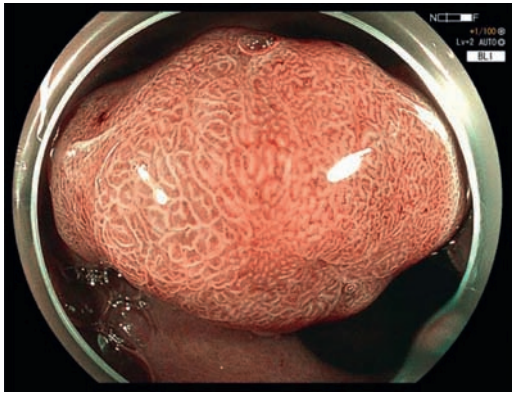
- 2 -



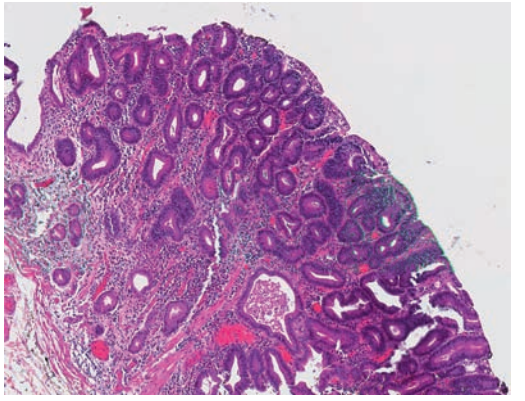
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

A 59-year-old patient with no notable medical history was referred for exploration for iron deficiency anemia. Gastroscopy revealed a large polypoid lesion developing near the pylorus. Analysis of the lesion using white light followed by virtual chromoendoscopy revealed an antral lesion of 30 mm long in the large axis, extending over approximately 5 mm into the bulb. A decision to perform an endoscopic resection of the lesion was reached.

Endoscopic description

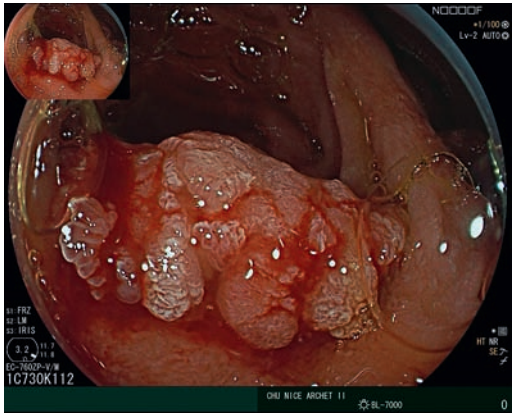
▶ **Images 1, 2 and 3:** On the left lateral surface of the antrum, an elevated lesion (Image 1) classified as 0-Is according to the Paris classification was present. Analysis of the lesion by chromoendoscopy showed clear boarders using BLI (Image 2) and LCI (Image 3).

▶ **Images 4 and 5:** The characterisation of the lesion using the BLI mode with zoom and cap made it possible to identify glandular (Image 4) and regular vascular (Image 5) patterns over the entire tumour mass. There was no loss of glandular architecture, no disappearance or modification of the branched vascularisation. Transpyloric endoscopic excision by submucosal dissection enabled a macroscopically complete monobloc resection.

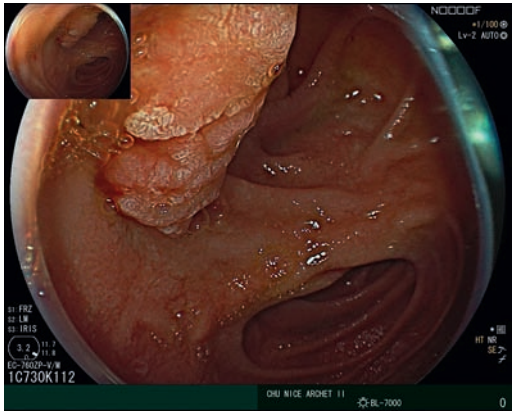
Histological description

The lesion was tubular and adenomatous, with a minor villous contingent representing approximately 10% of the lesion. The analysis of the glands showed a slight distortion (Image 6), without horizontalisation of the nuclei or loss of mucosecretion. This description was indicative of a tubular adenoma with low grade dysplasia. Clear resection margins, marked by the presence of an atrophic mucosa without metaplasia, were obtained.

