Electronic Imaging to Enhance Lesion Detection at Colonoscopy

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INTRODUCTION

Colorectal cancer (CRC) can be considered a heterogenous disease appearing in various clinical contexts, such as sporadically, in those with an inherited predisposition, or in chronic inflammatory processes of the colon such as inflammatory bowel disease (IBD).

There are multiple molecular pathways that can lead to CRC, reviewed in the article Colorectal Neoplasia Pathways: State-of-the-Art by Ijspeert and colleagues elsewhere in this issue. Adenomatous polyps undergo sporadic accumulation of genetic mutations in multiple molecular pathways, including the adenomatous polyposis coli tumor suppressor gene and DNA mismatch repair genes, which can lead to mutations in the KRAS oncogene and p53 suppressor gene. Sessile serrated adenomas/
polyps develop into CRC via a separate molecular pathway involving BRAF mutations and DNA methylation.\(^5,6\) Recent data suggest that traditional serrated adenomas develop through a pathway driven by epithelial over expression of the bone morphogenic protein antagonist GREM1.\(^7\)

Hereditary or familial syndromes give rise to approximately 3% of cases of CRC. The most common is hereditary nonpolyposis CRC or the Lynch syndrome, where a germline mutation in DNA mismatch repair genes occurs leading to microsatellite instability. The less well-recognized serrated polyposis syndrome is characterized by multiple serrated polyps, defined as patients with more than 20 serrated polyps throughout the colon or 5 or more serrated polyps proximal to the sigmoid with 2 or more that are at least 10 mm in size.\(^8\) Other genetic syndromes are either less common or produce so many polyps that advanced endoscopic imaging is not needed, for example, in familial adenomatous polyposis.

IBD has long been recognized to be associated with CRC, related to the carcinogenic effect of chronic inflammation combined with a genetic predisposition. A meta-analysis has estimated the cumulative probability of developing CRC in any patient, 30 years after a diagnosis of ulcerative colitis, at 18%,\(^9\) however, population-based studies suggest that for patients with IBD overall, the risk may in fact be minimally elevated.\(^10,11\) There are no large studies confirming that surveillance reduces the mortality of ulcerative colitis–associated CRC. However, the benefit of continued surveillance has been described\(^12\) and it remains recommended practice in all international guidelines,\(^13–17\) with increasing focus on risk stratification to target efforts on higher risk patients.

Recognition of lesions with malignant potential is crucial, because detection and early removal of polyps reduces CRC mortality compared with population risk estimates.\(^18\) No randomised studies for colonoscopy for CRC prevention are available; however, a meta-analysis looking at 4 randomised, controlled trials and 10 observational studies found that flexible sigmoidoscopy for population screening showed a reduction in CRC rates in the distal colon.\(^19\) Variation in adenoma detection correlates with the incidence of postcolonoscopy CRC and death from CRC.\(^20\) Current white light techniques for colonoscopic detection of polyps and neoplasia yield a high miss rate of up to 22% of all adenomas\(^21\) and 2% to 6% of advanced colorectal adenomas and cancers.\(^22\)

It is, therefore, imperative to maximize polyp detection rates and to avoid missing polyps to maximize cancer prevention and minimize the risk of postcolonoscopy CRCs. Missed polyps and subsequent cancers can arise through suboptimal mucosal visualization,\(^23\) failure of complete polyp resection,\(^24\) or failed polyp detection.\(^25\)

In this review, we assess the potential benefits of additional electronic imaging above and beyond standard white light to improve polyp detection at colonoscopy.

