Endoscopic Technologies Improve Diagnosis

Advances in endoscopic technology are allowing physicians at NewYork-Presbyterian Hospital to visualize the gastrointestinal (GI) tract and to detect mucosal and anatomic abnormalities in an unprecedented fashion. One advancement, narrow band imaging (NBI), is helping endoscopists detect precancerous mucosal changes earlier, potentially reducing the mortality associated with esophageal and colorectal cancers. Another new technology, balloon enteroscopy, is allowing gastroenterologists to access the small intestine, whereas it was previously mostly inaccessible with standard endoscopy.

“In patients with Barrett’s esophagus, NBI has improved our surveillance approach and has helped us target biopsies,” explained Charles Lightdale, MD. “It is also allowing us to detect residual and recurrent lesions in patients with advanced disease who have already undergone ablative treatment.”

“With high-definition endoscopy and NBI, we’re not just getting a better image, but also more information,” added Mark Pochapin, MD. “The image is so detailed, we can see flat polyps or lesions throughout the GI tract that we might have missed otherwise.”

NBI illuminates the mucosa with wavelengths of narrow bands of blue and green light. According to Drs. Lightdale and Pochapin, NBI enhances the visibility of capillaries, veins, and other suble tissue structures by optimizing the absorbance and scattering characteristics of light. Superficial blood vessels appear brown under NBI. Since precancerous areas of the mucosa often contain an increased concentration of this blood supply, NBI is an ideal technology to improve the appearance of these areas because it shows increased vascularity and, as Dr. Pochapin said, literally “outlines the polyps.”

The reigning standard of endoscopic care for patients with Barrett’s esophagus includes random biopsies in each of the 4 quadrants of the esophagus every 1 to 2 cm of Barrett’s length. However, Dr. Lightdale said, by using NBI, he can identify abnormal mucosa and target biopsies to only those areas that appear irregular. Indeed, research has shown this approach reduces the number of biopsies needed to perform an exhaustive endoscopic examination, while increasing the diagnostic yield of the procedure. Dr. Lightdale specifically looks for mucosa with villous patterns, or mucosa that appears fine or clumpy; if esophageal ridges are clubbed, enlarged, or thin, these areas require biopsy as well. Tiny islands of Barrett’s tissue remaining after the initial ablation stand out in much greater contrast using NBI, and are much easier to target for complete obliteration of all Barrett’s tissue.
Research Assesses Metabolic Surgery as Option for Diabetes

Columbia and Weill Cornell researchers at NewYork-Presbyterian Hospital, through the establishment of 2 dedicated research centers, are seeking to refine guidelines for the use of metabolic surgery in patients with type 2 diabetes who fail to respond to medical therapy and set the tone for future research into its efficacy.

“Diabetes has always been considered a medical disease,” noted Francesco Rubino, MD. “The concept that you could use surgery to intentionally treat diabetes is foreign to conventional medicine, and still has many skeptics.”

Indeed, unlike medical therapy, which often does not achieve adequate control of the diabetes, surgery in individuals who are morbidly obese can induce diabetes remission in up to 80% of cases, according to William B. Inabnet, MD. Dr. Inabnet believes that the current criteria for weight loss surgery, a body mass index greater than 35 with type 2 diabetes, established by the National Institutes of Health (NIH) in 1991, is overdue for revision.

“For years it was assumed that bariatric surgery improved diabetes only because of weight loss,” noted Dr. Rubino. “But this didn’t explain the rapid resolution of diabetes after certain types of procedures. We have learned that when you change the anatomy of the gastrointestinal tract, there are additional mechanisms that improve glucose metabolism.”