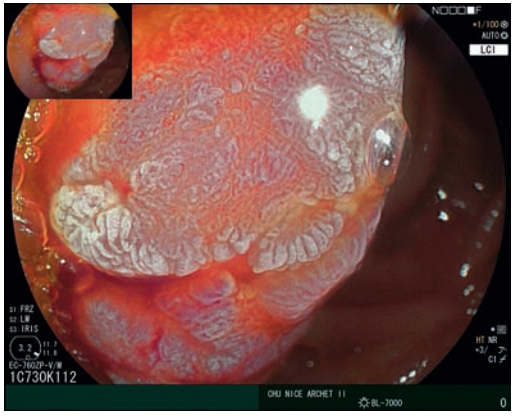
CC9 Low and high grade dysplastic adenoma of the duodenum. Complete excision by monobloc mucosectomy



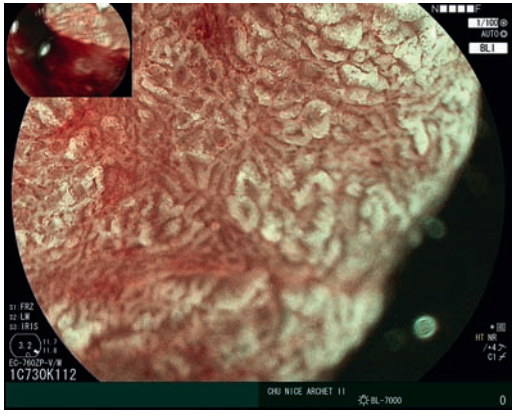
- 1 -



- 2 -



- 3 -



- 4 -

- 5 -

Clinical history

A 66-year-old patient with Lynch disease complicated by adenocarcinoma of the distal duodenum was operated on in 2011 (R0 resection without adjuvant therapy). During his last endoscopic check-up, a duodenal polypoid lesion developing upstream of the duodeno-jejunal anastomosis was identified. Endoscopic treatment of this lesion was initially proposed. Initial analysis included zoom, BLI and LCI before reaching a therapeutic decision.

Endoscopic description

▶ **Image 1:** Overview of the lesion using white light in the lower part of the second duodenum just above the anastomosis. The lesion was typically adenomatous, sessile (0-Is Paris classification) and measuring 15 to 20 mm with areas of demarcation, as is usually seen in these cases.

▶ **Image 2:** Again using white light without zoom and showing an overview of the anastomotic region. There was no ulceration or depression.

▶ **Image 3:** Using LCI plus zoom, the lesion had areas with a more irregular and eroded appearance of the glandular architecture and small, irregular vessels. These features were indicative of high grade dysplasia or even *in situ* carcinoma.

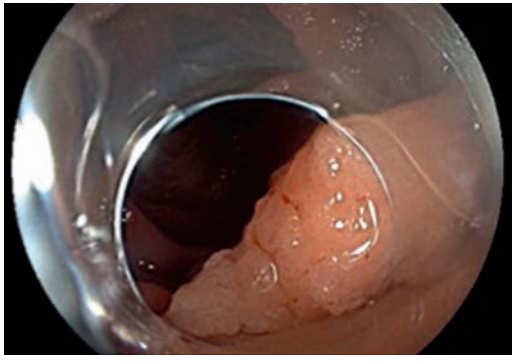
▶ **Image 4:** Using BLI with zoom on an adjacent area we observed the same features. A monobloc mucosectomy was selected as the therapeutic approach.

▶ **Image 5:** The appearance after monobloc mucosectomy – No adenomatous residue could be seen at the circumference of the resection site using white light.

