**Clinical Update** 

# Endoscopy: An Evolving Speciality

## Naila Arebi, Brian P Saunders

#### Abstract

The practice of endoscopy has been rapidly changing due to new emerging technologies and novel techniques. There has been more focus on colonoscopy training with the development of structured programmes including simulators. Chromoendoscopy and magnification endoscopy have enabled improved diagnosis of small neoplastic lesions and will be important for the success of colorectal cancer screening programmes. The small bowel is now accessible to diagnostic modalities like capsule endoscopy and to therapeutic tools through the double balloon enteroscope. Endoscopic therapy has also become more sophisticated with endoscopic therapy of reflux disease now possible. Excision of large colorectal adenomatous polyps by endoscopic mucosal resection and dissection of submucosal tumours may reduce the need for surgical intervention.

The practice of endoscopy has rapidly changed over the past few years. What was once a simple diagnostic procedure made possible by the development of fibre optics has become a speciality in its own right. This article will highlight some aspects of endoscopic practice that have undergone major changes over the past few years and that will shape endoscopy practice in the future.

#### **Keywords**

Colonoscopy training, chromoendoscopy, magnification endoscopy, capsule endoscopy, endoscopic therapy

Naila Arebi MD, PhD St Mark's Hospital, London, UK Email: naila.arebi@imperial.ac.uk

Brian P Saunders MD, FRCP Wolfson Unit for Endoscopy St Mark's Hospital, London, UK Email: b.saunders@imperial.ac.uk

### Training

There has been a major overhaul of colonoscopy training in the United Kingdom following the result of a large national colonoscopy audit carried out in 1997. The audit assessed colonoscopy skills. The caecal intubation rate was only 56.7% falling well below the standard of 90%.<sup>1</sup> The results of the audit reveal a deficiency in colonoscopy training and gave the Department of Health the impetus to invest large sums of money in colonoscopy training. Three national centres were set up to provide training with 7 supporting regional centres (Figure 1). In addition, an endoscopy modernisation agenda for future service development was established to compliment improved training. A similar audit on ERCP practice is currently underway and results are awaited.

Although the training methods may vary between the three national centres they follow the same principles. An introduction to the instruments, with initial didactic tuition, is followed by hands-on experience on endoscopy simulators, which may be animal models, mannequins or computerised programs. Hands-on experience on patients is accompanied by audio-visual recording of the trainee with a tri-split screen looking at the endoscopic view, trainee's handling of the scope and a 3D-image of the configuration of the endoscope in the third screen. Generation of the 3D image was made possible by the development of the ScopeGuide image (Figure 2), which allows the endoscopist to monitor looping and locate the scope without fluoroscopy and give feedback to the trainee on loop correction. Imager colonoscopes differ from standard colonoscopes in having sixteen or more 2mm in-built generator coils. Each coil is energized 10 times/sec, by a field generator connected to the scope by a cord plugged into the umbilicus. Each coil then generates a magnetic field of different frequency, which is then detected by larger coils in a sensor disk placed alongside the patient. The information is then analysed by a signal processor converted into a graph and subsequently to a 3D image of the colonoscope, which can be seen on the monitor. This technology is now available in most training units in the UK.

With the impending introduction of colorectal cancer screening for people over the age of 60, specialist accreditation for gastroenterologists wishing to provide a screening service may become necessary and specialist endoscopy training is likely to become mandatory.

# New Technology Diagnostics

## Chromoendoscopy

Chromoendoscopy describes the application of stains or dye through the endoscope to alter tissue appearance in order to improve localisation, characterization or diagnosis of lesions. The main dyes used in clinical and research practice are methylene blue and indigo carmine. Methylene blue enters the cytoplasm of absorptive tissues such as colonic and small bowel epithelia. In the stomach it identifies intestinal metaplasia and in the colon weak staining implies metaplastic, neoplastic, or inflammatory change. Biopsies can then be targeted from areas of intestinal metaplasia in Barrett's oesophagus<sup>2</sup> and from areas of poor uptake in ulcerative colitis increasing the yield of dysplasia.<sup>3</sup>

