

FALL/WINTER 2015

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SAVE THE DATE

Per-oral Endoscopic Myotomy (POEM) and Endoscopic Submucosal Dissection (ESD): Hands-on Course

January 8, 2016
7:30 am to 5 pm
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columbiasurgery.org/events/
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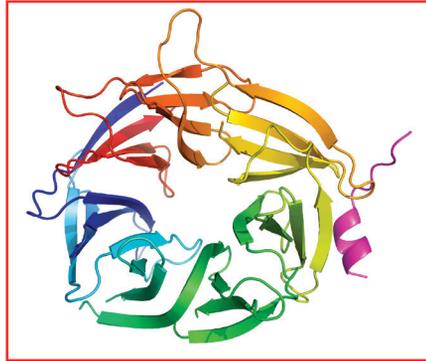
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Pancreatic and Breast Cancers Linked by BRCA Gene Mutation

“A mother in her forties, who has battled and survived breast cancer, is sitting opposite me at the other side of my desk,” says **John A. Chabot, MD**, Chief of the Division of GI/Endocrine Surgery and Executive Director of The Pancreas Center at NewYork-Presbyterian/Columbia University Medical Center. “I am very aware that she believed, or hoped, she was in the clear after a mastectomy and a bilateral oophorectomy. Yet, I find myself discussing with her our approach to the lesion the MRI revealed on her pancreas.”

Many patients know of the association of the



PALB2 WD40 domain in complex with a BRCA2 peptide

BRCA gene mutations with breast and ovarian cancers, and how work in this area has produced effective treatments and sometimes the means of prevention. “But very few patients,” Dr. Chabot says, “have heard that these germline mutations have been linked to several gastrointestinal cancers, including pancreatic ductal adenocarcinoma [PDAC]. For men and women who carry the *BRCA* mutations, there

is about a three- to four-fold higher risk for pancreatic cancer. Unfortunately, choices for treatment for the PDAC patient are very limited.”

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In MINT Condition: Redefining Gastrointestinal Surgery

For his terminally ill colon cancer patient in October 2014, **Jeffrey W. Milsom, MD**, Chief of Colon and Rectal Surgery and Executive Director of the Center for Advanced Digestive Care at NewYork-Presbyterian/Weill Cornell Medical Center, implanted the first bioabsorbable stent in a GI tract in North America to relieve a bowel obstruction. “I obtained the stent through the FDA’s Compassionate Use Program,” says Dr. Milsom. And for the placing of the stent, due to a second innovation developed at Weill Cornell in the Minimally Invasive New Technologies (MINT) program, there was no incision required at all. No cutting. No surgery.

“Instead of our patient undergoing an operation he would not have survived, we were able to relieve his intestinal obstruction in a novel manner,” says Dr. Milsom. “We were able to help him live more comfortably, and we improved his quality of life.” Dr. Milsom believes these important breakthroughs require a pool of talent such as is present in the MINT program at Weill Cornell Medicine and NewYork-Presbyterian Hospital. In a sense, while

“If we are going to drastically lower the cost and the morbidity of surgical procedures and improve outcomes that’s going to take innovation.”

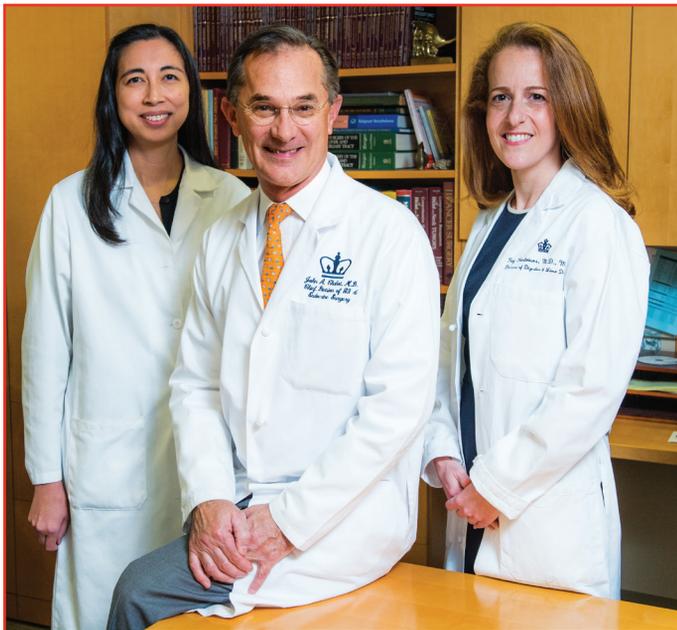
— Dr. Jeffrey W. Milsom

Dr. Milsom and his team are reimagining gastrointestinal care, they are also changing the nature of the interdisciplinary team.

