Improving Lesion Detection During Colonoscopy

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Abstract: Colonoscopy has changed since it was first introduced 50 years ago, with glass fibers being replaced by video electronics, the addition of water jets, better illumination, and the use of filters to enhance visual identification of polyps. In spite of these improvements, polyps and tumors of the colon are still overlooked even by the most meticulous examiner. Because missed lesions can develop into cancer, better imaging methods are required. The Third Eye Retroscope is a device that, in conjunction with the video colonoscope, may be able to find virtually all lesions in the colon. This novel device is described here and presents a new way to look into the colon.

Keywords
Retroscope, retroversion, Third Eye Retroscope, colonoscopy, polyps, adenoma, screening, surveillance

Colonoscopy

Since its introduction, colonoscopy has generally been accepted to be the most effective method for examining the colon. Colonoscopy became a popular diagnostic and therapeutic modality for the large bowel shortly after it was introduced. Because of its ability to visualize the mucosal surface of the colon and delineate stool from polyps, colonoscopy has displaced the barium enema as the primary imaging tool of the large bowel. Colonoscopy has the ability to suction pools of fluid from the large bowel to visualize the surface in full color, wash away debris such as fecal material or seeds, identify any protrusion as mucosal or submucosal in origin, and, with a high degree of certainty, distinguish benign from malignant lesions. Because of the visual clarity of colonoscopy, it has been hailed as the standard for colonic imaging since it was first introduced.[1] In addition to the diagnostic superiority of the colonoscope, colonoscopy has the ability to biopsy tissue, remove polyps, and control bleeding.

However, in spite of the known diagnostic accuracy of colonoscopy, it is not an infallible examination for the discovery of colonic lesions. When the first tandem study of the miss rate of polyps during colonoscopy was published, it was met with skepticism by the gastrointestinal community, which had fully embraced the overriding accuracy of colonoscopy.[2] This type of study was not repeated for another 6 years, when the Indiana group reported similar findings.[3] The third, and most recent, tandem study was published 11 years later.[4]

In the earlier studies, the overall miss rates for adenomas were 15–24%.[2,3] The most recent multicenter study reported that the miss rate for polyps of all types and sizes was 28%.[4] The investigators found that 31% of polyps were overlooked, as were 21% of adenomas. However, the miss rate for all polyps equal to or larger than 5 mm was 12%, whereas the miss rate of adenomas was 9%. Among the 14 polyps and 6 adenomas larger than 5 mm that were missed during the first examination, 6 were sessile and 14 were flat. The missed lesions ranged from 1 mm to 18 mm, with 37 adenomas (median size, 3 mm) overlooked in 286 patients. In this European study, 3 advanced adenomas, varying in size from 15 mm to 18 mm, were missed. Overall, there was a 27% miss rate for small adenomas (<5 mm in diameter) and 9% for larger lesions. In a previous study of 183 patients who underwent tandem colonoscopy, Rex and colleagues[3] reported a 27% miss rate for polyps smaller than 6 mm in diameter but a rate of only 6% for polyps larger than 9 mm. There was no significant difference in the distribution of the missed polyps, with 27% being missed in the right side of the colon and 21% of the polyps being overlooked in the left side of the colon. As expected, the larger the lesion, the greater the chance of detection, and the inverse was true as well. It is possible that the actual miss rate is higher than that reported, as the second examiner could have overlooked some polyps. In the summary of the report, Rex and associates pointed out the technical limitations of colonoscopy and recommended that technology be developed to solve the problem of missed lesions in the colon.[3]

Colonoscopic neoplasms are missed primarily due to their location on the proximal aspect of folds. The technique of an examination is critically important in the discovery of colonic polyps. It has been shown that not all missed lesions are hidden; for example, flat neoplasms can elude detection by the casual or untrained observer even when they are in the field of view of a straight forward-viewing standard colonoscope.[5] These flat neoplasms may contain early invasive cancer or may be frank carcinomas, even though they may not reveal any specific endoscopic red flags such as erythema, friability, or ulcerations. They often appear as a slightly thickened patch of mucosa, or they may look slightly opaque, with their presence heralded by a lack of normal vascular pattern in the colon.