Using a modified gastric bypass operation, Dr. Rubino demonstrated that surgery can directly improve glucose tolerance, independent of weight loss (Ann Surg 2004;240[2]:236-242). In further experiments, he found that a primary mediator of the effect of surgery on diabetes is the lack of nutrients that pass through the upper small intestine as a result of a duodeno-jejunal bypass. Dr. Rubino hypothesized that abnormal hormone or neural signaling stimulated by nutrient passage in the foregut of patients with diabetes may contribute to the pathophysiology of the disease. Accordingly, a duodeno-jejunal bypass may reverse these abnormalities, improving diabetes (Diabetes Care 2008;31[suppl 2]:S290-S296). As a consequence of Dr. Rubino’s research with rats, an endoscopic endoluminal sleeve that functionally bypasses the duodenum is currently being tested in humans for the treatment of diabetes.

Additionally, Dr. Inabnet is leading a randomized clinical trial to compare intensive medical therapy and lifestyle modifications to gastric bypass for moderately obese patients with a BMI of 30 to 34.9 who have severe diabetes and have failed conventional medical therapy (under the current NIH criteria, these patients would not be approved for bariatric surgery). The study will include 120 patients, 60 from the United States and 60 from Taiwan, and is currently recruiting patients. In this research, Dr. Inabnet is collaborating with other physicians at NewYork-Presbyterian Hospital/Columbia University Medical Center, including Judy Korner, MD, PhD, an endocrinologist who studies gut peptides in patients who are obese; Michelle Lee, MD, an expert in obesity and diabetes; and Marc Bessler, MD, a bariatric surgeon. Dr. Inabnet and his co-investigators hope to learn more about the effects of gastric bypass on pancreatic beta cell function in these moderately obese patients.

“This study will answer the question whether surgery is the best treatment for long-term, durable remission of type 2 diabetes, and hopefully will help lower the current BMI criteria for metabolic surgery in type 2 diabetes,” explained Dr. Inabnet.

At the Weill Cornell Diabetes Surgery Center at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, Dr. Rubino is also organizing a similar, multinational clinical trial, in collaboration with surgeons Alfonso Pomp, MD, and Greg Dakin, MD, and endocrinologists Louis Aronne, MD, Animesh A. Sinha, MD, David J. Brilllon, MD, and Julianne Leonore Imperato-McGinley, MD, as well as researchers from other centers in the United States, Europe, Asia, and South America.

“In the past 20 years, bariatric surgery has grown from 12,000 surgeries a year to close to 280,000,” said Dr. Rubino. “This explosion has been fueled by the obesity epidemic, technical advances in laparoscopic surgery, as well as a significant improvement in patient safety as demonstrated by the implementation of a national Center of Excellence program by the American Society for Metabolic and Bariatric Surgery. A recent review of more than 100,000 patient entries of the Surgical Review Corporation’s bariatric surgery national registry showed that the mortality of gastric bypass operations had decreased to 0.3%, lower than most commonly performed abdominal operations.”

According to Dr. Rubino, the Section of Metabolic Surgery at NewYork-

Figure. According to research led by Francesco Rubino, MD, at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, a duodeno-jejunal bypass may reverse abnormalities such as abnormal hormone or neural signaling that contribute to diabetes.
Presbyterian/Weill Cornell is the first academic-based program focused on the surgical treatment of diabetes. Dr. Rubino explained that the Diabetes Surgery Center complements the clinical mission of the metabolic surgery section by promoting research and education in this field. Meanwhile, at NewYork-Presbyterian/Columbia, Dr. Inabnet and his team have created the Center for Metabolic and Endocrine Surgery Research with the goal of advancing translational research and education in the emerging field of metabolic surgery.

“[Our] study will answer the question whether surgery is the best treatment for long-term, durable remission of type 2 diabetes, and help [change] the criteria ...”
—William B. Inabnet, MD

In March 2007, Dr. Rubino was the principal organizer of the Diabetes Surgery Summit, an international consensus conference that established recommendations for the use of surgery in the treatment of diabetes. As a result of this conference, many bariatric societies have changed their names to include metabolic surgery as part of their purview. For example, the American Society for Bariatric Surgery is now the American Society for Metabolic and Bariatric Surgery. In addition, an International Diabetes Surgery Task Force was created, with Dr. Rubino serving as a founding member.

