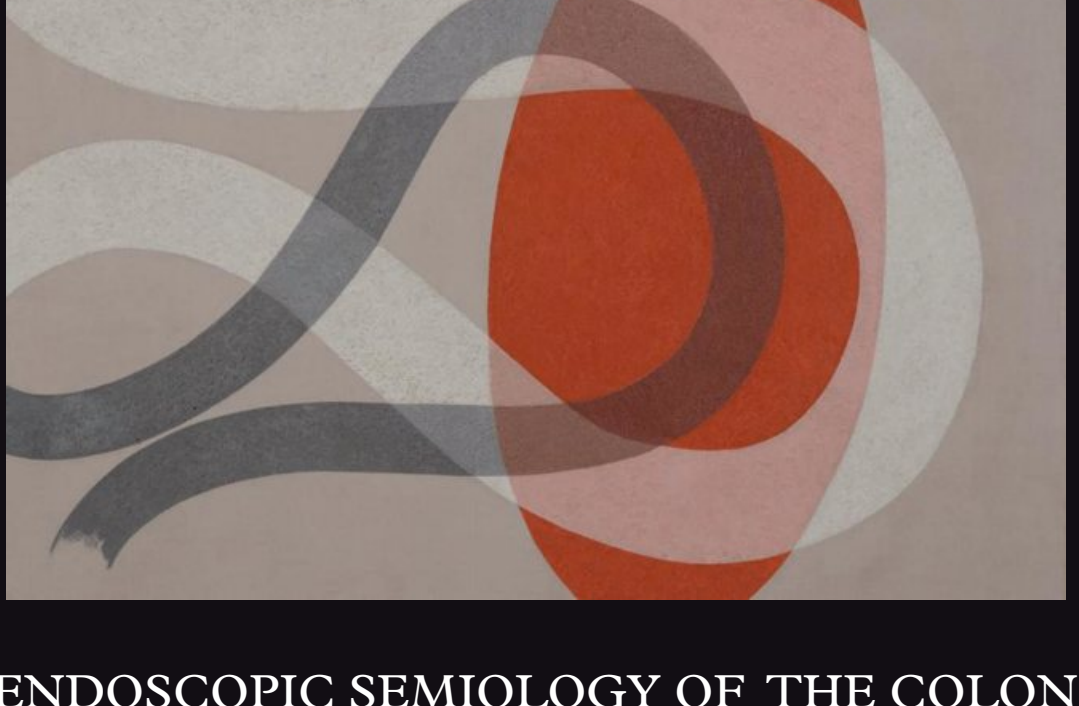

ENDOSCOPIC SEMIOLOGY OF THE COLON

From diagnosis to decision making

Coordinated by Emmanuel Coron, Gabriel Rahmi,

& Lucine Vuitton

Support by Fujifilm Europe

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General Summary

Foreword

This book, devoted to the endoscopic semiology of the colon, is the second in a series of three books (paper and e-book) dedicated to the endoscopic semiology of the digestive tract. The first book based on the oesophagus has received seemingly very favourable reception, so much so that an English version of the book has been produced for the UEGW 2018 (Vienna). The scientific coordinators are the same as for the first book, i.e. Emmanuel Coron and Gabriel Rahmi, but the team has been expanded with the arrival of Lucine Vuitton and Raf Bisschops, allowing us to better cover the field of chronic inflammatory bowel disease (IBD) and tackle some more futuristic topics such as help in decision making and artificial intelligence.

One point deserves particular attention; indeed, even if this book contains a large number of images, we were not aiming to create an atlas, since numerous atlases already exist. Our main ambition was to publish synthetic texts able to provide the reader (who is often very busy) with the "state of the art" of real *endoscopic science* that is rapidly evolving. In this sense, the short publication deadlines that we set for ourselves play a major role. As was the case for the first work in this collection, it was important to us to keep a balance between the first part of the book discussing the "developments" in the field and the second part discussing "clinical cases". For this work we have also included a small innovation presented in the appendix, containing an opinion poll based on the Delphi method, which consists of a list of 30 aphorisms that require a vote of whether you agree or disagree with the statements. While this is not based on high level of scientific evidence, we believe that the results may provide food for thought for future work.

As was the case for the first book we would like to especially thank Fujifim France and Fujifilm Europe, as well as our friends Flore Tésiorowski and Saskia Papa, who are personally involved in the publication of this book.

Finally, similarly to the first work, we have again avoided using "a beautiful endoscopic image" on the cover of the book and we have instead used a pictorial allegory... after surrealism here is the season of the Hungarian Constructivism (László Moholy-Nagy)[1].

1. The illiterate of the future will be the person ignorant of the use of the camera as well as the pen. Bauhaus 1928.

Endoscopic imaging of the colon and how technological developments will influence the paradigms of medical decision-making

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Looking inside a cavity that is inaccessible to the eye is the principle of endoscopy. A brief historical review shows that the first attempt to develop an endoscope dates back to 1868; it is attributed to Adolf Küssmaul who got the idea after attending a sword swallower show... However, the impossibility of having a sufficient source of light, prevented the development of the technique until Johann von Mikulicz-Radecki first observed the human stomach in 1881, after the invention of the electric bulb by Thomas Edison. The true revolution dates to 1957 when Basil Hirschowitz first used a flexible fiber endoscope (on himself!), thus paving the way for "modern" endoscopy and in particular the development of interventional techniques. The first golden age ensued in the following 30 years: the emergence of polypectomy (1969), retrograde cholangiopancreatograhy (1968), sphincterotomy (with retrieval of stones! -1974), endoscopic ultrasound (1980), CCD sensors (1983), hemostasis techniques for haemorrhagic ulcers (1985) and oesophageal ligation (1990). All these techniques have radically changed patient care, and there is no doubt that their impact goes far beyond the technical abilities of a few endoscopists working for the benefit of a few patients. Thus, having a colonoscopy reduces the risk of dying of colorectal cancer by 67% (1).

The second golden age extends from the first years of the millennium to today; it is marked by the revolution in the quality of the endoscopic images, with micrometer resolution. In addition, these very high-resolution images are further enriched by the possibility of applying virtual staining and structural enhancement techniques, thus making it possible to unmask certain anomalies that were undetectable with endoscopes of previous generations. However, these techniques are still inadequately evaluated in terms of clinical impact. Many questions remain unanswered: Can colonoscopy reliably assess the size of polyps? Is the optical characterisation of a polyp using white light sufficient to determine the choice of treatment and the subsequent monitoring interval? Is the strategy "Diagnose and discard" that is commonly used in English-speaking countries applicable in France? Is artificial intelligence going to guide endoscopic classification by the gastroenterologist? Can we say that a colon is normal without performing systematic biopsies?

Significant progress has already been made in the detection and characterisation of precancerous lesions. Firstly, it should be stressed that colonoscopy must meet a certain number of quality criteria in order to be regarded as a reliable exam. When these conditions are met, colonoscopy is the most effective test attesting to the absence of cancer or precancerous lesions. Endoscopic classifications are an invaluable aid for characterising lesions, predicting their nature and determining the risk of submucosal infiltration.

The Paris classification which was developed in 2003 is the most important classification in practice because it is the most easily applicable and it can be used to assess the topography of digestive lesions. It is in theory very simple;

it distinguishes protrusive pedunculated lesions (Paris 0-Ip) from sessile lesions (Paris 0-Is), discreetly raised flat lesions (Paris 0-IIa), perfectly flat lesions (Paris 0-IIb) or depressed lesions (Paris 0-IIc) and ulcerated lesions (Paris 0-III). However, this classification is imperfect, with a moderate inter-observer agreement even within expert groups (2). In addition, the risk of deep infiltration also largely depends on the size of the lesion and its mucous microarchitecture (pit-pattern), which makes real-time evaluation more complex. Finally, it has recently been shown that the risk of lymph node involvement also depends on a large number of other clinical and paraclinical factors. In this respect, the use of artificial intelligence could enable the selection of patients for a justified surgical intervention as opposed to no intervention, particularly in the case of an incomplete endoscopic resection (3). It is also clear that after assessing the topography of the lesion, some time must be devoted to the optical characterisation of its mucosal and vascular microarchitecture. The main classifications used (Nice, Wasp, Sano, BASIC) are detailed in the following chapter, and aim to classify the lesions into the following groups: hyperplastic polyps, classical adenomas or sessile serrated adenomas, thanks to the different virtual chromoendoscopy techniques that have been recently developed. These techniques are very appealing because unlike confocal endomicroscopic techniques which require special costly equipment, they can be used with standard endoscopes and are available to all gastroenterologists. However, they require a certain amount of time for observation and analysis, especially during the learning phase in order to be able to interpret the images correctly. This may explain the rather disappointing results when their application was tested in routine practice in the English study DISCARD2, even though the initial results obtained in the expert centers were excellent (4). The recommendations of this study were that narrow band imaging (NBI) cannot be recommended in routine clinical practice for the characterisation of polyps in real time. An important point is the possibility of zooming to have greater image detail, increasing the doctor's confidence in the histological prediction (5). However, we cannot ignore the growing difficulty of integrating all these parameters into the examination time. Lastly, it should not be forgotten that this endoscopic examination also requires the allocation of at least as much time to the performance of a macroscopically complete excision of the lesion, as well as securing haemostasis due to the increasing use of anticoagulants in elderly patients.

The problem of inflammatory bowel diseases is totally different, since the major issue is probably the therapeutic de-escalation in patients treated with immunosuppressive drugs, and conversely the therapeutic optimisation in patients at risk of relapse.

Standard endoscopy is largely deficient given (i) the difficulty of developing endoscopic scores that are easy to use outside of clinical research protocols, (ii) the near impossibility of performing a full-colon examination with a high

level of detail when the adoption of pancolonic chromoendoscopy recommendations combined with multilevel biopsies is very low, and (iii) the virtual absence of scientific proof regarding the benefits of virtual chromoendoscopy techniques in inflammatory diseases. However, scientific publications have demonstrated the value of endomicroscopic techniques in assessing mucosal damage, not only from a cellular morphology point of view but also from a functional one. Atreya *et al.* showed that it was possible to predict the 3-month clinical response in patients with Crohn's disease in which the mucosal characteristics were assessed by endomicroscopy after local application of fluorescent anti-TNF antibodies (6). Thus, even if it seems illusory to think that this type of approach, which requires special tools and a high level of expertise, can have an real immediate impact in clinical practice, this type of work opens up research possibilities for the use of endoscopy as a tool for functional characterisation of the mucosa. These innovative approaches are all the more desirable since the currently available biomarkers, such as fecal calprotectin, are insufficient to judge mucosal healing in patients whose symptoms may be related to functional disturbances and relapse of their inflammatory disease.

Regarding diseases of the colon, the essential issue is to show that technological progress has a real medical impact for a large number of patients. Let us hope that progress will come not only from diagnostic aids, such as those involving developments in the field of artificial intelligence, but also from the ability of gastroenterologists to adopt new paradigms and apply them to medical practice.

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Colorectal polyps: from screening to characterisation and how to choose the right therapeutic strategy

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Recent technological improvements, such as virtual chromoendoscopy techniques, including for example the Eluxeo system, make it possible to better analyse the surface of the colorectal mucosa during diagnostic colonoscopy. This is a prerequisite for the detection and characterisation of preneoplastic lesions and superficial colorectal cancers. The characterisation of polyps in order to predict their histological nature is an essential step in choosing the right therapeutic strategy, i.e. the appropriate resection type, endoscopic approach or less frequently surgical resection.

Adenoma is the most commonly encountered lesion found during a screening colonoscopy with an estimated prevalence of between 20 and 53% in patients over 50 years of age. For small adenomas, the risk of advanced lesions (high-grade dysplasia or adenocarcinoma) is low with rates ranging from 0.9 to 17.4% for adenomas ≤ 5 mm, and from 5.3 to 53% for adenomas of 6 to 9 mm. The definition of a small polyp is a polyp size of less than 10 mm, grouping very small polyps of 5 mm or less (diminutive polyps) and small polyps of 6 to 9 mm.

Detection of colorectal polyps

Firstly, it is important to mention that optimal colonic preparation, minimal withdrawal time (6 to 10 minutes) and the use of a high definition colonoscope are essential conditions for obtaining good results regarding the detection of colorectal adenomas whatever the technique used.

Virtual chromoendoscopy, now widely available, makes it possible to simply and rapidly increase the contrast between polyps and normal colonic mucosa. The benefit of this procedure for the detection of colorectal polyps has been evaluated. The majority of published studies have used the NBI chromoendoscopy (Olympus): they showed that there was only a small decrease in the risk of missed polyps and adenomas compared to colonoscopy with a high definition endoscope. More recently, in a randomised multicenter trial involving just under 1000 patients, the average number of adenomas diagnosed per patient was higher in the BLI group during a screening colonoscopy compared to the group using white light only (1). Another study showed that thanks to excellent contrast and high luminosity, the use of LCI improved the detection of flat polyps which are often more difficult to visualise (2).

Characterisation of colorectal polyps

Data from the literature show that the diagnostic accuracy for characterising and predicting polyp histology using virtual chromoendoscopy combined with optical zoom is excellent, reaching values of over 95%.

For the performance of a reliable and reproducible endoscopic analysis of colorectal polyps, several classifications are available. Most of them have been established using NBI, but their use can be extended to other virtual colouring systems like the Eluxeo system.

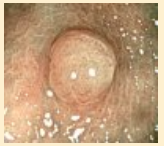
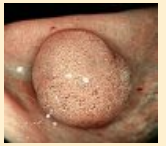
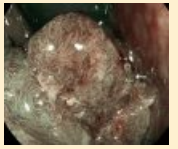
The "NICE" classification (NBI International Colorectal Endoscopic Classification) is based on an analysis without zoom of (i) the colour of the polyp, (ii) the presence of vessels (and their diameter) and (iii) the topography of the mucosa (Table 1). It can distinguish between hyperplastic polyps (type 1), adenomas (type 2) and invasive cancers.

This classification is simple to use and should be systematically included in endoscopy reports.

Regarding sessile serrated adenomas, the WASP classification (Workgroup serrAted polypS and Polyposis) can distinguish them from other hyperplastic polyps and adenomatous polyps. These lesions belong to the heterogeneous group of serrated polyps, corresponding to epithelial lesions with a morphological definition. They are characterised by a serrated or indented histological appearance of the epithelial crypts.

Their diagnosis is often difficult and they require special attention from endoscopists and pathologists because underestimation of their frequency and evolutionary potential could explain the occurrence of certain post-colonoscopy colorectal cancers (interval cancers).

Table 1: Classification using virtual chromoendoscopy without optical zoom, enabling the prediction of the histological nature of the polyps according to certain characteristics, such as colour, vascularity and the surface appearance.

	Type 1	Type 2	Type 3
			
Colour	Light	Brown	Dark or Black
Vessels	Absence (sometimes venous networks on the surface)	Regular, surrounding the glands	Irregular and sometimes absent
Surface	Homogeneous dark or white dots	Tubular or branched structures	Distorted zones or no pattern
Histology	Hyperplastic	Adenoma	Adenocarcinoma

The WASP classification for sessile serrated adenomas takes into account the following characteristics: sessile or slightly elevated, covered with mucus (yellow or red using BLI), lighter than the surrounding mucosa in BLI mode, irregular appearance resembling a plateau or a cloud, with a core of round crypts with a central black point, and badly defined edges (Figure 1).

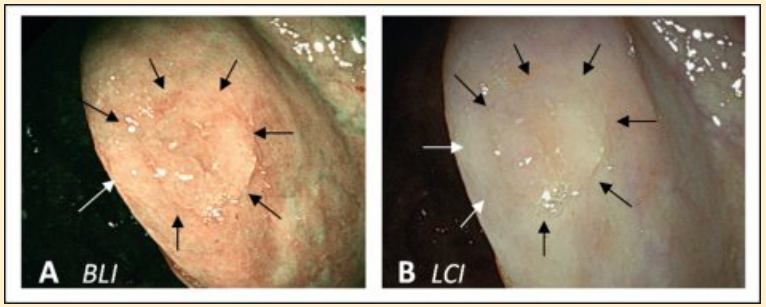


Figure 1: Sessile serrated adenoma of the right colon of around 6 mm, analysed by BLI followed by LCI. The selected technique was cold snare resection.

The Sano classification is another classification based on NBI virtual chromoendoscopy with high optical magnification used to analyse vessels (regular or tortuous) and their diameter (Table 2). The diagnostic accuracy and the negative predictive value of this classification are excellent. Analysis of the microvessels makes it possible to evaluate the in depth infiltration and thus to choose the appropriate resection technique.

Recently, a group of experts proposed a new classification called "BASIC" for the characterisation and prediction of deep invasion of colorectal polyps using the BLI mode (3). Following the Delphi method and through the analysis of images and videos, seven international experts proposed 12 criteria describing (i) the glandular architecture (pit pattern), (ii) the vascularisation and (iii) the surface of the polyp. The interobserver concordance was excellent or good for the surface criteria of the polyp (regular, presence of mucus) and for the vessels (absent, vascular networks, pericryptic, irregular). Regarding the glandular architecture, the concordance was good regarding the absence of contour and its appearance (rounded or not). In this study the diagnostic accuracy was not studied and will have to be the subject of a future prospective evaluation.

WHAT THERAPEUTIC STRATEGY TO ADOPT?

The macroscopic and microscopic *in vivo* endoscopic analyses of colorectal polyps make it possible to predict their histological nature, their depth of infiltration when it comes to cancer, and therefore to choose the appropriate treatment (Figure 2).

Table 2: Classification using virtual chromoendoscopy with optical zoom (magnification), making it possible to predict the histological nature of the polyp based on the appearance of the microvasculature. In the case of type IIIB the risk of invasion exceeding the deep submucosa is very high, and it is associated with the risk of lymph node invasion (in this case surgical treatment should be considered).