The clinical consequence of missed lesions is the progression of the adenomas to carcinomas. The National Polyp Study reported that the incidence of cancer can be markedly diminished by polyp removal, a prime reason for the popularity of screening colonoscopy in a population at risk for colorectal cancer.[6] There have been 2 reports from Canada that colonoscopy protects against the development of cancer in the left side of the colon but does not diminish the death rate for right-sided colorectal cancer, presumably because of missed adenomas.[7,8]

Wide-Angle Colonoscopy

For years, instrument manufacturers have tried to develop colonoscopes that afford a better, clearer, or new method of casting light on the mucosal surface (eg, narrow-band imaging) to enhance the ability to detect adenomas. The problem of missed lesions was demonstrated by Pickhardt and coworkers,[9] who performed a computed tomographic colonography (CTC) evaluation of over 1,200 individuals who underwent same-day CTC and colonoscopy. With segmental unblinding during a colonoscopic examination that followed CTC, 10% of polyps were missed by colonoscopy. Of the missed neoplasms found on the second-look colonoscopy after segmental unblinding, 17 were tubular adenomas, 3 were tubulovillous adenomas, and 1 was a small adenocarcinoma (range in size, 6–17 mm). The majority of these neoplasms were located on the edge or on the proximal aspect of a fold.

A more recent paper on CTC simulation reconstructions using a 90-degree imaging field of view corroborated a previous report that showed that 23.4% of the colonic surface is not visualized by direct, straight, end-on examinations.[10] This report by East and associates repeated the type of scan performed by Pickhardt and colleagues but varied the simulated fields of view to 90, 120, 140, and 170 degrees to match the angle of view of various colonoscopes.[9,10] In this study, the percentage of visualized colonic surface increased with each increasing angle-of-view increment. The total number of missed areas was approximately the same for the fields of view of 90–140 degrees but decreased when the field of view was 170 degrees. Only approximately 85% of the colonic surface was visualized using a 140-degree angle of view, and this percentage increased when the examination was repeated using a 170-degree angle of view comparable to the Olympus 180 series colonoscopes (Olympus Medical Instruments), signifying that more of the surface is seen when the angle of view increases. According to the optical colonoscopy simulation performed by CTC software, approximately 13% of the colonic surface is not seen with the commonly available 140-degree angle of view of most colonoscopes. Simulation of a colonoscope with a 170-degree field of view resulted in an almost 6% reduction in the percentage of surface missed.

Retroversion and Retroflexion

Realizing the problem of missed lesions, endoscopists have attempted to increase the amount of mucosa directly visualized. This thrust originally started in the rectum, where retroflexion was readily performed, and previously unseen areas were brought into view by purposely making a 180-degree rotation in the rectal ampulla.[11]

There have been few studies on the yield of finding significant pathology during rectal retroversion. A paper from the Indianapolis group examined rectal retroversion in 1,502 consecutive patients enrolled in a study of several aspects concerning rectal retroversion.[12] Retroflexion was successful in approximately 94% of patients, but it was not performed in 6% because the rectum appeared narrow. During this study, 7 polyps were visualized by retroflexion only (following a careful, planned extubation of the colonoscope, with special attention to the rectal mucosa right down to the anal verge). Of these polyps, 6 were hyperplastic sessile polyps and 1 was a 4-mm sessile tubular adenoma. In spite of this finding, most gastroenterologists are committed to the concept of performing rectal retroversion before or after total colonoscopy in order to visualize the area surrounding the dentate line and the distal rectum. Although there have been reports of perforation related to rectal retroversion and several reports of closing those perforations with clips, I recommend performing rectal retroversion, as it need not be uncomfortable nor place the patient at risk.

Should the patient complain of pain when the instrument is advanced into the rectum, that particular attempt should be abandoned and another direction chosen for retroflexion. Occasionally, the rectal vault may be small, a physical feature more common among patients who undergo radiation therapy to the pelvis, patients with inflammatory bowel disease, or slender women. Rectal retroversion may not be possible in these individuals; if it is attempted and is painful, the attempt should be stopped to avoid perforation.

The main reason that retroflexion is performed by endoscopists is to visualize more of the mucosal surface, particularly those areas that are not well seen by direct, end-on examination with a standard colonoscope.

It is possible to purposefully perform retroflexion of the instrument throughout various parts of the colon in a fashion similar to the one more routinely used in the rectum during colonoscopic examination. A comparison between a colonoscope with a shorter tip (or a more acutely angled bending section) and a pediatric or standard colonoscope showed that the prototype instruments were significantly better at performing retroflexion throughout the colon than a standard pediatric colonoscope.[13] The success rate of performing retroflexion in the cecum was 57% for the standard pediatric colonoscope and 91% and 94% for the prototype instruments. There was a 98% success rate for all instruments in terms of intubation of the terminal ileum. The rationale behind the quest for creating an instrument that can be easily retroflexed and yet is a useable instrument for colonoscopy is to detect polyps and adenomas that may be hidden behind folds. As retroflexion is not readily performed above the rectum, areas in the valleys between folds are often not amenable to inspection during colonoscopy with an obligatory straightforward-viewing angle, whether that angle is 140 degrees or 170 degrees.

