ASGE LEADING EDGE
Editor: Girish Mishra, MD, MSc, FASGE

Clinical Review:
How to Recognize Subtle Lesions in the Colon

Amit Rastogi, MD, FASGE
Associate Professor of Medicine
University of Kansas Medical Center

Introduction

Colonoscopy is the most common endoscopic procedure performed by gastroenterologists in the United States and continues to be the preferred method for colorectal cancer (CRC) screening.[1] Colonoscopy with polypectomy of adenomatous polyps has been shown to decrease the incidence and mortality associated with CRC. In spite of significant technological advancements, colonoscopy is still an imperfect tool for preventing CRC partly as a result of the highly operator-dependent nature of the procedure. Adenomas that are the precursor lesions for CRC can be missed even by experts, as shown in tandem colonoscopy studies. The miss rate can be substantial.[2] These missed adenomatous polyps can become cancer before the patient undergoes the next screening or surveillance exam. Herein lies the importance of the adenoma detection rate (ADR), which is a quality indicator of colonoscopy. Two recent studies have shown that a higher endoscopist ADR was associated with a reduced risk or hazard of developing interval CRC.[3, 4]Other studies have shown endoscopists' failure to detect adenomas as one of the major factors contributing to the development of interval CRC.[5]

Morphology of colorectal lesions

According to the Paris Classification[6], colonic polyps are divided morphologically into two broad categories: protruded or flat. The protruded lesions include: Type Ip (pedunculated); Type Isp (semi pedunculated); and Type Is (sessile). The flat lesions are subclassified into: Type 0 IIa (flat elevated--height less than 2.5 mm); Type 0 IIb (completely flat); and Type 0 IIc (depressed). The Japanese classification[7] is slightly different in that the sessile lesions are defined as having a height greater than half the diameter of the lesion, while flat or nonpolypoid lesions are defined as having a height less than half the diameter. Flat or nonpolypoid lesions can be subtle and technically challenging to detect during colonoscopy by virtue of not being raised significantly above the level of the surrounding mucosa. This review will focus on how to maximize the detection of these lesions.

Significance of flat/subtle lesions

Although described initially by Japanese endoscopists, recent data have shown that the prevalence of flat and depressed lesions in the western population is higher than previously thought and, in fact, is comparable to that seen in Japan.[7, 8] These lesions are not only difficult to detect endoscopically but also are more likely to harbor advanced histology such as high-grade dysplasia or early cancer compared to polypoid lesions, irrespective of the size.[7] [9] They also are more often located in the right side of the colon, which may partly account for why colonoscopy is less effective in preventing proximal (right sided) CRC as well as cancer deaths compared to distal CRC.[10, 11] Therefore, detection and subsequent removal of these lesions is of paramount importance in improving the efficacy of colonoscopy in preventing the development of CRC.

Detection of flat/subtle lesions

Cognitive knowledge and training:

In order to detect subtle/flat lesions (figure 1-3), it is imperative that endoscopists familiarize themselves with the endoscopic clues that should alert them of the presence of these lesions. These visual clues include subtle change or disruption in the mucosal vascular pattern, erythematous change in the color of the mucosa, friability, and convergence of folds, a distinct color/surface pattern/contour from the surrounding mucosa, and interruption of the innominate grooves. This cognitive knowledge is important for detecting subtle lesions as the “eyes do not see what the mind does not know.” Mucosal pattern recognition may require image enhanced endoscopy like dye-based chromoendoscopy or electronic chromoendoscopy. Different patterns have been described with dye-based methods (Kudo pit patterns)[12] and electronic chromoendoscopy (NICE classification with NBI).[13] It has been shown that there is a learning curve associated with the detection of flat lesions.[14] Following education and training that involved review of colonoscopy atlases and direct observation and discussions with Japanese experts, four endoscopists tracked their detection rates of non-polypoid lesions. The detection rates increased with time and experience. All endoscopists had a low detection rate (1.5-3.5%) during the first 200 colonoscopies following their training. The detection rate of flat lesions for three of the endoscopists was greater after performing 600 post-training colonoscopies. After their 1000th colonoscopy subsequent to training, the two highest-volume endoscopists had an overall detection rate of 7.4% for flat lesions. These data suggest that detection of flat lesions is a skill that must be learned, requires time and effort, and can improve with experience.

The importance of cognitive knowledge and training in detecting flat lesions has also been highlighted in other studies. Nicolas-Perez et al showed that training in detecting flat lesions was independently associated with flat adenoma detection rates of endoscopists (OR 2.02; P<.001)**.**[15] Kaltenbach et al showed that endoscopists trained to identify flat lesions detected them more frequently compared to those without supplemental training (OR 2.98).[16] Interestingly, this study also showed that endoscopists trained in detecting flat lesions also had a higher ADR than those not specifically trained (46% vs 35%; P = .02). The number of adenomas detected per patient and the proportion of neoplastic lesions detected were also significantly higher in the former group. Another study by Coe et al[17] demonstrated the positive impact of education and training on ADR. Fifteen endoscopists were evaluated for their baseline ADR. Eight were then randomized to an Endoscopic Quality Improvement Program (EQUIP) that included a training session conducted by an expert in which methods and techniques to improve ADR were reviewed. The ADRs were subsequently tracked. The group of endoscopists who did not undergo the training had similar ADRs in both phases (36% vs 35%). The trained endoscopists showed a significant increase in their ADRs in the post training phase (36% versus 47%; p=?). The effect of training on the ADRs was estimated with an odds ratio of 1.73; P=.0013). In another study, conducted in a large community practice, baseline data were collected on 2053 screening colonoscopies performed by 12 endoscopists without a specified withdrawal protocol. All 12 endoscopists then reviewed ideal withdrawal and inspection techniques. Following this, 2325 colonoscopies were performed employing these careful inspection techniques and a minimum of 8 minute withdrawal time.[18] In the post intervention phase, the ADR and the advanced adenomas detected per patient were significantly higher compared to the baseline measures (35% vs 24%, $P < .001$; 0.64 vs 0.47, $P < .001$; and 0.08 vs 0.055, $P < .01$, respectively). These and other studies highlight the utility of cognitive knowledge and training for increasing the detection of subtle/flat lesions as well as for improving the overall ADR.