“Surgery for diabetes is more than just a promising therapeutic option for selected patients,” said Dr. Rubino. “By understanding how surgery works, we might understand how diabetes itself works. Ultimately, surgery may help identify new targets for drug development and the effects of surgery may, one day, be replicated by medications. Paradoxically, surgery might facilitate pharmaceutical research. This is an important part of our work at the Diabetes Center.”

Contributing faculty for this article:
William B. Inabnet, MD; Francesco Rubino, MD

NewYork-Presbyterian Digestive Diseases

NewYork-Presbyterian Digestive Diseases is a publication of the Digestive Diseases Centers of NewYork-Presbyterian Hospital. The Digestive Diseases Centers are at the forefront of research and practice in the areas of gastroenterology; gastrointestinal surgery; and liver, bile duct, and pancreatic disorders. NewYork-Presbyterian Hospital/Columbia University Medical Center and NewYork-Presbyterian Hospital/Weill Cornell Medical Center are respectively affiliated with Columbia University College of Physicians and Surgeons and Weill Cornell Medical College.

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Researchers Explore New Options in MIS for Rectal Cancer

Due to several important initiatives, Columbia and Weill Cornell surgeons at NewYork-Presbyterian Hospital have been leading efforts to redefine minimally invasive rectal cancer resections through the use of and experimenttion with procedures such as transanal endoscopic microsurgery (TEMS) and minimally invasive techniques such as laparoscopy and endoluminal procedures.

"The whole concept of endolumenal surgery is moving rapidly because of new designs of scopes and tools that are expanding what we can achieve from a minimally invasive approach," said Jeffrey W. Milsom, MD. "We have been participating in formal arrangements with industry to help design the tools going forward. We are not just adapting the new technologies; we are contributing to the advances."

One of the major attributes of minimally invasive surgery is a quick recovery, but the Columbia and Weill Cornell investigators at NewYork-Presbyterian are proceeding only when it is clear that the quality of surgery will not be compromised. As the word "minimally" implies, the degree of invasiveness can range widely, depending on the procedure. Even when surgery is done through a laparoscope, it is important to use the minimally invasive technique that yields the best result. Surgeons at NewYork-Presbyterian Hospital/Weill Cornell Medical Center are leading a multicenter study in which the hypothesis is that hand-assisted laparoscopy will be superior to straight laparoscopy in the treatment of rectal cancer, even though it requires an extra incision.

"The laparoscopic approach to rectal cancer has been controversial because of initial reports that minimally invasive procedures led to an increase in positive margins, higher recurrence rates, and a higher rate of complications, such as anastomotic leaks. [But] we think that the hand-assisted approach will accelerate the process. There really seems to be no downside to the extra incision."

—Sang Lee, MD

At NewYork-Presbyterian, increasing numbers of procedures are being evaluated in which "minimally invasive" means circumventing the need for any external incisions. One of the best examples is the TEMS procedure, which allows removal of polyps not accessible with standard instruments through the anus. In TEMS, a circular piece of the rectal wall with the polyp in its center is excised through a special anoscope, which provides access to polyps that are otherwise out of reach. The wound is then closed with special suture. Unlike laparoscopy, the majority of patients after TEMS can return home after only an overnight hospitalization. Characteristic of endolumenal procedures being pursued at the Hospital, TEMS is redefining minimally invasive surgery.

"TEMS is technically challenging, but we have been deeply involved in minimally invasive surgery for several years and have a deep pool of surgeons with good skills in these types of techniques," said Richard L. Whelan, MD, who credited Daniel Feingold, MD, with refining the TEMS approach at NewYork-Presbyterian Hospital/Columbia University Medical Center. "Selecting the right candidate is important. However, for those who are suitable, TEMS has the potential to substantially reduce the dangers of and the trauma associated with a standard rectal cancer resection."