The Third Eye Retroscope

How It Works

The Third Eye Retroscope (TER; Avantis Medical Systems, Inc.) is a self-contained endoscope that can be advanced through the instrument channel of a standard colonoscope and was developed specifically because of the inability of the standard forward-viewing colonoscope to detect all polyps located behind folds and flexures in the colon during screening procedures.

When the TER is positioned beyond the tip of the colonoscope, it permits a retrograde view of the colon. Whereas the colonoscope reveals an image of the colon in a forward direction, the TER looks backward, toward and beyond the tip of the colonoscope, providing a view of the proximal aspect of the folds as the colonoscope simultaneously views their distal surfaces. The disposable TER has a 2.5-mm external diameter, and the tip enclosing the camera is 3.5 mm wide. To prevent triggering the automatic iris (a brightness reduction feature) built into the colonoscope, the TER has a polarized light emitting diode (LED) matched to a polarized filter affixed to the colonoscope tip before the procedure begins. As a result, the colonoscope light is as bright as usual and is not diminished in intensity by the built-in light sensor, leading to full illumination for both forward and retrograde viewing.

The working end of the TER is composed of 3 connected units with a straightforward-viewing camera at the end. When the instrument emerges from the colonoscope, the tip flexes so that the camera segment points backward at 180 degrees. This brings it face to face with the lens of the colonoscope and parallel with the colonoscope's long axis (Figure 1). The short section carrying the light assumes its position parallel to the faceplate of the colonoscope; thus, its illumination is directed toward the colonoscope tip and reveals the proximal aspect of folds while the colonoscope views their distal sides. As the TER is advanced from the colonoscope's instrumentation channel, the shaft of the TER is then adjusted to place the camera several centimeters from the tip of the colonoscope. The TER lens is rotated to place it in line with the water jet from the colonoscope. This affords the ability to clean the lens if it becomes soiled. The TER, containing an integrated light source and microchip for visualization, depends upon a separate image processor. The images are

Figure 1. The Third Eye Retroscope automatically turns 180 degrees when extended from the instrument channel of the standard colonoscope. A miniature video camera is housed in its tip and provides a continuous retrograde image during withdrawal through the colon. The light-emitting diode in the bent portion of the instrument provides illumination for the camera. A polarized hood on the tip of the colonoscope prevents the bright light emitted by the retroscope from interfering with the automatic iris of the colonoscope.

transmitted by a tiny complementary metal oxide semiconductor chip to the processor and then to the monitor, where side-by-side live video is projected with the colonoscopic image on the left and the TER image on the right (Figure 2).

When the TER is advanced several centimeters beyond the tip of the colonoscope, the area behind the folds and the valleys between the folds can be readily observed, providing a complete evaluation of the areas hidden from the forward-viewing colonoscope. Because of the self-contained LED illumination and the 135-degree angle of view, the previously dark area behind the colonoscope tip can be visualized for several centimeters. The transmitted images from the microchip on the TER and the colonoscope are viewed simultaneously by a trained endoscopist. A CTC simulation model has shown that a retrograde 135-degree angle of view device, coupled with a standard forward-viewing colonoscope (140-degree angle of view), will permit almost full optical visualization of the entire distal and proximal colonic surfaces and the crevices between colonic folds.[10]

In the CTC simulation study, the addition of a simulated retrograde-viewing auxiliary imaging device to a standard forward-viewing 140-degree angle of vision led to nearly complete surface visualization, with a 10-fold decrease in the area that would have been missed with a simulation model having a 170-degree angle of view.

The marked additional mucosal visualization seen in simulation models combining 140 degrees of forward view and 135 degrees of reverse view (such as with the TER) may be preferred to recently developed optics providing a 360-degree view (Aer-O-Scope, GI View), which has a substantial fish-eye effect.[14] In this simulation model, there does not appear to be any additional benefit to using a 170-degree angle-of-view colonoscope instead of a 140-degree instrument when associated with the additional advantage of the TER.