Quality colonoscopy relies not only on cognitive knowledge and training concerning the features of subtle lesions, but also to proper techniques during the withdrawal phase of colonoscopy that includes three aspects: adequate luminal distension; cleaning all pools of fluids and feces; and examining the mucosa behind folds, flexures, ileocecal valve, and rectal valves. Withdrawal technique is difficult to assess as it is subjective and requires real time observation, which is logistically not possible. In an interesting study, Lee et al[19] video recorded the withdrawal phase of 10 procedures each performed by 11 endoscopists. Based on their baseline ADR, these endoscopists were divided into low, moderate, and high adenoma detectors. The videos were reviewed and subjectively scored for the three above-mentioned aspects of withdrawal technique by three blinded investigators. The moderate and high adenoma detectors had a significantly superior withdrawal technique score compared to the low detectors. Comparing the lowest and the highest adenoma detector, they found that while the withdrawal times were similar, their technique scores were significantly different, being higher for the latter.

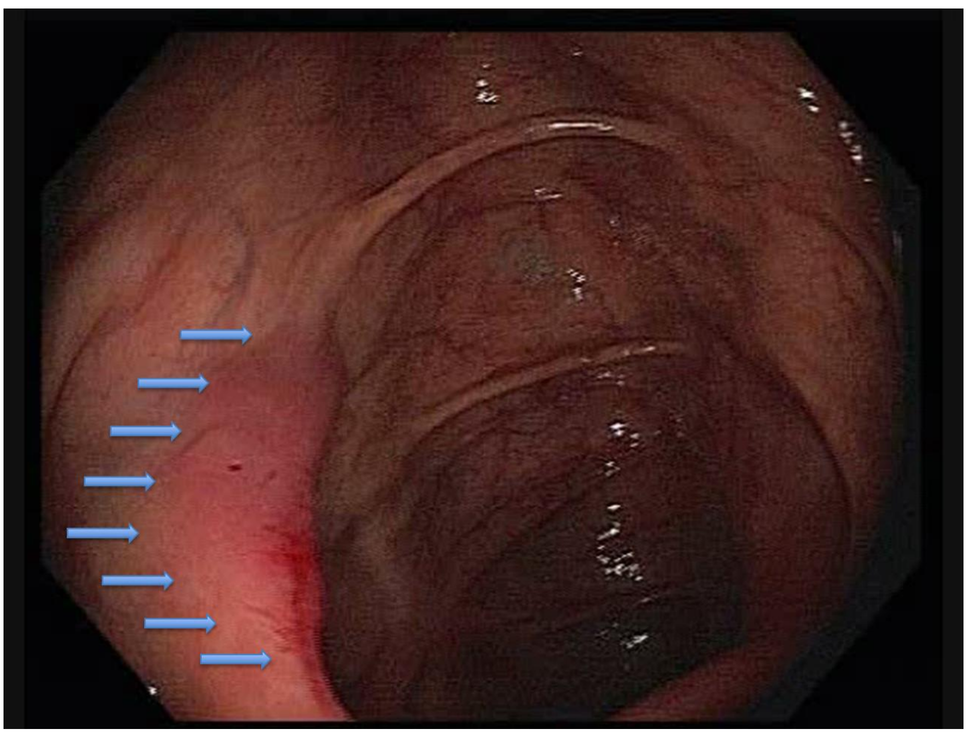

Figure 1: Flat polyp seen as erythematous change in the color of mucosa and alteration in the contour from surrounding mucosa.

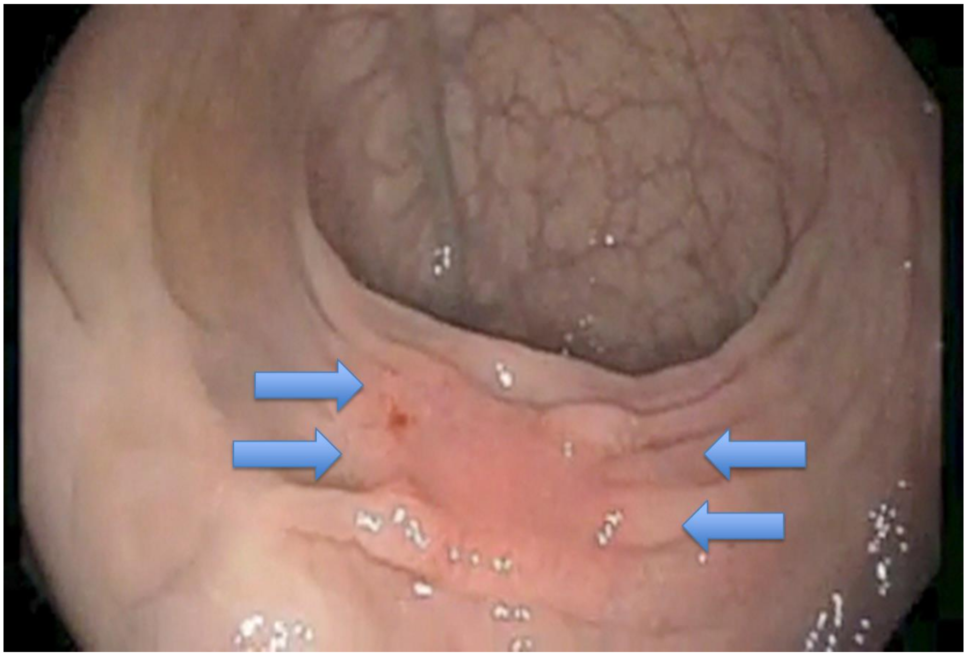

Figure 2: Depressed lesion seen as erythematous change in color of mucosa, convergence of folds.