TEMS is seen as another step on the road to a reorientation in gastrointestinal surgery at NewYork-Presbyterian. According to Dr. Milsom, the Hospital recently recruited Fred Cornhill, DPhil, previously Director of the Institute of Biomedical Engineering at the University of Oxford, to participate in their effort to rethink approaches to minimally invasive surgery that include not only better instrumentation, but better intraoperative imaging.

"What we are seeing is a drastic redesign of the operating room that will allow imaging to play a far more important role in guiding the procedure," Dr. Milsom said, adding that the Helmsley Operating Room at NewYork-Presbyterian/Weill Cornell has been designed so that intraoperative 3-dimensional imaging can be used to achieve a precision that is as good as or better than that found in open surgeries. In general, the advances at the Hospital are expected to facilitate a growing number of resections for rectal tumors to be performed without any external excisions. Whenever a minimally invasive procedure can be substituted for an open technique with similar results, it yields major benefits for the patient.

"We are dedicated to this concept and are helping to bring it forward," Dr. Whelan said. "For the right patient, minimally invasive surgery allows us to greatly improve the experience of surgery for the patient without compromising the result."

Contributing faculty for this article:
Sang Lee, MD; Jeffrey W. Milsom, MD; Richard L. Whelan, MD
Pancreatic Cancer: Registry Emphasizes Early Detection

Columbia and Weill Cornell researchers at NewYork-Presbyterian Hospital are studying the genetic or molecular changes that may be involved in the development of pancreatic cancer as well as the potential benefit of screening in individuals with a strong family history of this disease. The hope is that such screening may result in earlier detection and more effective treatment.

In collaboration with Memorial Sloan-Kettering Cancer Center, The Jay Monahan Center for Gastrointestinal Health at NewYork-Presbyterian Hospital/Weill Cornell Medical Center—led by Felice Schnoll-Sussman, MD, and colleagues—is in the process of building a large national registry of DNA samples from people who have been diagnosed with or have family members with pancreatic cancer.

“Our goal is to collect a broad genetic sampling from individuals with pancreatic cancer or with first-degree relatives who have pancreatic cancer,” noted Dr. Schnoll-Sussman. “The registry will help researchers determine, for example, to what degree genetic abnormalities can predict a patient’s risk for pancreatic cancer.” In addition to studying the epidemiologic and genetic factors involved in pancreatic cancer, Dr. Schnoll-Sussman’s team is investigating the potential benefit of endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography screening in people with a family history of pancreatic cancer. “It is early in the study, but the hope is that such screening efforts in higher-risk families may lead to early detection of cancers, or even detection of precancerous lesions that are known to have the potential to progress to pancreatic cancer,” she said.

Through a separate registry at NewYork-Presbyterian Hospital/Columbia University Medical Center, Harold Frucht, MD, is hoping to follow patients with a personal or familial history of pancreatic cancer in an effort to detect cancers earlier and, ultimately, to improve survival among patients with pancreatic cancer. According to Dr. Frucht, patients with high-risk genetic or lifestyle traits undergo an aggressive surveillance screening protocol with MRI and/or EUS with possible tissue aspiration of detected lesions—an approach that has been effective in identifying early lesions, said Dr. Frucht. Patients with histologically confirmed pancreatic intraepithelial neoplasia lesions then undergo an intensive screening schedule and possible surgical and/or medical treatment. Using MRI for surveillance allows Dr. Frucht and his colleagues to detect other cancerous lesions for which patients with genetic cancer susceptibility syndromes may be at risk.

“Because of our broad and aggressive approach, we’ve also detected 2 early ovarian cancers, 1 carcinoid tumor, a thyroid cancer, and several precancerous pancreatic lesions,” Dr. Frucht said. “The only way to truly get ahead with those who have these susceptibility syndromes or a genetic risk for pancreatic cancer is to put them on an aggressive surveillance schedule.”