### HISTORY OF COLORECTAL POLYP DETECTION

The ability to reliably detect subcentimeter polyps is a relatively new phenomenon that has come with the advent of increasingly sophisticated endoscopic equipment. Before the 1950s, barium radiographic studies and rigid sigmoidoscopy were used for investigation of the colon. Flexible endoscopic visualization of the mucosa of the gastrointestinal tract was made possible by the development of a coherent optical fiber bundle by Hopkins and Kapany.\(^26\) This led to the development of the first flexible gastroscopy “fiberscope” reported in 1958, which was developed commercially by 1960.\(^27\) Combined with the use of fluoroscopy, endoscope location could be confirmed and correlated with the endoscopic findings.\(^28\) The next major development in endoscopy came when Sivak and Fleischer\(^29\) published findings of a new endoscope where the optical
fiber bundle was replaced with an image sensor or charge-coupled device at the tip of the endoscope. This allowed the conversion of the light into electrical charges and reconstruction on a television monitor. By the 1990s, videocolonoscopy had largely replaced fiberoptic colonoscopy and as technology advanced, high-resolution endoscopy (HRE), and most recently high-definition endoscopy with 1080 lines of pixels was introduced in 2005 (see Fig 1A and 2A). Nevertheless, polyp miss rates continued to be significant for both adenomas and polyps.30

Colonoscopic chromoendoscopy was introduced in the 1970s and involves enhancement of the mucosa by segmentally applying stains, such as methylene blue or indigo carmine.31 This not only improves localization and characterization of lesions during endoscopy (see Fig. 2B), but also allows targeted biopsies of enhanced mucosal abnormality improving dysplasia detection in long-standing IBD,32 as well as increasing detection of neoplastic lesions in average risk subjects.33 Despite evidence supporting the use of chromoendoscopy, it has not become a widely adopted practice. This low use may be owing to a number of factors, including increased time required, cost, inadequate training, and interobserver variability.

**Narrowed Spectrum Endoscopy (Virtual Chromoendoscopy)**

Virtual chromoendoscopy may provide an alternative to conventional chromoendoscopy, because it does not require dye spray catheters and the use of dye. Rather, it relies on built-in technologies within the endoscope and processor that uses the innate properties of light to generate a tissue enhanced pseudoimage.

Conventional white light endoscopy (WLE) generates endoscopic images by shining white light (400–700 nm) onto tissue and uses a charge-coupled device to capture reflected light. Specific components of the mucosa and submucosa can be enhanced by manipulating the light reflected and the generated endoscopic images. This maneuver allows for detailed endoscopic examination of the mucosa and any abnormalities, without the need for dye.

Currently there are 3 different systems that enhance the mucosal appearance that are available commercially: (1) narrow band imaging (NBI) by Olympus (Tokyo, Japan), (2) Fuji intelligent color enhancement (FICE) by Fujinon (Tokyo, Japan), and (3) i-scan (Pentax, Tokyo, Japan).

NBI utilizes the principle that light wavelength determines depth of tissue penetration. Special filters are placed in front of the xenon lamp that narrows the spectrum to blue light of 400 to 430 nm and green light of 525 to 555 nm. The blue short wavelength (centered at 415 nm) not only has penetration limited to the mucosa, but has been shown to correspond with the peak absorption spectrum of hemoglobin34; thus, mucosal structures containing high hemoglobin content, such that vessels seem to be brown. The longer wavelength light (centered at 540 nm) penetrates deeper into the submucosa and corresponds with a secondary absorption peak of hemoglobin, highlighting submucosal vasculature as cyan (Figs. 1 and 2C).

FICE uses an algorithm that takes an ordinary endoscope image and decomposes the light according to wavelengths. Selective wavelength images are then combined to reconstruct a real-time image. There are 10 channels with each channel corresponding with 3 specific virtual, electronic filters resulting in images with various tissue depth penetrations, and hence tissue enhancements.35

I-scan uses 3 algorithms for image enhancement. (1) Surface enhancement allows minor changes in structure to be seen by enhancing the edge. This is achieved by analyzing the difference in luminance intensity of the pixels in this area with the edge components being enhanced. (2) Contrast enhancement identifies pixels of lower luminance intensity and subsequently enhancing the blue component of these
pixels. This gives areas of low luminance such as depressed areas a bluish color. (3) Tone enhancement decomposes the ordinary color image into light wavelength components of red, green, and blue. These components are then adjusted along a tone curve and reconstructed to produce an image with increased contrast of color tone.36

