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Review Article

# State of Art Update: Detection and Classification of Early Colonic Neoplasia

## Abstract

Colonoscopy has been shown to be effective in the detection and removal of precancerous lesions and early cancers, and as a result, colorectal screening programs are in preparation, or in place throughout the world. Screening efforts are reducing the incidence of colorectal cancer (CRC) and allow diagnosis CRCs at an earlier stage. It is increasingly evident that colonoscopic polypectomy including endoscopic mucosal resection and submucosal dissection has become a means of cancer prevention with evidence of reduced predicted incidence and mortality of colorectal malignancies.

However, the risk of interval CRC relates to the skill of the performing colonoscopist, rather than any patient or polyp characteristic. Every endoscopist needs to actively look for proximal and flat or depressed lesions. For the general endoscopist, this means the ability to find and accurately assess a lesion is vital. In addition, advancing endotherapeutics means more lesions are potentially removable, and so endoscopists must be able to describe lesions in a standard fashion. This review deals with the current means of describing lesion morphology and surface characteristics, together with the significance of these. We also discuss the developing adjuncts to endoscopic imaging.

## Introduction

Since the recognition of adenomatous polyps as a precursor to colorectal cancer (CRC), there has been great interest in early identification and treatment of colonic lesions. Colonoscopic polypectomy has become a means of cancer prevention with evidence of reduced predicted incidence and mortality of colorectal malignancies [1,2].

Colonoscopy has been shown to be effective in the detection and removal of precancerous lesions and early cancers, and as a result, colorectal screening programs are in preparation, or in place throughout the world. Screening efforts are reducing the incidence of CRC [2,3] and allow diagnosis CRCs at an earlier stage [4]. Endoscopic mucosal resection (EMR) and submucosal dissection (ESD) provide means to treat lesions that previously had required surgical intervention.

Despite organisational and technical improvements, current colonoscopic surveillance is not 100% protective from CRC. The degree to which colonoscopy can reduce CRC incidence, particularly proximally to the splenic flexure is variably reported [5]. Suggested reasons for post colonoscopy CRCs include incomplete examinations, inadequate bowel preparation, incomplete polypectomy, and missed flat lesions. Back to back colonoscopies have suggested an adenoma miss rate of up to 27% [6] and flat lesions, notoriously easy to miss, may account for approaching 40% of adenomas in western series [7].

It is recognised that right-sided lesions are particularly challenging to identify, in part due to the difficulties in assessing the entire mucosal surface in the proximal colon [8], in addition, adenomatous changes are found in smaller lesions proximally, compared to distal lesions [9]. Proximal serrated polyps have been implicated as a further reason for the reduced effectiveness of colonoscopic screening. The term encompasses hyperplastic, sessile serrated and traditional serrated polyps, and while previously thought benign there is suggestion that some have neoplastic potential [10].

Despite this, the risk of interval proximal CRC relates to the skill of the performing colonoscopist, rather than any patient or polyp characteristic [11,12].

Undoubtedly, every endoscopist needs to actively look for proximal and flat or depressed lesions. For the general endoscopist, this means the ability to find and accurately



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assess a lesion is vital. Advancing endotherapeutics means more lesions are potentially removable, and so endoscopists must be able to describe lesions in a standard fashion whether removing in-house or referring to a tertiary unit.

We present a review of the current means of describing lesion morphology and surface characteristics, together with the significance of these. We also discuss the developing adjuncts to endoscopic imaging.

## Essentials of pre-treatment staging

The ability to accurately classify lesions is the key to pretreatment staging of early colonic neoplasia

Unlike the upper GI tract, the colorectal mucosa has no lymphatics in the mucosal layer, therefore, mucosal lesions have no risk of lymphatic metastases. If carcinoma is contained completely within the mucosa, the risk of lymph node and vascular invasion is nil and as a rule endoscopic resection is legimate for those lesions. Lesions may grow upwards, downwards or laterall, this is significant as indicates the likelihood of submucosal invasion, and so, the suitability for endoscopic intervention.

The Paris Classification [13], provides a simple and internationally valid classification, allowing an accurate, standardised method of describing the macroscopic appearance of superficial tumours from the oesophagus to colon. It allows prediction of the likelihood of submucosal invasion, and so decide if a lesion may be safely removed at the time of index colonoscopy, relisted for EMR by expert endoscopist or referred for surgery (Figure 1).

