Artificial intelligence (AI) is emerging as a tool with which gastroenterologists can improve colon polyp detection rates, characterization and management. This branch of computer science attempts to mimic the intelligence and behavior of human beings. A process called deep learning is integral to the development of AI tools in gastroenterology, especially in imaging technologies. AI tools use general purpose algorithms specialized through training to perform tasks such as image classification and enhancement, diagnosis, or outcomes prediction. These deep neural networks analyze large, previously annotated datasets of images to learn in an iterative fashion. And with ongoing use, they get smarter.

An article published in *Endoscopy* in 2012 noted that up to 25% of polyps can be missed during colonoscopy. Factors related to these misses include withdrawal time, preparation quality and endoscopist-specific variables, such as the extent of lining visualized and the ability to recognize flat polyps (Figure).

Computer-aided polyp detection systems using deep learning have been shown to increase the ability of endoscopists to detect polyps and aid in their characterization during routine screening and surveillance colonoscopy. In an article published in *Gut* in 2019, researchers prospectively examined the effect of a computer-aided polyp detection system based on deep learning on polyp detection rate and adenoma detection rate (ADR). Most of the additional polyps identified were small and hyperplastic, thus limiting the clinical relevance of the study. But the authors demonstrated that the computer-aided diagnosis system yielded a significantly higher ADR than those achieved with standard colonoscopy (29.1% versus 20.3%, p < 0.001) and a higher mean number of adenomas detected per patient as well (0.53 versus 0.31, p < 0.001).

According to Nayantara Coelho Prabhu, M.B.B.S., AI deep learning tools may be particularly helpful in detection of certain types of polyps, such as flat and serrated lesions, that are more commonly missed by endoscopists. Dr. Coelho Prabhu is a gastroenterologist at Mayo Clinic’s campus in Rochester, Minnesota, whose research focuses on endoscopy. AI tools can also provide endoscopists with objective data that indicate whether they are performing a high-quality colonoscopy. “These tools can
account for variables such as prep quality, segments of colon visualized and completeness of examination,” explains Dr. Coelho Prabhu.

Use of AI tools in patients with inflammatory bowel disease (IBD) is another area of interest because of the difficulties associated with polyp detection in patients with mucosal inflammation. “Because IBD increases an individual’s risk of colorectal cancer, the potential utility of AI to enhance polyp detection in these patients is very exciting,” explains Dr. Coelho Prabhu. “Once they are trained on adequate images, AI systems will be able to help gastroenterologists identify areas of higher risk of dysplasia and preneoplastic changes in these colons.”

**Role of AI in polyp classification and management**

Characterization of polyps, as premalignant adenomatous or serrated lesions versus benign hyperplastic lesions, is an important feature of currently available AI systems. “This differentiation is important because it determines the patient’s colon cancer risk and the surveillance intervals. The currently available tools for classification are yet to be perfected but show potential for future development,” says Dr. Coelho Prabhu.

Newer AI technologies are emerging that may have the potential to help endoscopists determine the depth of submucosal invasion of various parts of a lesion. “The information provided by these tools could help endoscopists determine whether a simple mucosal resection versus a deeper submucosal dissection of the lesion is required to ensure complete removal,” explains Dr. Coelho Prabhu.

Dr. Coelho Prabhu notes that AI can be trained to help endoscopists identify the margin of polyps, which can sometimes be difficult to identify, especially in lesions that spread laterally. “Training AI on various filtered-light images will improve the tool’s accuracy and specificity,” explains Dr. Coelho Prabhu. “And with deep learning, the AI systems will continue to learn while they are being implemented, to improve and yield more fine-tuned results.”

Dr. Coelho Prabhu notes that AI tools can also be trained to perform the following tasks:

- Outline polyps before resection and identify residual preneoplastic tissue to guide the complete resection of the adenomatous tissue that is required to prevent recurrence
- Standardize the quality of exams and guide accurate follow-up intervals
- Identify patients who are at higher risk of complications during resection, including bleeding, cardiorespiratory complications and perforation

**AI in GI at Mayo Clinic**

Dr. Coelho Prabhu notes that Mayo Clinic is well positioned to develop and validate AI tools. “Our depth of highly specialized physicians in each field of gastroenterology and the high volume of patients we see and treat both make our organization uniquely suited to this vein of research.”