Study Results

Up to this time, there have been 5 published reports on the TER. The first report was a feasibility study using colon models implanted with 40 simulated polyps, 27 of which were attached to the proximal aspect of folds and 13 of which were placed in obvious locations readily seen by the straight forward-viewing colonoscope.[15] Six gastrointestinal endoscopists examined these models with either a straightforward colonoscope or the same instrument using the TER during withdrawal. The round, brightly colored, simulated polyps were 3 mm in diameter and 1.5 mm in height. Twelve percent of the polyps located on the proximal aspect of folds were detected with the straight-viewing colonoscope, and 81% were seen with the first-generation auxiliary retrograde-viewing

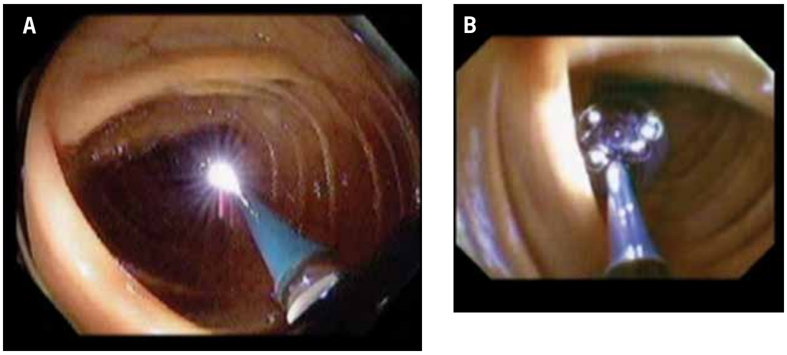

Figure 2. In the forward view of the colonoscope, the shaft of the Third Eye Retroscope is visible, as is light from the light-emitting diode **(A)**. The retrograde view from the retroscope reveals the area behind folds and flexures **(B)**. The retroscope looks back at the colonoscope, and the proximal edges and valleys between folds are brightly illuminated by its integrated light source.

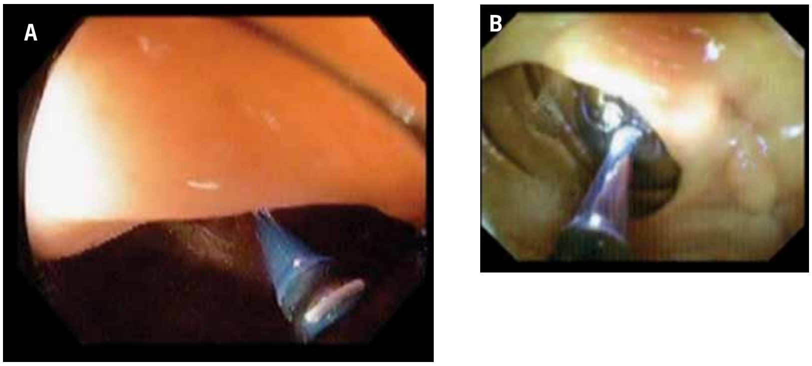

Figure 3. The forward view of the colonoscope, looking toward the Third Eye Retroscope, is obscured by the fold **(A)**. However, in the retrograde view, the retroscope is examining the area behind that fold **(B)** and reveals an adenoma hidden deep behind the fold. This polyp was not visualized by the colonoscope.

device. This marked ability to detect polyps hidden from straightforward-viewing stimulated further interest in the development of the device. In the first human pilot study, the TER was associated with an 11.8% increase in polyp detection compared to the straight end-on colonoscope.[16] During this study, a total of 38 polyps were identified in 29 patients as the colonoscope and TER were withdrawn together from the cecum. Thirty of the polyps were seen with the colonoscope, 4 were visualized by both endoscopes, and an additional 4 were seen only with the TER, as they were located on the proximal aspect of folds. The polyps found only by the TER measured 0.3 cm, 0.3 cm, 0.2 cm, and 0.7 cm in size. All of these polyps were subsequently located by the colonoscope and removed. Histopathologic examination of the tissue showed that 3 were hyperplastic and the largest was a tubular adenoma. The mean time for the total examination was 22 minutes, which included the time for removal of the polyps and the replacement of the device.