In contrast indigo carmine is not taken up by cells but instead highlights the tissue surface by entering mucosal depressions and crevices. It has been studied as a tool in the assessment of the severity of ulcerative colitis and in the identification of dysplastic lesions arising as complication of longstanding ulcerative colitis.<sup>4</sup> In non-colitis patients the appearance of the surface pattern after the application of indigo carmine has been shown to be useful to discriminate between neoplastic and non-neoplastic polyps.<sup>5</sup>



**Figure 1.** Wolfson Unit for Endoscopy, one of the three UK National Training Centres for endoscopy. The centre offers a 4-day accelerated colonoscopy course and Train the Trainers course. Additional courses on offer include basic therapeutic skills and colonoscopy workshop.

Detection of diminutive polyps (polyps <5mm) has been reported to be greater with dye spray compared to conventional endoscopy.  $^{6}$ 

#### Magnification endoscopy

Although modern high resolution video-endoscopes permit detailed views of the gastrointestinal mucosa, magnification endoscopes can further enhance image detail. The Olympus magnifying videoendoscope can magnify the mucosal surface by 100 times and has been shown to provide an accurate assessment of the histology of colorectal tumour.<sup>7</sup> Kudo's group have shown that interpretation of the pit pattern by an expert colonoscopist enabled a clinical decision on the best management to be made without awaiting the histology (Figure 3).

#### Capsule endoscopy

Until recently, endoscopic visualisation of the small bowel was limited to the upper jejunum by enteroscopy and the distal end of the terminal ileum at colonoscopy. The limited access to the small bowel at enteroscopy was largely due to the mobility of the small intestine on its mesentery making fixation and forward movement of the endoscope uncomfortable for the patient. However, the introduction of the innovative wireless



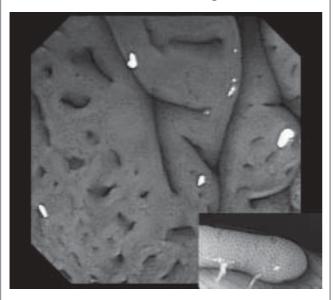
**Figure 2.** ScopeGuide imager. Specially designed colonoscopes have inbuilt coils which are energised and generate magnetic fields of different frequency. The magnetic fields are detected by the round sensor disk, which is placed in front of the patient. Information from the disc is analysed to produce a 3D image of the endoscope shown here in the top screen. Trainees can modify their technique according to the image on the screen.

**Table 1.** Indications for capsule endoscopy from a seriesof 150 patients

	Number of cases (%)
Obscure Gastrointestinal bleeding	100 (66)
Peutz-Jeghers syndrome	30 (20)
Pain	10 (6.6)
Possible Crohn's disease	4 (2.6)
Recurrence of Crohn's disease	2 (1.3)
Other (vomiting, Cowden's diseas abnormal Barium imaging,	e
follow-up ileal carcinoma)	4 (2.6)

capsule endoscopy now allows easy, safe and effective small bowel examination. This new technology consists of a capsule (Pillcam<sup>®</sup>), a portable hard drive with antenna array (Given system<sup>™</sup>) and a workstation (Rapid diagnostics<sup>®</sup>) (Figure 4).

The capsule contains a metal oxide silicon chip camera, a short focal length lens, 4 white light emitting diode (LED) illumination sources, two silver oxide batteries, and a UHF band radio telemetry transmitter. It measures 11mm in diameter and 26 mm in length and is easily ingested by most patients. It weighs 3.7g and is passively propelled through the intestine by peristalsis. The activated capsule provides image accrual and transmission at a frequency of 2 frames per second until the battery expires after  $7 \pm 1$  hours. During the examination the patient wears a belt pack holding a power supply containing batteries together with a small 305gb hard drive for storing received images. Before ingestion of the capsule, a series of electrodes are taped to the patient's abdomen in a designated pattern. This is then connected to the hard drive on the belt so that luminal findings can be correlated with general capsule location in the abdomen.8 After eight hours, data are



**Figure 3.** Magnified view of a colonic polyp. This image shows a magnified polyp (x110) after the application of indigo carmine dye spray. The pit pattern resembles cerebral sulci and is characteristic of an adenoma. A normal punctate pit pattern is shown inset.

downloaded from the belt pack recorder to a customized PC workstation. Proprietary software is then used to review the images and a report generated.