Having well-annotated datasets that can be used to train AI tools is an essential component in building effective and accurate AI tools. “We have records from a large volume of procedures performed, and we are working to create a rich database of high-quality images and videos needed to support AI tools. This work will position us at the forefront of AI tool development,” says Dr. Coelho Prabhu.

Dr. Coelho Prabhu and colleagues are currently focused on using AI to help accurately identify the precise location of polyps and cancer in the colon to aid surgeons in cases where resection is needed, and to improve surveillance efforts, especially when these lesions are endoscopically resected.

Mayo Clinic researchers are also conducting clinical trials involving advanced imaging techniques, including the use of AI tools and blue light imaging, narrow band imaging, and colon capsule endoscopy.

Dr. Coelho Prabhu anticipates that AI tools will be used regularly in the clinical setting within the next five years to guide endoscopy (including colonoscopy), esophagogastroduodenoscopy, capsule enteroscopy, endoscopic ultrasound and endoscopic retrograde cholangiopancreatography. “I also expect to see AI employed to optimize procedure scheduling, for diagnosis augmentation and to guide surveillance,” says Dr. Coelho Prabhu.

“Overall, the advances provided by AI-based learning can help us determine the best treatment option for each patient, and this will enhance our ability to offer patients truly individualized therapeutic approaches,” says Dr. Coelho Prabhu.

**For more information**


Prepless Colon Capsule Technology: New Research Examines This Less Invasive Approach to Colorectal Cancer Screening

Optical colonoscopy facilitates the detection and removal of premalignant polyps and is the gold standard as a screening and surveillance tool for colorectal cancer (CRC). Despite the demonstrated track record of the procedure, a number of factors limit patient acceptance of this test. Concerns about adverse events, the required colon-cleansing prep, the need for sedation and pain control, loss of work time, and costs associated with optical colonoscopy are among the issues that negatively affect patient tolerance. In addition, inadequate cleansing before the test can reduce cancer detection rates and lead to the need for repeat procedures.

Mayo Clinic researchers, in collaboration with others, are working to assess and advance capsule-based technology for CRC screening. According to Elizabeth Rajan, M.D., a gastroenterologist and researcher from Mayo Clinic’s campus in Rochester, Minnesota, one of the newest capsule imaging systems currently being studied is a prepless, disposable and ingestible X-ray imaging capsule.

The capsule system that Dr. Rajan and others are studying uses an ingestible capsule that emits and detects ultra-low-dose radiation and requires no cathartic cleansing or sedation (Figure). The capsule generates a 3D reconstruction of the colonic lumen for detection of polyps and cancer. The system also includes a tracking device that utilizes processing units combined with radiofrequency (RF) communication to allow data transmission to an externally worn recorder attached to the lower back. In addition, it utilizes electromagnetic tracking technology to enable the device to track the capsule’s 3D position and orientation within the body.

After ingesting the capsule, patients drink a small amount of contrast agent and fiber supplements with each meal during capsule passage. Patients can go about their daily activities and return to work. While the capsule travels naturally through the gastrointestinal tract, it scans the colon in a 360-degree arc and sends information to a recorder. Once the capsule is excreted, data from the recorder is downloaded to a workstation and analyzed to create a map of the colon.

Results from clinical trials
Safety and feasibility
Researchers from Germany and Israel first assessed the safety of this new generation of the prepless capsule system in two separate studies. The results of those studies were published in *Abdominal Radiology* in 2017 and demonstrated the safety and feasibility of this device in 141 study participants.

The same prepless capsule device underwent additional testing in a prospective multicenter trial conducted in Israel. During that trial, study participants underwent the capsule procedure and concomitant fecal immunochemical test (FIT) followed by colonoscopy, with removal of all visualized polyps.