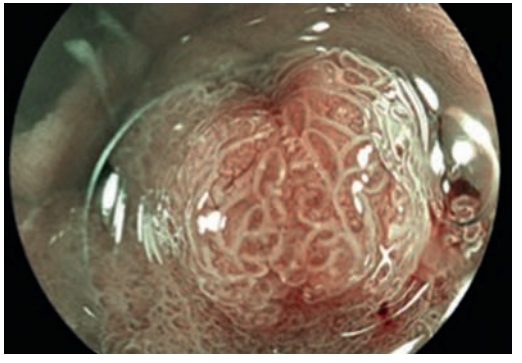
Histological description

The final histology was indicative of complete excision of a dysplastic adenoma of low and high grade.

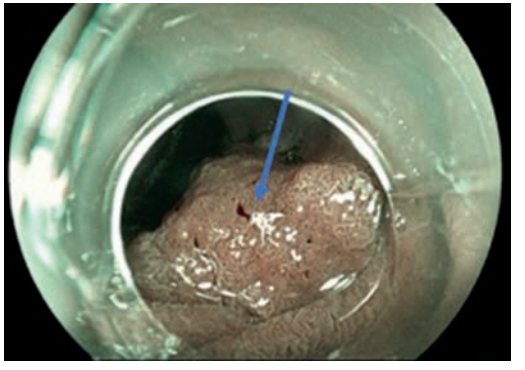
CC10 Duodenal adenoma with high grade dysplasia