“In our MINT program, we have surgeons, gastroenterologists, pharmacologists, engineers, MBAs, social workers, imaging specialists, lawyers, and students from Cornell University and other medical schools,” notes Dr. Milsom. “We have a Fulbright surgical fellow who came here to study from England and is now completing his training in New York. Each of the members of this multidisciplinary team is working on innovations that will help us define a new era in gastrointestinal care.”

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Pancreatic and Breast Cancers Linked by *BRCA* Gene Mutation (continued from page 1)



Dr. Katherine D. Crew, Dr. John A. Chabot, and Dr. Fay Kastrinos

The *BRCA* Connection

According to Dr. Chabot, the discovery of the connection between the *BRCA1* and *BRCA2* mutations as a predisposing factor for PDAC grew out of a set of associations. “We started to ask the question, ‘Could people have any predisposing conditions for pancreatic cancer?’ We had already established a high-risk program focused on identifying other family members of the patient who might be at risk or have pancreatic cancer. We then wanted to see if we could determine a more complete cancer risk assessment for the other members of the patient’s family. So we decided to take this to its furthest step to see if we could figure out the mutations that predispose a particular family.”

The presence of the *BRCA* gene mutations has calculable genetic risk factors for breast cancer. About 1 in 400 individuals in the general population may test positive for a mutation in the *BRCA1* and *BRCA2* genes. Mutation in *BRCA1* and *BRCA2* are responsible for about 5 to 10 percent of all breast cancers, and for approximately 50 percent of all hereditary breast cancers. Additionally, 8 percent of all women in the general population will develop breast cancer by age 70; whereas 66 percent of *BRCA* positive women will manifest the disease. Approximately 1 percent of the general population will develop ovarian cancer by age 70; but 31 percent of *BRCA* positive women will, by age 70, develop ovarian cancer.

Additionally, certain populations are more likely to carry mutations of the *BRCA* genes. Individuals with Ashkenazi Jewish ancestry have a significantly higher risk than the general population – about 1 in 40. *BRCA* gene mutations are also more common in Norwegian, Dutch, and Icelandic populations.

Research conducted by faculty at The Pancreas Center published in 2014 found that approximately 10 percent of pancreatic cancers seen in The Pancreas Center are associated with breast and ovarian cancer syndromes caused by *BRCA1* and *BRCA2* mutations. Other researchers have found the link between pancreatic cancer and *BRCA2* mutations to be as high as 19 percent.

Why Genetic Testing?

“The patient who is identified as *BRCA* positive when diagnosed with pancreatic cancer should be screened for ovarian and breast cancer and vice versa,” says Dr. Chabot. “We need to manage the patient’s care, but also advise the patient’s family members and encourage them to be evaluated. If a family member is identified with a *BRCA1* and/or *BRCA2* gene mutation, there are implications for treatment. For example, early screening for pancreatic cancer may be recommended when certain risk factors, particularly positive genetic associations, are present. Early screening can lead to early diagnosis of pancreatic cancer at a stage when it is most treatable. If a specific gene is identified, it is generally accepted that screening with an MRI or endoscopic ultrasound should begin at an age of 10 years younger than the youngest family member affected.”

In addition, pancreatic tumors have increased susceptibility to certain chemotherapies. “Identifying someone with pancreatic cancer with these gene mutations may guide the type of chemotherapy recommended,” adds Dr. Chabot. “Our patients have had improved responses to individually tailored therapy regimens based on genetic testing.”

“We recommend that patients who have pancreatic cancer and are identified as *BRCA* positive should also be screened for ovarian and breast cancer and vice versa.”

— Dr. John A. Chabot

Fay Kastrinos, MD, a gastroenterologist in the Division of Digestive and Liver Diseases, NewYork-Presbyterian/Columbia, works with families who are at a high risk for almost all of the inherited gastrointestinal cancers. “Pancreatic cancer can be associated with multiple familial cancer syndromes. The connection and risk of pancreatic cancer may be with cancer syndromes involving breast, ovarian, and colorectal cancers, as well as melanoma. The connections can be very broad,” Dr. Kastrinos says. “And now, because genetic testing has expanded to where we can simultaneously test multiple genes associated with cancer, we have more information beyond family history alone to define at-risk families.”