	Type I	Type II	Type IIIA	Type IIIB
				
Micro-vasculature	Vessels surrounding the crypts, but not branched	Connected appearance of the vessels, regular, medium density	Irregular branched vessels without avascular zones, high density	Almost avascular or very few vessels, very irregular
Histology	Hyperplastic	Simple adenoma	Degenerated adenoma WITHOUT deep invasion	Degenerated adenoma WITH deep invasion

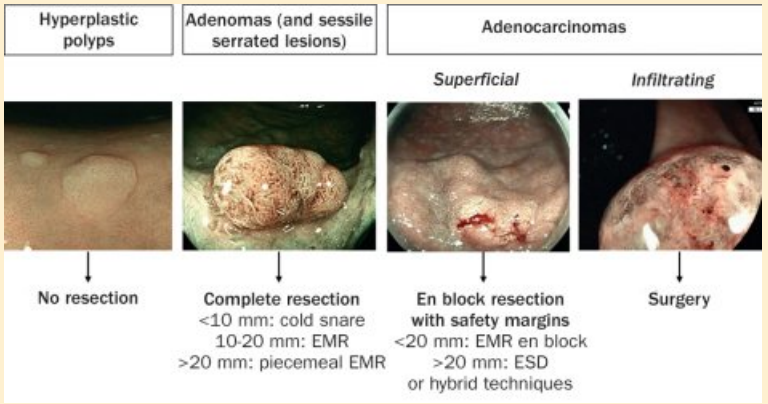


Figure 2: Therapeutic strategy based on the histological prediction of colorectal polyps (ESD: endoscopic submucosal dissection, EMR: endoscopic mucosal resection).

Nearly half of the polyps diagnosed during a screening colonoscopy are hyperplastic polyps with no potential for degeneration to cancer. Their resection represents a considerable cost (medical time, endotherapy equipment, histological analysis) and can be associated with complications (though rare). It is therefore legitimate to consider other strategies than systematic resection of all polyps; the idea is then to try to resect only the adenomatous polyps and to leave the small polyps that are very probably hyperplastic untouched ("predict-resect-leave" strategy) or simply to discard them ("predict-resect-discard ").

According to the European and American endoscopy societies, it is thus recommended to leave in place a simple hyperplastic polyp (type 1 of the NICE classification)

especially when it is located in the rectosigmoid. The same is true for more proximal hyperplastic polyps when the operator has high confidence in his in vivo analysis.

For sessile serrated adenomas and simple adenomas without any sign of degeneration, endoscopic resection is recommended. The goal is to do a complete resection that can be either one-piece or fragmented. Mucosectomy (EMR: endoscopic mucosal resection) is therefore the first-line technique.

For adenomas with a high risk of containing degenerated zones or for superficial adenocarcinomas, the objective is to obtain a curative R0 resection and monoblock resection is therefore preferred. Depending on the size of the polyp, mucosectomy (< 20 mm) or submucosal dissection (> 20 mm) (ESD: endoscopic submucosal dissection) are the two preferred techniques. The so-called "hybrid" technique (submucosal dissection and mucosectomy) consists of starting the resection with a circumferential dissection and finishing it with a diathermic loop.

The macroscopic appearance is an important factor to consider in order to evaluate the risk of submucosal invasion and therefore the choice of the resection technique. The risk is high (i) in the case of a depressed lesion classified as IIc according to the Paris classification; (ii) when there is a macronodule of more than 1 cm within an adenomatous laterally spreading polyp (LST G) (risk of around 20%), (iii) when the polyp is flat with lateral spreading (LST NG) associated with a depressed zone (risk of about 40%); and (iv) when the size exceeds 30 mm for LST G and 20 mm for LST NG (Figure 3).

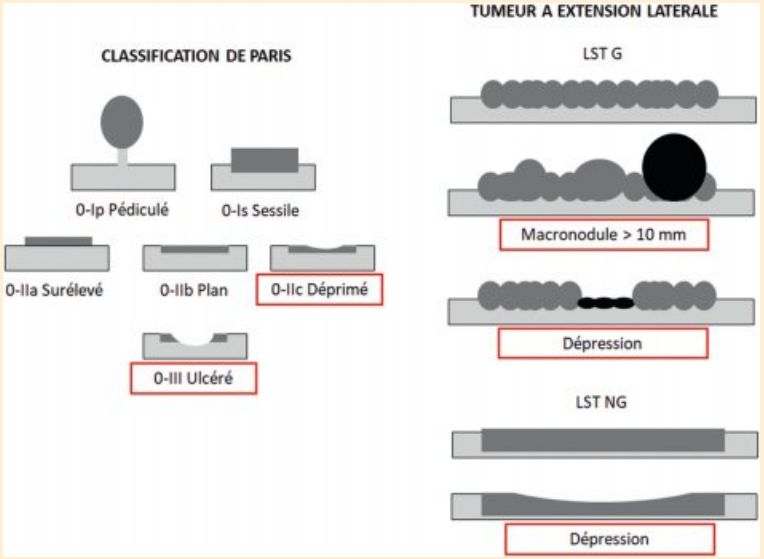


Figure 3: Macroscopic morphological classification of colorectal polyps. Cases that are framed in red are at a high risk of invasion of the deep submucosa.

Finally, for adenocarcinoma with suspected deep invasion, it is necessary to choose surgery with lymph node dissection.

In conclusion, the current technological revolution in digestive endoscopy makes it possible to better detect and characterise colorectal polyps. Pre-cancerous and superficial cancerous tumors can be conveniently removed, minimally invasive, and with the primary objective of preserving the integrity and function of the colon and rectum.

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Colonoscopy in the context of inflammatory bowel disease (IBD): an indispensable tool for all stages of care

The role of colonoscopy in chronic inflammatory bowel disease (IBD)

Colonoscopy is an essential examination in the management of IBD: it is used to confirm the initial diagnosis, and diagnose relapse, as well as the follow-up of the disease, when the clinical symptoms can be unclear (1). In addition to a positive diagnosis, colonoscopy makes it possible to distinguish between Crohn's disease (CD) and ulcerative colitis (UC), and to specify the severity and topography of inflammatory lesions, which are necessary for clinical management. This examination is therefore a prerequisite for the initial choice or change of treatment, and it is also currently the "Gold standard" used to confirm that the goal of treatment is achieved, especially regarding the endoscopic response, and ideally also the endoscopic mucosal healing. A major breakthrough in the last ten years, in parallel with the development of biotherapeutics, is the demonstration that achieving remission, in particular endoscopic remission, makes it possible to modify the natural history of these chronic diseases, as can be evaluated by different criteria: hospitalisations, surgery and destruction of the intestine. For these reasons, significant evolution has taken place regarding the number and quality of endoscopic examinations in this field of gastroenterology.

In addition to being a diagnostic and therapeutic tool, colonoscopy is also a screening tool. The risk of colorectal cancer in patients with colitis is 2.4 times higher than in the general population, as was shown in population cohort studies (2): a major challenge of colonoscopic screening is the prevention of colorectal cancer in this population, and recently it was shown to be effective for this purpose (3, 4). Finally, colonoscopy can be a therapeutic tool (1), especially for resection of dysplastic lesions and dilation of ileocolic stenoses.

Practical aspects of colonoscopy for IBD

In practice, the preparation for colonoscopy must be excellent to allow for a thorough assessment; this must include exploration of the ileum, and effective screening for pre-neoplastic lesions. The quality factors for the preparation are the same as in the general population, namely, split dose, minimum delay between the intake of the last preparation and colonoscopy, residue-free diet the day before and use of a washing pump.

Screening colonoscopies should be performed with new generation endoscopes with high definition (5).

Biopsies should be performed systematically on inflammatory lesions, and macroscopically healthy zones in each segment, with a minimum of two representative samples (ileum, right colon, transverse colon, left colon, sigmoid, rectum) at initial diagnosis (1). Then, during follow-up, systematic segmental colonic biopsies can be used to determine the level of histological inflammation, which is itself correlated with prolonged remission, particularly in UC, and the risk of dysplasia (1, 4).

Endoscopic semiology of IBD injuries

It is important to use standard terminology to describe the appearance of abnormalities encountered in IBD. Endoscopic abnormalities that we describe, called "Elementary lesions" are those that are both characteristic of the endoscopic appearance of the pathology and have a good intra- and inter-observer correlation (6, 7). The way endoscopic lesions are described differs in UC and CD. In UC, the elementary lesions are the presence of blood (on the mucosa and / or in the lumen), the visibility of the vascular framework (complete or partial disappearance), and the presence of ulcers (erosions or ulcers) (Table 1). In CD the elementary lesions are erythema, oedema, aphthous ulcers, ulcers (superficial, deep, wide), stenoses, pseudo-polyps, and scars (Table 2).

These endoscopic features are nevertheless not specific to one disease, and the diagnosis between UC and CD may be difficult in about 10-15% of the cases (1). The most useful criteria for the diagnosis of UC are the continuous and confluent nature of rectal or colorectal involvement from the anal margin. Rectal involvement is constant in UC at the initial diagnosis and in the absence of prior treatment. The most discriminating endoscopic aspects in favour of CD are the discontinuous nature of the lesions observed with intervals of healthy mucosa, the presence of stenoses and fistulas, and the perianal involvement, which must be carefully studied during the colonoscopy.

The specificity of the elementary lesions described above is not excellent and is not sufficient to diagnose IBD. Several differential diagnoses may have identical endoscopic signs: acute infectious colitis (for example: Salmonella spp., Shigella spp., or Campylobacter spp., Chlamydiae spp.), or ischemic colitis; tuberculous enterocolitis; and medicated enterocolitis.

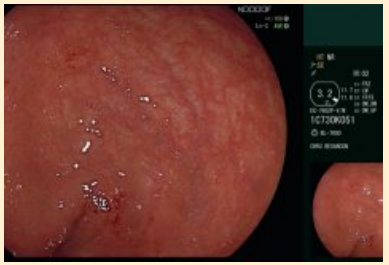
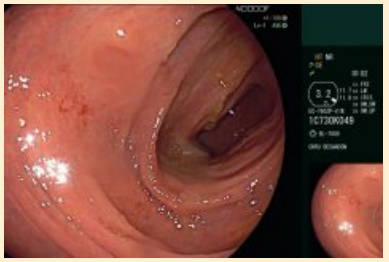
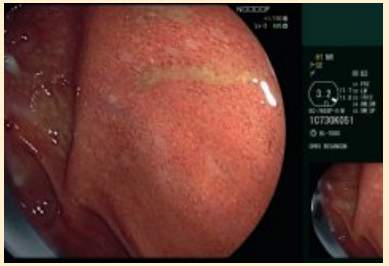
The colonoscopy report for IBD should describe only the elementary lesions for each segment, their extent in the segment (as percentage for simplicity reasons), and associate a representative photograph of each segment. For UC, the upper limit of the lesions at the junction with healthy colon should be specified. The goal is to adopt a common vocabulary understandable by another practitioner, and to allow for accurate and comparative assessment of colonoscopies over time. This also makes it possible to determine the endoscopic response to the treatments undertaken.

Endoscopic scores

The use of endoscopic scores is not restricted to research, but it also facilitates the follow up of patients by using a common language in order to compare exams over time. Furthermore, validated scores are composed of elementary endoscopic lesions, and can serve as a guide for the gastroenterologist when preparing the endoscopy report.

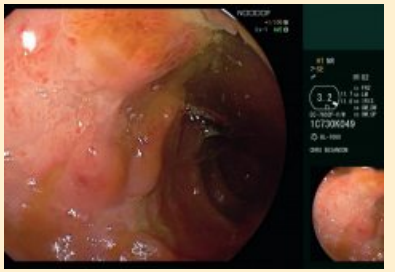
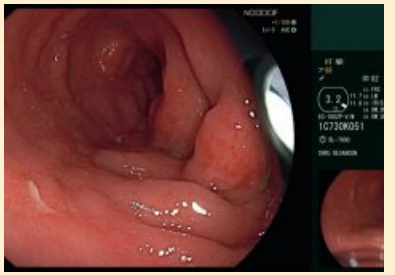
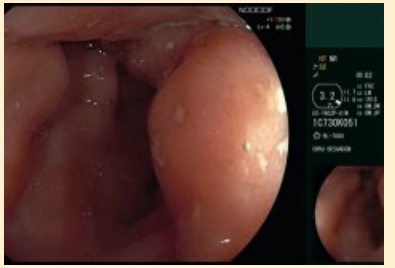
For UC, the "Mayo endoscopic subscore", which was originally described in clinical research but that has never

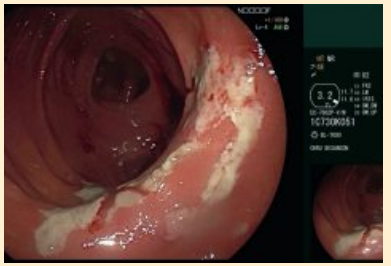
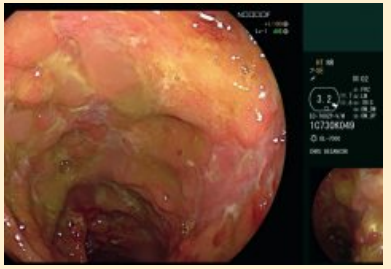
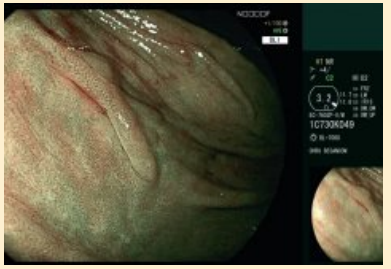
Table 1: Elementary endoscopic lesions of ulcerative colitis.

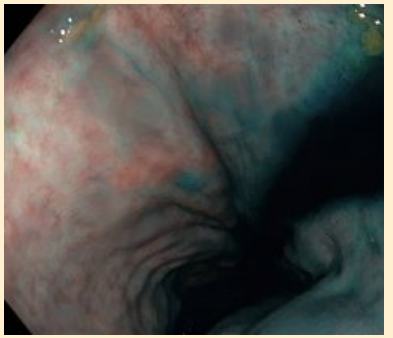
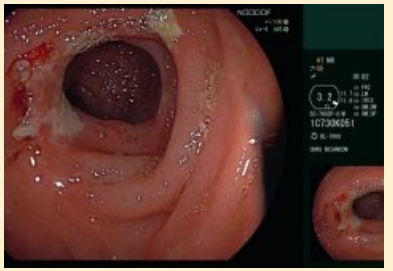
Lesion	Description	Endoscopic illustration *
Vascular network	Network of submucosal vessels visible under normal conditions. The loss of visibility of the vascular network can be partial or total.	
Bleeding	Washable coagulated hemorrhagic points or streaks, or fresh blood in the colic lumen.	
Ulcers	Loss of mucosal integrity with fibrinous coating. Erosion ≤ 5 mm or larger ulcers, +/- indentation.	

* Fujifilm Eluxeo™ EC-760ZP Colonoscope - 700 Series

Table 2: Elementary endoscopic lesions of Crohn's disease.

Lesion	Description	Endoscopic illustration*
Marked oedema	Disappearance of the vascular network, puffy appearance Mild or moderate oedema should be ignored.	
Marked erythema	Abnormal redness of the mucous membrane Mild or moderate erythema should be ignored.	
Aphthous ulcers	Small (≤ 3 mm) raised or flat lesion, white in the center, +/- erythematous halo.	

Superficial ulcer	Loss of mucosal integrity neither aphthoid nor deep. The width should be described (≤ 5 mm, 5-20 mm, > 20 mm, large ulcer).	
Deep ulcer	Loss of mucosal integrity with raised edges, and/or mucosal detachment. Width (≤ 5 mm, 5-20 mm, > 20 mm, large ulcer).	
Pseudo polyp	Polypoidal lesion, non adenomatous, pit pattern Kudo I	

Healed ulcer	Whitish area with “frosted glass” appearance, stellate scars	
Stenosis	Impossible or difficult passage through the tube	

* Fujifilm Eluxeo™ EC-760ZP Colonoscope - 700 Series

been validated, is widely used in clinical practice around the world.

It is a simple score, which ranks the severity of the disease from 0 to 3 (0 = normal mucosa, 1 = erythema, partial reduction of the vascular pattern, 2 = marked erythema, disappearance of the vascular pattern, erosions, 3 = spontaneous bleeding, ulcers).

More recently, the more robust and validated UCEIS (Ulative Colitis Endoscopic Index of Severity) score has been used in clinical research; its ease of use also allows its application when preparing the endoscopic report. It is composed of the 3 most reproducible elementary lesions of UC: the vascular network, bleeding and ulcers, which are noted according to their level of severity (8) (Table 3). In

CD, two scores have been validated, the CDEIS (Crohn's Disease Endoscopic Index of Severity), developed in the late 80s, and the SES-CD (Simple Endoscopic Score for Crohn's Disease) derived from CDEIS for simplification reasons (9) (Table 4).

Finally, the description of CD after ileocolic surgery must use the Rutgeerts score, which has not been validated, but predicts postoperative recurrence. This is an easy and very widely used score (Table 5) that describes ileocolic anastomosis and upstream neo-terminal ileum (aphthous ulcers, ulcers, stenosis) (9).

The definitions of endosopic response and remission have not yet been validated. In UC, remission corresponds to at least the disappearance of the ulcerated lesions and blood. In CD remission corresponds to at least the disappearance of ulcers. A consensus of experts has proposed the following definitions for UC: endoscopic response, decrease in the Mayo endoscoopic score ≥ 1 or a decrease in the UCEIS score ≥ 2; endoscopic remission: UCEIS score 0. For CD: endoscopic response, > 50% decrease in CDEIS or SES-CD score; endoscopic remission: SES-CD score 0-2. After surgery, Rutgeerts score of i0 or i1 is the current consensus for defining remission (8, 9).