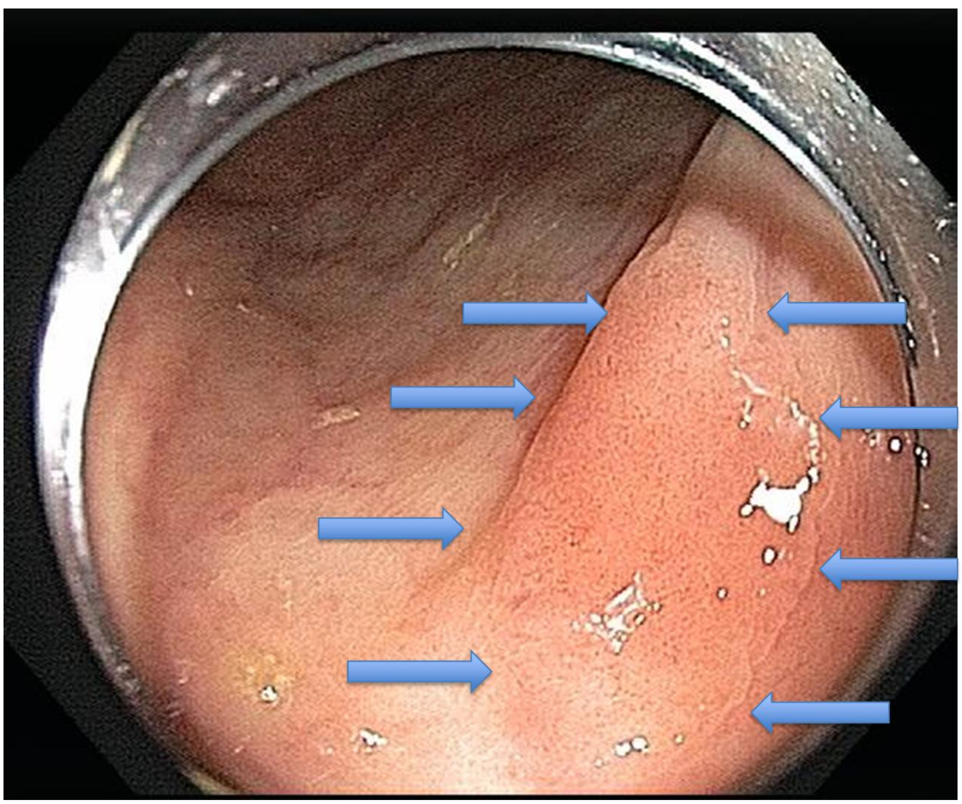

Figure 3: Subtle, flat polyp detected by a distinct surface pattern from the surrounding mucosa and interruption of the innominate grooves.

Bowel preparation:

The quality of bowel preparation is another important factor for optimizing adenoma detection, especially flat/subtle lesions. A recent meta-analysis showed that ADRs were significantly higher with intermediate-quality (fair) and high-quality preparation (excellent/good) vs. low-quality preparation (poor/insufficient): OR=1.39 and 1.41, with an absolute risk increase of 5% for both. ADR and advanced ADR were significantly higher with adequate vs. inadequate preparation: OR=1.30 and 1.30, respectively.[20] In a study analyzing more than 30,000 colonoscopies, a higher quality bowel preparation was one of the factors that significantly increased the relative risk of adenoma detection.[21] While these studies showed that poor/inadequate bowel prep was associated with lower ADR, there are other studies that have specifically looked at the detection rates of flat adenomas with varying quality of bowel preparation. Oh et al[22] evaluated 6097 screening examinations and showed that the detection of flat adenomas was significantly lower with fair- or poor-quality bowel preparation, versus adequate-quality preparation (adjusted odds ratio: 0.55 and 0.49, respectively). They concluded that suboptimal (fair or poor) bowel preparation significantly impairs detection of flat or non-polypoid lesions. In another study, Xiang et al[23] showed that poor bowel preparation was one of the factors on multivariate analysis associated with a higher miss rate of flat adenomas. Given that the prevalence of flat lesions is substantial in our average-risk screening cohort, efforts to improve bowel preparation quality are valuable in increasing their detection, thereby improving the efficacy of screening colonoscopies.

Chromoendoscopy:

Dye-based chromoendoscopy involves the spraying of dyes such as methylene blue, cresyl violet, and indigo carmine over the colonic mucosa. Methylene blue and cresyl violet stain the surface of the lesion through active absorption and interaction with cellular constituents. Indigo carmine and similar dyes are not absorbed by the mucosa and pool in the pits and mucosal crevices on the surface of polyps. This highlights the borders of subtle and flat lesion and unravels different patterns on the surface of polyps called “pit patterns.”[12] A recent meta-analysis showed that chromoendoscopy improved adenoma detection (RR: 1.36; 95% CI: 1.23 – 1.51).[25] An earlier Cochrane review showed that chromoendoscopy detects at least 1 neoplastic lesion in a higher number of patients and detects 3 or more neoplastic lesions in more patients compared to standard colonoscopy.