Results from this trial were published in *Gut* in 2019 and included these relevant findings:

- An analysis of 45 procedures performed demonstrated the sensitivity of both approaches for polyp detection: 44% using the capsule and 37% using FIT.
- Capsule sensitivity increased to 78% to 100% when more than 50% to 70% of the colon surface area was imaged, respectively, with a linear correlation between imaged area and sensitivity. Specificity varied from 86% to 90%. Optimized scanning algorithms will be applied to future studies.
- The average transit time was 52 hours with no device-related serious adverse events.

Ongoing and future trials
Dr. Rajan and colleagues are collaborating in the first U.S. prospective single-arm pilot study evaluating the safety and compliance of this prepless capsule in asymptomatic participants considered to be of average risk of polyps and colon cancer. Preliminary results are promising, and Dr. Rajan and co-investigators expect to publish results from that trial in early 2020. The next step will be a multicenter pivotal study.

*“Each phase of this research helps us progress toward the...*
goal of offering patients the option of a prepless, X-ray-based imaging capsule as a screening tool for CRC,” says Dr. Rajan. Establishing the safety and efficacy of this screening test may encourage more nonadhering patients to comply with recommended screening, which would, in turn, help reduce the overall incidence of CRC.

**For more information**


**Update on Hereditary Gastrointestinal Cancers: Lynch Syndrome and Familial Adenomatous Polyposis Syndromes**

Hereditary causes, due to defects in certain genes, account for up to 10% of all colorectal cancers (CRCs). These high-risk hereditary predisposition syndromes have been associated with a significantly increased lifetime risk of cancer, with some approaching 100%. In addition, up to 20% of patients with CRC have common familial cancer, meaning there is a strong family history of CRC but no one genetic defect has been identified.

In an article published in *Mayo Clinic Proceedings* in 2019, Niloy Jewel (Jewel) Samadder, M.D., and co-authors present a primer on the diagnosis and management of these hereditary conditions and the gastrointestinal cancers with which they are associated. Dr. Samadder is a gastroenterologist and hepatologist specializing in inherited cancers at Mayo Clinic’s campus in Arizona.

In this article, Dr. Samadder shares information about Lynch syndrome (LS), familial adenomatous polyposis (FAP) and attenuated FAP (AFAP) to provide clinicians with tools to understand the genetic bases of these conditions and the appropriate diagnosis and management.

**Lynch syndrome (LS)**
**Overview and clinical presentation**
Hereditary nonpolyposis CRC, also known as LS, is the most common hereditary CRC predisposition syndrome and accounts for 2% to 4% of all colorectal neoplasias. Individuals with LS have an elevated lifetime risk of CRC (80%) and endometrial cancer (60%).

In addition to colorectal and endometrial cancers, individuals with LS have a predisposition for these extracolonic cancers: gastric, ovarian, breast, liver and bile duct, genitourinary, pancreatic, small bowel, brain, sebaceous gland adenomas, and keratoacanthomas. The lifetime risk of each of these cancers varies and is affected by the individual’s age, sex and the specific mismatch repair (MMR) germline mutation involved.

**Genetics and diagnosis**
LS is an autosomal dominant disorder caused by a germline mutation in one of several DNA MMR genes on chromosome 3p21 that are responsible for post-replicative proofreading — MLH1, MSH2, MSH6, PMS2 and EPCAM.

“The accelerated rate at which these cancers develop and the associated risk of multiple malignancies make early diagnosis critical,” explains Dr. Samadder. In addition to a review of family and personal cancer history, the Amsterdam and revised Bethesda criteria can help identify patients carrying mutations.

Tumor testing for LS can include microsatellite instability (MSI) status testing and immunohistochemical (IHC) analysis to assess for MMR protein expression. Current guidelines recommend these tests for every CRC tumor specimen to identify LS-related cancers. If multigene testing is performed, it should be accompanied by professional pretest and posttest counseling.

**Colorectal cancer surveillance and management**
The National Comprehensive Cancer Network and others recommend performing surveillance colonoscopy every one to two years in confirmed LS mutation carriers, beginning at age 20 to 25, or two to five years before the age at which the youngest family member was diagnosed, whichever comes first.