The original classification of polypoid and non polypoid lesions has latterly been expanded to encompass laterally spreading tumours (LST). LST are defined as lesions larger than 10mm in circumference with height less than their diameter. They may be granular or non-granular and typically are slow growing. Lesions demonstrating depression, whether in its entirety or focally are associated with higher rates of submucosal invasion and severe dysplasia [7]. Non granular LST, particularly with nodules greater than 10mm or demarcated depression, are particularly associated with high rates of submucosal invasion (Figure 2) [14,15].

## Endoscopic adjuvants to aid detection and classification

Having recognized that colonic lesions are missed, attempts have been made to optimise mucosal visualisation and assessment. Basic improvement, such as optimising bowel prep [16] and ensuring minimum individual endoscopist annual numbers [17], have contributed to reduced adenoma miss rates. A minimum withdrawal time has been shown to increase ADR and is now accepted as standard in all colonoscopies [18], while patient position changes in each area of the bowel [19] and the routine administration of buscopan on intubating the caecum [20], have been suggested to improve mucosal visualization. Other groups have focused on endoscopic adjuvants, such as cap-assisted [21], retroview colonoscopy [22] and superwide views [23].

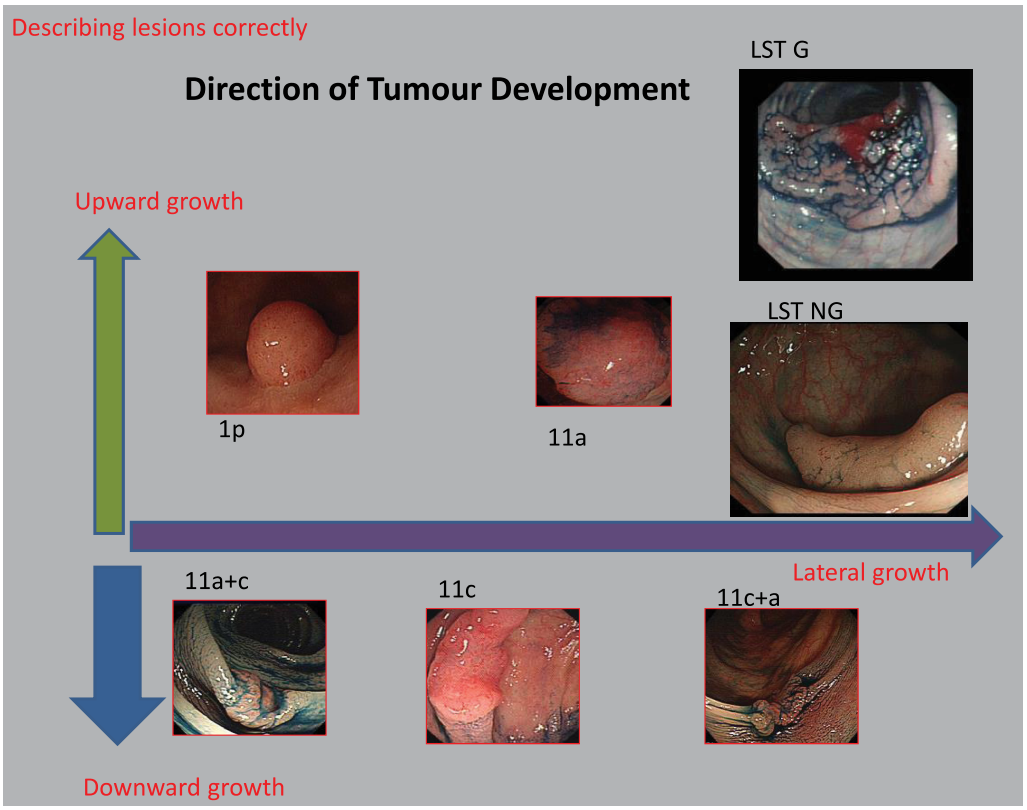


**Figure 1:** Paris Classification of early colonic neoplasia.



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In addition to optimising the bowel and the endoscopic technique, image-enhanced endoscopy is increasingly utilized. Numerous studies have reviewed its use, both to aid detection, but also aid histological diagnosis.