**AUTOFLUORESCENCE IMAGING**

Autofluorescence imaging (AFI) is another modality of mucosal enhancement manufactured by Olympus (Tokyo, Japan). Autofluorescence is the natural emission of light from biological molecules, endogenous fluorophores, when light of a suitable wavelength is absorbed. When cellular components and tissue state changes during pathologic processes, this alters the amount and distribution of endogenous fluorophores; hence, the autofluorescence generated. In neoplastic epithelial cells, there is increased fluorescence from mitochondrial cofactors nicotinamide adenine dinucleotide (plus hydrogen) and flavin adenine dinucleotide (FAD), but reduced fluorescence from collagen in the stroma.37 Thickening of the mucosa and increased blood flow in adenomatous lesions also attenuate excitation light and block the autofluorescence signal.

The autofluorescence endoscope generates blue light (390–470 nm) and green light (540–560 nm) via rotating color filters in front of the xenon light. After excitation by the shorter wavelength blue light, fluorophores emit autofluorescence of longer wavelengths (500–630 nm). A filter in front of the separate AFI charge-coupled device blocks the reflected blue excitation light, but enables the tissue autofluorescence as well as the reflected green light to filter through. These images are then integrated by the processor to generate a pseudocolor image where normal tissue and vessels appear green and dysplastic tissue as magenta (see Fig. 2D).

**CLINICAL APPLICATION OF ELECTRONIC IMAGING AT COLONOSCOPY**

**Average-Risk Populations**

In average-risk populations, the use of NBI has been compared with WLE for detection of colonic lesions in 5 meta-analyses (Table 1). Overall, the evidence that NBI is better than WLE for adenoma detection is not convincing. Similarly, polyp detection was not
improved with NBI and only 1 meta-analysis found that NBI increased detection of flat adenomas (95% CI, 1.09–3.52, \( P = .02 \)).

Other virtual chromoendoscopy modalities have limited data. A randomized, tandem trial in patients undergoing surveillance colonoscopy compared NBI, FICE, and WLE on first withdrawal. The authors recruited 550 patients into each group and neither NBI nor FICE improved adenoma detection or miss rates, with no benefit over WLE demonstrated. Two prospective, randomized, controlled trials, which enrolled a total of 1230 patients combined, compared WLE with FICE. These trials did not demonstrate an improvement in adenoma miss rate of FICE over WLE. A third prospective trial of 1318 patients (68% undergoing screening colonoscopies, the remaining diagnostic) also did not demonstrate significant benefit of FICE over white light for adenoma detection. Similarly, when assessing i-scan, 1 study has not