Detection of dysplasia

Screening colonoscopies are intended for patients with former and more extensive colitis (CD or UC), given the risk of colorectal cancer associated with IBD (1, 5, 10). A first evaluation is proposed approximately 8 to 10 years after the diagnosis, then the regularity of the controls is adapted to the level of inflammatory activity of the disease, its extent, the presence of pseudo polyps or stenoses, and the patient's

Table 3: UCEIS (Ulcerative Colitis Endoscopic Index of Severity) Score (7).

Item	Appearance	Score
Vascular network	Normal	0
	Decreased	1
	Disappeared	2
Bleeding	Absent	0
	Coagulated, washable dots or streaks	1
	Some luminal fresh blood	2
	Abundant luminal blood and / or spontaneous bleeding	3
Erosions and ulcerations	Absent	0
	< 5 mm, superficial	1
	> 5 mm, fibrinous coating	2
	Indented	3
Total		0-8

Table 4: SES-CD Score (Simple Endoscopic Score for Crohn's Disease).

Variable	0	1	2	3
Size of ulcers	None	Aphthous ulcers (0.1-0.5 cm)	Wide ulcers (0.5-2 cm)	Very wide ulcers (> 2 cm)
Ulcerated surface	None	< 10%	10-30%	> 30%
Affected surface	None	< 50%	50-70%	> 75%
Stenosis	None	One, Crossable	Multiple, Crossable	Impassable

The score is calculated for each segment, then the total sum of all the segments that have been explored is determined.

Table 5: Rutgeerts postoperative endoscopic score

Endoscopic score	Definition
i0	No injury
i1	≤ 5 aphthous ulcers
i2	> 5 aphthous ulcers within normal mucosa or larger but limited lesions; or lesions confined to the anastomosis
i3	Diffuse aphthous ileitis in a diffusely inflammatory mucosa
i4	Diffuse inflammation with large ulcers, nodules or stenosis
Remission: i0-i1; Recurrence: i2-i4	

antecedents (primary sclerosing cholangitis (PSC), history of colorectal cancer in the immediate family, personal antecedents of adenoma or colonic dysplasia). To carry out this screening, international consensus insists on the operator's experience in IBD specific endoscopy, and on the use of high-definition endoscopes. When these conditions are not met, it is advisable to seek an expert center (1, 5, 10).

In IBD, numerous studies have demonstrated the diagnostic benefit of using blue staining (indigo carmine blue or methylene blue) to detect pre-neoplastic lesions (5). In the era of high-definition endoscopy, with image magnification, the blue colouring remains valid and is still recommended (5). In practice, blue can be diluted with saline or water (1/6-1/10 dilution), and used directly in the wash pump. Studies using virtual staining have so far focused on the Olympus® narrow band imaging (NBI) system; they did not show any benefit of this approach compared to using

high-definition white-light endoscopy or high definition blue-chromoendoscopy (5). The pre-neoplastic lesions of the colon found in IBD may be sporadic adenomas or serrated polyps, located within inflammatory lesions or in healthy zones. They may also be non-adenomatous dysplastic lesions, which may develop in inflammatory or formerly inflammatory areas, as occurs for example in stenoses. The characterisation of the observed lesions makes it possible to discriminate between adenomatous lesions and lesions that are specific to IBD. A description should be made, as is the case when screening for adenomas, using the Paris classification (pedunculated lesion 0-Ip, sessile lesion 0-Is, flat lesion 0-IIa and b, depressed lesion 0-IIc, ulcerated lesion 0-III); it must specify the "pit pattern" (according to Kudo for example), and the size of the lesion.

More specifically, it is necessary to specify whether the lesion is located within inflammatory lesions, stenoses or scars, and to describe the presence or absence of edges, and clear limits that may provide enough reason to contemplate endoscopic resection (10). If the lesion is not immediately resectable in order to obtain complete histological analysis, any suspected dysplastic lesions should be biopsied. The aim of biopsies targeted by chromoendoscopy is to have a better diagnostic efficiency. There is an ongoing debate regarding the usefulness of performing systematic multilevel biopsies (4 per 10 cm segment) in addition to targeted biopsies, since this approach provides very little benefit (5). The current scientific consensus (1, 10) suggests that only targeted biopsies should be performed on detected abnormalities, provided that high quality chromoendoscopic equipment and an expert in the field are available. It should be noted however, that at least two biopsies in each colonic segment are recommended in any case to establish the histological extension of colonic inflammation. Furthermore, the surveillance of patients with PSC is different, since past literature has described the occurrence of dysplasia that is endoscopically "invisible" in these patients, but it is possible to detect in random biopsies. Monitoring examinations for these patients should be annual, with numerous, multilevel biopsies (both targeted and systematic) in all segments.

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Artificial intelligence: Perspectives in the developments in the field of digestive endoscopy

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The life of an endoscopist is hard these days. The caseload is getting heavier each year and for a large portion of time, the endoscopist is merely a machine processing a large number of images whilst looking for abnormalities in order to provide the correct diagnosis. This is not only a long and tiresome process but it is also inherently difficult due to the large variety of possible diseases and their appearance. This makes the effectiveness of a colonoscopy depend largely on the operator's skill and thoroughness, which vary largely with the training they have received and the operational environment of their institution. Even with today's high definition endoscopes and advanced classification systems, a suboptimal performance is achieved for many tasks especially in non-expert settings. Indeed, the quality of colonoscopy differs significantly and these differences translate into considerable clinical consequences for patients. For example, it is well established that post-colonoscopy colorectal cancers (PCCRC) arise from missed lesions or incomplete polypectomy (1,2). Back-to-back colonoscopy studies have shown that up to 22% of all adenomas are missed (3) and that there is a significant variation in adenoma detection rates between endoscopists (4). The latter correlates very well to the risk of PCCRC (5). Also in the upper GI tract, quality differs significantly between endoscopists. Gastric cancers and precursor lesions are frequently missed: in one series, in 7.2% of patients with gastric cancer the lesion was not detected at a previous endoscopy performed within the past year (6). A recent study from Singapore indicated that, as is the case for the colon, inspection time for lesion detection is important: slow endoscopists with an inspection time of seven minutes or more detected significantly more high risk lesions in the stomach in comparison to fast endoscopists (14% versus 6%) (7).

Similarly, in most epidemiological studies on Barrett's oesophagus, it was shown that up to 36% of cancers are detected within 1 year of diagnosis indicating that these lesions were probably missed during the first endoscopy (8). In patients referred with Barrett's dysplasia without clearly visible lesions, expert eyes can detect lesions in 75% of cases, even including lesions that need straight referral for surgery (9).

As a first step, introduction of automated procedures in the field of endoscopy could help in lesion detection in order to eventually improve the outcome for patients (if easy to use and accurate). Endoscopy also entails a lot of image-based decision-making. Tremendous costs are involved, especially with the huge numbers of resected polyps. Diagnosis based on optical analysis could be potentially cost saving (10,11). Although initial results of the NICE classification using NBI looked very promising with an accuracy of 95-98% (12), the recent DISCARD II and REDEFINE trials demonstrated that we are a long way from implementing such algorithms in a real life setting with sufficiently high quality (13,14).

An automated system for detection, diagnosis and disease monitoring has many advantages. First of all, it is

objective and repeatable, removing the ubiquitous inter- and intra-observer variability, which is inherent to any guideline or classification system used by an endoscopist. On top of this, a computer is never tired or hungry, so the last patient of the day will get the exact same level of attention as the first one. As an additional advantage, it is also potentially a lot faster than human beings and it can take into account more information than a typical endoscopist would use to make a diagnosis. In recent years, it has even been shown that artificial intelligence can surpass human performance in tasks that require a certain level of expertise. A mobile phone application exists today that can discriminate malignant skin melanomas from benign lesions more accurately than a dermatologist (15).

Artificial intelligence (AI) is the general term for any type of machine that can perform tasks in an automated way with some sort of reasoning or algorithm behind it. Even though this concept has existed for many years, it is only recently that AI has become very popular in the medical world. This is mainly due to i) the increased computational power that we have today, ii) the easier access to data and iii) most importantly due to the rise of the deep learning paradigm. Deep learning (DL) has revolutionised the world of computer-aided analysis and has shown its remarkably high performance in classifying spatially correlated data, such as images. The most recent methods for image analysis almost exclusively use this paradigm and consistently outperform more traditional methods in nearly every application. The reason for this superior performance is that DL uses neural networks which, much like a human brain can learn to discriminate certain features. For example, the algorithm is never told what a polyp typically looks like but instead it learns from (a large number of) examples how to recognise them. This also implies that the power of a neural network depends chiefly on the data that it is presented during training. Therefore, the utmost importance is given to the data and one could almost say: “the data is the algorithm”. More and more resources are therefore allocated to gathering large, validated datasets.

Detection and diagnosis of endoscopically visible lesions requires the processing of long videos with typically only very sparse display of areas of interest. There are numerous cases where the endoscopist could benefit from being assisted by an AI system. Some examples include polyp detection and characterisation (see Figure 1), gastric cancer diagnosis, endoscopic staging of adenocarcinoma, optimal biopsy site selection, delineation of lesions, among many others. This kind of support module would be integrated within the endoscope’s processor and it would be accessible to any endoscopist. This would not only lower the detection miss rates but it would also lower the dependency on histopathological analysis, allowing less specialised doctors/hospitals to make more difficult diagnoses and in general make the endoscopists more confident in their clinical decisions.

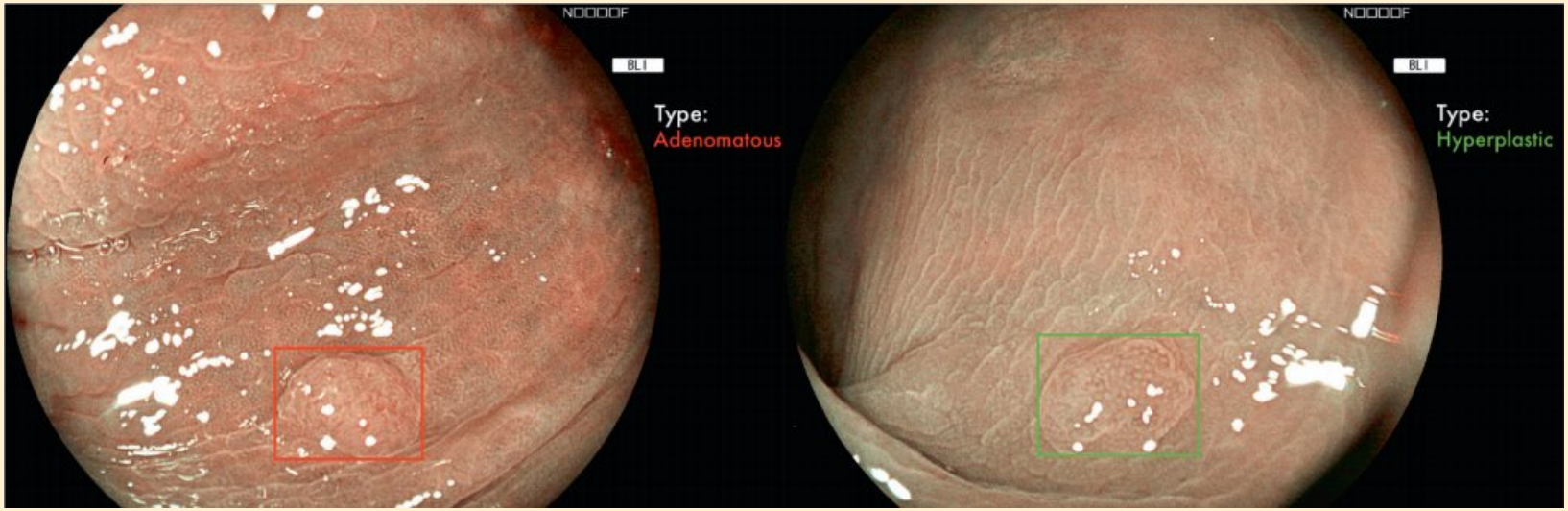

Figure 1: AI assistive tool for polyp detection and characterization.

Recent publications suggest that the progress in this field is moving us closer to realistic applications of these technologies in practice. Chen *et al.* showed that an accurate automated discrimination between hyperplastic and adenomatous polyps is possible. In their study a deep convolutional neural network was trained and tested on manually selected ROIs from high magnification and high quality images (16). Very recently, a video-based approach where each frame is classified as a whole image was proposed by Byrne *et al.* The results of this classification were then used to update a credibility score over the course of the full video (17). Finally, a pilot trial for the detection of Barrett's neoplasia showed at the patient level, that the AI system achieved a sensitivity and specificity of 0.86 and 0.87, respectively (18)

In the next 5 to 10 years, AI will start to be more and more integrated into routine clinical practice. The more image-based a certain field is, the bigger the impact will be. The profession of a radiologist or pathologist will not be the same anymore. Pure image interpretation will become less

important and the clinician will contribute in a more holistic way to the diagnosis and personalised treatment of the patient. On the other hand, some major limitations to AI systems still exist today. Because of these limitations the clinicians will more likely be assisted by AI instead of being replaced by it. The applications of AI today are very narrow, meaning that they can only perform one specific task and thus a higher level of context is missing. In addition, the level of interpretation that a human can provide when making a decision is still lacking for neural networks. Having a human in the loop will therefore probably remain important for decades to come (19).

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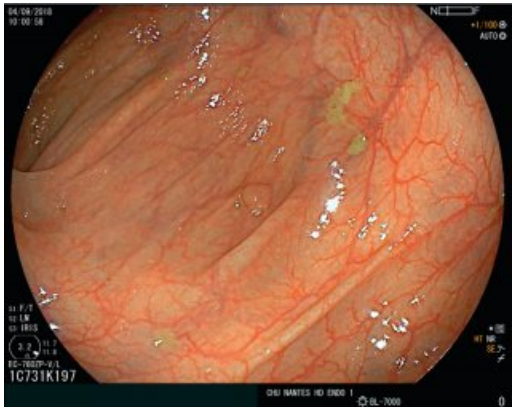
List of clinical cases

CC1: Is the strategy of "diagnose and discard" applicable in France? The example of very small polyps (< 6 mm)
CC2: Superficial adenocarcinoma of the rectum resectable by submucosal dissection
CC3: Adenoma with high grade dysplasia and infiltrating microcarcinoma (mixed LST) of the ileocecal valve
CC4: Management of a rectal tumour of the LST G type with Sano IIIB macronodule
CC5: Development of adenocarcinoma on a scar of an irradiated coloanal anastomosis
CC6: Submucosal dissection of a fixed sigmoid colon with multiple diverticula
CC7: Invasive adenocarcinoma of the rectum type LST in the context of Lynch syndrome
CC8: Difficult diagnosis of Crohn's disease
CC9: Ulcerative colitis with multiple polyps without adenomatous or dysplastic lesions
CC10: Tubulovillous adenoma with dysplasia (high and low grade) complicating antecedent ulcerative colitis
CC11: A flat dysplastic lesion in the context of antecedent Crohn's colitis

Main abbreviations used in the text
LCI: Linked Color Imaging
BLI: Blue Light Imaging
LST: Laterally Spreading Tumour

CC1 Is the strategy of "diagnose and discard" applicable in France? The example of very small polyps (< 6 mm)



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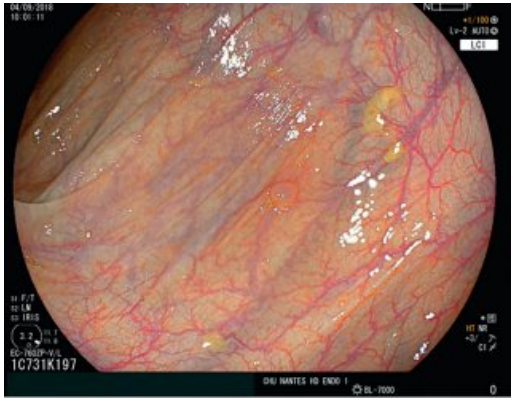

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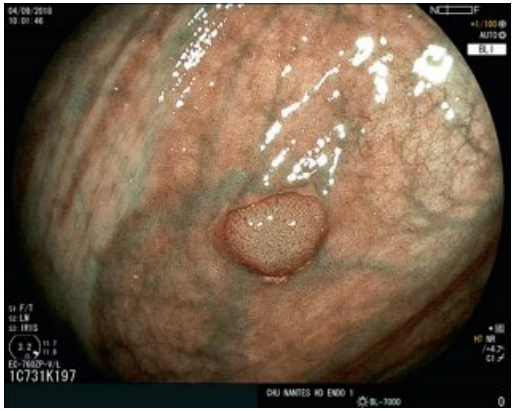

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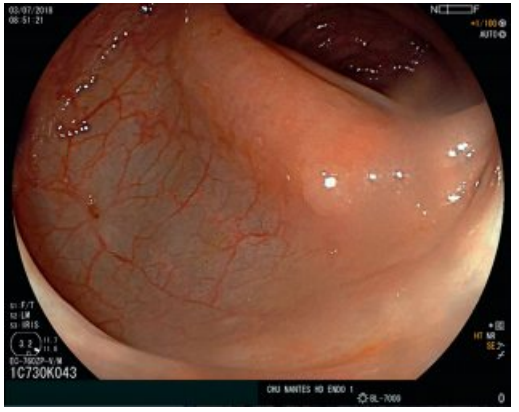

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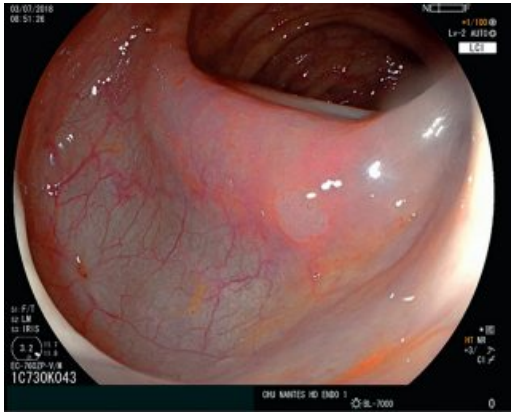

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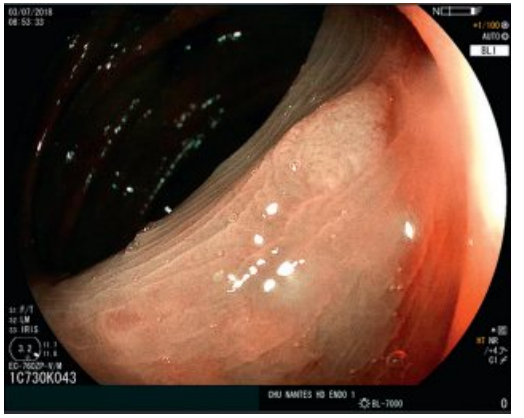


- 6 -

Clinical description

A 72-year-old patient with a first-degree family history of colorectal cancer and adenomatous polyps was referred for surveillance colonoscopy. She also had a history of severe smoking complicated by lower extremity arteritis and right carotid endarterectomy 2 years ago following a stroke. Clopidogrel treatment was discontinued 5 days before the procedure. Two polyps of 3 mm and 5 mm in size located in the left colon were found during colonoscopy.