Standard white light endoscopy relies on careful assessment of slight color changes (faint redness, or loss of color), mucosal irregularity and interruption or loss of underlying vessels. It is regarded as inaccurate in the prediction of histological classification (Figure 3) [24].

Dye based chromendoscopy was the first adjunct to assessment of lesions. It was originally described using indigo carmine as a means of creating contrast between normal and abnormal mucosa. A 2010 meta-analysis of five randomised control trials estimated a 50% increase in polyp detection [25].

Its adoption has been limited as it is labour intensive, time-consuming and does not allow switching between chromo- and normal endoscopic views. There are attempts to use novel techniques to deliver contrast staining, including the use of delayed release tablets [26], but newer endoscopic equipment aims to provide a virtual means of appreciating the same features without the imitations.

## High definition white light endoscopy

Studies show promise in differentiating between adenomatous and hyperplastic polyps [27] and new generations of endoscopes promise to make new techniques easier to adopt. The Kudo system, by using high definition white light endoscopy, provides a further means of stratifying risk of submucosal invasion or malignancy. Kudo is a now well-described means of describing mucosal pit patterns. Developed in Japan, it has been shown to be an accurate means of classifying polyps prior to formal histological assessment [28].

In addition to assisting the identification of polyps, there is suggestion that HD-WLE may also improve detection of lesions, particularly small, flat, right sided adenomas [29]. There is not yet supporting evidence that this has a significant effect on patient outcome however.

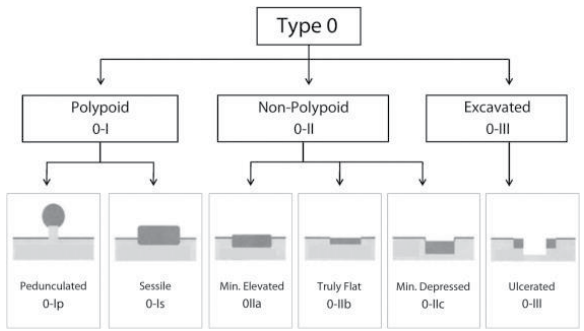


**Figure 2:** The original classification of polypoid and non polypoid lesions and its expanded to encompass laterally spreading tumours (LST), Tadepalli US, et al.

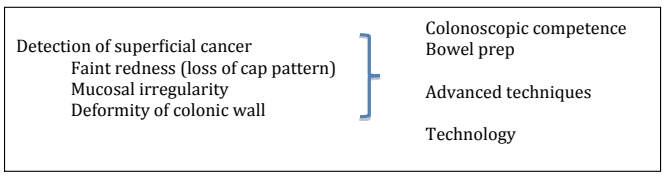


**Figure 3:** Considerations in lesion detection.

## Virtual Image processing

Narrow band imaging uses light filters to narrow the bandwidth of the light projected from the endoscope. The resultant spectrum of blue-green light highlights mucosal vessels and gives an impression of the pit pattern as a result. Post-processing imaging techniques such as FICE (Fuginon intelligent chromoendoscopy) and iSCAN use computer algorithms to further highlight the mucosal features.

Sano classification uses observation of microvessels and pit-like patterns of polyps seen by narrow band imaging to differentiate between adenomatous polyps and carcinoma [30]. NBI prediction of histological diagnosis is highly accurate [31], but there is not yet evidence that initial detection rates are significantly increased (Figure 4) [32,33].

Confident use of endoscopic lesion recognition adjuvants has allowed the American Association of Gastrointestinal Endoscopy to propose a "resect and discard" treatment algorithm whereby following optical assessment, lesions <5mm are either left in situ (rectosigmoid) or resected and discarded without histopathological analysis (outwith rectosigmoid) [34]. This is hoped to best utilize endoscopic resources and prevent exposing patients to the risk of unnecessary poylpectomy. However, while imaged enhanced techniques have been proven to be accurate in high volume centres. The wider application in non-specialist centres is less certain due to unacceptably low rates of sensitivity and specificity [35]. There is no standard means of training but a variety of groups have proposed that a greater than 90% diagnostic accuracy can be achieved by NBI following various computer based training [36,37].