The advances in gene discovery and the increase in speed in performing genetic testing has lowered costs and broadened the number and variety of genes being examined. It has, furthermore, created an ever-deepening pool of information and exciting developments in understanding the genetic predisposition to multiple malignancies.

“A lot of information is continually becoming available,” notes Dr. Kastrinos, underscoring how quickly technology is changing the knowledge related to the inherited predisposition of certain cancers. “What is important to achieve in a high-risk cancer genetics and prevention program is identifying which genes are important to consider testing for, interpreting the results of testing, and the associated risks of cancer, and concluding which results are clinically actionable and meaningful, where options for screening for cancer prevention can be considered. How are we going to translate this better understanding into what we recommend for patients who are diagnosed with cancer, but also extend this to the at-risk family members, many of whom are yet to be affected by cancer?”

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Pancreatic and Breast Cancers Linked by *BRCA* Gene Mutation (continued from page 2)

“What is important to achieve in a high risk program is defining what is clinically actionable and meaningful. How are we going to translate this better understanding into what we recommend for patients who are diagnosed with cancer, but also for the at-risk family members?”

— Dr. Fay Kastrinos

While these questions seem to be better addressed for breast and colorectal cancer, it is intensely poignant for the pancreatic cancer patient identified to carry an inherited cancer gene, such as *BRCA*, or a family member who is predisposed for it.”

Dr. Kastrinos stresses the necessity for a comprehensive multidisciplinary approach to taking care of patients and families with these gene mutations. It involves a team of oncologists, surgeons, pathologists, radiologists, gastroenterologists, and genetic counselors, and the approach to each patient and family is personalized. “In our program, we hone in on each individual and the details related to their personal cancer and also that in his or her family,” she says. “Cascade testing is performed to expand genetic risk assessment to family members and gives us the ability to prevent cancer before it develops.” Each time there is a new development, Dr. Kastrinos and her colleagues bring any actionable advances to the families.

The developments in early treatment and targeted therapies for colorectal cancers are far clearer than for pancreatic cancer. For pancreatic cancer the picture is still complex. The options for surgery are greatly reduced, and there are few opportunities for examining the specific tumor, as in colon or breast surgeries. Early detection remains the best defense.

“For example,” says Dr. Kastrinos, “in colorectal cancer we can actually look at the tumor and do DNA testing, and different stains of the tumor can give us some insight as to what’s happening on a genetic basis. The results from tumor studies can guide our decision-making related to genetic testing. With pancreatic cancer we have to rely more heavily on the family history and the presence, or absence, of multiple cancers. When looking at the family history of those who come in with pancreatic cancer, we have been surprised to find previously unseen connections – pancreatic cancer related to breast-ovarian cancer syndrome, melanoma, or related to a colon cancer familial syndrome. Not every physician is going to know all of the different clinical criteria associated with familial cancer syndromes that will drive when genetic testing should be considered.”

The optimum step for the family with a history of pancreatic cancer is a referral for a genetics evaluation. “These families need specialized attention, which includes genetic referral and evaluation,” advises Dr. Kastrinos. “Here at Columbia, our families receive counseling pre-testing and post-testing, which is very important for appropriate and timely follow-up. The evaluation is comprehensive from whom should have genetic testing, how do we interpret the results, and how do the results guide the care and clinical management of our patients and families.”

Both Drs. Chabot and Kastrinos are extremely sensitive to the issues involved in genetic testing for the patient and their family members. “We generally recommend to the patient that they deal with the cancer that they’re facing first,” says Dr. Chabot. “After they

recover, we then focus on prevention for the other organs that could potentially be involved, as well as testing of family members.”

Drs. Chabot and Kastrinos are in regular communication with their breast cancer colleagues at NewYork-Presbyterian/Columbia. Among them is **Katherine D. Crew, MD, MS**, a medical oncologist in the Division of Hematology/Oncology at NewYork-Presbyterian/Columbia.

“In our clinical breast cancer prevention program, we counsel women who may be at high-risk for developing breast cancer,” says Dr. Crew. “Those who test positive for a *BRCA* mutation will be followed in our high-risk prevention program so that we can counsel them on the potential for risk-reducing surgery, medical management, and intensive screening. In this program it becomes much more about comprehensive care working together with the geneticist, the surgeon, our social workers, and our psychiatrists. This is not only for the patient, but also for their family members as well in terms of discussing options that are available for them to help manage their cancer risk.”

“In light of what we now know for both men and women who carry the *BRCA* mutations and the link to pancreatic cancer prompts us to refer patients to Dr. Chabot’s Pancreas Center and Fay Kastrinos’ program.”