Endoscopic description

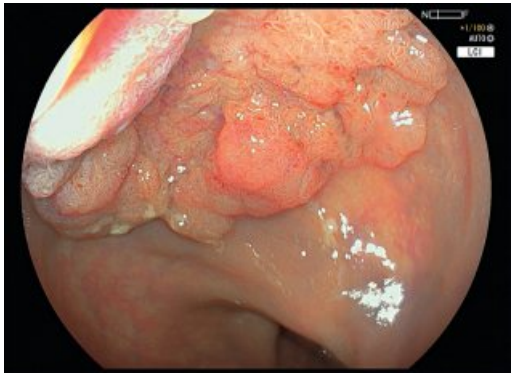
▶ **Images 1, 2 and 3:** Polyp number 1 was located 50 cm from the anal margin. It was detected with white light (Image 1) but the visibility was better using the LCI mode (Image 2). Its size was estimated to be 5 mm. It was classified as Paris 0-Is with regular and elongated crypts, surrounded by brown vessels using the BLI mode (Image 3). According to this optical characterisation, it had a typical appearance of a benign tubular adenoma, and was resected with cold snare.

▶ **Images 4, 5 and 6:** Polyp number 2 was located 30 cm from the anal margin. It was also detected using white light (Image 4) but it was easier to identify using the LCI mode (Image 5). Its size was estimated to be 3 mm. It was classified as Paris 0IIa with a paler appearance than the adjacent mucosa in BLI mode. Note that zoom was necessary to characterise the appearance of mucosal microarchitecture, revealing the absence of peri-cryptic vessels and the presence of black dots within round crypts (Fig. 6); it therefore had a typical appearance of a hyperplastic polyp. This polyp was left untouched.

Histological description

Polyp number 1 consisted of tubes lined with cylindrical cells with reduced mucus secretion. The pits were globular, hyperchromatic with a tendency to ascend, but they remained however arranged at the basal pole of the cells. The excision of the lesion was complete. It was characterised as a tubular adenoma with low grade dysplasia.

CC2 Superficial adenocarcinoma of the rectum resectable by submucosal dissection



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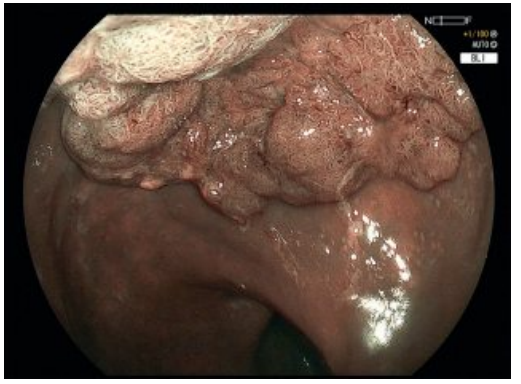

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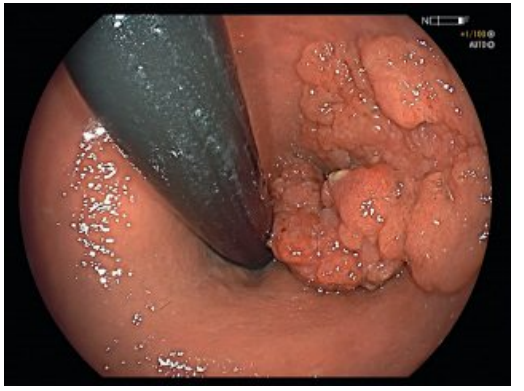

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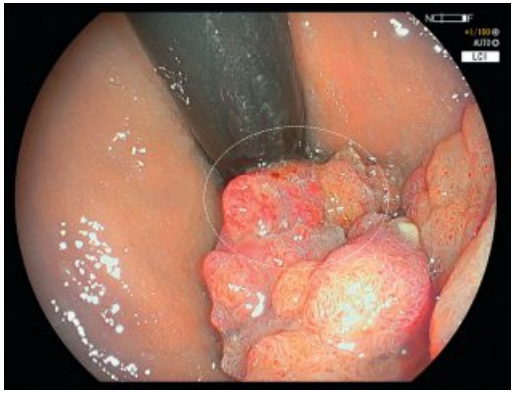

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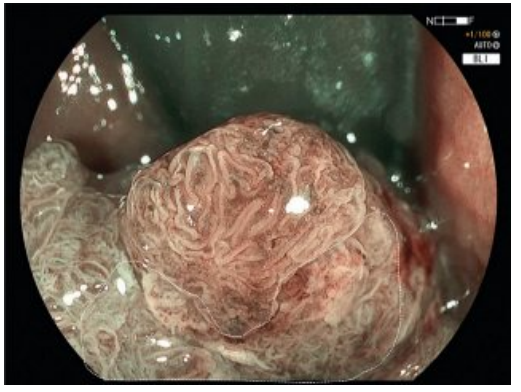

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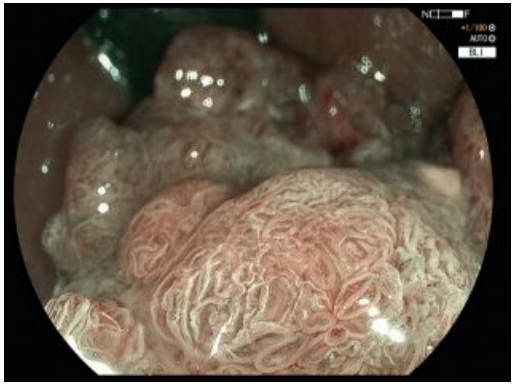


- 6 -

Clinical description

A 57-year-old patient with no notable antecedents was referred for endoscopic resection of a large lesion of the rectum. This lesion was discovered during a screening colonoscopy performed after a positive FIT test 3 months earlier. A previous endoscopic ultrasound was not indicative of muscle invasion or lymph node involvement (usT1N0).

Endoscopic description

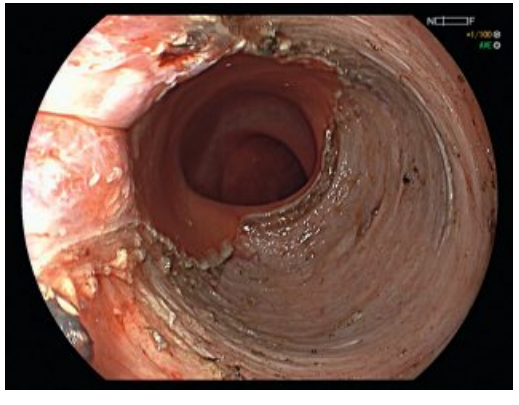
▶ **Images 1, 2 and 3:** Endoscopic analysis identified a bulky lesion with lateral extension with a macronodule (LST-G), extending from the anal margin to 6 cm above the pectinate line (Image 1) using direct vision followed by retroflexion. Using the LCI mode followed by BLI made it possible to identify the borders of the lesion. No ulcerated areas were identified.

▶ **Images 4, 5 and 6:** using the LCI mode facilitated the search for red areas with high risk of degeneration (Image 4). The characterisation of this zone, using the BLI mode with zoom, made it possible to identify a distinct microvasculature and to classify this zone as IIIA in the Sano classification; it was characterised by irregular branched vessels, that were sometimes terminal and dilated (Image 5). The rest of the lesion had a regular Sano II-like vasculature (Image 6). This characterisation confirmed the endoscopic resectability of this lesion.

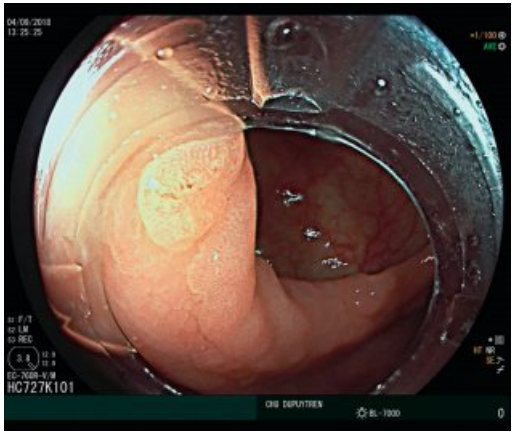
▶ **Image 7:** The submucosal dissection technique enabled a macroscopically complete monoblock resection of the lesion (performed during a demonstration session at the HEGP by Prof T. Toyonaga of Kobe University in Japan).

Histological description

Histological analysis supported the classification of a well-differentiated superficial adenocarcinoma, invading the submucosa over 350 micrometers next to the macronodule, classifying the lesion as T1sm1. The lateral and deep margins were healthy and there were no lymphatic or vascular emboli. It was therefore classified as a R0 curative monoblock endoscopic resection, requiring endoscopic inspection in 6-12 months according to the European and Japanese recommendations.



CC3 Adenoma with high grade dysplasia and infiltrating microcarcinoma (mixed LST) of the ileocecal valve



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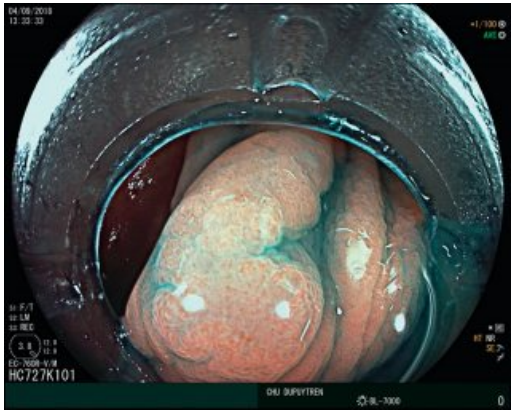

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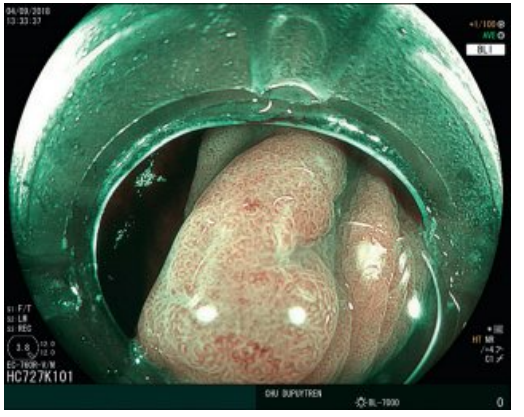

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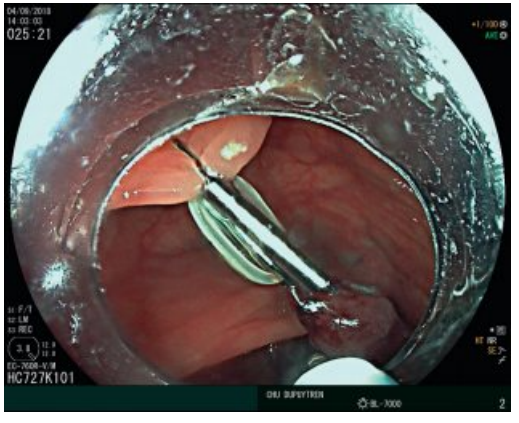

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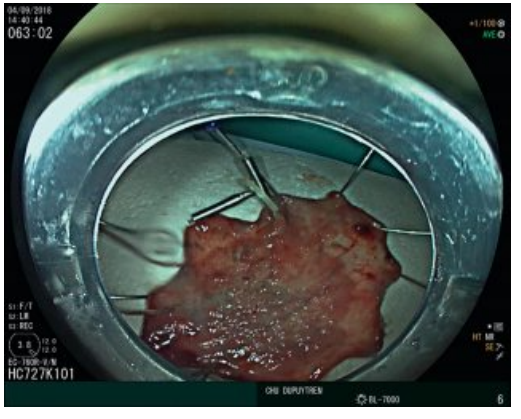

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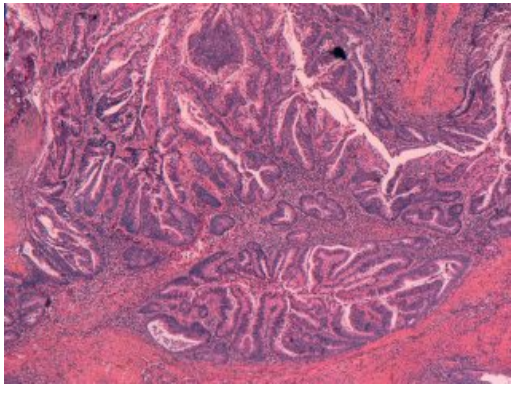

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Clinical description

A 71-year-old man was referred for endoscopic resection of a superficial lesion of the ileocecal valve. A colonoscopy was performed three months earlier as part of a screening and the immunological test came back positive; it revealed three pedunculated polyps of the left colon corresponding to tubulovillous adenomas with high grade dysplasia, as was demonstrated after resection. A flat lesion, barely visible in white light, was also observed; no biopsy was performed and the patient was assigned to an expert center for endoscopic resection.

Endoscopic description

▶ **Image 1:** During the colonoscopy, a mixed LST was demonstrated and classified as 0-IIa according to the Paris classification. A non-granular zone was shown near the valvular orifice as well as a granular zone further away.

▶ **Image 2:** After staining with indigo-carmine, the existence of a small zone characterised by irregularity of the glands led to the classification of the lesion as Vi according to the Kudo classification.

▶ **Image 3:** The same zone was observed with BLI showing the presence of irregular, tortuous vessels, corresponding to stage IIIA of the Sano classification.

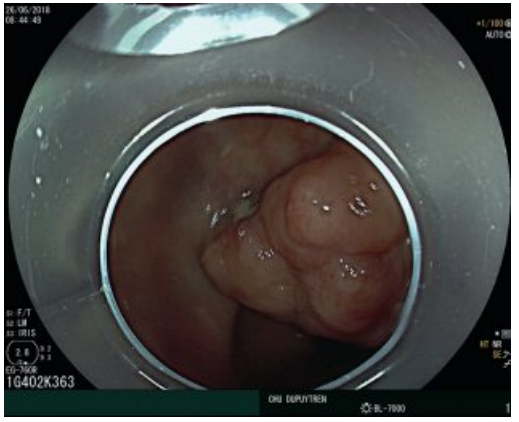
▶ **Image 4:** Given the suspicion of superficial submucosal cancer, a submucosal dissection was performed using the counter-traction strategy based on the use of two clips and a rubber band, permitting a monoblock resection in less than 40 minutes.

▶ **Image 5:** Monoblock resection with satisfactory safety margins.

Histological description

▶ **Image 6:** Histological analysis showed a lesion of 55 mm by 40 mm, corresponding to an adenoma with high grade dysplasia with an adenocarcinoma focal point in the millimetric range infiltrating the submucosa over 100 micrometers. There were no vascular emboli or budding. The safety margin was 2 mm. The endoscopic resection was considered curative and a control colonoscopy was planned in one year.

CC4 Management of a LST G type rectal tumour with Sano IIIB macronodule



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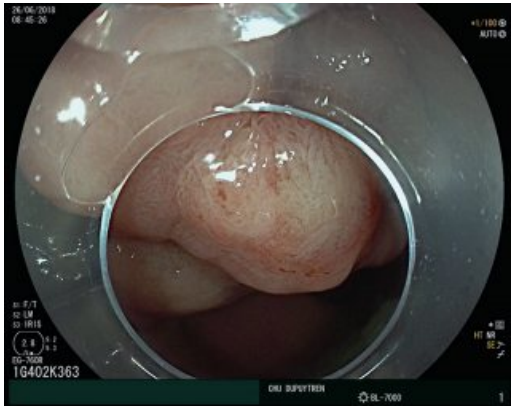

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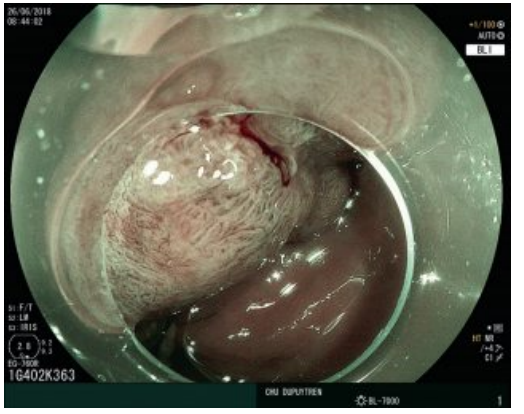

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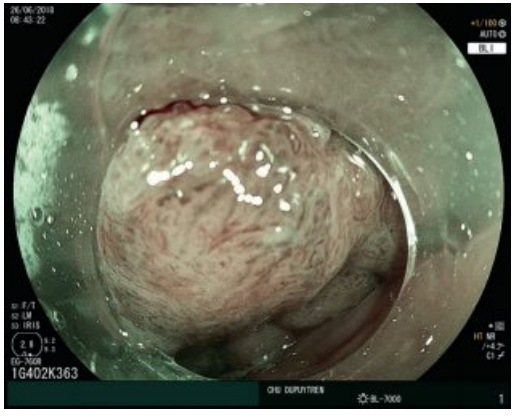

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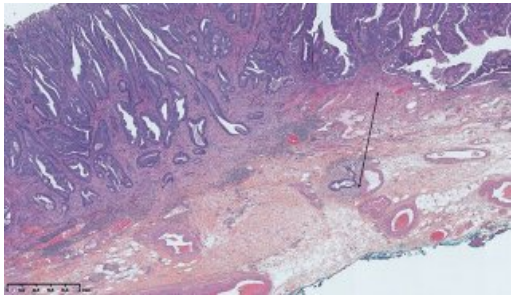

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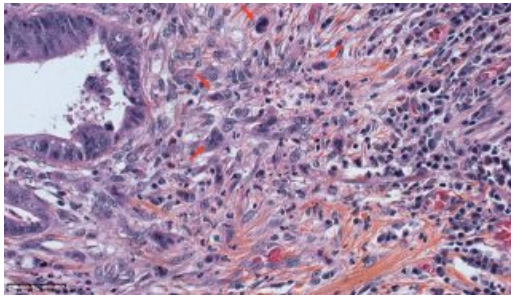

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Clinical description

A 65-year-old man was referred to an expert center for endoscopic resection of a granular lesion of the rectum. A month earlier, a colonoscopy was performed in the context of rectal bleeding and it demonstrated the presence of two pedunculated polyps of the left colon, which after resection were shown to correspond to tubulovillous adenomas with low grade dysplasia. There was also a sessile rectal lesion of about 4 cm, which the biopsies showed to be an adenoma with high grade dysplasia.