## Approach when considering polypectomy

There are different areas to consider when assessing the suitability of a lesion for polypectomy. Several approaches are available, from conventional polypectomy for lesions less than 20mm, to EMR (Endoscopic Mucosal Resection) or ESD (Endoscopic Submucosal Dissection) for larger lesions or surgery, whether laparoscopic assisted colectomy (LAC) or open surgery, if deep invasion present (Figure 5). An appropriate, available support framework is vital prior to any colonoscopy. This is even more important if there is a possibility that larger polyps, with the potential for higher rates of complication may be removed. Familiar kit and appropriately trained nursing staff must be on hand. The endoscopist must have received appropriate training and mentoring. Support staff including surgeons, pathologists and accommodating managers are essential.

On assessing the polyp itself, the first consideration should be a judgment of the neoplastic potential. Pit pattern assessment by chromoendoscopy or vascular pattern by NBI together with morphological features; fixity, in drawing of folds, depression or non-lifting sign (Kato sign). Following



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this, the respectability should be assessed. A wide base or overlying of a haustral fold add complexity to polypectomy and should encourage caution.

Finally, prior to removal, any hazards should be taken in to consideration. Right sided lesions, particularly caecal lesions in proximity to the appendix, and those close to or involving diverticulae should encourage caution due to the increased risk of perforation. There may be significant scarring present from previous attempted at removal which may make the procedure more technically challenging.

We propose a pathway as an easy to follow guide for the management of larger colonic polyps, suitable for display in endoscopy rooms (Figure 6).

## Future directions

Colonoscopy is effective in reducing incidence of CRC, however it is not simply a case of "getting round" to the caecum. Endoscopic technology has advanced dramatically over the preceding years and will continue to do so. We are now able to assess and categorise lesions with increasing confidence, to the extent that resect and discard approaches are being advocated by national bodies, removing the need for histological assessment in selected lesions.

The definition of an endoscopically treatable lesion is changing. Accurate assessment of invasion, together with novel equipment and techniques allow endoscopists to remove lesions previously referred for surgery. The importance of good bowel prep, technique and adequate withdrawal time are now well recognised as vital in optimising polyp detection rate. Complex lesions are best managed in high volume expert centers, making it all the more important that every endoscopist use the Paris Classification as a means of assessing and describing every lesion found, whether removed or referred.

While additional techniques such as narrow band imaging or high definition white light microscopy may not yet be universally available, simple, universally adoptable approaches

