

Title

Endoscopic approach to polyp recognition

Authors

Dr Conor Lahiff, Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, UK

Dr James E. East, Translational Gastroenterology Unit, John Radcliffe Hospital, Oxford, UK

Address for Correspondence

Dr. James E. East, Translational Gastroenterology Unit, Experimental Medicine Division, Nuffield

Dept of Clinical Medicine, University of Oxford, John Radcliffe Hospital, Headley Way, Headington,

Oxford, OX3 9DU, United Kingdom

Telephone: +44 [0]1865 228753

Fax: +44 [0]1865 228763

E-mail: james.east@ndm.ox.ac.uk

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Abstract

Identification and complete resection of colorectal polyps provides a significant mortality benefit from colorectal cancer. With improvements in colonoscopic technique and advanced endoscopic imaging techniques, polyp detection has taken on greater complexity since the establishment of Bowel Cancer Screening programmes internationally. All endoscopists operating within symptomatic and screening populations should be aware of endoscopic features associated with advanced neoplasia. Chromoendoscopy and advanced imaging techniques such as narrow spectrum technologies (NBI, FICE, i-SCAN) have specific classification systems to support accurate lesion characterisation. This review summarises the evidence in relation to polyp detection, recognition and characterisation as well as the identification of features of invasion. Future areas of interest include optimal management of large polyps, incorporation of a “detect, resect and discard” strategy for small and diminutive polyps, expected wider use of computer decision support tools (artificial intelligence, deep learning) and the use of fluorescently labelled molecular probes to improve detection and assessment of neoplasia.

Background

The detection of colorectal polyps has become an area of intense interest since the original description of the adenoma-carcinoma sequence and further strengthened by robust large scale trial data supporting the role for colonoscopy and resection of adenomatous polyps as being associated with reduced colorectal cancer related mortality¹. As endoscopic technology advances, our understanding of appropriate colonoscopic surveillance and identification and management of specific polyp sub-types that may place individuals at higher risk of developing cancer has become clearer. In the era of national bowel cancer screening we are detecting increasing numbers of polyps and those polyps that we are detecting are increasingly complex, requiring specialized methods for their characterization and management.

Polyp detection

There is now clear epidemiological data from multiple large studies linking the adenoma detection rate (ADR; the percentage of colonoscopies where at least one adenoma is detected) with outcomes such as interval colorectal cancer incidence and interval cancer mortality². Adenoma detection is influenced by many factors, including patient factors such as age, gender and bowel preparation; and endoscopist factors such as experience, withdrawal time, time of day, use of anti-spasmodics, adequate luminal distension and rectal retroflexion. Specific technologies such as high definition endoscopes, chromoendoscopy and devices e.g. cap attachments can also influence the ADR. Adequate bowel preparation is a prerequisite for acceptable polyp detection, particularly for right sided, smaller, and flat polyps. The British Society of Gastroenterology (BSG) guidance on bowel cleansing considers sodium phosphate preparations and polyethylene glycol based preparation to be equivalent, however they do recognize that most studies show a superior cleansing effect in the proximal colon with PEG-based preparations³. The importance of "split dose" prep in achieving high quality bowel preparation is emphasised in the 2014 US multi-society task force on colorectal cancer guidelines and is now the standard of care, demonstrating improved adenoma detection in

randomised trials⁴.

Increased lesion recognition may be achieved with the use of an anti-spasmodic such as hyoscine butylbromide (Buscopan; Boehringer Ingelheim, United Kingdom) prior to scope withdrawal, dynamic position changes (luminal distension), and adherence to key performance indicators such as a six-minute withdrawal time and retroflexion in the rectum. Combining these four factors in an "evidence bundle" and supporting endoscopists and units to make these practice changes improves adenoma detection, particularly for the lowest detectors⁵. Within specific higher risk groups such as IBD and Lynch syndrome chromoendoscopy has been shown to result in improved lesion recognition^{6,7}.

Polyp characterisation

Polyps have been classically defined as pedunculated or sessile, with "flat" or non-polypoid lesions only recently widely appreciated by Western endoscopists. In research studies characterisation is usually with the Paris Classification for gastrointestinal polyps, and the NHS Bowel cancer screening programme has recently adopted this for clinical use⁸. However there are doubts about its reproducibility, especially for diminutive polyps where interobserver kappa values were 0.27 (fair) even amongst experts⁹. Invasive potential can be estimated based on morphology. Polypoid lesions (Paris 0-I), sessile or pedunculated polyps (>10mm) have a low invasive potential (7%), whereas as those with a depressed component (either Paris IIc or IIa+c) have a 31% risk of submucosal invasion¹⁰. Type III (excavated) lesions are invasive and should be biopsied and referred for MDT discussion with surgical management unless co-morbidity precludes this approach.