Patients with LS who are diagnosed with CRC may benefit from a completion colectomy with ileorectal anastomosis to eliminate future risk of CRC. A segmental resection may be considered if postoperative surveillance can be performed every one to two years.

**Extracolonic cancer surveillance and management recommendations**
Currently there are no universal guidelines to guide screening for extracolonic cancers associated
with LS. A few general recommendations for each cancer are listed below.

Endometrial cancer: Patient education about symptoms and instructions to report symptoms; annual endometrial biopsy can also be considered.

Ovarian cancer: Transvaginal ultrasonography and serum cancer antigen 125 measurement can be considered, although data about their efficacy are limited.

To reduce the risk of both endometrial and ovarian cancers, prophylactic total abdominal hysterectomy and bilateral salpingo-oophorectomy are recommended in women beyond the childbearing years.

Gastric and duodenal cancers: Baseline esophagogastroduodenoscopy, extended to the distal duodenum, by age 30 to 35 years; gastric biopsies to detect and treat Helicobacter pylori infection; surveillance endoscopy performed every three to five years, although there is limited evidence supporting this practice.

Genitourinary, pancreaticobiliary and breast cancers: At this time, there is insufficient evidence to recommend deviating from the population-based screening guidelines developed for the average-risk population. Screening efforts should be tailored to the individual’s family history of the specific cancers. At the very least, patients with LS should continue to undergo population-based breast cancer screening, including mammography by age 40 years.

**Familial adenomatous polyposis (FAP) and attenuated FAP (AFAP)**

**Overview and clinical presentation**

This rare, autosomal dominant, inherited condition presents with the development of hundreds of colorectal adenomas, generally during early adolescence. Although data about this syndrome are limited, the incidence of FAP is estimated to be 1 in 10,000 across all populations, and it accounts for less than 1% of all CRCs. In its early stages, FAP can present with nonspecific gastrointestinal symptoms (such as change in bowel movement pattern) and rectal bleeding (Figure).

“If left untreated, FAP is associated with a lifetime risk of CRC of nearly 100%,” says Dr. Samadder. A less severe form of this disease, called AFAP, is characterized by later onset of polyps, fewer polyps (0 to 100 colon adenomas) and a lower overall risk of CRC (70%).

**Genetic causes and diagnosis**

Both FAP and AFAP are caused by germline mutations in the APC gene, a tumor suppressor gene that is part of the Wnt signaling pathway. Although FAP is an inherited disorder, up to 30% of cases of FAP are due to de novo APC mutations.

Genetic testing for FAP and AFAP should be considered in any of these situations:

- More than 10 adenomas detected during a single colonoscopy
- More than 20 adenomas in the colon or rectum over the patient’s lifetime
- Known diagnosis of FAP in the family
- Family or personal history of early-onset CRC and extraintestinal features often associated with FAP, including congenital hypertrophy of the retinal pigment epithelium (CHRPE), osteomas and desmoid tumors

“FAP, AFAP and another hereditary cancer called MUTYH-associated polyposis have similar features, so confirming a molecular diagnosis of these syndromes via genetic testing is critical,” says Dr. Samadder.

Patients with classic FAP symptoms whose genetic testing results do not confirm an APC mutation may have other mutations.
Colorectal cancer surveillance
“Aggressive early diagnosis and management are warranted for patients with FAP” explains Dr. Samadder.

Recommendations: For FAP, colonoscopy is typically initiated by age 10 to 12 years and repeated annually, until the number of polyps present makes endoscopic management impractical. For AFAP, colonoscopy can begin at a slightly later age (late teens) and be repeated every one to two years.

Surgical management
Colectomy is generally recommended for patients with FAP and any of the following findings:
- Confirmed diagnosis of CRC
- Advanced histologic features in polyps (vil- lous or high-grade dysplasia)
- Large adenomatous polyps (> 1 cm)
- Polyp burden exceeds capacity for endoscopic control (> 20 to 40 adenomatous polyps)

Proctocolectomy with ileal pouch-anal anastomosis and colectomy with ileorectal anastomosis are the two most commonly performed surgical approaches for patients with FAP. “The burden of disease in the rectum and the capacity to continue annual surveillance help guide the choice between these two surgical options,” says Dr. Samadder.