Fig. 2. A nonpolypoid colorectal neoplasm in quiescent ulcerative colitis. (A) An area of abnormal pit pattern with a “velvety” appearance was seen during high definition white light colonoscopy for surveillance of longstanding ulcerative colitis. (B) Use of chromoendoscopy (dye spray) with indigocarmine 0.2% revealed a flat (Paris 0-IIb) lesion with a circumscribed border with a diameter of approximately 30 mm. (C) Assessment with narrow band imaging (NBI; Olympus, Tokyo, Japan) is also shown to clarify the pit pattern, but the border is not as distinct as with chromoendoscopy. (D) Assessment with autofluorescence imaging (AFI; Olympus) also helps to differentiate the neoplastic tissue (pink/purple) from the surrounding normal mucosa (green). Biopsy confirmed low-grade dysplasia.
<table>
<thead>
<tr>
<th>Author, Year of Publication</th>
<th>No. of Studies Included</th>
<th>Method</th>
<th>Study Design</th>
<th>No. of Patients</th>
<th>Adenoma Detection Rate</th>
<th>Polyps per Patient</th>
<th>Flat Adenoma Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasha et al, 2012</td>
<td>9</td>
<td>NBI vs WLE</td>
<td>Meta-analysis</td>
<td>3059</td>
<td>OR, 1.01; 95% CI, 0.74–1.37</td>
<td>OR, 1.17; 95% CI, 0.8–1.71</td>
<td>OR, 1.26; 95% CI, 0.62–2.57</td>
</tr>
<tr>
<td>Dinesen et al, 2012</td>
<td>7</td>
<td>NBI vs WLE</td>
<td>Meta-analysis</td>
<td>2936</td>
<td>RR, 1.06; 95% CI, 0.97–1.16</td>
<td>RR, 1.22; 95% CI, 0.85–1.76</td>
<td>WMD 0.06; 95% CI, -0.01–0.13</td>
</tr>
<tr>
<td>Nagorni et al, 2012</td>
<td>8</td>
<td>NBI vs WLE</td>
<td>Meta-analysis</td>
<td>3673</td>
<td>RR, 1.03; 95% CI, 0.92–1.16</td>
<td>RR, 1.01; 95% CI, 0.96–1.06</td>
<td>RR, 0.87; 95% CI, 0.72–1.04</td>
</tr>
<tr>
<td>Jin et al, 2011</td>
<td>8</td>
<td>NBI vs WLE</td>
<td>Meta-analysis</td>
<td>3049</td>
<td>RR, 1.09; 95% CI, 1.00–1.19</td>
<td>—</td>
<td>RR, 1.96; 95% CI, 1.09–3.52</td>
</tr>
<tr>
<td>Omata et al, 2014</td>
<td>5</td>
<td>AFI vs WLE</td>
<td>Meta-analysis</td>
<td>758</td>
<td>RR, 1.04; 95% CI, 0.87–1.24</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>FICE/i-scan vs WLE</td>
<td>Meta-analysis</td>
<td>3032</td>
<td>RR, 1.09; 95% CI, 0.97–1.23</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>14</td>
<td>NBI vs WLE</td>
<td>Meta-analysis</td>
<td>5074</td>
<td>RR, 1.03; 95% CI, 0.96–1.11</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Zhao et al, 2014</td>
<td>6</td>
<td>AFI vs WLE</td>
<td>Meta-analysis</td>
<td>1199</td>
<td>OR, 1.01; 95% CI, 0.74–1.37</td>
<td>OR, 0.86; 95% CI, 0.57–1.30</td>
<td>—</td>
</tr>
</tbody>
</table>

**Abbreviations:** AFI, autofluorescence imaging; FICE, Fujinon intelligent color enhancement; NBI, narrow band imaging; OR, Odds ratio; RR, relative risk; WLE, white light endoscopy; WMD, weighted mean difference.

* Polyp detection rate.
demonstrated improvement in adenoma detection during screening colonoscopy. A meta-analysis that combined FICE and i-scan also showed no benefit of these modalities. Regarding AFI versus high-definition (HD)-WLE in average risk populations, the results are inconsistent, with 2 Japanese studies finding improved outcome with AFI. One study found that the miss rate for all polyps with AFI (30%) was significantly less than with WLE (49%; \( P = .01 \)) and a second study detected significantly more colorectal neoplasms with AFI, although a transparent hood was also used in this study. Interestingly, 3 European trials have not demonstrated a significant adenoma miss rate difference. Two meta-analyses of AFI did not find that it improved adenoma detection.

In summary, there is insufficient evidence to support the routine use of electronic imaging enhancement in average-risk populations to increase adenoma yield during colonoscopy, irrespective of the system used.

**Hereditary Syndromes**

Screening of patients with hereditary nonpolyposis syndromes reduces the risk of CRC by one half. A prospective cohort study of patients with the Lynch syndrome found that an additional pass with NBI compared with a single pass with HD-WLE significantly increased adenoma detection (absolute difference, 15%; 95% CI, 4%–25%).

Pancolonic chromoendoscopy seems to have benefit in screening colonoscopies in this patient population. Chromoendoscopy compared with conventional colonoscopy significantly improved detection of significant neoplastic lesions (24 lesions in 13 patients compared with 52 lesions in 16 patients; \( P = .004 \)). In another cohort study, an additional pass with conventional chromoendoscopy after a first pass with HD-NBI significantly increased the number of adenomas detected. A further study found that chromoendoscopy is superior to white light, AFI, and NBI for the detection of diminutive polyps in adenomatous polyposis. However, some studies have found that chromoendoscopy did not perform better for missed adenomas than intensive inspection. Data using other virtual chromoendoscopy modalities are very limited.