Kudo pit pattern with Narrow Band Imaging (NBI) and has high sensitivity and specificity for distinguishing adenomas (type III/IV) from hyperplastic (type I/II), particularly when used by experts. Even polyps less than 10mm have a malignant potential and this can be largely determined by careful endoscopic evaluation. Kudo type V pit pattern is associated with a 56% rate of submucosal invasion, compared with 5% for type III/IV and 0% for type I/II¹¹.

The Sano classification uses blood vessel irregularity and capillary patterns to predict invasive potential and considers meshed (type I) or branched around crypts (type II) vessels to indicate hyperplastic and adenomatous histopathology respectively, while irregular, blind ending, branched or absent vessel pattern (type III) indicates submucosal invasion (Table 1).

Narrow band imaging International Colorectal Endoscopic (NICE) classification¹² is a consensus-derived, validated classification system based on colour change, vessel thickness and surface pattern and divides polyps into type I (hyperplastic), type II (adenoma), and was extended to include type III (deep submucosal invasion or cancer). Further to this the Japanese NBI Expert Team (JNET) classification subdivides into type IIa (adenoma) or type IIb (high grade shallow submucosal invasive cancers, SM1). This latest classification system, which attempts to unify aspects of all of the others (and includes Hiroshima, Showa and Jikei classifications, not mentioned in this article) has been recognized by the World Endoscopy Organisation (WEO) but is limited by its requirement for optical zoom magnification and lack of validation outside of expert Japanese endoscopists to date (Table 1)¹³.

For serrated polyps, a modification of the Kudo pit pattern classification has been proposed with type II-O (open) pits proposed to indicate sessile serrated polyps¹⁴. The Dutch “Workgroup serrated polypS and Polyposis” (WASP) classification¹⁵ combines the NICE classification (types I and II) and four typical sessile serrated features, i.e. clouded surface, indistinct border, irregular shape, and dark spots inside the crypts. This classification appears to have good accuracy (in diminutive and small polyps) both for differentiating hyperplastic and serrated lesions from adenomas and for identifying neoplasia. Further predictors of neoplasia identified in a recent retrospective series of serrated polyps included (semi) pedunculated morphology, double elevation, central depression and reddishness, along with pit pattern analysis by Kudo classification¹⁶. The features of these classifications and how they interact are summarised in Table 1.

Specific descriptive features for inflammatory or post-inflammatory polyps (PIPs) in patients with IBD have not been well studied and the application of advanced digital imaging technology (NBI) has

not been shown to be helpful, although chromoendoscopy is suggested to improve accuracy.

Characteristic features of PIPs include the presence of a fibrinous cap, surface friability, ulceration, an appendage-like or filiform appearance and a halo sign on application of dye.

The classification systems mentioned above which use pit pattern or microvessel patterns to determine risk can be complementary to one another and it is suggested that they be used in combination, depending on the information required (Table 1). To determine invasive potential of a polyp before embarking upon attempted resection, a combination of Kudo and Sano (in conjunction with other factors) has been suggested (Box 1)¹⁰, while to differentiate adenomas, hyperplastic polyps and serrated polyps from one another, a combination of NICE and WASP classifications has been suggested¹².

Classification systems for FICE and iSCAN exist and show good accuracy for optical diagnosis of polyps, but these are not necessarily interchangeable with those derived for use with NBI, such as NICE and JNET.

For pedunculated polyps (Paris, 0-Ip), careful assessment of the polyp by one or more of the classification systems above is recommended. Invasive characteristics should favour a lower resection point on the stalk i.e. closer to the mucosal surface and further from the polyp head, to maximize the chances of a clear margin and to facilitate the pathologist in being able to make an assessment using the Haggitt classification¹⁷.