[26] Two large, randomized controlled studies have shown that chromoendoscopy detects a higher number of flat adenomas compared to either standard definition or high definition white light.[27,28] Kahi et al[27] compared pan colonic chromoendoscopy with high-definition white light. The flat ADR was significantly higher with chromoendoscopy: 0.6±1.2 vs 0.4±0.9; P = .01. Pohl et al[28] compared chromoendoscopy with standard resolution white light and similarly found a higher detection rate of flat adenomas per patient with the former: 0.58 vs 0.28; P < .001. Chromoendoscopy has not been embraced and utilized in the western countries for detecting adenomas due to the perceived hassle, cost, and time associated with spraying dye. Another approach that has been recommended by some experts is targeted chromoendoscopy with white light upon suspicion of a flat or subtle lesion. This involves meticulous inspection with white light with special focus on the features discussed above that suggest the presence of a flat or subtle lesion. Upon suspicion of a subtle lesion, contrast dye can be sprayed over the lesion to highlight the borders as well as the surface pattern to confirm its presence. This accentuation of the borders and margins of the lesion also assists in polypectomy and ensuring complete removal (Figure 4).

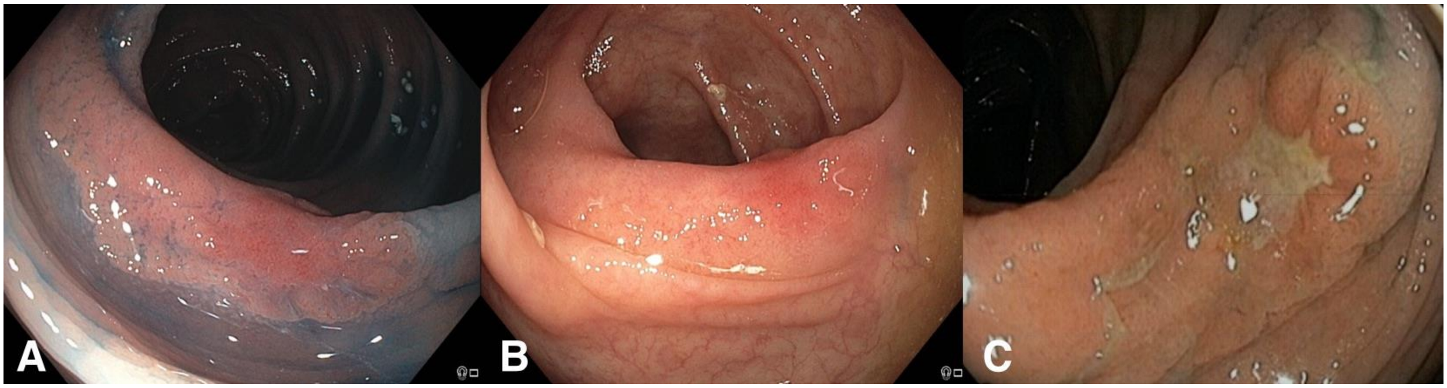

Figure 4: A, 3-cm, nonpolypoid, superficial, elevated lesion after indigo carmine chromoendoscopy. **B**, The area of the lesion before dye spray. **C**, The same lesion had likely been photographed approximately a year earlier (on fold to left of ulcer), but it was not recognized to be dysplastic. Histologic examination showed low-grade dysplasia. (Image used with permission from *GIE: Gastrointestinal Endoscopy*)

Electronic chromoendoscopy:

This provides a visual contrast akin to chromoendoscopy without the need to spray dye. There are three platforms: narrow band imaging (NBI) (Olympus), Flexible spectral Imaging Colour Enhancement (FICE) (Fujinon), and i-Scan (Pentax). NBI uses an optical filter in the endoscopy system to transmit an increased proportion of blue light (415 nm) and a decreased proportion of red light. It narrows the white light spectrum into two wavelengths, blue (390 - 445 nm) and green (530 - 550 nm) light. These wavelengths correspond to the peak absorption spectrum of hemoglobin, the major tissue chromophore. Therefore, mucosal vasculature appears dark. Also, blue light has a shorter wavelength and hence penetrates superficially compared to red light that has longer wavelength and penetrates deeper. This accentuates the mucosal architecture. These two principles combine to enhance superficial mucosal vasculature by optimizing absorption and scattering of light. As the surface mucosal and vascular pattern of adenomas is different from normal colonic mucosa, the contrast could help detect subtle lesions that might not be appreciated by white light. An initial study using NBI showed that it had a learning effect on the ability of endoscopists to detect polyps with white light.[29] However, multiple studies showed that there was no increase in ADR with NBI. A recent meta-analysis confirmed the lack of superiority of NBI over white light for ADR.[25] The newer version of NBI (190 series) is brighter than the previous version (180 series) and has been shown in one study to improve the ADR compared to high-definition white light (48% vs 34%; P = .01).[30] However, more data is required before any definitive conclusions can be made.

FICE utilizes a post processing technique in which the regular endoscopic image from the processor is altered by computerized spectral estimation technology. The reflected photons of the original image are arithmetically processed to reconstitute a virtual image. There are 10 preprogrammed FICE settings using optimal sets of wavelengths that can be selected. Each setting differs in terms of the estimated red, green, and blue wavelengths. Image color varies as different wavelengths are applied, i.e., shorter wavelengths for surface structures and longer for deeper vessels. As a result, enhancement of the superficial mucosal vascular pattern on the polyp can be achieved.