The diagnostic yield of capsule endoscopy has been shown to be highest when used to investigate the cause of obscure gastrointestinal bleeding.9 Its place in clinical practice is after negative upper endoscopy, push enteroscopy, colonoscopy, and possibly small bowel radiography. Other indications include surveillance in patients with polyposis syndromes and evaluation of malabsorptive, inflammatory or infiltrative conditions. Our unit has undertaken 150 procedures and the indications are listed in Table 1. The diagnostic yield for obscure gastrointestinal bleeding was 43% i.e. the cause for bleeding was found in 43% of cases (unpublished data). This is comparable to the yield in a small series of 43 patients investigated for obscure gastrointestinal bleeding9 but lower than the yield of 47% reported in a larger series of 100 patients with obscure bleeding.10 In two patients the investigation was complicated by capsule retention necessitating surgery in one case.

#### Therapeutics

The use of band ligation, injection therapy, heater probes and argon plasma coagulators for haemostasis are widely accepted practices together with other interventional procedure such as polypectomy, percutaneous endoscopic gastrostomies, stents and dilation. These simple therapeutic procedures are leading the way to more invasive endo-surgical approaches to treat gastrointestinal diseases.

#### Gastro-oesophageal reflux disease

The commonest surgical procedure used to control gastrooesophageal reflux disease is the Nissen fundoplication either laparoscopically or by an open technique. However the past few years have seen the introduction of a new surgical approach via the endoscope also known as endoluminal antireflux procedures.<sup>11</sup> The site of intervention classifies these procedures into one of three types: augmentation of the lower

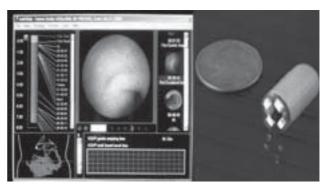


Figure 4. Capsule endoscopy. The capsule is shown compared to a dime coin. The images from the capsule can then be downloaded onto the computer and analysed using the RAPID programme. The view of the workstation is shown here.

oesophageal sphincter (usually by intramural injection of a substance or placement of a device); suturing or plication techniques; and radiofrequency ablation of the lower esophagus and/or cardia. Access to endoluminal therapies is still restricted to use in clinical trials, as there remain a number of unresolved features. Questions about the underlying mechanisms of action, the long-term efficacy and safety along with the appropriate selection of patient for each technique need to be addressed before they enter routine clinical practice.

#### Endoscopic mucosal resection

Endoscopic mucosal resection (EMR) completely removes diseased mucosa by resecting through the middle or deeper part of the submucosa. Although there are many variations of the technique, the basic principle is the same - the diseased mucosa is raised off the muscularis propria by the creation of a submucosal bleb, strangulated by a snare or ligator, and subsequently resected by an electrosurgical snare (Figure 5). The purpose of EMR is twofold: to provide endoscopic cure of early cancers in which the risk of lymph-node metastasis is minimal and to obtain specimens for accurate pathologic staging. For all types of gastrointestinal cancers for the outcome to be favourable there must be no evidence of venous or lymphatic involvement. In this context a useful discriminating technique for colonic tumours as to whether it is amenable to EMR removal is the effect of submucosal fluid injection. Invasion, more than 2/3, into submucosa triggers substantial submucosal fibrosis preventing tissue separation after attempts at submucosal fluid injection (non-lifting sign). The diagnostic accuracy of the non-lifting sign in early cancer of the colon has