AFI was found to improve adenoma detection in a prospective single-center study that enrolled 75 asymptomatic patients with the Lynch syndrome or familial CRC families (\( P = .01 \)). In the context of serrated polyposis syndrome, a randomized cross-over study of consecutive patients who underwent tandem colonoscopy with HRE and NBI found the polyp miss rates was 36% (95% CI, 28%–45%) for HRE compared with a significantly lower 10% (95% CI, 5.5%–19%) for NBI (\( P < .001 \)). Similarly, a pilot study comparing HRE, AFI, and NBI showed significantly lower polyp miss rates with HD-NBI compared with HD WLE. Endoscopic differentiation between hyperplastic polyps and sessile serrated adenomas/polyps using endoscopic trimodal imaging did not demonstrate a significant difference; however, hyperplastic polyps and adenomas could be differentiated with NBI but not AFI.

The use of electronic imaging in the high-risk populations of hereditary syndromes may have some benefit, but has not been shown to be superior to conventional chromoendoscopy.

**Inflammatory Bowel Disease**

Patients with long-standing and extensive ulcerative colitis benefit from colonoscopic surveillance given their increased risk of CRC compared with the average-risk population. In 3 randomized, controlled trials comparing NBI with WLE for the detection of neoplasia in long-standing IBD, it was found that NBI did not increase significantly the detection rate of neoplastic lesions compared with WLE. Random biopsies taken with both NBI as well as WLE (\( n = 1348 \) and 1359, respectively) yielded only 1 biopsy
demonstrating histologic evidence of low-grade dysplasia, suggesting that this prac-
tice should be abandoned.61

Two randomized, controlled trials have compared the detection of neoplasia in long-
standing IBD using HD-NBI with HD conventional chromoendoscopy. One study
found that NBI had a significantly inferior false-positive biopsy rate \( (P = .001) \) but a
higher percentage of missed neoplastic lesions (31.8% with NBI compared with
13.6% using chromoendoscopy).64 Similarly, a second study found that chromoendo-
scopy identified more lesions than NBI (131 vs 102; \( P < .001 \)), but histology revealed
most of these lesions to be nondysplastic. In the same study, chromoendoscopy iden-
tified more neoplastic lesions (23 lesions in 11 patients vs 20 lesions in 10 patients), but
this difference was not statistically significant \( (P = .180) \).65

There are 2 studies comparing HD-WLE with AFI for the detection of colorectal
neoplasia in IBD. A pilot study showed that protruding lesions with a low autofluores-
cence signal were more likely to be neoplastic than lesions with a high autofluores-
cence signal,66 and in a randomized, controlled trial, the miss rate for neoplastic
lesions was statistically significantly lower with AFI compared with HD-WLE.67

Overall, advanced electronic imaging has demonstrated limited utility compared
with conventional chromoendoscopy in the detection of neoplastic lesions in patients
with long-standing IBD.

**MOLECULAR IMAGING ENHANCED ELECTRONIC IMAGING: AN EMERGING
TECHNOLOGY**

Given the overall lack of evidence supporting the routine use of electronic imaging
modalities in surveillance colonoscopy to enhance polyp detection, further technolog-
ical advancements are needed. Molecular imaging has the potential to facilitate this
step forward in our endoscopic diagnostic and perhaps even prognostic ability. This
technique takes advantage of molecular changes that occur early in the pathogenesis
of disease and allows these molecular changes to be detected at endoscopy to high-
light areas of concern. The key to success in this technique will be the ability to detect
these molecular changes using an endoscope with a wide field of view (ie, not needing
confocal endomicroscopy), without the need for specialist interpretation or expensive
equipment, and to identify imaging probes for the molecular changes that are suffi-
ciently sensitive and specific in their binding to a defined target. Ultimately, such a
technique may even allow a degree of quantification of biomarker expression.