Laterally spreading tumours (LSTs, Figure 1) are those with a horizontal growth pattern around the circumference of the bowel wall, and are greater than 10mm and can be divided into granular (G) and non-granular (NG) subtypes. Further distinction should be made to identify LST-G where a dominant nodule is present. LST-NG and LST-G with dominant nodule >10mm have a high risk of invasion (30%) compared with a LST-G without a nodule (<5%). Depressed (Paris 0-IIc or 0-IIa+c) lesions can carry as high as 60-75% risk of deep submucosal invasion^{10,18}. Key points in the identification and initial endoscopic management of these larger lesions are considered to be; photograph or video upon discovery (after washing), estimate size (ideally against an open snare),

characterize by Paris and Kudo/NICE NBI classifications, and biopsy only where there is concern for invasion (targeted biopsies from most suspicious area) (Box 1).

A broad approach to assess difficulty of colorectal polyp resection has been recommended by consensus guidelines¹⁰. Lesion assessment should include four components, i.e. size, morphology, site and access (SMSA) and polyps are thus assigned points for each component and assigned a level of difficulty (I-IV) based a cumulative points total. Level I and II polyps should be within the capability of all fully trained independent colonoscopists, while those participating in Bowel Cancer Screening should be comfortable with level III polyps. Specialist referral or surgery should be considered for level IV polyps. Size >4cm, right-sided/caecal location and endoscopist inexperience are factors that are suggested to be associated with higher risk for adverse outcomes. Location including involving the appendix, ileo-caecal valve or adjacent to the dentate line, as well as polyps within a segment of previous colitis or previous attempt at resection are all factors associated with higher risk for incomplete resection. Specialist referral should be considered in these circumstances, along with careful discussion at Complex polyp Multi-disciplinary team meetings (MDTs) and informed consent for the patient including alternative management and subsequent requirements for follow-up. Polyps which have not been biopsied or partly resected (scarred) with a non-lifting sign after accurate submucosal injection¹⁹ should be considered to have a high risk of deep submucosal invasion and these lesions should be assessed by an experienced colonoscopist to assess endoscopic resectability, combining other factors which may indicate invasive risk. The challenges in and importance of correct decision making for Suspicious Polyps and Early Colorectal Cancer (SPECC) have recently been highlighted in a national series of ongoing development lectures and case presentations that aims to promote multi-disciplinary approaches to make sure patients receive optimal care, with regional or even supra-regional referral if necessary (<http://www.pelicanancer.org/specc>). Current variations in surgical referral rates for large polyps which are seven-fold in the bowel cancer screening programme in the North of England are not acceptable.

Recent Developments

Device assisted colonoscopy (cap assisted colonoscopy, Endocuff, Endorings) may confer a benefit in terms of increased adenoma detection but early studies have shown mixed results and the benefit in terms of adenoma detection remains unclear.

New generation endoscopes with bright illumination, high definition, surface / edge enhancement, optical and digital zoom magnification, and wider field of visualization (170 degrees or more) endoscopes and endoscopy systems, may further improve white light detection rates. ESGE guidelines suggest use of high definition endoscopes for detection of colorectal neoplasia in average risk populations¹².

An expert group of gastroenterologists, interventional endoscopists, pathologists and colorectal surgeons recently published guidance on the management of large non-pedunculated colorectal polyps (LNPCP)¹⁰. In this guideline a structured approach to polyp recognition and further management is suggested, along with evidence based recommendations for the identification of technically challenging and high risk lesions both in terms of identification of markers of deep or submucosal invasion (Box 1) and polyps with high risk or procedure related complications, best managed by expert colonoscopists. The approach described above is largely in concordance with these guidelines.

Future Potential

Evidence suggests that there is good correlation between optical diagnosis (using NICE criteria) for small and diminutive polyps and pathology, especially where the optical diagnosis is made with high confidence. This is true for colonoscopy carried out by experts in academic settings but more recent evidence suggests that the correlation is significantly less strong when applied in the general hospital or non-expert setting, even after a defined period of training¹². The National Institute for Clinical and Health Excellence is considering the clinical efficacy and cost effectiveness of Virtual Chromoendoscopy for this application and is expected to deliver a final report in May 2017

[\[https://www.nice.org.uk/guidance/indevelopment/gid-dg10004\]](https://www.nice.org.uk/guidance/indevelopment/gid-dg10004).