Endoscopic description

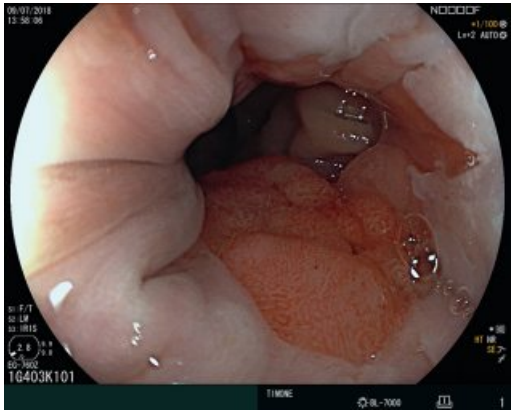
▶ **Images 1 and 2:** The tumour was located in the upper rectum and it was classified as a granular LST type, O-Is + O-IIa according to the Paris classification, with a macronodule of more than 1 cm. White light analysis showed a smooth whitish zone on the macronodule.

▶ **Images 3 and 4:** Using BLI, deep invasion was suspected in one zone due to the absence of vessels over a few millimeters and it corresponded to a Sano IIIB stage.
The performance of an endoscopic ultrasound enabled the elimination of damaged muscularis and it confirmed the absence of perirectal lymphadenopathies (lesion classified usT1NO). A submucosal dissection was decided on, in order to obtain a precise histological analysis and to confirm the depth of involvement.

Histological description

▶ **Image 5:** Histological analysis showed a lesion of 50 mm by 40 mm corresponding to an adenoma with high grade dysplasia with a focal adenocarcinoma of less than 1 cm infiltrating the submucosa over 3 mm with emboli.
▶ **Image 6:** Typical representation of tumour budding.
The safety margins were more than 1 cm for adenocarcinoma and 2 mm for adenoma. Endoscopic resection was therefore considered R0 but not curative and complementary surgery was performed. No tumour residue or ganglionic invasion was found in the surgical specimen.

CC5 Development of adenocarcinoma on a scar of an irradiated coloanal anastomosis



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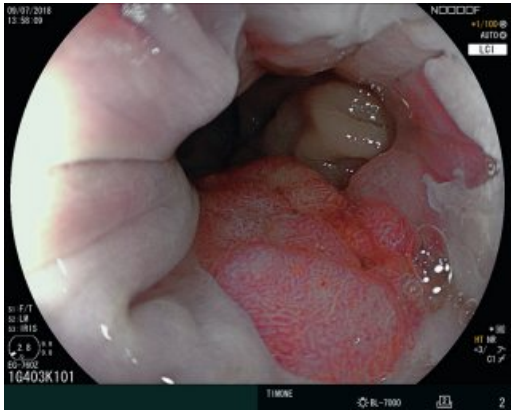

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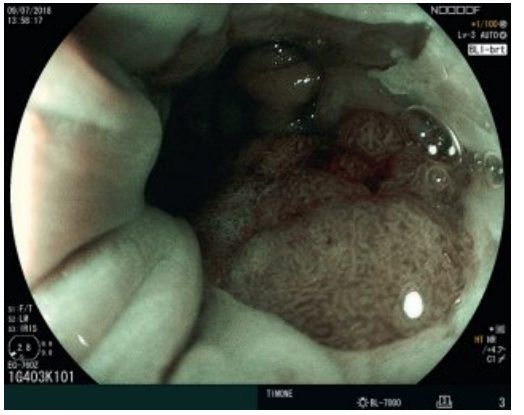

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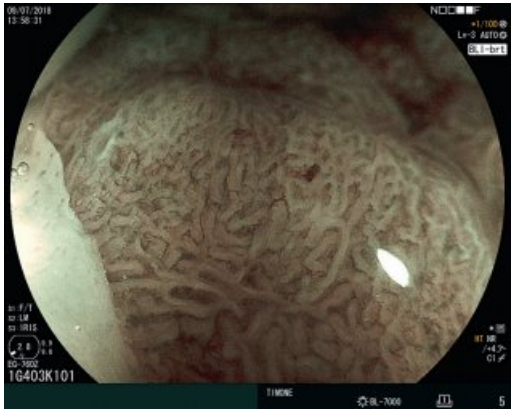

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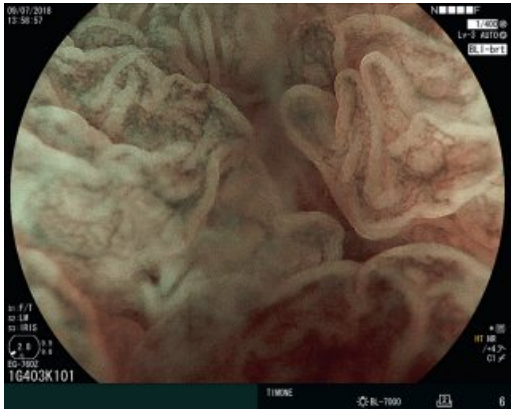

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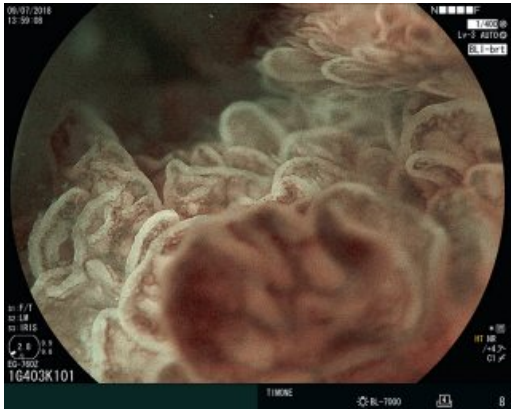

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Clinical description

A 43-year-old man with previous adenocarcinoma of the rectum treated by radiochemotherapy and then by surgery in 2015 was treated for a flat lesion developed on colorectal anastomosis; biopsies showed the presence of low grade dysplasia. Endoscopic ultrasound and MRI found an intramucosal lesion without pelvic lymphadenopathy. The selected approach was resection by submucosal dissection.

Endoscopic description

The lesion was examined with a gastroscope, using white light (Image 1) and then by chromoendoscopy using LCI (Image 2), BLI (Images 3, 4), and zoom. It was shown to be a flat lesion classified as 0IIa using the Paris classification, about 25 mm in diameter starting at the pectinate line over a quarter of the circumference. The lesion was rather granular without macronodules or depressed zones and could be described as having a mucosal topography of type 3 of the Kudo classification. Resection by submucosal dissection was difficult because of rectostenosis, the absence of uplift due to major radicular fibrosis and the extension to the superior pole of the anal canal.

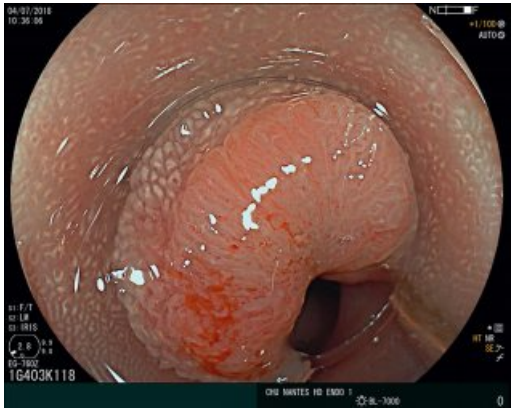
Histological description

A villous lesion was present on the surface with varying degrees of atypia (low and high grade) and positive labeling with anti-P53 and Ki67 antibodies. Atypical glands dissected and infiltrated the deep muscularis mucosa. There were no tumour emboli and the invasive lesion came into contact with the lateral and deep excision margins. It was a well-differentiated adenocarcinoma developed on the irradiated coloanal anastomosis scar with non-healthy resection margins (category 4.4 of the modified Vienna Classification, stage pTis). Surgery was decided on.

Comments

This case illustrates the difficulty of analysing superficial lesions in the case of prior irradiation.
The retrospective analysis of the images before resection shows aspects that are compatible with low grade dysplasia on the side closest to the anal margin, especially in the zoomed images (Images 5, 6). In image 2, using LCI mode, the central and left part of the lesion shows more disturbing appearance with irregular glands, a mucosa that is less pink, and a vascular rarefaction when using the BLI mode.

CC6 Submucosal dissection of a fixed sigmoid colon with multiple diverticula



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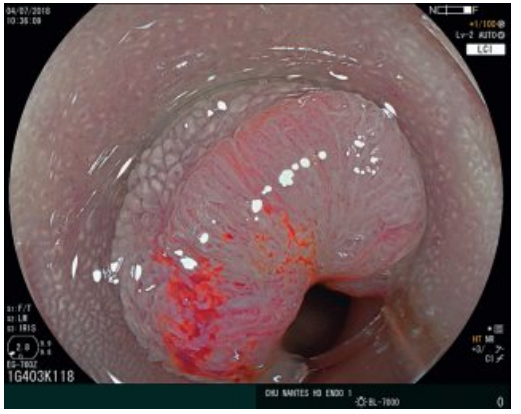

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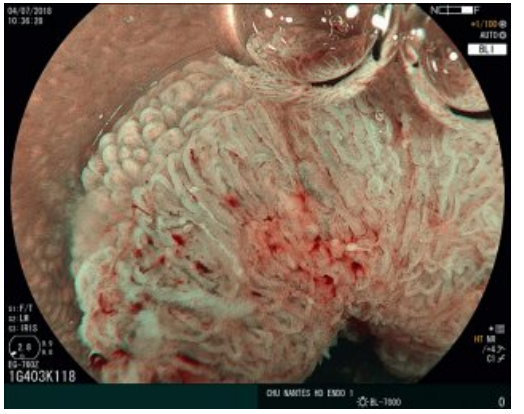

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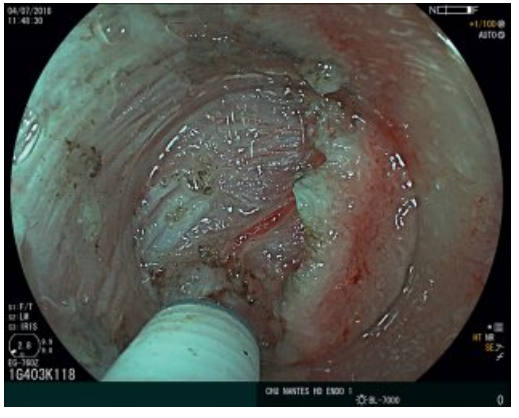

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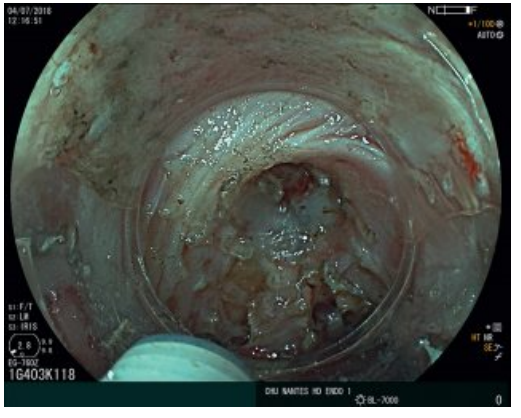

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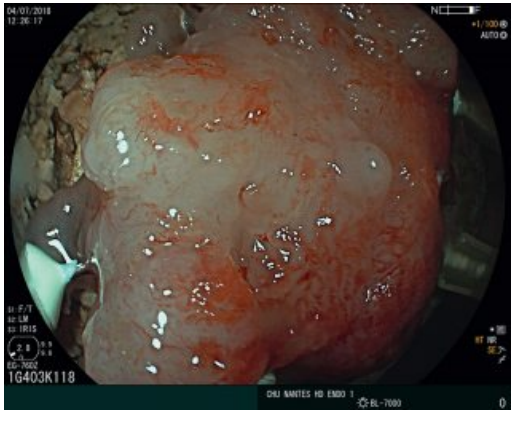

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Clinical description

An 82-year-old man with a history of arterial hypertension, stroke and glaucoma was referred for an exam because of rectal bleeding. Rectosigmoidoscopy was difficult but showed a sigmoid lesion located 35 cm from the anal margin, within a fixed and multidiverticular sigmoid. There were no other lesions detected during this examination, and it was decided that a colonoscopy should be performed in order to (i) eliminate an overlying lesion and (ii) resect the sigmoid lesion either by submucosal dissection or by multifragmentary mucosectomy according to the appearance of the lesion in zoom mode and virtual coloration.

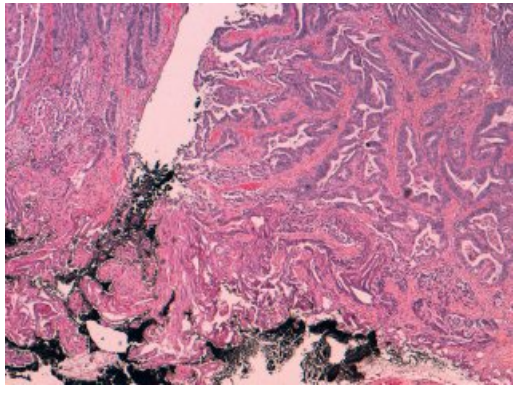
Endoscopic description

▶ **Images 1, 2 and 3:** The lesion was classified as Paris 0-Is and it measured about 25 mm in the long axis. Using the white light mode (Image 1) and especially with LCI (Image 2), areas of spontaneous bleeding were visualised within the lesion. Using the BLI mode and zoom (Image 3), the central part was very irregular with loss of mucosal and vascular microarchitecture evocative of an adenocarcinoma with deep infiltration. Because of this appearance, performing a dissection rather than a multifragmental mucosectomy was selected.

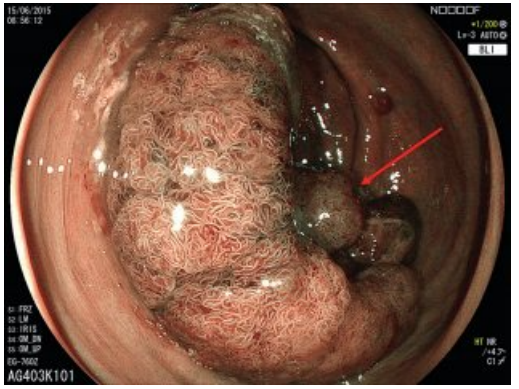
▶ **Images 4, 5 and 6:** The submucosal dissection was performed using the FlushKnife, step by step in contact with the muscular layer (Image 4), despite the difficult detachment and the difficulties of positioning in this digestive segment. It was possible to resect the lesion in a macroscopically complete manner, including at the level of the diverticular zones (Image 5). The specimen was extended and stretched, then sent for pathological examination (Image 6).

Histological description

▶ **Image 7:** The histological analysis was indicative of moderately differentiated adenocarcinoma that developed on a tubulovillous adenoma with low and high grade dysplasia. Adenocarcinoma deeply invaded the submucosa reaching contact with the resection margins (classified T1sm2). The lateral margins were healthy and there were no vascular emboli. It was therefore classified as a non-curative monoblock endoscopic resection according to European and Japanese recommendations. However, this result made it possible to validate the decision of adjuvant chemotherapy at a multidisciplinary meeting regarding “superficial tumors”.