Ideally, probes would have a high binding affinity to a specific target relative to back-
ground; they would remain structurally stable until imaging is complete, and be rapidly
cleared in a nontoxic manner. It must also be possible to combine the probe with a
fluorescent tag to allow its endoscopic detection, without alteration in the binding
properties of the probe. The ideal endoscopic detector for such a system would be
able to excite at a specific wavelength to excite the fluorochrome labeling the probe
to emit light, which can then be identified by the endoscope. To avoid confounding
signal from autofluorescence, it is expected that it will be optimal to undertake this
endoscopic imaging in the near infrared spectrum. Optical imaging is the most sensi-
tive way of detecting molecular changes and this is perfectly suited to endoscopic
imaging of the epithelium where we have the ability to get close to the epithelium
with our endoscopes.

Molecular imaging for the endoscopic detection of dysplasia that is not macroscop-
ically evident has been shown, in proof-of-principle work, to allow identification of
dysplasia within the esophagus using lectin probes.68 Molecular imaging has also
been used within the colon for endoscopic detection of the tumor necrosis factor in
Crohn’s disease, using a fluorescently labeled antibody to predict clinical response to anti-tumor necrosis factor therapy, although these molecular changes were detected using confocal endoscopy and therefore subject to the same sampling error encountered with random biopsies.69

Studies of molecular imaging for the detection of dysplasia within the human colon are few and are listed in Table 2. Part of the problem has been getting probes through the necessary regulatory steps before in vivo use. This process is costly and regulatory bodies have not yet defined pathways for approval of these imaging agents, which are currently subject to the same standards as new, intravenously administered drugs. The possibility of topical application of these probes at microdosing quantities is not likely to be associated with significant toxicity, particularly within the colon. These regulatory issues have led investigators to pragmatically choose probes that are already used as therapeutic agents and have therefore already gone through the regulatory processes, such as the anti-tumor necrosis factor antibodies.69

Antibodies as probes have the advantage of excellent specificity; however, their cost would prohibit their use in the routine clinical setting. They are also associated with a degree of immunogenicity and therefore risk toxicity, and their binding specificity can be altered when labeled with a fluorescent probe. Keller and colleagues70 used antibodies to carcinoembryonic antigen; however, the limitations associated with antibody probes, as well as lack of early abnormal expression of carcinoembryonic antigen in the majority of patients, limit the clinical usefulness of this probe.

Peptide probes have been considered as an alternative to antibodies, because their smaller size means that they are associated with a lower degree of antigenicity and they are cheap to produce from phage libraries; however, their smaller size is associated with decreased binding specificity and an increased risk that their binding will be altered when labeled. Another problem, as seen with Hsiung and colleagues,71 is that the molecular target of the probe may be unknown. This issue of unclear target was overcome by Hardwick and colleagues72 when they looked for a peptide probe against a specific molecular change, known to occur early in colon cancer carcinogenesis (c-MET); however, the need for intravenous application makes such a probe more problematic to use in the routine clinical setting.

Lectin probes are an alternative to antibodies and peptides. They are naturally occurring and can therefore be obtained at low cost. They are large and relatively stable and their specificity is therefore less likely to be altered when labeled. A great deal is known about their binding specificities, but their binding to glycans is not as specific as the antibody–antigen interaction.68 Lectin probes have been used topically in colon resection specimens to highlight dysplasia in IBD, flat polyps, and cancers using standard wide-field of view endoscopes73 and are now being taken forward to in vivo use (Fig. 3). It is interesting that lectin molecular imaging probes have thus far been used as negative markers, in that they bind to normal tissue, but not to precancerous tissue,68,73 whereas most other molecular imaging techniques have looked at increases in probe binding as disease develops. This is not a problem for endoscopic molecular imaging, because it still creates a clear color difference owing to the alteration of lectin binding that can be seen endoscopically, with a good signal:background ratio and signal:noise ratio of 5.2 (SD, 1.2–9.1) and 30.3 (SD, 15.2–45.5), respectively, in the esophagus.68 The key to these imaging modalities is that lesions are not missed, whereas the level of false positives does not need to be controlled tightly.