While i-Scan is also a post processing technology, it utilizes different software algorithms with Real Time Image Mapping (RIM) to enhance different elements of the mucosa. There are three adjustable modes of image enhancement: surface enhancement, contrast enhancement, and tone enhancement. Surface enhancement highlights light to dark contrast, thereby making the edges of the lesion well demarcated. This can potentially help in identifying subtle and flat lesions. Contrast enhancement highlights low intensity areas and can help in identifying depressed lesions. Tone enhancement highlights vascular structures. Both FICE and i-Scan have not been shown to improve the ADR.[25]

High-definition white light:
With advancements in miniaturization and specialized design of charged couple device chips, images with a three-fold higher pixel density (over a million pixels) and 1080 effective scan lines can be generated with high-definition colonoscopes combined with a high-definition video processor and monitor. Detection of flat adenomas was shown to be higher with high-definition white light compared to standard definition in some studies.[31, 32] However, a meta-analysis has shown that the pooled incremental yield of high-definition over standard video endoscopy for the detection of polyp and adenomas was marginal (<4%).[33]

Technologies that increase the field of view by examining blind mucosal areas:
Flat and subtle lesions can evade detection by virtue of their location on the proximal aspects of haustral folds, ileocecal valve, flexures, and rectal valves. This is due to the physical limitation of torqueing and turning capabilities of the flexible bending portion of the colonoscope. There are several devices and technologies that have been developed and tested to address this issue.

Cap-assisted colonoscopy is among the most extensively evaluated. This involves attaching a plastic cap to the colonoscope that protrudes about 4 mm beyond the tip. The edge of this cap can help flatten the haustral folds and also keeps the colonic mucosa away from the tip of colonoscope to prevent a red out, thus helping to visualize the blind mucosal areas. The results on ADR from different studies using cap-assisted colonoscopy showed varied results and a meta-analysis showed that while it did increase polyp detection, there was no benefit in terms of the ADR.[34] Nonetheless, this is a simple, inexpensive, and easy-to-use device that may assist in detecting lesions that are located on proximal aspects of folds, especially the flat ones.

The Third Eye® Retroscope® is a retrograde-viewing auxiliary device that is passed through the working channel of the colonoscope. As it extends beyond the tip of the colonoscope, it turns 180 degrees. In the locked position the lens protrudes about 4 cm beyond the tip of the colonoscope. The device is connected to an external power source and videoprocessing system and provides a retrograde view of the colonic mucosa. Images from the colonoscope and the Third Eye Retroscope are viewed simultaneously, and complete visualization of both sides of the folds is possible. A large multicenter, tandem colonoscopy study showed that the relative risk of missing adenomas with standard colonoscopy compared to the Third Eye Retroscope was 1.92 (P=.029).[35] The hurdles to using this device in clinical practice include the cost, trouble of having to remove it upon detecting a polyp for polypectomy and then reinserting it, increased withdrawal time (making the procedure less efficient) and need to acclimatize to viewing the forward and retrograde views simultaneously.

The full spectrum colonoscope (FUSE) has three lenses and light-emitting diode groups at the front and on two sides of the flexible tip and a 300-degree, ultra wide view. Three images, one from each lens, are viewed simultaneously. In a multicenter, randomized, controlled, tandem colonoscopy study, FUSE showed a significantly lower adenoma miss rate (7%) versus standard colonoscopy (41%; p =?).[36]

Other recently available devices include the Endocuff™, EndoRings™, and balloon colonoscope that work on the principle of flattening the haustral folds during withdrawal and therefore expanding the surface area of the colonic mucosa being visualized. There are limited studies with these devices, and their use in routine clinical practice cannot be recommended. However, while they may serve as a useful adjunct for low adenoma detectors, they cannot be a substitute for cognitive knowledge and good withdrawal technique.

Retroflexion in the proximal colon:
This is a useful technique that can be successfully performed in a majority of patients except when there is looping of the colonoscope.[37] Withdrawal in the ascending colon in the retroflexed position can help examine the mucosal areas that may have not been clearly visualized on the forward view exam. Studies have shown that additional adenomas are detected by re-examining the proximal colon in retroflexion.[37, 38] However, it can be argued that a second forward view exam of the ascending colon could also have detected these lesions. This premise was tested in a randomized controlled study showing that a second exam of the right side of the colon with either forward view or retroflexed view detected at least 1 additional adenoma in similar proportions (10.5% vs 7.5%; P = .13).[39] Predictors of identifying adenomas on the second withdrawal included older age (OR=1.04), adenomas seen on initial withdrawal (OR=2.8), and low endoscopist confidence in quality of first examination of the right side of the colon (OR=4.8). Therefore, although retroflexion in the right side of the colon cannot be routinely recommended, a second exam of the right side of the colon either in forward or retroflexed view should be considered, especially when an adenoma is detected in the right side of the colon on the initial exam, or when the endoscopist's confidence in the quality of initial examination is low.

Sessile serrated adenoma/polyp (SSA/P)
These lesions are usually flat and subtle or inconspicuous and located predominantly in the right side of the colon.[40] Proximal serrated polyps can be easily missed during colonoscopy, as was shown in a study analyzing more than 6500 screening colonoscopies performed by 15 gastroenterologists.[41] The detection of proximal serrated polyps was highly variable and endoscopist-dependent in this study. The odds of detecting at least 1 proximal serrated polyp for individual endoscopists ranged from 0.05 to 0.67 compared to the highest level detector. Another study showed that the detection rate of proximal serrated polyps differed significantly among endoscopists, ranging from 6% to 22% (P < .001). Longer withdrawal time (OR = 1.12) was significantly associated with better proximal serrated polyp detection.[42] A recent study from the New Hampshire Colonoscopy Registry showed that a withdrawal time of 9 minutes resulted in a significantly higher detection of SSA/P and proximal hyperplastic polyps.[43]