The early research regarding the development of the device and its specifications was published in 2009 and described the increase in mucosal visualization provided by the device.[17] A multicenter prospective study was performed in 249 patients in 8 locations.[18] During this investigation, an attempt was made to determine whether detected polyps were identified first by the colonoscope or by the TER. This report revealed an additional 13.2% increase in polyp detection, with an 11.0% increase in adenoma detection (Figure 3). Nine adenomas measuring over 10 mm in diameter were seen with the standard forward-viewing colonoscope; 3 additional adenomas of that size were seen with the TER but not the forward-viewing colonoscope, representing a 33% increase in adenoma yield. Most of the 257 polyps seen and removed during this study were visualized simultaneously by both the forward-viewing colonoscope and the TER. The 8 investigators and their study coordinators were instructed to specifically exclude from the TER discovery set lesions that were initially seen with the TER but were readily apparent on the forward view of the colonoscope. These lesions were not considered "additional polyps detected by TER." The final result was that 34 of 257 polyps were first seen by the TER. Among adenomas, 15 of a total of 136 were first seen by the TER. In this group of adenomas, 8 of a total of 40 adenomas greater than 6 mm in diameter were first seen by the TER (20% yield) and 3 of 12 were larger than 10 mm.

It should be noted that the TER is pointed backward and examines folds after they, and the space behind them, have been seen and already cleared by the forward-viewing colonoscope as it is being withdrawn. The mean size of all polyps detected with the TER was 4.6 mm compared to 4.2 mm for those detected with the colonoscope alone. The mean size of adenomas detected with the TER was 5.2 mm compared to 4.4 mm for those detected with the colonoscope. Of the 34 polyps detected with the TER, 10 were over 6 mm and 4 were greater than 10 mm in diameter. The withdrawal phase of both endoscopes took 10.9 minutes during this investigation. This time did not include the actual time required for polyp removal, as all polyps seen by either device were removed immediately. The ability of a retrograde-viewing device to find additional polyps highlights the inability of forward-viewing colonoscopy to locate all of the polyps in the colon. Colonoscopy is the most effective imaging modality currently available for the large bowel, though it may be an imperfect tool against colorectal cancer. As recent guidelines for colorectal cancer screening and surveillance depend upon whether polyps are found on colonoscopy and upon their size, the need to identify all of the neoplasia in the colon has assumed greater importance.

Another major study examined the impact of experience with the device on adenoma detection rates.[19] This multicenter prospective study demonstrated that the learning curve for using the TER is relatively short and confirms the increase in polyp detection with the device. This study was designed to determine how much experience was required for a previously untrained individual to acquire the necessary skills to find polyps and become proficient in its use. The endoscopists participating in this study had no previous experience with the TER. The protocol required each endoscopist to complete 20 procedures. During this study, when a polyp was seen, the endoscopist indicated whether it could have been seen using a routine withdrawal technique or whether it could only have been detected with the TER. If the polyp was seen with both endoscopes, it was credited as being found by the colonoscope. All polyps seen with the colonoscope or the TER were subsequently found with the colonoscope and removed. In these 298 subjects, 182 polyps were detected with the colonoscope, and an additional 27 polyps were detected with the TER, representing a 14% increase. The 20 subjects who were assigned to each endoscopist were examined in groups of 5 as the study progressed. The learning curve was evaluated by comparing results among each group examined by an individual physician. For all polyps, the additional detection rate for the TER was 17.8% in the first group and 17% in the fourth group to be examined. For adenomas, the additional detection for the TER increased from 15.4% in the first group to be examined to 25% in the fourth group. The mean size of all polyps detected with the TER was 6.5 mm, compared to 5.5 mm for those detected with the colonoscope alone. The mean size of adenomas detected with the TER was 6.8 mm compared to 6.5 mm for those found with the colonoscope. Nineteen percent of additional adenomas with a size of 10 mm or larger were detected with the TER compared to the colonoscope. This study suggests that there is a trend toward improvement of adenoma detection with increasing experience and that the basic mechanical skills are acquired rapidly, though varying amounts of experience are required to develop optimal technique.

Summary

In the beginning of the colonoscopy era, this technique was accepted as the most accurate method of investigation for the large bowel. Since then, studies have shown that colonoscopy may miss lesions that may be responsible for cancer of the right colon. Endoscopists have tried several methods for increasing the ability to visualize the right colon, including retroflexion of the colonoscope. However, this procedure frequently cannot be performed in the right colon and often cannot be performed in the narrowed left colon. A novel device, the TER, has been introduced to find lesions hidden behind the proximal aspect of folds in the colon. Use of this device has been associated with increased detection of adenomas in the colon. This device is introduced through the instrumentation channel of a standard colonoscope, providing a retrograde view of the colon as the straightforward colonoscope visualizes the distal portions of folds. This device holds promise for discovery of most, if not all, of the adenomas in the colon, though additional research is necessary.

Dr. Waye has no disclosures or conflicts of interest to report.

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