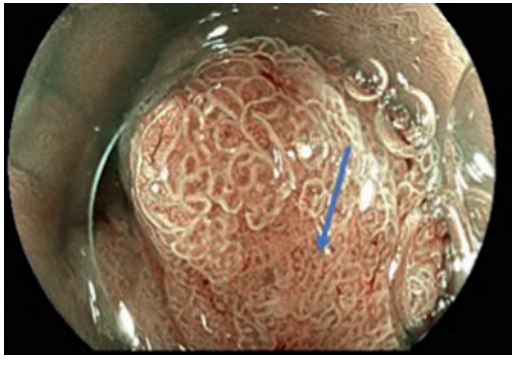
- 1 -



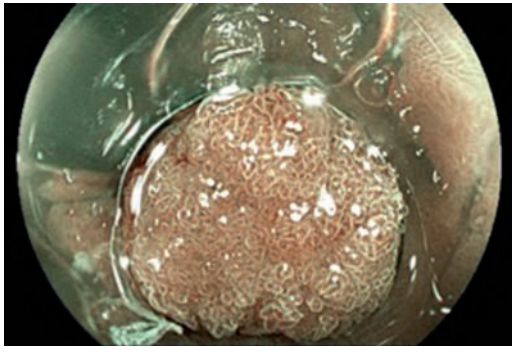
- 2 -



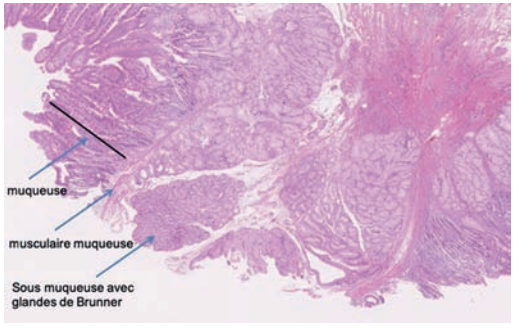
- 3 -



- 4 -



- 5 -



- 6 -

Clinical description

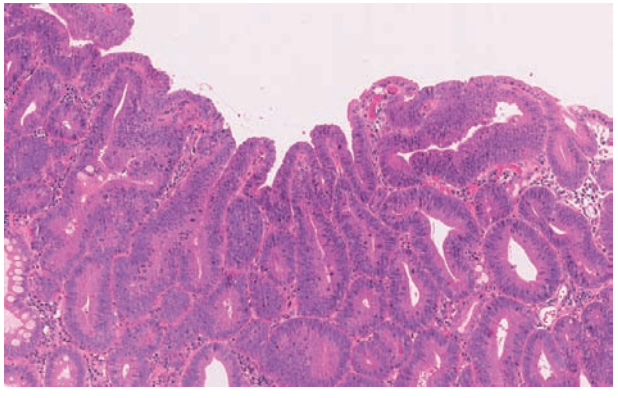
A 72-year-old patient was referred for endoscopic resection of a lesion of 15 mm in diameter located by the D2 duodenum. A previous endoscopy reported a villous appearance. The histological analysis of the biopsies performed at the first endoscopy described an adenoma with low grade dysplasia. The context was not suggestive of genetic polyposis.

Endoscopic description

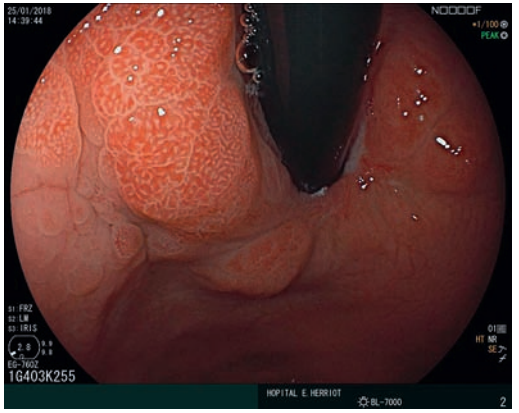
▶ **Image 1:** In the middle part of D2, on the anti-mesenteric edge, an adenoma of 15 mm in diameter of type 0-IIa of the Paris classification was located.
▶ **Image 2:** Using BLI with zoom, it had an adenomatous appearance with a regular, large and tubular type IIIL pit pattern in the Kudo classification. The capillary network was homogeneous with regular caliber, i.e. type II of the Sano classification.
▶ **Images 3, 4 and 5:** Using the BLI mode with zoom, the pit pattern was different at the center of the lesion, with tubular, smaller glands but with regular organisation (possibly high grade dysplasia). The lesion was resected by monobloc mucosectomy, after satisfactory detachment and the resection area was closed using 5 clips.

Histological description

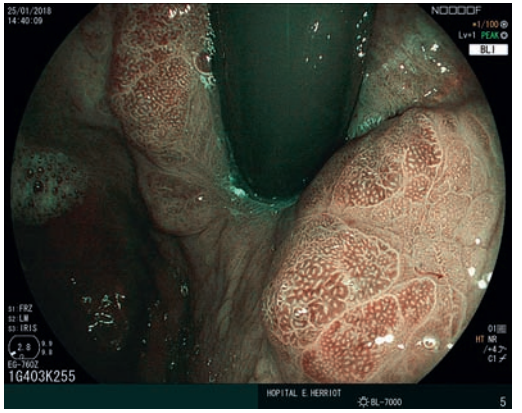
▶ **Image 6:** Normal histological appearance of one of the resection margins.
▶ **Image 7:** Tubular adenoma with high grade dysplasia, 15 mm in diameter, the resection of which was complete without affecting the deep submucosa. The epithelial cells had enlarged nuclei and a pseudo-stratified aspect reaching the surface, an aspect characteristic of high grade dysplasia.



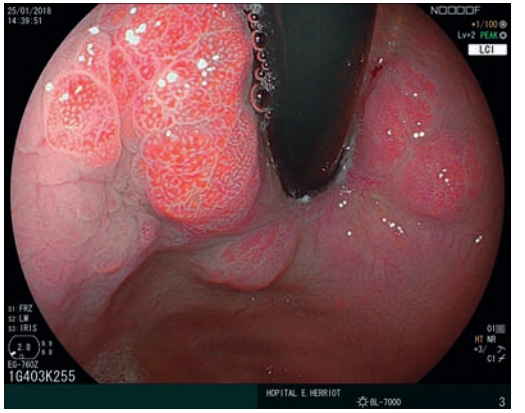
CC11 Juvenile gastrointestinal polyposis: a separate entity