Knowledge and familiarity of their appearance are key to detection of these lesions. Tadepalli et al[44] evaluated the prevalence of morphologic characteristics related to polyp shape, color, and texture in 158 sessile serrated polyps (SSPs). The most prevalent visual descriptors (figure 5) were the presence of a mucous cap (63.9%), rim of debris or bubbles (51.9%), alteration of the contour of a fold (37.3%), and interruption of the underlying mucosal vascular pattern (32.3%). Because SSPs are easily overlooked, the investigators analyzed the gross morphologic characteristic of each lesion that first captured the attention of colonoscopists during colonoscope withdrawal. The most common "sentinel signs" were the presence of a mucous cap and alteration of the contour of a mucosal fold (each 24.6%), rim of debris or bubbles (21.7%), and a dome-shaped protuberance (20.3%). When comparing SSPs with adenomatous polyps, the frequencies of 5 of 7 morphologic characteristics and the distribution of sentinel signs differed (P < .01). Hazewinkel et al[45] also described the endoscopic appearance of SSA/Ps that might help endoscopists to recognize these lesions. High-resolution white light and NBI images of 50 SSA/Ps, hyperplastic polyps, and adenomas each were assessed by five international experts using various endoscopic descriptors. Indistinct borders (OR= 3.11) and a cloud-like surface (OR=2.65) were associated with SSA/P histology on high-resolution white light. Under NBI, a cloud-like surface (OR= 4.91), indistinct borders (OR= 2.38), irregular shape (OR= 3.17), and dark spots inside the crypts (OR= 2.05) were found to be endoscopic predictors of SSA/P histology (figure 6). The sensitivity, specificity, and accuracy of NBI for differentiating serrated polyps containing either none or all four endoscopic features were 89%, 96%, and 93%, respectively.

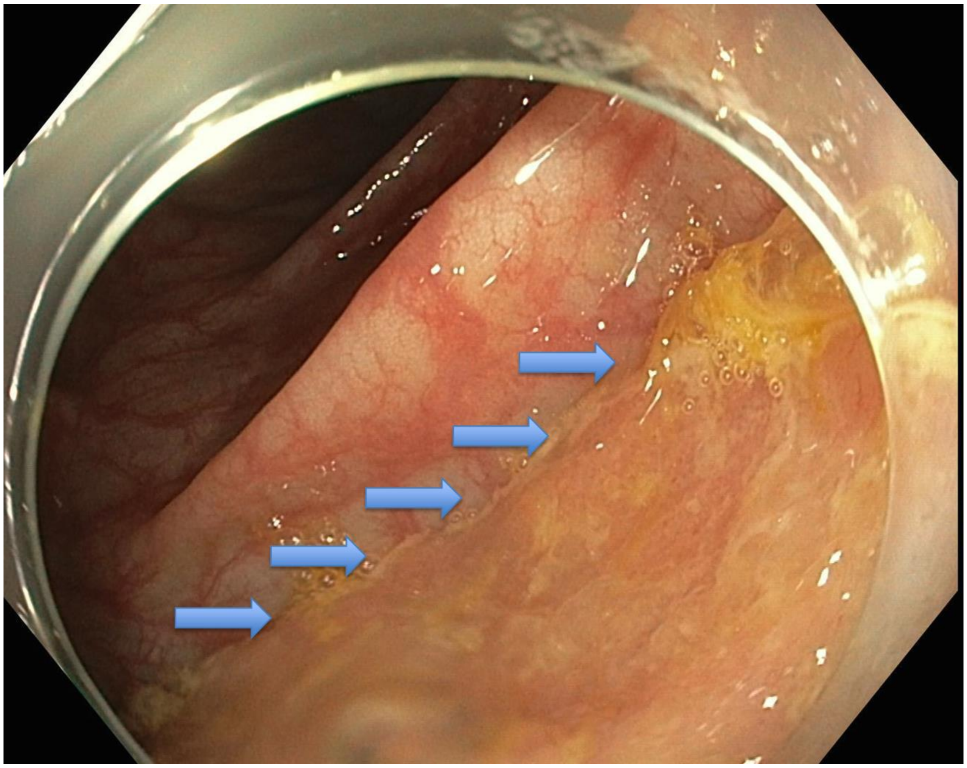

Figure 5: Sessile serrated adenoma – covered with a mucus cap with rim of debris and bubbles.

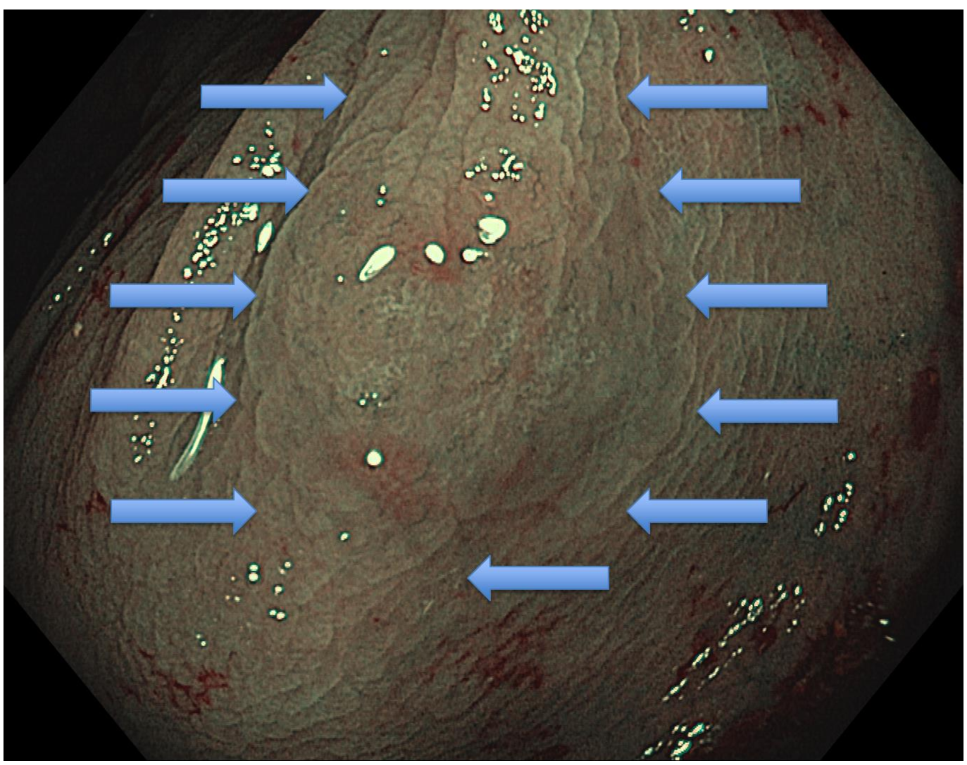

Figure 6: Sessile serrated adenoma under NBI: cloud like surface, indistinct borders, irregular shape and dark spots inside crypts.