This exciting progress in molecular probe development, combined with endoscopic detection, offers the potential for a giant leap forward in our endoscopic diagnostic ability and may simultaneously facilitate the guidance of endoscopic and surgical therapy, assist in risk prognostication for individual patients, and even allow more
<table>
<thead>
<tr>
<th>Author, Year of Publication</th>
<th>Molecular Target</th>
<th>Probe</th>
<th>Route of Administration</th>
<th>Detector System</th>
<th>Tissue Used</th>
<th>Key Statistics</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hsiung et al, 2008</td>
<td>Unknown</td>
<td>Fluorescein conjugated heptapeptide</td>
<td>Topical</td>
<td>Confocal laser endoscopy</td>
<td>During colonoscopy</td>
<td>81% sensitivity and 82% specificity for dysplastic colonocytes</td>
<td>Polyps identified were visible with white light. Field of view. Unclear molecular target.</td>
</tr>
<tr>
<td>Keller et al, 2002</td>
<td>CEA</td>
<td>Fluorescein-labelled antibody against CEA</td>
<td>Topical</td>
<td>Conventional endoscope with 2 narrow-band filters</td>
<td>During colonoscopy</td>
<td>Fluorescence was present in 19/25 CRCs and 3/8 adenomas. If cases with bleeding or ulceration were excluded specificity 100%, sensitivity 78.6%, accuracy 89.3%.</td>
<td>Rate of CEA expression in early lesions</td>
</tr>
<tr>
<td>Yeung et al, 2013</td>
<td>Terminal β1-4-linked GalNAc residues</td>
<td>Fluorescently labeled lectin (WFA)</td>
<td>Topical</td>
<td>Conventional endoscope or IVIS camera</td>
<td>Colectomy specimens</td>
<td>WFA binds more strongly to normal colonic epithelium than to cancer tissue from the same patient. Mean fluorescence 27.6 vs 4.80 arbitrary units, P&lt;.0001</td>
<td>In vivo trials pending</td>
</tr>
<tr>
<td>Hardwick et al, 2014</td>
<td>c-Met</td>
<td>Fluorescent cyanine-labelled 26-amino acid cyclic peptide</td>
<td>Intravenous</td>
<td>Dual white-light and near infrared fluorescent light endoscopic imaging system</td>
<td>During colonoscopy</td>
<td>All neoplastic lesions had increased fluorescence. 9 nonpolypoid adenomas were visible with fluorescent light but not with white light</td>
<td>Need for IV administration means high dose and cost and increased risk of toxicity. c-MET expression was reported as higher in adenomas and hyperplastic polyps</td>
</tr>
</tbody>
</table>

**Abbreviations:** CEA, carcinoembryonic antigen; IVIS, in vivo imaging system; WFA, Wisteria floribunda.
personalized drug therapies based on the individual molecular abnormalities that we may be able to detect in real time at endoscopy.

SUMMARY

The current generation of electronic imaging either via virtual chromoendoscopy or AFI has not delivered the hoped for benefits in terms of polyp and specifically adenoma detection. Their use is not supported in average-risk patients in recent guidelines, and is only recommended for certain specific indications (the Lynch syndrome and serrated polyposis syndrome surveillance). The reasons for this may include a darker image, insufficient contrast versus background mucosa, and loss of resolution and image quality. The current reference standard, now HD-WLE, has improved. There has been a focus on quality in endoscopy and on the detection of subtle and flat lesions, which may have improved endoscopist performance, obviating the need for additional enhancements beyond high-quality white light examinations. Nevertheless, adenomas and sessile serrated adenomas/polyps are still missed at an alarming rate and seem likely to be significant factors in postcolonoscopy CRC. Molecular imaging is an alternate modality that may offer specific highlighting of lesions to allow adequate contrast in the detection of CRC precursor lesions.

REFERENCES

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