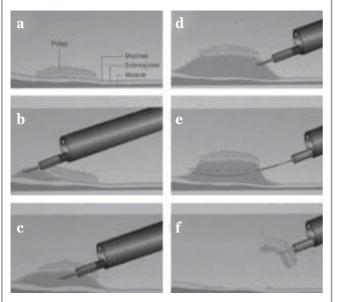


Figure 5. Schematic view of endoscopic mucosal resection. (a) The three main layers of the colonic wall are shown in relation to a polyp. (b,c,d) After a submucosal injection of fluid the mucosa is lifted and the polyp is cushioned from the underlying tissue. (e) The polyp can then be snared through the submucosa. (f) The polyp with a superficial surface of the submucosa was then removed.

been investigated; one study has shown a positive predictive value of 83% for invasive carcinoma.<sup>12</sup>

In the colon, the EMR is also used to safely remove flat lesions and broad-based sessile polyps. Injection of fluid into the submucosa beneath the polyp increases the distance between the base of the polyp and the deeper tissues of the bowel wall. The large submucosal cushion of saline solution increases the safety of polypectomy by preventing thermal injury to these deeper tissues.<sup>13</sup> In our unit we have removed 177 polyps ranging 2-8cm in diameter with this technique with only one case requiring hospitalisation for post-polypectomy bleeding (Figure 6). EMR can be safe, effective, and applicable to a variety of clinical situations. If practiced in the right setting and with

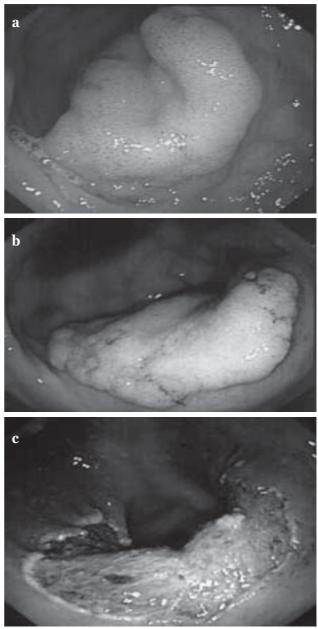


Figure 6. A polyp removed by endoscopic mucosal resection. (a) The polyp is first located (b) a mixture of saline, adrenaline and methylene blue is injected in the submucosal (c) the residual defect after polypectomy showing the muscular layer.

expertise, the technique should be considered in selected cases of superficial early cancer in which the risk of leaving lymph node metastases is nil or at least judged to be lower than the risk of surgery or death.

#### En bloc resection techniques

En-bloc resection for adenomas, early mucosal cancers and submucosal tumours using an insulated tip knife (IT knife) has been reported for tumours of the upper GIT. The advantages of this approach are that the tumour can be resected in one piece enabling completed histo-pathological assessment. Less recurrence has been reported when this procedure is used for the removal of large colorectal polyps.<sup>14</sup> However further comparative studies are warranted to confirm the safety and efficacy of this technique.

#### The future

With the introduction of colorectal cancer screening maximal detection of premalignant polyps will be of paramount importance in the success of the program. Confocal laser endoscopy, in which a confocal laser microsope is intergrated into the distal end of the endoscopy, permits the diagnosis of neoplasia at endoscopy.<sup>15</sup>

The clinical application of this new technology will probably be as a two-stage procedure: firstly highlighting abnormal mucosa by dye spray or autofluorescence followed by the detailed examination using the confocal laser endoscope.

In the small bowel, progress in imaging has been made with the introduction of the double balloon enteroscope which can provide access to all the small bowel and now allows therapy for lesions seen on capsule endoscopy.<sup>16</sup>

Further technological improvements to the capsule endoscope have been directed toward additional abilities, such as means to label the bowel wall, sample the luminal contents, biopsy the mucosa, or control the movement of the device.<sup>17</sup> What was once believed to be science fiction is fast becoming a reality.