The different technologies discussed above for improving ADR can be utilized for detecting SSA/Ps. Although these technologies have not been specifically studied for improving the detection of SSA/Ps, a post hoc analysis of a randomized controlled trial comparing cap-assisted colonoscopy to standard high definition colonoscopy showed that the former detected a significantly higher proportion of patients with significant serrated polyps as well as a higher total number of significant serrated polyps (12.8% vs 6.6%; *P* =.047 and 40 vs 20; *P*=.03, respectively).[46] This requires confirmation in future prospective studies.

In conclusion, detection of flat, subtle lesions in the colon as well as SSA/Ps continues to be a challenge for endoscopists. This is an important issue given that their identification and resection are key to decreasing the incidence and mortality associated with CRC. Cognitive knowledge regarding their appearance, along with training and good withdrawal technique, is paramount in optimizing their detection. Good bowel preparation remains a prerequisite. Other ancillary techniques including chromoendoscopy, high-definition colonoscopy, retroflexion in the right side of the colon, cap-assisted colonoscopy, and wider angle colonoscopes can be useful adjuncts.

References:

1. *Vital signs: colorectal cancer screening test use--United States, 2012.* MMWR Morb Mortal Wkly Rep, 2013. **62**(44): p. 881-8.
2. van Rijn, J.C., et al., *Polyp miss rate determined by tandem colonoscopy: a systematic review.* Am J Gastroenterol, 2006. **101**(2): p. 343-50.
3. Kaminski, M.F., et al., *Quality indicators for colonoscopy and the risk of interval cancer.* N Engl J Med, 2010. **362**(19): p. 1795-803.
4. Corley, D.A., et al., *Adenoma detection rate and risk of colorectal cancer and death.* N Engl J Med, 2014. **370**(14): p. 1298-306.
5. Robertson, D.J., et al., *Colorectal cancer in patients under close colonoscopic surveillance.* Gastroenterology, 2005. **129**(1): p. 34-41.
6. *The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach, and colon: November 30 to December 1, 2002.* Gastrointest Endosc, 2003. **58**(6 Suppl): p. S3-43.
7. Soetikno, R.M., et al., *Prevalence of nonpolypoid (flat and depressed) colorectal neoplasms in asymptomatic and symptomatic adults.* Jama, 2008. **299**(9): p. 1027-35.
8. Saitoh, Y., et al., *Prevalence and distinctive biologic features of flat colorectal adenomas in a North American population.* Gastroenterology, 2001. **120**(7): p. 1657-65.
9. Hurlstone, D.P., et al., *A prospective clinicopathological and endoscopic evaluation of flat and depressed colorectal lesions in the United Kingdom.* Am J Gastroenterol, 2003. **98**(11): p. 2543-9.
10. Brenner, H., et al., *Protection from colorectal cancer after colonoscopy: a population-based, case-control study.* Ann Intern Med, 2011. **154**(1): p. 22-30.
11. Baxter, N.N., et al., *Association of colonoscopy and death from colorectal cancer.* Ann Intern Med, 2009. **150**(1): p. 1-8.
12. Kudo, S., et al., *Diagnosis of colorectal tumorous lesions by magnifying endoscopy.* Gastrointest Endosc, 1996. **44**(1): p. 8-14.
13. Hewett, D.G., et al., *Validation of a simple classification system for endoscopic diagnosis of small colorectal polyps using narrow-band imaging.* Gastroenterology, 2012. **143**(3): p. 599-607.e1.
14. McGill, S.K., et al., *The learning curve for detection of non-polypoid (flat and depressed) colorectal neoplasms.* Gut, 2015. **64**(1): p. 184-5.
15. Nicolas-Perez, D., et al., *Risk factors associated with colorectal flat adenoma detection.* Eur J Gastroenterol Hepatol, 2013. **25**(3): p. 302-8.