CC7 LST type invasive adenocarcinoma of the rectum in the context of Lynch syndrome



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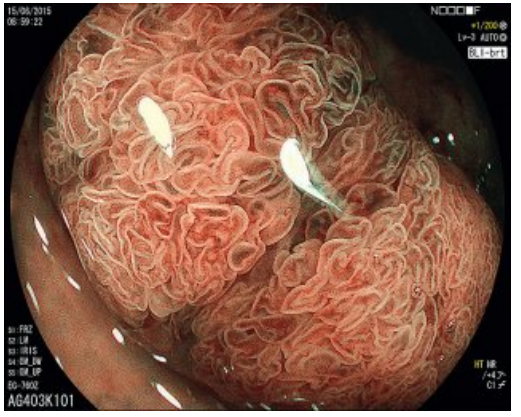

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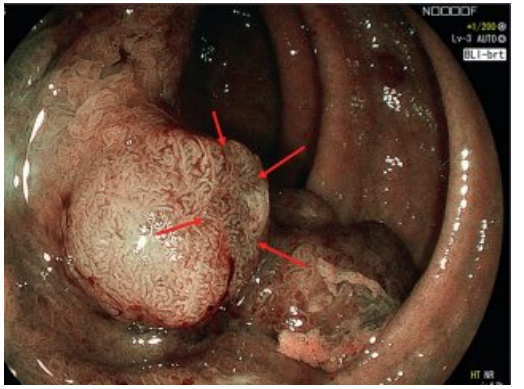

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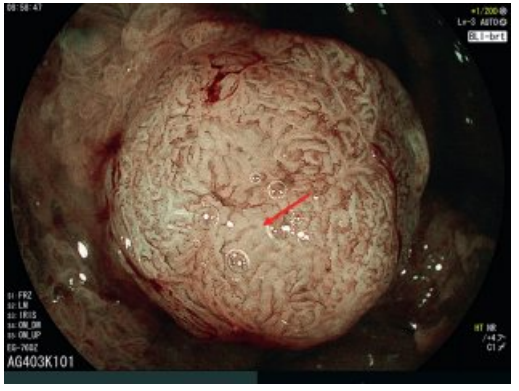

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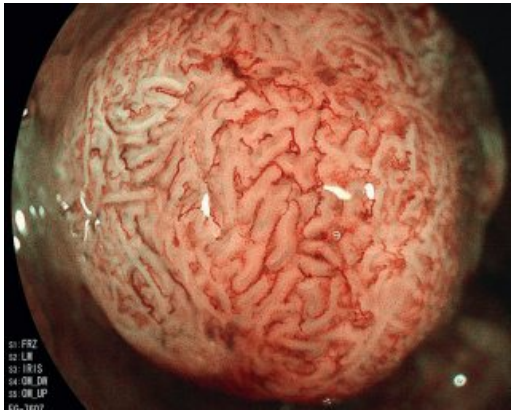

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Clinical description

A 30-year-old patient with Lynch Syndrome was treated for a villous lesion of the mid-rectum that corresponded to a Laterally Spreading Tumor (LST) of the rectum and was found during a check-up due to a history of rectal bleeding.

Endoscopic description

▶ **Images 1 and 2:** The appearance of granular LST of the rectum (Image 1). The peripheral part of the LST was homogeneous with a regular pattern (Image 2) and villous, classified as type IV in the Kudo classification; the vascular topography followed the mucous topography (Sano II).

▶ **Image 3:** A central nodule was present with a very suspicious appearance, evocative of neoplasia. This nodule, which was about 1 centimeter in size, was detached from the rest of the lesion with a much more irregular pit pattern and vascular topography, resembling type Vi in the Kudo classification and Sano IIIa. Within this nodule of type Is of the Paris classification, there was a well-defined discrete depression at the top (red arrow).

▶ **Image 4:** Elevated appearance of the vascular pattern by location (arrow). However, there were no areas without any mucosal or vascular topography.

▶ **Image 5:** By increasing the zoom level, we observed a tortuous and irregular vascular topography, which was present in the whole area that was explored. In the absence of formal criteria for deep submucosal invasion (Vn pit pattern, Sano IIIb vascular pattern), submucosal dissection was performed.

▶ **Image 6:** The extended resection specimen showing the suspected nodule in the center (blue arrow).

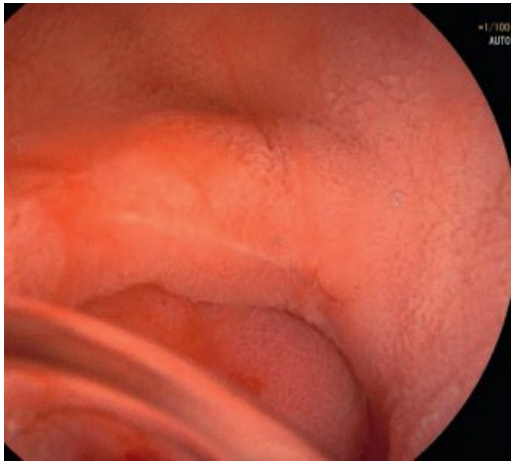
Histological description

A well differentiated invasive adenocarcinoma of 1750 micrometers without lymph node involvement. Since the resection was not curative (invasion > 1000 micrometers), the patient underwent a proctectomy with lymphadenectomy; no tumour residue was detected.

Comments

As demonstrated by the Japanese authors, the presence of a macronodule of around 1 centimeter in size (risk of 8%) and a depressed delineated zone (risk > 20%) within a nodule are risk factors for deep submucosal invasion but insufficient to contraindicate submucosal dissection.

CC8 Difficult diagnosis of Crohn's disease



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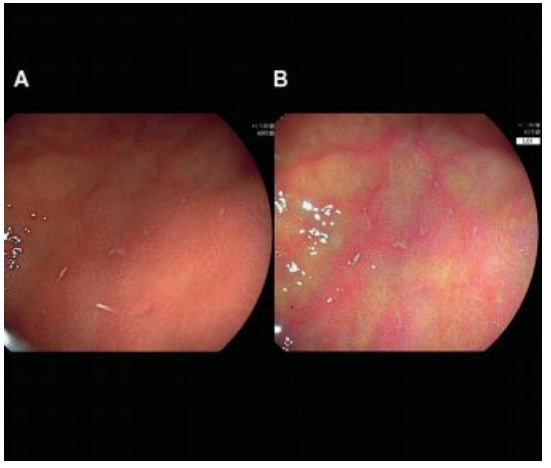

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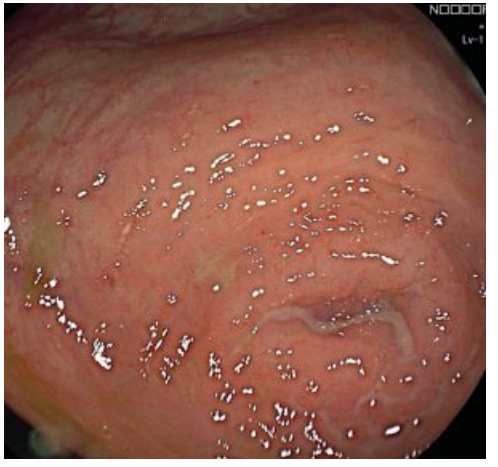

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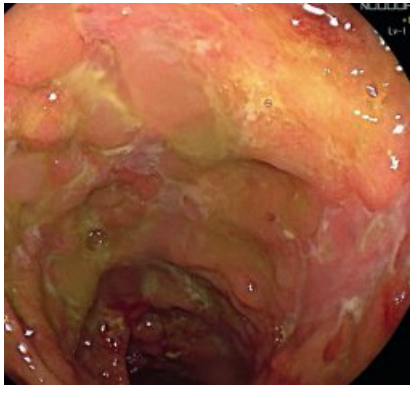

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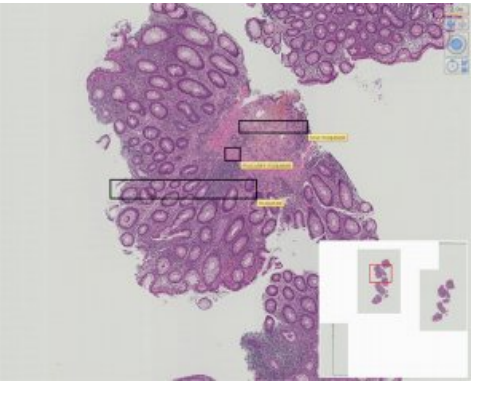

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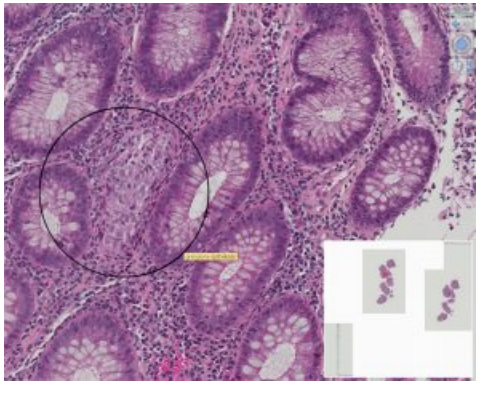


- 6 -

Clinical description

A 35-year-old patient who had received a kidney transplant 10 years ago for end-stage renal failure of unidentified origin had diarrhea for 4 months, dyspeptic disturbances, peripheral joint pain and weight loss of 4 kg. The patient received anti-rejection treatment with tacrolimus, mycophenolate mofetil, and low doses of corticosteroids.

Endoscopic description

Gastroscopy revealed ulcers and marked erythema in the gastric antrum; the duodenum and oesophagus were normal.

▶ **Image 1:** A linear superficial prepyloric ulcer visualised using white light plus immersion.

▶ **Images 2A and B:** Superficial aphthoid ulcers of the gastric antrum, within a marked erythema, the inflammatory appearance was enhanced and highlighted by the LCI mode (2B).

Colonoscopy was conducted up to the ileocecal valve which was ulcerated and impassable, suggestive of stenosis. The transverse colon was the most affected segment with inflammatory lesions (erythema, oedema, ulcers) occupying 100% of the segment surface and superficial and deep ulcers occupying 30% of the surface. The sigmoid colon and the rectum were affected with aphthous ulcers. The CDEIS (Crohn's Disease Endoscopic Index of Severity) score was 14.

▶ **Image 3:** The appendix was the site of marked oedema, confirmed by the disappearance of the vascular network compared to the adjacent normal cecal mucosa, with superficial ulcers leading to the disappearance of the cryptic topography.

▶ **Image 4:** Extensive and circumferential involvement of the transversal colon by inflammatory lesions, and deep ulcers with raised margins.

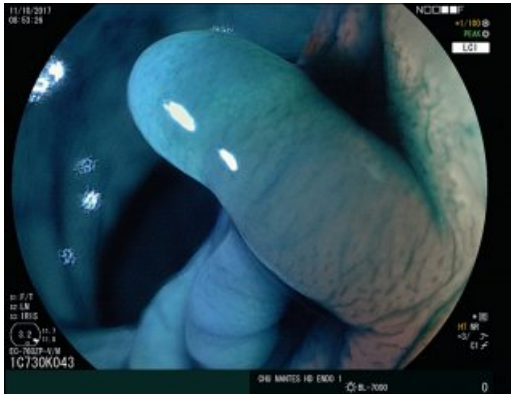
Histological description

▶ **Images 5 and 6:** Gastric and colonic biopsies were the site of a marked inflammatory infiltrate with a predominance of lymphatic cells. Distortions of the glands indicated chronic architectural changes. Several epithelioid and giant cell granulomas were observed.

Comments

The diagnosis of Crohn's disease was based on the chronic nature of the clinical symptoms, the presence of elementary endoscopic lesions evocative of the disease, the topographic distribution of the lesions and histological analysis. The differential diagnosis of mycophenolate-associated enterocolitis was discarded in view of the severity of the endoscopic lesions and the absence of apoptotic bodies, a weak representation of eosinophilic polynuclear cells in the inflammatory infiltrate, and the presence of granulomas.

CC9 Ulcerative colitis with multiple polyps without adenomatous or dysplastic lesions



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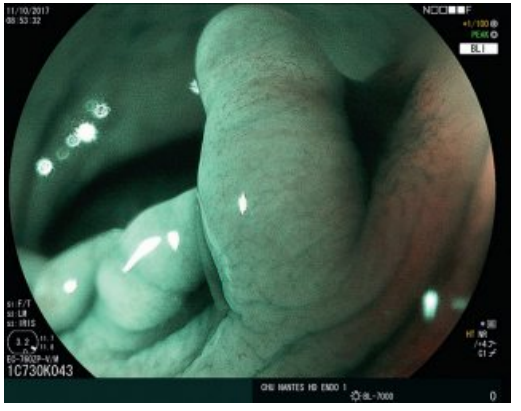

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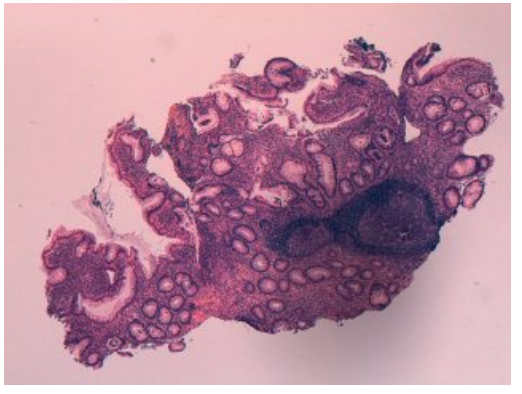

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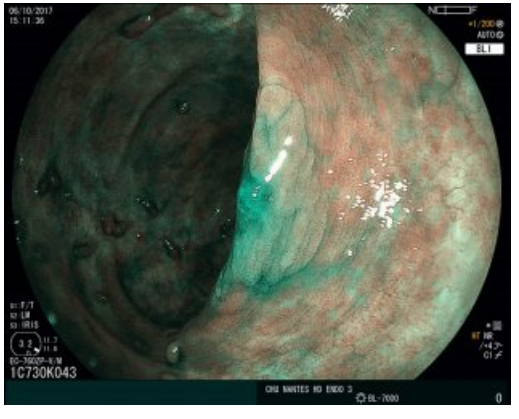

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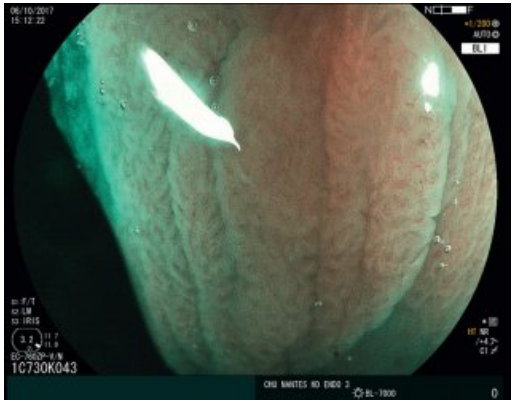

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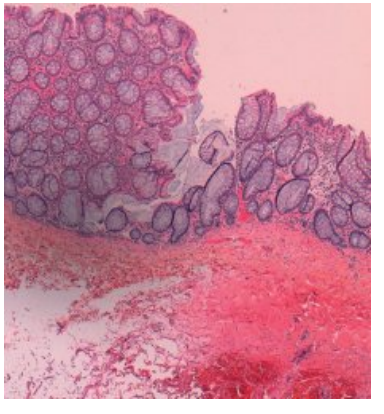


- 6 -

Clinical description

A 60-year-old patient followed due to pancreatic colitis diagnosed in 1999, and currently in clinical remission had a screening colonoscopy with indigo carmine chromoendoscopy in accordance with European recommendations.

Endoscopic description

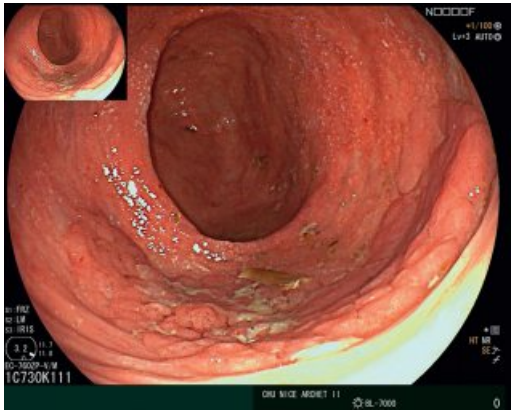
There were multiple white, soft, translucent pseudo polyps throughout the colon of less than 1 cm in size. The colonic mucosa showed no sign of inflammation; the vascular network was clearly visible, without any erosion or ulceration and without any traces of blood. A polyp was shown to be present in the transverse colon and it was ranked as 0-IIa according to the Paris classification. Its surface was regular, non-ulcerated, and its margins well delineated with a regular mucous pattern, classified as type II according to Kudo classification; the adjacent mucosa was non-inflammatory. The lesions were characterised by white light, Linked Color Imaging (LCI) and Blue Light Imaging (BLI), prior to chromoendoscopy with indigo carmine. The polyp was then resected by monoblock mucosectomy after satisfactory separation and biopsies of the adjacent mucosa were taken. A pseudo polyp was resected by polypectomy with cold snare.

▶ **Images 1, 2 and 3:** Pseudo polyps: chromoendoscopy with indigo carmine (1), virtual chromoendoscopy using BLI with zoom (2) and histological section (3): the mucosal pattern was comparable to the normal colonic mucosa of type I according to Kudo; the vascular structures were regular.
▶ **Images 4, 5 and 6:** Flat polyp of type 0-IIa, with a hyperplastic appearance (Kudo type II) using virtual BLI chromoendoscopy (4), BLI with zoom (5), and a histological section (6). On the same colonic segment, the presence of some polyps was noted which were classified as post-inflammatory "pseudo polyps", with identical endoscopic semiology as the polyp described above (Images 1, 2, 3).

Histological description

▶ **Image 3:** Histological analysis confirmed a pseudo polyp with evenly distributed glands, without lymphocytic exocytosis, within a fibrous chorion whose cellularity was not increased. Some crypts were unoccupied. There was no dysplasia.
▶ **Image 6:** The analysis of the mucosectomy specimen confirmed the existence of a hyperplastic polyp of 10 mm. There was a focal length extension of the crypts that were bordered by cells of variable height, which gave a very characteristic indented appearance to their lumen. The subepithelial collagen lamina was thickened. There were no associated adenomatous lesions. There was an oedematous restructuring. The adjacent mucosa was normal.