#### References

- Bowles CJ, Leicester R, Romaya C, Swarbrick E, Williams CB, Epstein O. A prospective study of colonoscopy practice in the UK today: are we adequately prepared for national colorectal cancer screening tomorrow? Gut 2004; 53:277-83.
- Ragunath K, Krasner N, Raman VS, Haqqani MT, Cheung WY. A randomized, prospective cross-over trial comparing methylene blue-directed biopsy and conventional random biopsy for detecting intestinal metaplasia and dysplasia in Barrett's esophagus. Endoscopy 2003; 35:998-1003
- Kiesslich R, Fritsch J, Holtmann M, Koehler HH, Stolte M, Kanzler S, Nafe B, Jung M, Galle PR, Neurath MF. Methylene blue-aided chromoendoscopy for the detection of intraepithelial neoplasia and colon cancer in ulcerative colitis. Gastroenterology 2003; 124:880-8.
- 4. Rutter MD, Saunders BP, Schofield G, Forbes A, Price AB, Talbot IC. Pancolonic indigo carmine dye spraying for the detection of dysplasia in ulcerative colitis. Gut 2004; 53:256-60.
- Axelrad AM, Fleischer DE, Geller AJ, Nguyen CC, Lewis JH, Al-Kawas FH, Avigan MI, Montgomery EA, Benjamin SB. Highresolution chromoendoscopy for the diagnosis of dimunutive colon polyps: implications of colon cancer screening. Gastroenterology 1996; 110:1253-8.
- 6. Brooker JC, Saunders BP, Shah SG, Thapar CJ, Thomas HJ, Atkin WS, Cardwell CR, Williams CB. Total colonic dye-spray increases the detection of diminutive adenomas during routine colonoscopy: a randomized controlled trial. Gastrointest Endosc 2002; 56(3):333-8.
- 7. Kudo S, Tamura S, Nakajima T, Yamano H, Kusaka H, Watanabe H. Diagnosis of colorectal tumorous lesions by magnifying endoscopy. Gastrointest Endosc 1996; 44:8-14.
- 8. Mylonaki M, Fritscher-Ravens A, Swain P. Wireless capsule endoscopy: a comparison with push enteroscopy in patients with gastroscopy and colonoscopy negative gastrointestinal bleeding. Gut 2003; 52:1122-6.
- Rastogi M, Schoen RE , Slivka, A. Diagnostic yield and clinical outcomes of capsule endoscopy. Gastrointest Endosc 2004; 60:959-64.
- 10. Pennazio M, Santucci R, Rondonotti E, Abbiati C, Beccari G, Rossini FP, De Franchis R. Outcome of patients with obscure gastrointestinal bleeding after capsule endoscopy: report of 100 consecutive cases. Gastroenterology 2004; 126:643-53.
- 11. Palmer K. Review article: indications for anti-reflux surgery and endoscopic anti-reflux procedures. Aliment Pharmacol Ther 2004; 20 Suppl 8:32-5.
- 12. Ishiguro A, Uno Y, Ishiguro Y, Munakata A, Morita T. Correlation of lifting versus non-lifting and microscopic depth of invasion in early colorectal cancer. Gastrointest.Endosc 1999; 50:329-333.
- 13. Norton ID, Wang L, Levine SA, Burgart LJ, Hofmeister EK, Rumalla A, Gostout CJ, Petersen BT. Efficacy of colonic submucosal saline solution injection for the reduction of iatrogenic thermal injury. Gastrointest Endosc 2002; 56:95-99.
- 14. Miyamoto S, Muto M, Hamamoto Y, Boku N, Ohtsu A, Baba S, Yoshida M, Ohkuwa M, Hosokawa K, Tajiri H, Yoshida S. A new technique for endoscopic mucosal resection with an insulated-tip electrosurgical knife improves the completeness of resection of intramucosal gastric neoplasms. Gastrointest Endosc 2002; 55:576-81.
- 15. Kiesslich R, Burg J, Vieth M, Gnaendiger J, Enders M, Delaney P, Polglase A, McLaren W, Janell D, Thomas S, Nafe B, Galle PR, Neurath MF. Confocal laser endoscopy for diagnosing intraepithelial neoplasias and colorectal cancer in vivo. Gastroenterology 2004; 127:706-13.
- May A, Nachbar L, Wardak A, Yamamoto H, Ell C. Double-balloon enteroscopy: preliminary experience in patients with obscure gastrointestinal bleeding or chronic abdominal pain. Endoscopy 2003; 35:985-91.
- 17. Available at: http://www.rfnorika.com/index.html.