16. Kaltenbach, T., et al., *Proficiency in the diagnosis of nonpolypoid colorectal neoplasm yields high adenoma detection rates.* Dig Dis Sci, 2012. **57**(3): p. 764-70.
17. Coe, S.G., et al., *An endoscopic quality improvement program improves detection of colorectal adenomas.* Am J Gastroenterol, 2013. **108**(2): p. 219-26; quiz 227.
18. Barclay, R.L., J.J. Vicari, and R.L. Greenlaw, *Effect of a time-dependent colonoscopic withdrawal protocol on adenoma detection during screening colonoscopy.* Clin Gastroenterol Hepatol, 2008. **6**(10): p. 1091-8.
19. Lee, R.H., et al., *Quality of colonoscopy withdrawal technique and variability in adenoma detection rates (with videos).* Gastrointest Endosc, 2011. **74**(1): p. 128-34.
20. Clark, B.T., T. Rustagi, and L. Laine, *What level of bowel prep quality requires early repeat colonoscopy: systematic review and meta-analysis of the impact of preparation quality on adenoma detection rate.* Am J Gastroenterol, 2014. **109**(11): p. 1714-23; quiz 1724.
21. Lee, T.J., et al., *Colonoscopic factors associated with adenoma detection in a national colorectal cancer screening program.* Endoscopy, 2014. **46**(3): p. 203-11.
22. Oh, C.H., et al., *Suboptimal Bowel Preparation Significantly Impairs Colonoscopic Detection of Non-polypoid Colorectal Neoplasms.* Dig Dis Sci, 2015.
23. Xiang, L., et al., *Risk factors associated with missed colorectal flat adenoma: a multicenter retrospective tandem colonoscopy study.* World J Gastroenterol, 2014. **20**(31): p. 10927-37.
24. Siddiqui, A.A., et al., *Duration of the interval between the completion of bowel preparation and the start of colonoscopy predicts bowel-preparation quality.* Gastrointest Endosc, 2009. **69**(3 Pt 2): p. 700-6.
25. Omata, F., et al., *Image-enhanced, chromo, and cap-assisted colonoscopy for improving adenoma/neoplasia detection rate: a systematic review and meta-analysis.* Scand J Gastroenterol, 2014. **49**(2): p. 222-37.
26. Brown, S.R. and W. Baraza, *Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum.* Cochrane Database Syst Rev, 2010(10): p. Cd006439.
27. Kahi, C.J., et al., *High-definition chromocolonoscopy vs. high-definition white light colonoscopy for average-risk colorectal cancer screening.* Am J Gastroenterol, 2010. **105**(6): p. 1301-7.
28. Pohl, J., et al., *Pancolonic chromoendoscopy with indigo carmine versus standard colonoscopy for detection of neoplastic lesions: a randomised two-centre trial.* Gut, 2011. **60**(4): p. 485-90.
29. Adler, A., et al., *A prospective randomised study on narrow-band imaging versus conventional colonoscopy for adenoma detection: does narrow-band imaging induce a learning effect?* Gut, 2008. **57**(1): p. 59-64.
30. Leung, W.K., et al., *Detection of colorectal adenoma by narrow band imaging (HQ190) vs. high-definition white light colonoscopy: a randomized controlled trial.* Am J Gastroenterol, 2014. **109**(6): p. 855-63.
31. East, J.E., et al., *Narrow band imaging for colonoscopic surveillance in hereditary non-polyposis colorectal cancer.* Gut, 2008. **57**(1): p. 65-70.
32. Rastogi, A., et al., *Randomized, controlled trial of standard-definition white-light, high-definition white-light, and narrow-band imaging colonoscopy for the detection of colon polyps and prediction of polyp histology.* Gastrointest Endosc, 2011. **74**(3): p. 593-602.
33. Subramanian, V., et al., *High definition colonoscopy vs. standard video endoscopy for the detection of colonic polyps: a meta-analysis.* Endoscopy, 2011. **43**(6): p. 499-505.
34. Ng, S.C., et al., *The efficacy of cap-assisted colonoscopy in polyp detection and cecal intubation: a meta-analysis of randomized controlled trials.* Am J Gastroenterol, 2012. **107**(8): p. 1165-73.
35. Leufkens, A.M., et al., *Effect of a retrograde-viewing device on adenoma detection rate during colonoscopy: the TERRACE study.* Gastrointest Endosc, 2011. **73**(3): p. 480-9.

36. Gralnek, I.M., et al., *Standard forward-viewing colonoscopy versus full-spectrum endoscopy: an international, multicentre, randomised, tandem colonoscopy trial.* Lancet Oncol, 2014. **15**(3): p. 353-60.
37. Chandran, S., et al., *Right-sided adenoma detection with retroflexion versus forward-view colonoscopy.* Gastrointest Endosc, 2015. **81**(3): p. 608-13.
38. Hewett, D.G. and D.K. Rex, *Miss rate of right-sided colon examination during colonoscopy defined by retroflexion: an observational study.* Gastrointest Endosc, 2011. **74**(2): p. 246-52.
39. Kushnir, V.M., et al., *Impact of retroflexion vs. Second forward view examination of the right colon on adenoma detection: a comparison study.* Am J Gastroenterol, 2015. **110**(3): p. 415-22.
40. Yang, J.F., et al., *Anatomic distribution of sessile serrated adenoma/polyp with and without cytologic dysplasia.* Arch Pathol Lab Med, 2015. **139**(3): p. 388-93.
41. Kahi, C.J., et al., *Prevalence and variable detection of proximal colon serrated polyps during screening colonoscopy.* Clin Gastroenterol Hepatol, 2011. **9**(1): p. 42-6.
42. de Wijkerslooth, T.R., et al., *Differences in proximal serrated polyp detection among endoscopists are associated with variability in withdrawal time.* Gastrointest Endosc, 2013. **77**(4): p. 617-23.
43. Butterly, L., et al., *Serrated and adenomatous polyp detection increases with longer withdrawal time: results from the New Hampshire Colonoscopy Registry.* Am J Gastroenterol, 2014. **109**(3): p. 417-26.
44. Tadepalli, U.S., et al., *A morphologic analysis of sessile serrated polyps observed during routine colonoscopy (with video).* Gastrointest Endosc, 2011. **74**(6): p. 1360-8.
45. Hazewinkel, Y., et al., *Endoscopic features of sessile serrated adenomas: validation by international experts using high-resolution white-light endoscopy and narrow-band imaging.* Gastrointest Endosc, 2013. **77**(6): p. 916-24.
46. Rzouq, F., et al., *Cap assisted colonoscopy for the detection of serrated polyps: a post-hoc analysis.* BMC Gastroenterol, 2015. **15**(1): p. 11.

Author contact information:

Amit Rastogi, MD, FASGE
Associate Professor of Medicine
University of Kansas Medical Center
Kansas City VA Medical Center
Kansas City, KS - 66160

Disclosures: Consultant – Olympus America
Research Grant Support - Olympus America