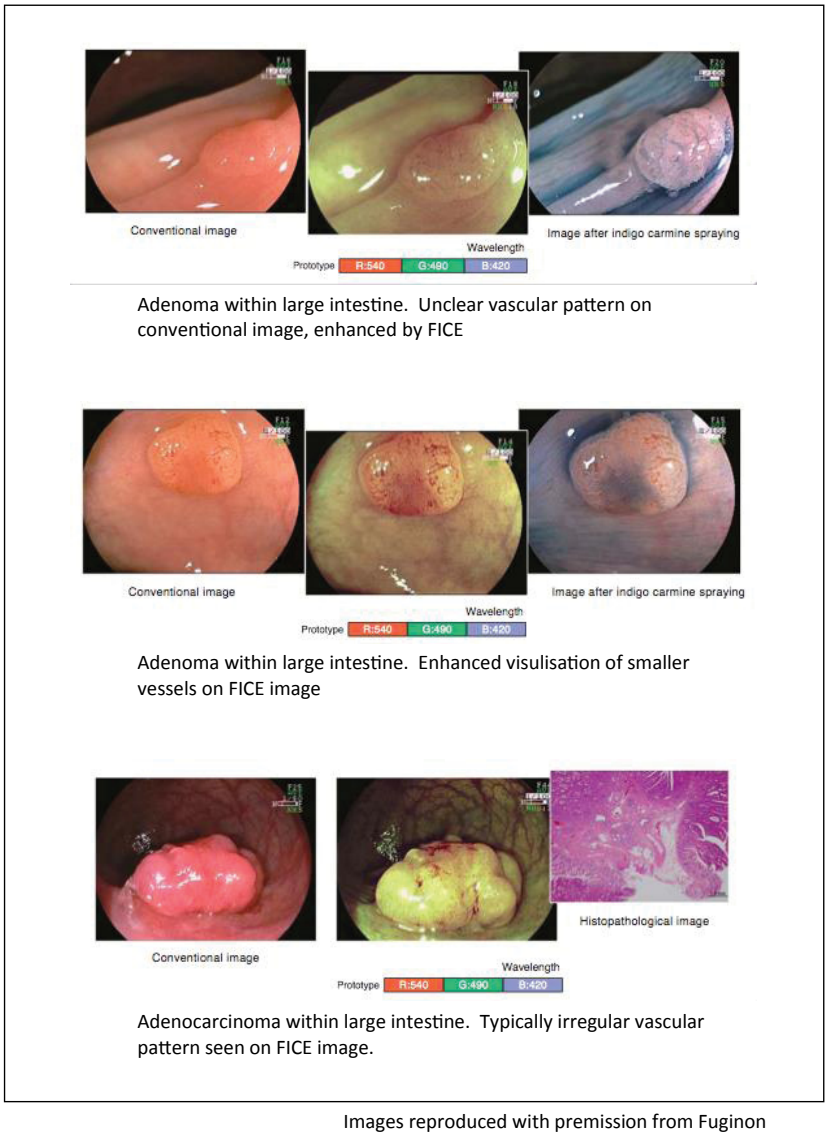


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**Figure 4:** Sano classification uses observation of microvessels and pit-like patterns of polyps, examples using Fuji Intelligent Color Enhancement technology.



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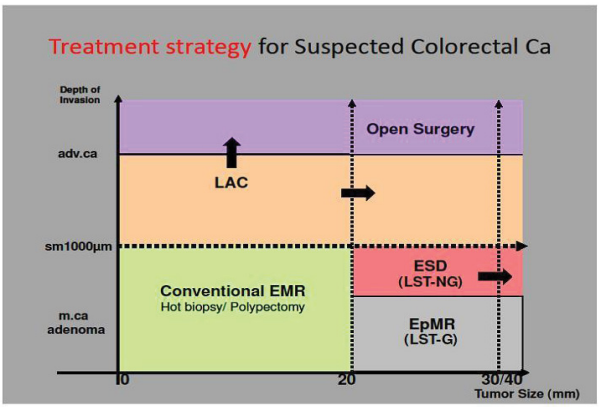


**Figure 5:** Treatment Strategy for treatment of suspected cancer with kind permission of Dr Y Saito, NCCH, Tokyo.
**Abbreviations:** EMR (Endoscopic Mucosal Resection) or ESD (Endoscopic Submucosal Dissection), LAC (laparoscopic assisted colectomy), LST-NG (Lateral Spreading Tumour –None Granular Type) or LST-G (Lateral Spreading Tumour – Granular Type).

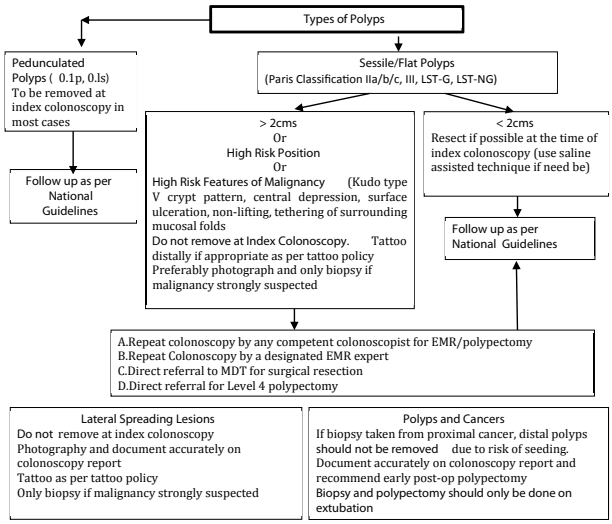


**Figure 6:** Management of Larger Colon polyp.

have been shown to improve lesion detection rates. The utility of advanced technology has been proven in expert centers in discriminating between lesions. As availability expands and its application broadens, it seems inevitable that its use will become more widespread and require incorporation into endoscopic training programs.

In conclusion, an appreciation of the available techniques, together with the proposed management strategy will allow useful referral information to be given. This will lead to the optimal management of early colonic neoplasia.

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