At the Monahan Center, Ann Carlson, MS, CGC, is available to provide genetic counseling and, if appropriate, genetic testing. As part of a session, Ms. Carlson records a patient’s personal medical history, as well as any familial history of cancer, and constructs a pedigree to help assess the risk of pancreatic cancer. Those with a family history of pancreatic cancer, but without evidence of pancreatic cancer themselves, undergo full medical and lifestyle evaluations, and, if they choose to, genetic testing to determine their estimated risk of developing cancer. Depending on the patient’s family history, there are a number of genetic mutations for which Ms. Carlson may recommend testing. One possible set of mutations includes those in the MLH1, MSH2, and MSH6 genes. These are associated with Lynch syndrome, or hereditary non-polyposis colorectal cancer. Other possible genetic mutations for which Ms. Carlson may offer testing include the PRSS1 gene, which is linked with hereditary pancreatitis, a condition that is associated with an increased risk of developing pancreatic cancer, and STK11, which is thought to be responsible for Peutz-Jeghers syndrome (PJS). Individuals with PJS have approximately a 36% chance of developing pancreatic cancer in their lifetime. Women with PJS also have an approximately 20% risk of developing ovarian cancer, while families with PJS are at increased risk of breast, uterine, and lung cancers.

Mutations in the CDKN2A gene, meanwhile, are associated with familial atypical multiple mole melanoma and pancreatic cancer (FAMMM-PC), and are linked to a 17% lifetime risk of developing pancreatic cancer. People with CDKN2A mutations also have a nearly 70% risk of melanoma during their lifetime. Finally, mutations in the BRCA1 or BRCA2 genes are seen in individuals with hereditary breast and ovarian cancer (HBOC) syndrome. Those with the BRCA2 gene are 10 times more likely to develop pancreatic cancer than individuals without this gene. One study also has reported a small increased risk of pancreatic cancer in families with BRCA1 gene mutations.

In addition to comprehensive counseling regarding the patient’s family medical history, Ms. Carlson assesses whether patients are comfortable with the idea of genetic testing and are equipped with the knowledge that will help them cope, should they be carriers of a pancreatic cancer gene. To do so, she discusses the syndrome as well as the benefits and drawbacks of genetic testing with patients. She explains what it might mean if the patient were found to carry a mutation in one of the associated genes, in terms of appropriate surveillance testing, the importance of notifying other at-risk family members, and issues of privacy and confidentiality.

According to Dr. Frucht, enhanced surveillance seems to improve outcomes. Of the approximately 100 patients at NewYork-Presbyterian/Columbia who have been identified as high risk for pancreatic cancer within the past 2 years, none have developed the disease during surveillance. Dr. Frucht believes this outcome reflects the importance of early identification and aggressive surveillance.

Contributing faculty for this article: Harold Frucht, MD; Felice Schnoll-Sussman, MD
Table. Results from the ENACT Trial: Change From Baseline in CDAI
Score Over Time

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<tr>
<th>Week Of Visit</th>
<th>Placebo (N=250)</th>
<th>Natalizumab (N=259)</th>
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<tr>
<td></td>
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<td>Mean</td>
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<tr>
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</tr>
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<td>8</td>
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<td>-65.8</td>
</tr>
<tr>
<td>12</td>
<td>249</td>
<td>-68.3</td>
</tr>
</tbody>
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Note: Last observation carried forward was used to replace the missing data. Also, the data collected at the time points after the failure date (the earliest of early discontinuation, start date of rescue intervention, or onset date of adverse events that led to discontinuation of study drug) were replaced by the last available data before the failure date using last observation carried forward.

CDAI, Crohn’s Disease Activity Index; SD, standard deviation.
Source: Gastroenterology. 2007;132(5):1672-1683

Contributing faculty for this article:
Brian Bosworth, MD; Ellen J. Scherl, MD; Arun Swaminath, MD
According to Dr. Pochapin, the use of NBI has become the standard of care at the Hospital for all GI procedures. Brian Bosworth, MD, for example, is using NBI to detect early dysplastic changes in ulcerative colitis patients at risk for developing colorectal cancer. The ability to screen for dysplasia using NBI is “a quantum leap above standard endoscopy and microscopy,” Dr. Bosworth said. “It allows us to quickly and efficiently image the mucosa.”