Patients with an ileorectal anastomosis have a continued substantial risk of rectal cancer and require continued endoscopic surveillance every six to 12 months. Similarly, patients with an ileal pouch-anal anastomosis or ileostomy should undergo periodic endoscopic surveillance because of increased cancer risk related to the presence of preneoplastic lesions that can develop in the ileum, J pouch and anal transition zone.

Extracolonic cancer surveillance and management
A few of the more common types of extracolonic cancers associated with FAP and available recommendations for their surveillance and management are described below.

Duodenal cancer: This is the most common extracolonic malignancy and a major cause of mortality in patients who have undergone risk-reducing colectomy. Up to 80% of patients with FAP will develop duodenal adenomas, and the lifetime risk of duodenal cancer is 12%. The Spigelman classification score can guide endoscopic surveillance intervals. Recommendation: Baseline endoscopy, performed at 25 to 30 years of age or just prior to colectomy and repeated at intervals (from every one to five years) based on the patient’s Spigelman score and stage.

Gastric polyps: Although gastric polyps are a frequent finding, the lifetime risk of gastric cancer is only 1%. Recommendation: Biopsy when observed during endoscopic surveillance.

Cancers of the thyroid: The lifetime risk of these cancers is 2%. Most occur in women, and some data suggest that Hispanic individuals are at increased risk. Recommendation: Annual thyroid clinical examination and consideration for thyroid ultrasonography.

Hepatoblastomas: These very rare liver tumors occur mostly in males, and children under the age of five years are at greatest risk. Recommendation: Alpha fetoprotein and liver ultrasonography can be considered every three to six months.

Dr. Samadder and colleagues at Mayo Clinic’s multidisciplinary inherited cancers clinic are available to help identify high-risk patients and families, tailor approaches to cancer screening to detect cancers earlier, and formulate more-effective individualized treatment protocols for these patients.

For more information

Use of ESD for Treatment of Gastrointestinal Lesions

Norio Fukami, M.D.

In this Q and A, three experienced therapeutic endoscopists from Mayo Clinic answer questions about the role of endoscopic submucosal dissection (ESD) in treating lesions within the gastrointestinal tract. Norio Fukami, M.D., from Mayo Clinic’s campus in Phoenix/Scottsdale, Arizona; Michael B. Wallace, M.D., from Mayo Clinic’s campus in Jacksonville, Florida; and Louis M. Wong Kee Song, M.D., from Mayo Clinic’s campus in Rochester, Minnesota, share best practices and updates about the role of ESD within the United States.

What are the indications for ESD for treatment of early gastric cancers?
ESD has enabled en bloc resection of lesions that are too large for endoscopic mucosal resection (EMR) and those that are suspected superficial malignancies. An AGA Institute Clinical Practice Update published in Clinical Gastroenterology and Hepatology in 2019 outlines several best practices for ESD. Peter V. Draganov, M.D., Dr. Fukami and co-authors note that, historically, absolute indications for endoscopic resection have included mucosal cancers ≤ 2 cm.
that are moderately and well differentiated, and nonulcerated. The authors also state that ESD has enabled the expansion of endoscopic resection criteria, so it may also be appropriate to include: moderately and well-differentiated superficial gastric cancers that are larger than 2 cm, lesions ≤ 3 cm with ulceration or those that contain early submucosal invasion, and poorly differentiated superficial cancers ≤ 2 cm. However, performing ESD for these expanded indications can lead to including patients who have an elevated risk of lymph node metastasis. So success in completing safe ESD and an analysis of post-resection pathological findings are extremely important to consider when assessing the need for additional oncologic therapy.

Is ESD appropriate for patients with Barrett’s esophagus-related neoplasms? Although EMR is performed in most cases, ESD may be considered for select patients with Barrett’s esophagus. Experienced endoscopists are more likely to use this approach in patients with suspected superficial cancers (T1a and early T1b lesions) that are larger than 10 to 15 mm, and those with poor lifting. The AGA update states that ESD may be considered for lesions that have a large or bulky area of nodularity, lesions where superficial submucosal invasion is suspected, and lesions with evidence of recurrent dysplasia, invasive carcinoma with positive margins, equivocal pre-procedural histology or intramucosal carcinoma.