CC10 Tubulovillous adenoma with dysplasia (high and low grade) complicating antecedent ulcerative colitis



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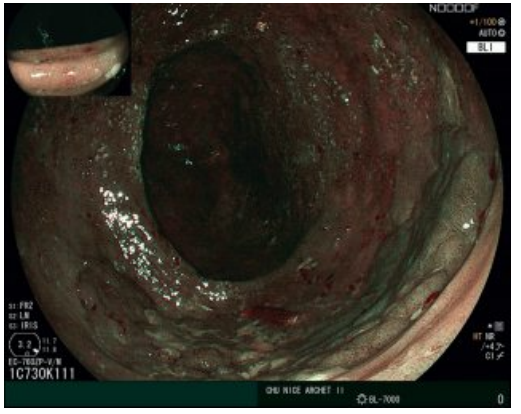

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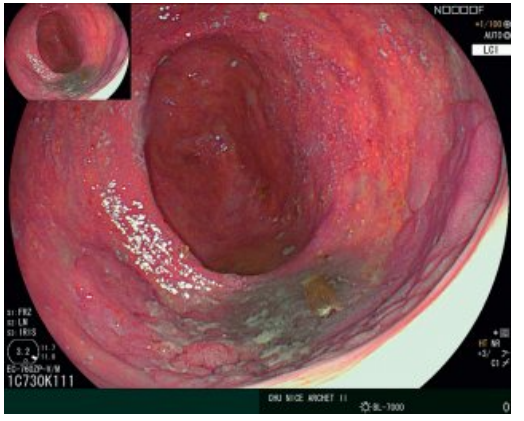

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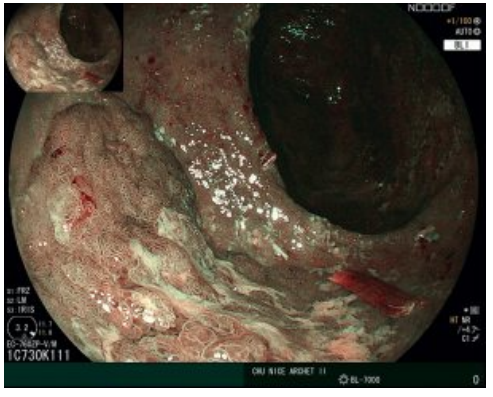

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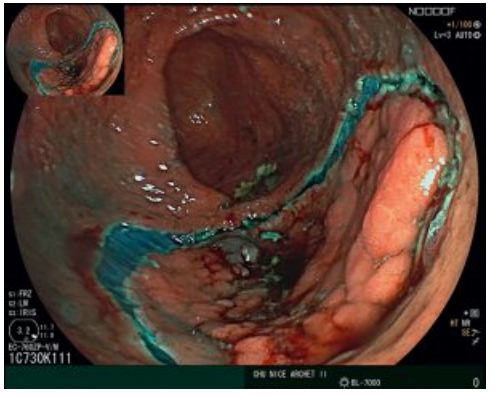

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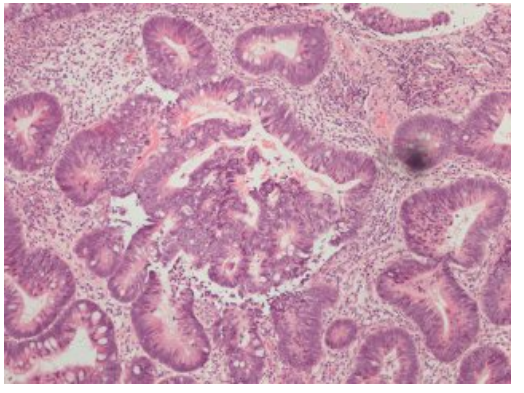

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Clinical description

A 70-year-old man had a pancolonic ulcero-haemorrhagic rectocolitis of moderate extent at the time of the endoscopic procedure (moderate inflammatory syndrome, UCDAI score of 4). The inflammatory disease had been evolving since 1989 and in 2007 three polyps were resected endoscopically with high grade dysplasia. The patient had always refused treatment with 5-ASA.

Endoscopic description

▶ **Image 1:** Discovery of a single adenovillous layer in the right colon of 6 to 7 cm in size of the LST-G type within a mucosa with aphthoid ulcerations; note the moderate loss of the vascular network and mucosal fragility.

▶ **Image 2:** A well-defined lesion inspected with BLI, with a regular surface and no depressed zones or ulcerations.

▶ **Image 3:** Assessment of the extent of the lesion using LCI.

▶ **Image 4:** Assessment of the pit and the vascular pattern using BLI: the lesion was classified according to the Paris classification: 0-Is, Kudo classification: IIIL, and Sano classification: III.

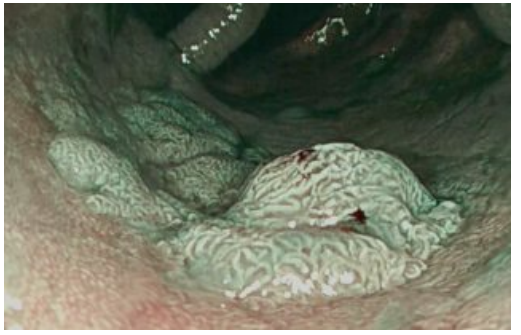
▶ **Image 5:** Hybrid mucosectomy resection without incident.

Histological description

▶ **Image 6:** Presence of tubulovillous adenoma with low and high grade dysplasia (category 4.1 of the modified Vienna Classification).

CC11 A flat dysplastic lesion in the context of antecedent Crohn's colitis

- 1 -



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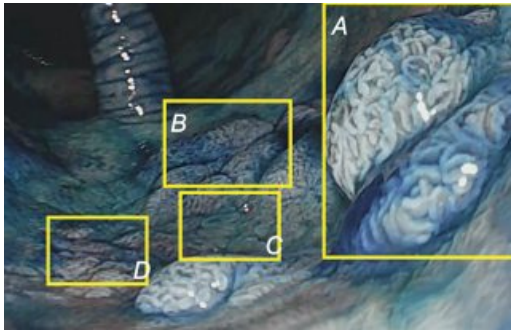

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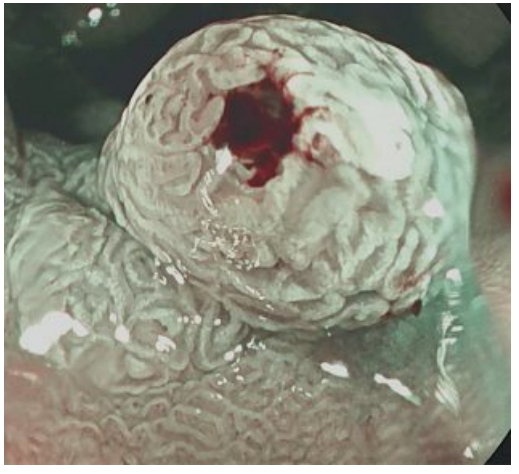

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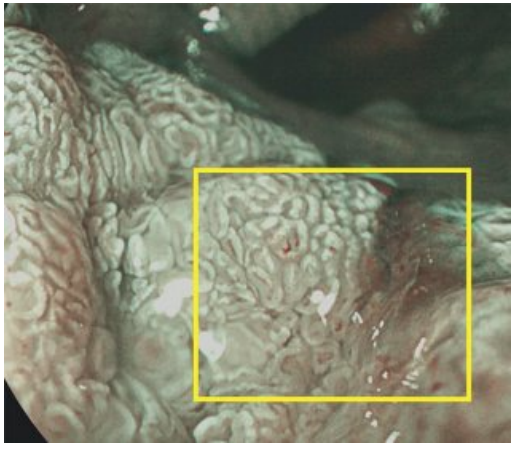

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Clinical description

A 57-year-old patient with Crohn's disease with pancolonic topography that has been evolving for the past 17 years had a screening colonoscopy because of his age and the extent of his disease. He was totally asymptomatic and treated with azathioprine for 5 years. The colonoscopy detected a lesion in the right colon.

Endoscopic description

Indigo carmine chromoendoscopy revealed a wide mixed lesion (Image 1 in blue and Image 2 with BLI) composed of elevations or sessile lesions of type Is of the Paris classification (Image 3A), and flat, elevated areas of type IIa (Image 3B), and flat areas of type IIb (Image 3 C and D). The adjacent mucosa had irregular, non-inflammatory crypts when studied using BLI (Image 2). The lesion was therefore poorly delineated, measuring approximately 2.5 cm in the long axis.
At the level of the sessile zones (zone A, Image 3), the crypts appeared well delineated, rounded, a little elongated but mainly of type IIIs, IIIL according to the Kudo classification. Using BLI, the vascularisation was regular (Image 4). It was noted that the crypts around the lesion were also elongated (Image 2).
The same appearance was visualised in the raised flat areas with unclear borders (area B, Image 3).
In the central flat zone of type IIb (Image 3, zone C), the crypts appeared more irregular with elongated crypts of type IIlL according to the Kudo classification or less well developed, and vessels that were spark-like in their form (zoom image 5). At the periphery of the lesion, the flat area was irregular (zone D image 3, zoom image 6) and poorly delineated with elongated crypts in some places.

Histological description

In the biopsies performed, the colonic glands were dilated and lined with a serrated Lieberkuhnian coating without dysplasia. Furthermore, in the flat areas (C and D) the mucosa contained a pseudostratified epithelium, dilated glands of variable caliber lined with a hypercrinic coating. High grade dysplasia was noted. The chorion harbored a polymorphic inflammatory infiltrate of mild intensity.

2018: Do we live in an ideal world?

Writing a book like this one has first and foremost an essentially practical goal: how to recognise, describe and interpret endoscopic semiology that is constantly evolving. However, this exercise is not a simple educational project! It is also an opportunity to become fully aware of the differences of opinion and the differences in practice that exist within a group of experts in digestive endoscopy. There are multiple reasons for these differences; the first and most important is probably the lack of scientific data validated in a large number of cases. The rapid evolution of technologies, as is illustrated in this book, inevitably creates a time "gap" compared to clinical trials that are slower due to the difficulties involved in their set-up and the magnitude of the trials. Therefore, the principles of "evidence-based medicine", while excellent as a concept, cannot be applied to the multitude and complexity of situations that clinicians face today. At the very least, it is important to question the necessary prerequisites regarding the possibility to generalise the results obtained in a trial using a particular type of technology to a non-selected real-life population. Finally, even with identical information two practitioners will not necessarily interpret the results in the same way and therefore would not necessarily follow the same strategy. This subjectivity in medical practice must be accepted but also evaluated. This is why it seemed relevant to us to conduct an opinion poll in parallel to writing this book. We used a method related to the Delphi method, which is based on first asking a group of experts to express their agreement or disagreement with about thirty aphorisms (Table 1) written by the group of coordinators of this book. We warmly thank our colleagues and in particular the GRAPHE group for having responded to this survey. We would like to increase the number of participants in order to improve the representativeness of the results, but we believed that it would already be interesting to present some "preview" results that suggest that a strong consensus exists but also some great differences. We have to recognise and admit that we do not live in an ideal world!

We strongly hope that the results of this survey will facilitate better analysis in practice and will stimulate future work that is more focused on the concerns of the clinicians and the profession as a whole.

Table 1: Common practice surrounding colonoscopy: a multicenter survey among gastroenterologists based on the Delphi method⋆.*

Statements
Part One: Endoscopy Technique and Polyps
1. To state that a colon is normal, it is absolutely required to take one or multiple biopsies in each colonic segment.
2. To state that a colon is normal, a list of quality indicators for colonoscopy first must be met.
3. The polyp detection rate (PDR) is not related to the quality of the bowel preparation.
4. If an endoscopy system is at least technically equivalent to that of its competitor, then the scientific data acquired with the former is also applicable to the latter.
5. A colonoscopy allows for a reliable evaluation of polyp size.
6. All polyps must be removed except for diminutive (< 6 mm) rectosigmoid polyps that are predicted with high confidence to be hyperplastic.
7. The "resect and discard" strategy is applicable for all diminutive polyps (< 6 mm) in all centers in Europe.
8. The optical characterization of polyps using high-definition white light endoscopy is sufficient to guide management and post-polypectomy surveillance intervals.
9. The use of magnification for colorectal polyps improves the level of confidence in predicting a histological diagnosis.
10. Virtual chromoendoscopy must be routinely used because it allows for better characterization and histological prediction of colonic polyps.
11. During optical characterization of a colonic polyp, the use of the BLI (Fujifilm®) or NBI (Olympus®) mode is required to ensure appropriate management and post-polypectomy surveillance interval.
12. The LCI (Fujifilm®) mode is useful for the detection of flat colonic lesions.
13. Currently, the learning process of diagnostic colonoscopy and basic resection techniques is adequate in Europe.
14. It is recommended for endoscopists to undergo virtual chromoendoscopy training in order to improve their performance in colonic polyp characterization.
15. In the near future, artifical intelligence (AI) systems will guide endoscopists in their management decisions during colonoscopy.
16. In the future, endoscopists could use AI systems instead of learning multiple endoscopic classifications.

Part Two: Inflammatory Bowel Disease (IBD)

Diagnosis

17. The colonoscopy report in the context of IBD requires at least the description of disease-related features and their extent in each segment.
18. The colonoscopy report in the context of IBD must include a validated and/or generally accepted score such as the CDEIS or SES-CD in Crohn's disease or the UCEIS or Mayo endoscopic subscore in ulcerative colitis.
19. In the course of IBD, the endoscopic assessment must be based on validated classifications in order to properly evaluate disease severity.
20. An ileocolonoscopy allows for an adequate evaluation of the small bowel in IBD.

Treatment

21. A colonoscopy without biopsies is sufficient for the assessment of mucosal healing in the course of IBD.
22. Performing a colonoscopy is essential before starting or changing medical therapy for IBD.
23. Performing a colonoscopy is essential before optimization of therapy in IBD.
24. Performing a colonoscopy is essential before discontinuation of an anti-TNF.
25. Biopsies from each colonic segment must be performed systematically for the assessment of mucosal healing in the course of IBD.
26. The presence of histological (microscopic) inflammation must prompt an optimization of therapy in Crohn's disease.
27. The presence of histological (microscopic) inflammation must prompt an optimization of therapy in ulcerative colitis.

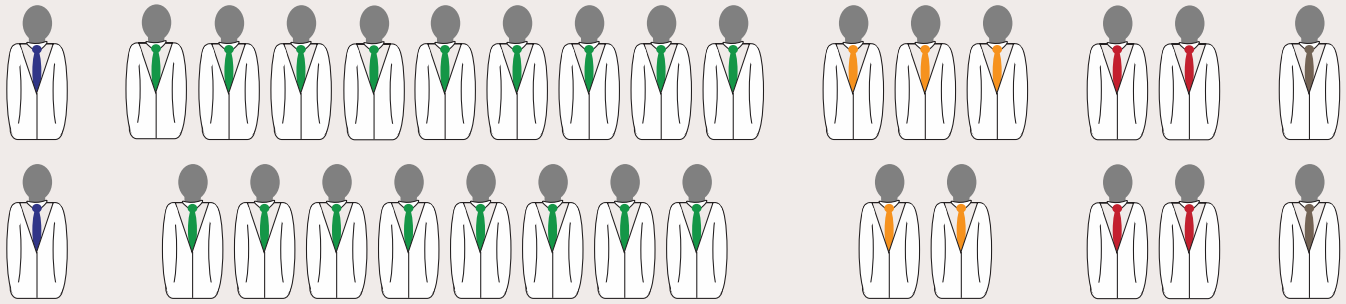
Dysplasia surveillance

28. Chromoendoscopy with targeted biopsies is sufficient for dysplasia detection (i.e., without the need for random biopsies under white light endoscopy).
29. Virtual chromoendoscopy is at least equivalent to dye chromoendoscopy for dysplasia surveillance in the context of IBD.
30. In the course of IBD, the description of colonic lesions detected during dysplasia surveillance may be achieved by using the same classifications as in colorectal cancer screening (e.g. Paris, Kudo classifications).