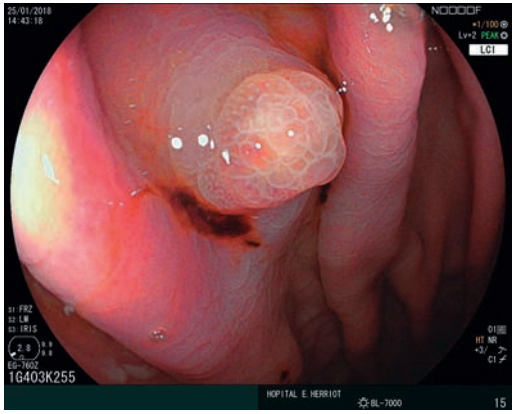
- 1 -



- 2 -



- 3 -



- 4 -

- 5 -

Clinical description

A 34-year-old woman was followed after submucosal dissection of a cardial lesion in the context of juvenile gastrointestinal polyposis with a mutation in the SMAD4 gene. The main current hypothesis regarding the development of SMAD4 polyposis is that the initial lesions develop around the cardia and then extend to the entire stomach. This explains why a monobloc exeresis, which was complete, both macroscopically and histologically, was perfomed. A surveillance endoscopy was scheduled 3 months after the submucosal dissection.

Endoscopic description

▶ **Images 1, 2 and 3:** Despite the initial complete resection, after the examination of the cardia in white light the recurrence of the lesion was apparent. This recurrence was characterised by a hyperplastic-looking tissue, with a regular but enlarged mucosal surface, the crypts of which appeared either round or star-shaped but enlarged, around the initial scar that was depressed and retractile (Image 1). Using BLI, it was possible to characterise the mucosal surface with more contrast (Image 2). Examination using the LCI mode enhanced the red appearance of the lesion and facilitated the demarcation of the lesion in relation to the surrounding non-lesion mucosa (Image 3).

▶ **Images 4 and 5:** The LCI examination also demonstrated the presence of another juvenile polyp located lower in the fundus that was hyperplastic in appearance, with or without zoom. The crypts appeared round or star-shaped and enlarged, producing the typical aspect of hyperplastic gastric polyps.

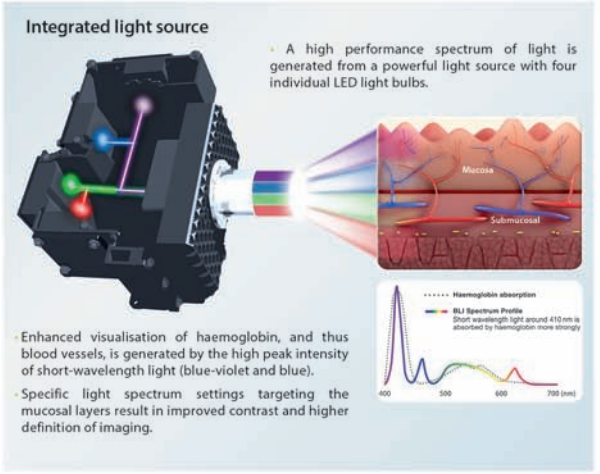
Histological description

The histological appearance of SMAD4 polyposis is extremely specific, with extensive hyperplastic lesions around the cardia. Complete resection does not prevent recurrence in the fundus.

FUJIFILM
Value from Innovation

ELUXEO

The ELUXEO endoscopy system which consists of a processor (VP 7000) and an innovative light source (BL 7000), offers new light intensity thanks to Fujifilm's exclusive Multi Light™ technology.