What role can ESD play in treating esophageal squamous cell carcinoma (ESCC)? According to the AGA update, ESD is the primary modality for treating ESCC confined to the superficial esophageal mucosa. The authors also note that alternative or additional therapy should be considered for lesions with pathological evidence of submucosal invasion, due to increased risk of lymph node metastasis. A large uninterrupted specimen removed by ESD technique would facilitate the pathological evaluation of the lesion to determine tumor staging and a risk of metastasis. The European Society of Gastrointestinal Endoscopy (ESGE) guideline published in Endoscopy in 2015 recommends en bloc resection with ESD instead of EMR for ESCC lesions 10 mm or larger.

Data from large trials with head-to-head comparisons between ESD and esophagectomy using a validated assessment tool in patients with ESCC still remain scarce.

In an article published in Gastrointestinal Endoscopy in 2018, Yang Won Min, M.D., Ph.D., and co-authors shared the results from a retrospective, single-center analysis comparing outcomes between two groups of patients. One group underwent ESD for ESCC. The other underwent esophagectomy, but the patients were later deemed candidates for ESD by a retrospective review of images, as determined by the study protocol. Both groups received long-term follow-up with serial upper endoscopy and chest CT at set intervals until five years after intervention. Patients in the ESD group had outcomes that were similar to those in the group that underwent surgical therapy. The ESD group also had lower adverse event occurrences, even though metachronous lesions were more frequent in this group.

In an editorial published in Gastrointestinal Endoscopy in 2018 and commenting on this study, Dr. Fukami and co-author Tiffany Y. Chua, M.D., note that the study results suggest that ESD can serve as a first line treatment for superficial ESCC when endoscopic features do not indicate submucosal invasion and when there is no clinical evidence of metastasis.

What has recent research shown about the use of ESD for colorectal lesions? Advanced endoscopic techniques should be considered for complex colorectal lesions without signs of deep submucosal invasion or advanced cancer. The ESGE guideline notes that ESD is generally appropriate for colonic lesions larger than 2 cm that are suspected invasive cancer with limited (shallow) invasion depth, all rectal lesions larger than 2 cm that are nongranular, and those larger than 3 cm that are granular or mixed. The AGA update also notes that neoplasms containing dysplasia confined to the mucosa have no risk of lymph node metastasis, and therefore endoscopic resection should be the primary mode of therapy. ESD should be considered for large lesions or those with concerning features for superficial colorectal cancer.

What challenges do larger or more-complex colorectal lesions pose? Experienced endoscopists agree that patients with lesions larger than 2 cm and complex colorectal polyps should be referred to a high-volume, specialized center for endoscopic removal using EMR or ESD. Piecemeal removal of larger lesions is associated with an increased rate of recurrence up to 20%, and an incomplete first attempt is associated with an increased rate of failure of future
endoscopic therapy. ESD can facilitate en bloc resection and reduce recurrence rates in patients with these larger, more-complex lesions (Figure, see page 7).

**What do ESD practitioners need to know about closure devices?**
The AGA update notes that familiarity with closure devices, including clips and endoscopic suturing, is important. Available data show that both approaches are effective in managing intraprocedural perforation.

**How can clinicians acquire ESD training in the United States?**
While there is no standardized approach to ESD training within the U.S., it is still possible to achieve a high level of competency in this procedure. Self-guided study, practice on explant and animated models, and training courses offered by Mayo Clinic and other high-volume, advanced endoscopy centers and GI societies can provide the needed exposure and opportunities for skill development.

**Are there new technologies that will make ESD simpler?**
One of the major limitations of ESD is the very long time needed to complete the procedure. ESD typically requires two to three hours, which is nearly two times longer than EMR and four to six times longer than the time required for diagnostic colonoscopy. Several new devices that allow traction and countertraction, as well as electrosurgical knives with integrated water jets to lift and cut simultaneously, have recently been introduced and are under study.

**For more information**