Computer aided diagnosis (CAD) systems have developed rapidly in the last few years, especially since the advent of "deep learning" methods^{12,20}. Such technology is already in use in within radiology to support clinical decision making and it is envisaged that similar applications within gastrointestinal endoscopy will be available shortly. A key criterion not yet fully overcome will be the ability of such systems to detect and characterize lesions, where current models are unable to define the borders of a specific lesion of interest, though this seems to be less problematic with deep learning based approaches (<https://vimeo.com/185052677>). Currently described accuracy levels are approaching that considered to be required to support community based endoscopists to adopt a "resect and discard" strategy for diminutive colorectal polyps, perhaps as a "second reader".

Molecular imaging using fluorescently labelled molecular probes such as lectins have shown promise in the detection of Barrett's dysplasia in the oesophagus. Lectins and other molecular probes e.g. c-Met and may have utility in the identification and characterisation of colonic neoplasia with detection using fluorescence enabled endoscopes for wide field "red flag" detection²¹.

These technologies may be of particular benefit in situations where detection and characterisation are challenging e.g. IBD associated dysplasia.

The ESGE guideline on advanced endoscopic imaging techniques and BSG-ACPGBI guideline on large non-pedunculated colorectal polyps identify areas where evidence is lacking in relation to lesion recognition and management. Both guidelines suggest several areas where we can improve our knowledge as a community, including training in lesion recognition. By use of virtual and standard chromoendoscopy in selected settings and validation of competency measures / key performance indicators for polyp recognition and resection, we can achieve improved pre-resection identification of malignant features and enhance polyp management in general endoscopy. Correct diagnosis of invasiveness risk by the endoscopist first encountering a large polyp is the key step to making correct management decisions.

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Figure Legends

Figure 1.

40mm Granular-type laterally spreading tumour (LST-G type) in the caecum from a patient referred after diagnostic colonoscopy at another centre. 1A. High Definition (CF-H290DL, Olympus, Tokyo) white light image. 1B After dye spray with indigo carmine chromoendoscopy. This lesion was resected with piecemeal EMR and histology showed a tubulovillous adenoma with low grade dysplasia. Images provided courtesy of Dr. Malcolm Tan, Translational Gastroenterology Unit, Oxford / Changi General Hospital, Singapore.

Table 1. Pit pattern, microvessels and surface pattern classifications.

Classification	Hyperplastic	SSP	Dysplasia	Early invasion (SM1)	Deep invasion (SM2/3)
Kudo	Asteroid or star shaped pit (type II)	Asteroid or star shaped pit (type II) or type II-O (open shape)	Tubular or round pit either smaller (III _s) or larger (III _L) than regular pits . Gyrus / branched type pits (IV)	Irregular aggregation of type III _s , III _L and IV pits (V _i)	Loss of pit pattern, amorphous (V _n) non-structural
Sano	Meshed capillary vessels invisible with NBI (type I)	-	Broader meshed capillary vessels surround mucosal glands (type II)	Broad irregular vessels, unevenly sized and branching (type IIIA)	Avascular appearance due to desmoplastic change in stroma (type IIIB)
NICE NBI	Type I		Type II		Type III
- Colour (vs. background)	Same or lighter	-	Brown	-	Brown to dark brown
- Vessels	None, or isolated lacy	-	Brown vessels surround (white) pits	-	Disrupted vessels
- Surface	Dark or white uniform spots	-	Tubular or branched	-	Amorphous or absent pattern
WASP				-	-
- Clouded surface	<2 features present	≥2 features present	<2 features present		
- Indistinct border					
- Irregular shape					
- Dark spots inside pits					
JNET	Type 1	Type 1	Type 2a	Type 2b	Type 3
- Vessel pattern	Invisible	Invisible	Regular calibre Meshed pattern	Variable calibre Irregular distribution	Loose vessel areas Interruption of thick vessels
- Surface pattern	Regular white or dark spots, similar to surrounding mucosa	Regular white or dark spots, similar to surrounding mucosa	Tubular, branched or papillary	Irregular or obscure	Amorphous areas

Box 1. Polyp features that indicate higher risk of malignant invasion (Adapted from Rutter *et al.* Gut 2015¹⁰).

- Kudo type V pit pattern (irregular or loss of pit pattern)
- Paris 0-IIc or 0-IIa+IIc morphology (depressed component)
- Non-granular laterally spreading type polyp (LST-NG "flat or smooth")
- Granular type LST (G-LST) with dominant nodule (≥ 10 mm in size)
- Distorted surface pattern, colour and vessels (NICE type III)
- Thick and irregular microvessels (Sano capillary pattern type III)