Multi-Light Technology

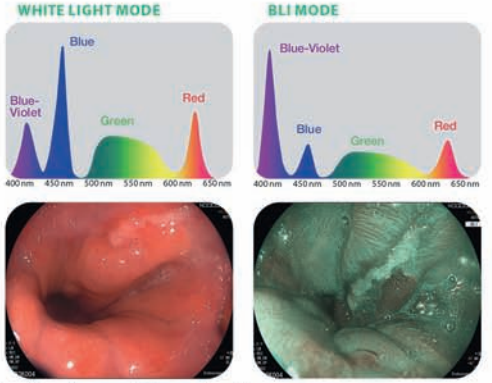
4-LED Multi Light™ technology : the new definition of light

The Multi Light™ technology is based on optimal quality white light obtained through the combination of **4 LEDs of focused colors**.
With the participation of numerous clinical experts, these wavelengths have been illustrated to correspond to the optimal absorption of haemoglobin from the vascular network of the different layers of the mucosa, from the most superficial layer to the deepest layer : blue-violet, blue, green and red. The intensity of each source creates a stable and homogeneous illumination.

In addition, by modifying the spectrum of these 4 independent LEDs, **two new observation modes** are generated: the **BLI (Blue Light Imaging)** and the **LCI (Linked Color Imaging).**

BLI

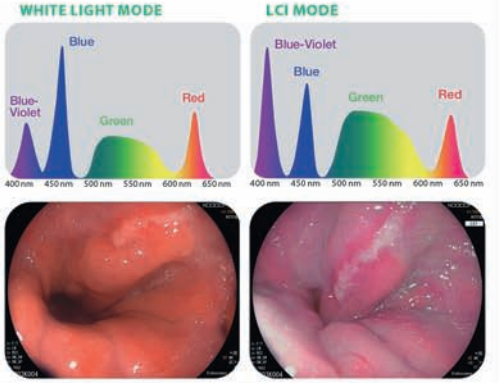
The **BLI** is targeted illumination that provides excellent visibility of the mucosal surface and better contrast of its vascular network. Associated with zoom endoscopes from the 700 series, with a magnification capacity of up to 135x, the images obtained are more detailed **facilitating the characterisation of neoplastic lesions.**



Los Angeles grade B esophagitis

LCI

Fujifilm's new exclusive **LCI** mode is based on the similar spectrum of BLI with amplification and post-processing of its signal. It enables increased contrast between the different shades of red of the mucosa. The resulting images are brighter than when using BLI illumination. LCI is therefore recommended for the **detection of adenomas and inflammatory lesions.**



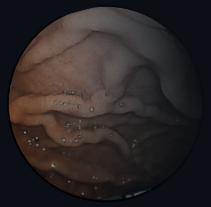
Los Angeles grade B esophagitis

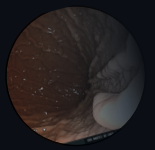
The endoscopes of the new 700 series are compatible with these two observation modes and 760 scopes are equipped with CMOS technology. A simple push of a button on the endoscope handle allows for an easy switch between the LCI / BLI observation modes.

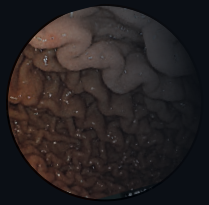
« Eluxeo represents a real revolution in the endoscopic analysis of the colorectal mucosa. Firstly, the use of LCI and BLI modes in combination with a high-definition image obviously reinforces the analysis of the mucosal surface with the aim of improving the detection of polyps. Specificaly the BLI mode associated with a high optical magnification allows you to switch easily and quickly from macro to microscopic analysis, disclosing the glandular architecture and microvascular pattern. The performance of the Eluxeo system to characterise colorectal tumors in order to predict their histology and in-depth infiltration are excellent.».

Pr Gabriel Rahmi, MD, PhD - Hôpital Européen Georges Pompidou - Paris - France

Information & studies
Multi-Light Technology LCI BLI
VISIT
BLI.eu







In recent years, endoscopy has been transformed thanks to the introduction of optical magnification, high definition and chromoendoscopy. Today, this novel mastery of detail is combined with a global overview of the whole stomach and duodenum. Screening and micro-semiology are today guided by the expertise of our Japanese colleagues.