* Vote (Delphi method)
A. Totally agrees
B. Agrees with some restraint
C. Totally disagrees
D. Disagrees with some restraint
E. Doesn't know or believes it is impossible to answer

Guidelines

Statement n° 4. *If an endoscopy system is at least technically equivalent to that of its competitor, then the scientific data acquired with the former is also applicable to the latter.*



7% totally agree

56% agree with some restraint

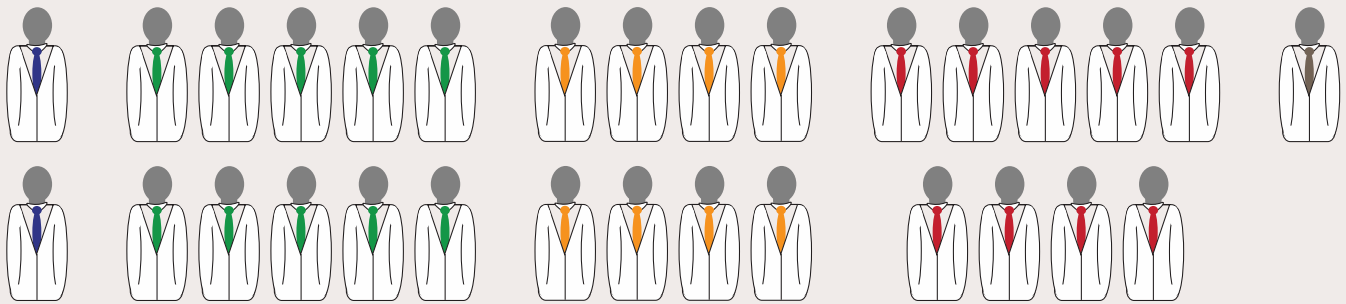
17% disagree with some restraint

13% totally disagree

7% don't know

Polyps

Statement n° 7. *The "resect and discard" strategy is applicable for all diminutive polyps (<6 mm) in all centers in Europe.*



7% totally agree

33% agree with some restraint

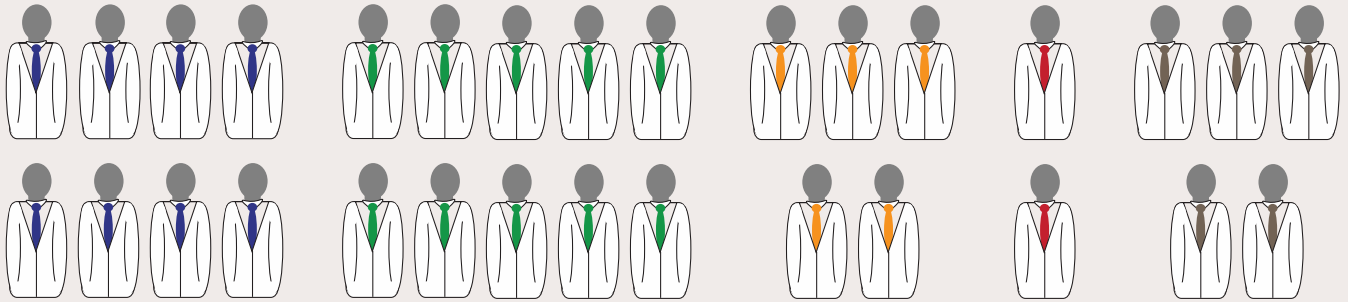
27% disagree with some restraint

30% totally disagree

3% don't know

Polyps

Statement n° 11. *During optical characterization of a colonic polyp, the use of the BLI (Fujifilm®) mode is required to ensure appropriate management and post-polypectomy surveillance interval.*



26% totally agree

33% agree with some restraint

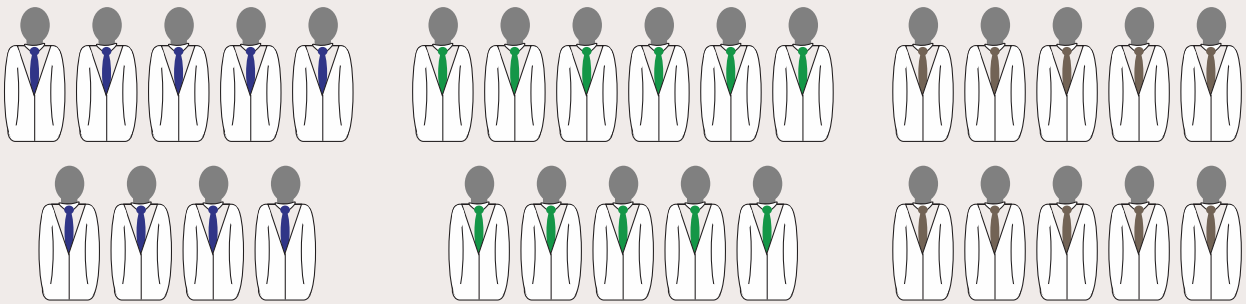
17% disagree with some restraint

7% totally disagree

17% don't know

Polyps

Statement n° 12. *The LCI (Fujifilm®) mode is useful for the detection of flat colonic lesions.*



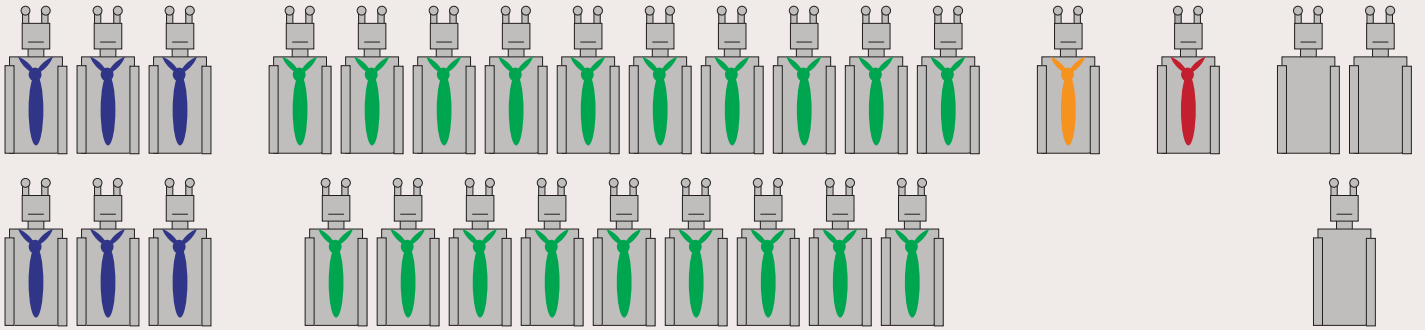
30% totally agree

37% agree with some restraint

33% don't know

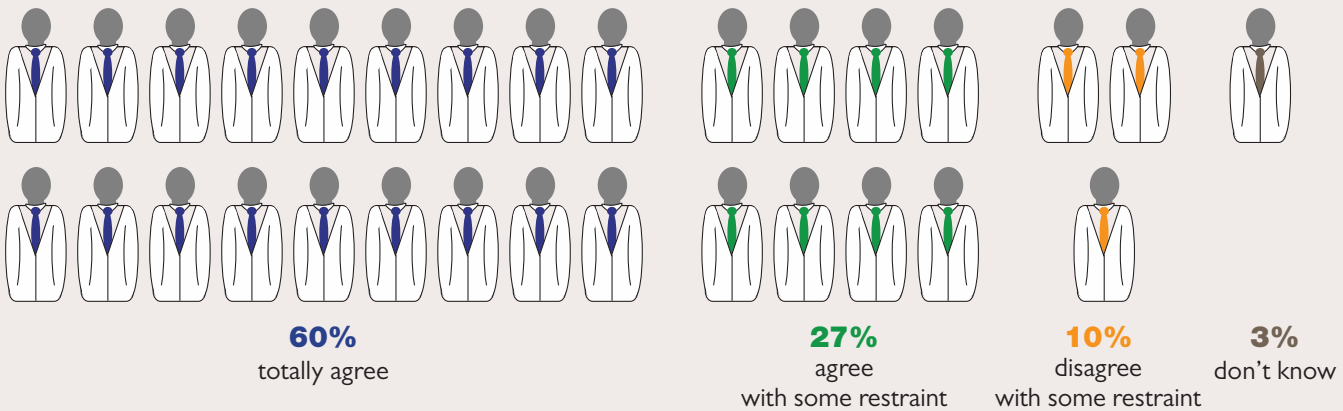
Artificial Intelligence

Statement n° 15. *In the near future, artifical intelligence (AI) systems will guide endoscopists in their management decisions during colonoscopy.*

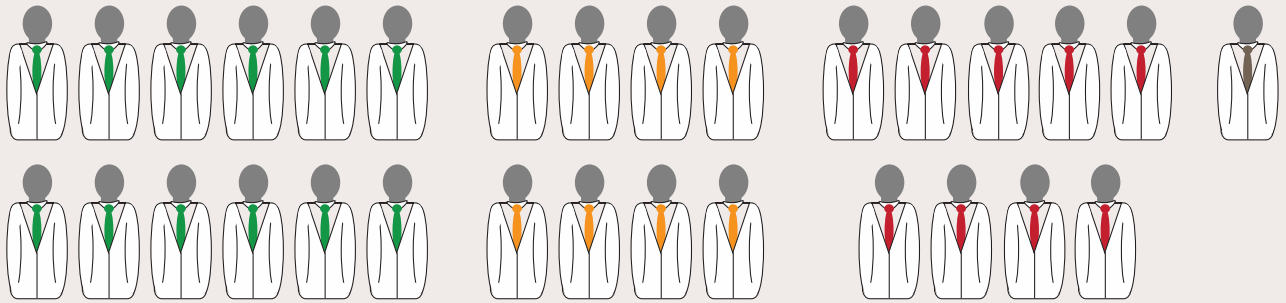


IBD

Statement n° 18. *The colonoscopy report in the context of IBD must include a validated and/or generally accepted score such as the CDEIS or SES-CD in Crohn's disease or the UCEIS or Mayo endoscopic subscore in ulcerative colitis.*



Statement n° 21. *A colonoscopy without biopsies is sufficient for the assessment of mucosal healing in the course of IBD.*



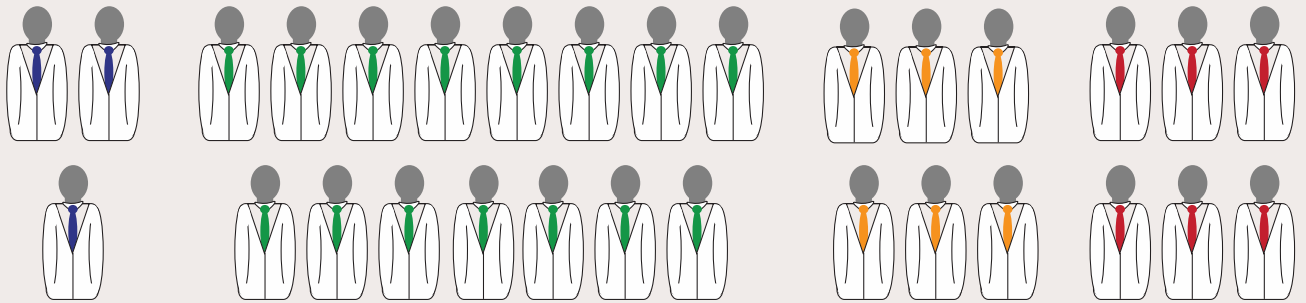
40%
agree with some restraint

27%
disagree with some restraint

30%
totally disagree

3%
don't know

Statement n° 28. *Chromoendoscopy with targeted biopsies is sufficient for dysplasia detection (i.e., without the need for random biopsies under white light endoscopy).*



10%
totally agree

50%
agree with some restraint

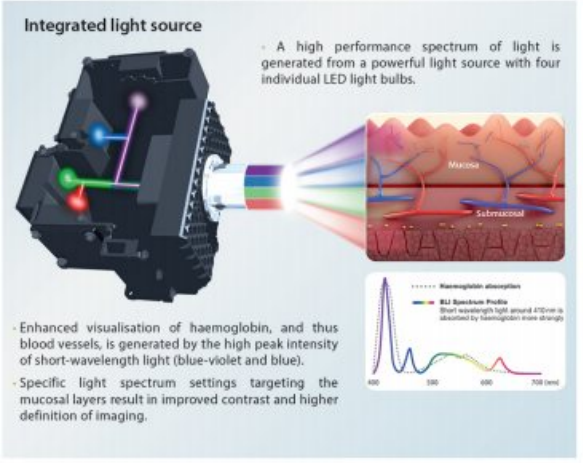
20%
disagree with some restraint

20%
totally disagree

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.



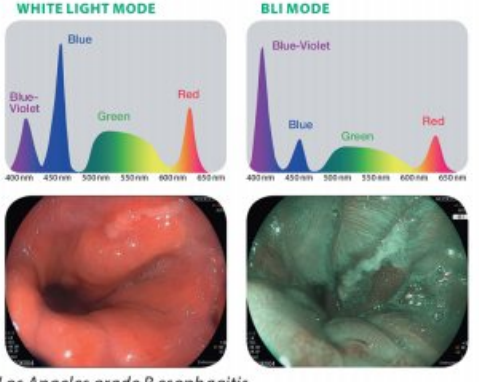
4-LED Multi Light™ technology : the new definition of light

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

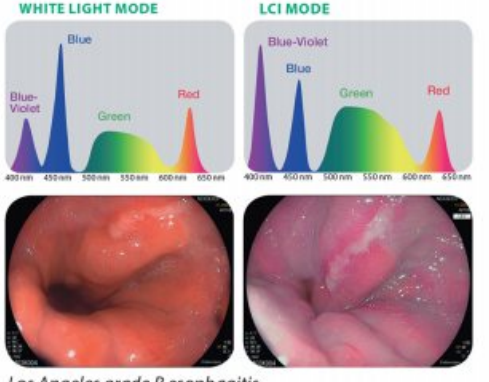
The **BLI** is targeted illumination that provides excellent visibility of the mucosal surface and better contrast of its vascular network. Associated with zoom endoscopes from the 700 series, with a magnification capacity of up to 135x, the images obtained are more detailed **facilitating the characterisation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

Informations & Studies
LCI BLI
VISIT
BLI.eu

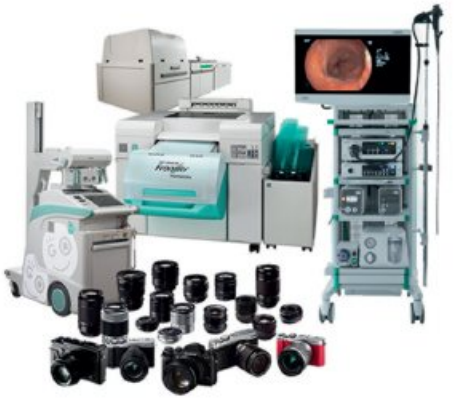
FUJIFILM
Value from Innovation

A pioneer in digital imaging, Fujifilm also offers innovative solutions in the fields of medical diagnostic imaging for prevention or treatment: digital radiography, mammography, endoscopy systems, ultrasound, chemical analysers ...

Discover our solutions dedicated to women's imaging, paediatric imaging, orthopaedic imaging or veterinary imaging.

The Fujifilm brand also proposes services for storage and diffusion of images using the latest web technologies.

Every year, Fujifilm invests approximately 7% of its turnover in Research & Development, or 3.5 million euros / day, in order to meet the challenges of developing new products capable of improving the quality of life for all. Our vision was born from this strength: «Value from innovation».



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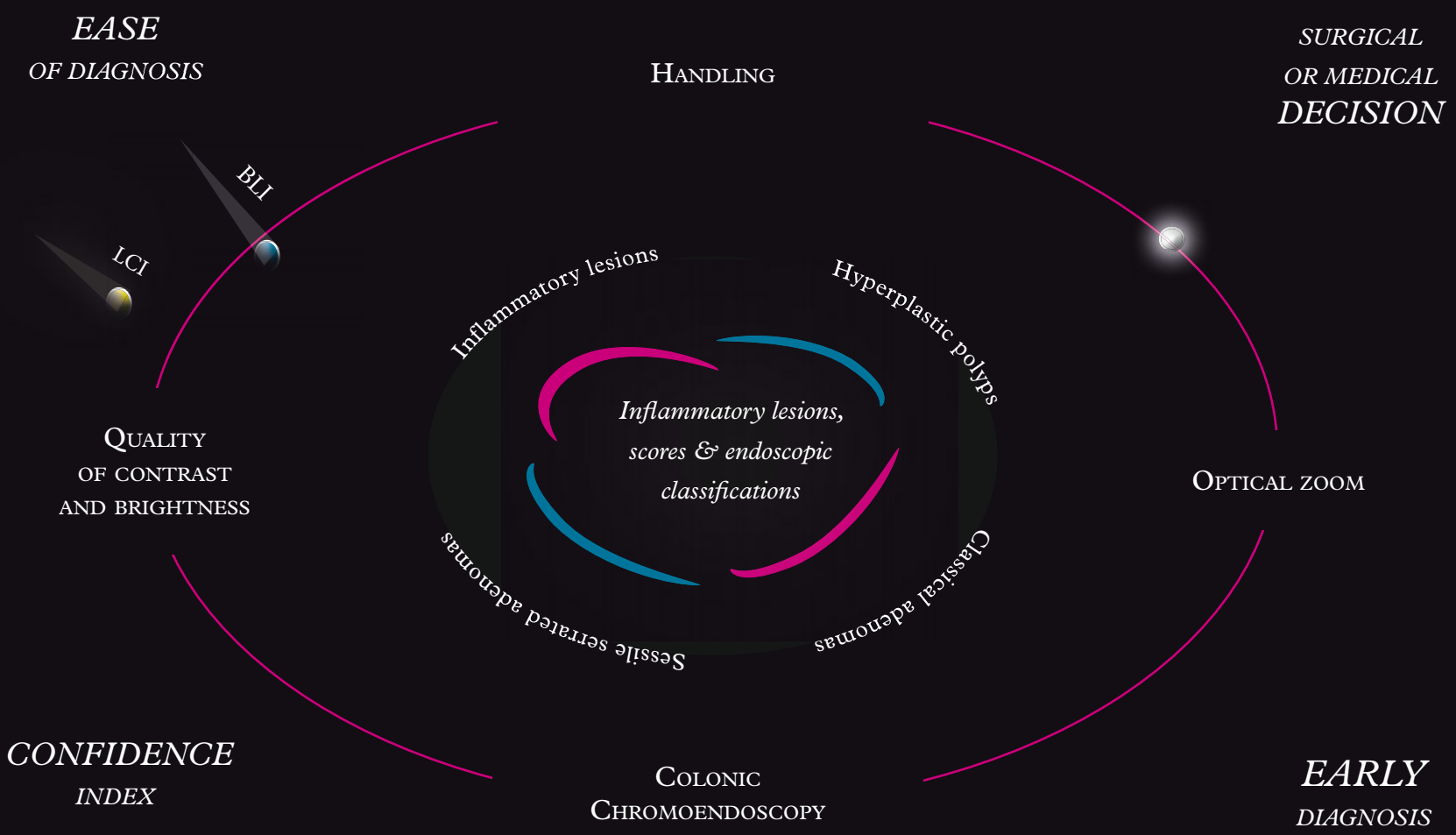
"Fujifilm has been the engine of innovation for more than 80 years, and as a result of the production of photographic film, the brand has been able to translate its historical know-how to the development of innovative products dedicated to health. In endoscopy, Fujifilm offers a range of advanced solutions to accompany Gastroenterologists and Pulmonologist in their daily lives. They facilitate the optimisation of certain procedures, but above all, they increase their diagnostic and therapeutic performance thanks to the exclusive tools dedicated to the detection and characterisation of lesions that are often difficult to identify and treat".

Mr. Takemasa KOJIMA - Senior Manager Marketing & Sales for Endoscopy European department.

Medical devices, see the product-specific instructions for more information. These medical devices are regulated health products that bear the CE marking based on this regulation.

The authors would like to thank the endoscopy and pathological anatomy teams for their help in obtaining the documents shown in this book
An electronic version is available at www.bli.eu



Chromoendoscopy: the latest technological leap contributing to the «second endoscopic golden age». Thanks to the latest advances and soon with the help of artificial intelligence, the endoscopist is becoming more than ever a strategist.