He pointed to 2 studies presented at the 2008 Digestive Diseases Week (Rastogi et al; Abstract 1163) showing that NBI increases the detection of more lesions with dysplasia than white light endoscopy does. Regarding the diagnostic advantage NBI confers on Barrett’s esophagus–related endoscopic examinations, Dr. Bosworth agreed that “this means we can do fewer biopsies on normal tissue, and focus on only the areas that raise suspicion.”

Low-grade dysplasia is not visible under white light endoscopy, but is clearly seen under NBI, Dr. Bosworth emphasized. Furthermore, NBI requires approximately half the time of chromoendoscopy. As it has transformed the management of Barrett’s esophagus–related lesions, patients with noncirrumscribed lesions without defined borders still undergo colectomy.

“We are building a robust database of our colitis patients with dysplasia in an effort to identify endoscopic, pathologic, and serologic markers that may help us predict who will develop dysplasia,” said Dr. Bosworth, who is co-investigator on this study with senior researcher Ellen Scherl, MD. “The idea is that the risk for colorectal cancer if these lesions are removed early and completely may be no higher among our colitis patients than among any other individuals.”

In addition to the NBI scopes, some gastroenterologists at the Hospital are also researching a new technology called the “third eye” retroscope—so named, according to Dr. Pochapin, because “it is a tiny camera in a catheter which goes out the tip of the endoscope and turns back in on itself, almost in the shape of a ‘J.’” Research has shown that even the most astute GI surgeons miss approximately 6% of all GI polyps because they are not visible in standard colonoscopy. This scope’s design characteristic allows surgeons to spot more flat polyps or polyps located behind folds in the colon. Dr. Pochapin’s group plans to lead a study using the device in patients deemed at high risk for colon cancer to determine if the technology will allow for the identification of polypos.

Physicians and surgeons at the Hospital are also using 2 relatively new techniques and/or devices designed to assist in the performance of diagnostic and therapeutic procedures within the bowel. Led by Jeffrey W. Milson, MD, and Richard L. Whelan, MD, the first, carbon dioxide (CO2) insufflation, distends the bowel with CO2 gas, allowing surgeons increased access without the complications associated with standard insufflation (ie, abdominal pain). The second, double-balloon endoscopy, uses a specialized endoscope featuring 2 balloons—the first attached to the distal end of the scope, the second to a transparent tube sliding over the endoscope. When inflated with air, the balloons cling to sections of the small intestine and pleat it over the endoscope, effectively “shortening” it. Shortening of the small intestine over the endoscope enables a comprehensive examination of the entire small intestine, enabling targeted intervention that makes biopsies, injections, and removal and ablation techniques in the small intestine possible, without surgery.

The double-balloon endoscopy device, which received FDA approval in 2004, produces high-quality images and reduces patient discomfort. If a lesion is found in the small intestine that requires surgery, “tattooing” of the region and biopsies for tissue diagnosis by double-balloon endoscopy can also provide important information to help surgeons plan for the appropriate type of surgery, potentially resulting in smaller incisions and less-invasive operations as well as shorter recovery times; however, double-balloon endoscopy often mitigates the need for surgery, according to Peter D. Stevens, MD.

“Double-balloon endoscopy is particularly helpful in patients with celiac disease, lymphoma or other therapeutic challenges,” he noted. “It fits in where intraoperative endoscopy or surgery would have been before.”

Contributing faculty for this article:
Brian Bosworth, MD; Vinita Jacob, MD; Charles Lighthall, MD; Mark B. Pochapin, MD; Ellen J. Scherl, MD; Peter D. Stevens, MD

NewYork-Presbyterian Hospital physicians are using NBI technology to detect early dysplastic changes in ulcerative colitis patients at risk for developing colorectal cancer.
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Important news from the Digestive Diseases Centers of NewYork-Presbyterian Hospital—current research, clinical trials, and advances in the diagnosis and treatment of gastrointestinal, liver, bile duct, pancreatic, and nutritional disorders.

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