— Dr. Katherine D. Crew

Dr. Crew points out that it is much more difficult to elicit a family history for abdominal, ovarian, and pancreatic cancer. “People can usually remember if a woman had a mastectomy or some sort of breast surgery, which we can assume could have been breast cancer. But for cancers that present in the abdomen with very late stage disease, you can’t pinpoint where that cancer started and whether it was in the ovaries, pancreas, stomach, or elsewhere in the body,” says Dr. Crew. “In light of what we now know for both men and women who carry the *BRCA* mutations and the link to pancreatic cancer prompts us to refer patients to Dr. Chabot’s Pancreas Center and Fay Kastrinos’ program.”

“We see hundreds of people from this region who are carrying *BRCA* gene mutations, and we employ a truly interdisciplinary team, which personalizes and creates targeted treatment or prevention if possible,” says Dr. Chabot. “As we discover these unforeseen connections, such as the link among breast, ovarian, and pancreatic cancers, we can continue to develop and offer effective clinical protocols and remain hopeful.”

Reference Article

Lucas AL, Frado LE, Hwang C, Kumar S, Khanna LG, Levinson EJ, Chabot JA, Chung WK, Frucht H. *BRCA1* and *BRCA2* germline mutations are frequently demonstrated in both high-risk pancreatic cancer screening and pancreatic cancer cohorts. *Cancer*. 2014 Jul 1; 120(13):1960-67.

For More Information

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In MINT Condition: Redefining Gastrointestinal Surgery *(continued from page 1)*

Device Development

A major turning point in this quest began with the development of CELS – combined endo-laparoscopic surgery – one of a series of procedures under study in the MINT program in 2013. At that time, Dr. Milsom, Sang W. Lee, MD, and their colleagues at Weill Cornell reported on their review of the long-term outcomes of patients undergoing CELS for large benign colon polyps that were unsuitable for endoscopic removal. They found the CELS procedure to be a safe and effective alternative to colectomy for treatment of benign polyps not removable with colonoscopy alone. They followed this up with a publication on alternate procedures, drawing the same conclusion.

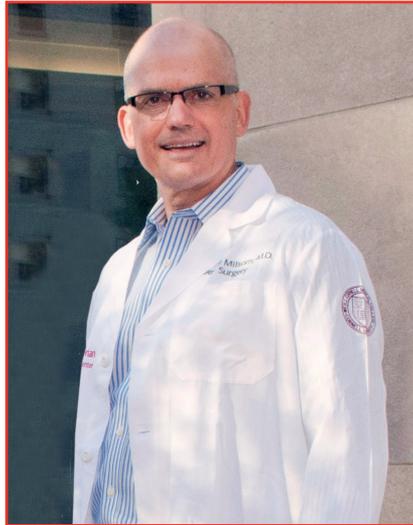
At that time, Dr. Milsom said their ultimate goal was to evolve better procedures that would render CELS obsolete. “Scope instability within the intestine prevents clinicians from using endoscopes as true surgical tools,” he said. The MINT team was already several steps ahead, developing an adjunct device to current endoscopes that enables clinicians to create an isolated, stable, and manipulable zone to enhance visualization and therapeutic capability of the scope.

Just two years later, the surgical platform prototype they developed to make the endoscope, in essence, a surgical tool, is now on its way to becoming a commercial product. The Endolumenal Surgical Platform (ESP) is under development through a new startup company called Lumendi, in partnership with entrepreneurs and investors. ESP fits over a standard endoscope like a sleeve and is disposable. Utilizing the two balloons with one that extends from the end of the device, the clinician can move within the channel of the intestine with unprecedented visualization and control while controlling the surgical environment.

The ESP’s visual enhancement is also a remarkable step forward. “If you’re working through a two-meter-long scope, you don’t have the tools that can reach all over the area of the disease,” explains Dr. Milsom. “You have to work in a limited field. We’ve made this device so that you can effectively move the field back and forth, thus work on the disease in a way that’s currently not possible.”

The ability to maneuver the field more precisely within the intestine will allow for more complex procedures to be performed endolumenally, without necessitating open or laparoscopic surgery, thereby dramatically lessening trauma for the patient, considerably shortening recovery, and greatly reducing costs. ESP has been designed to allow clinicians to remove large polyps, and in the future it will be able to treat early cancers, Crohn’s strictures, diverticulitis, serious other lesions or fistulas, and other complicated problems that affect the intestines.

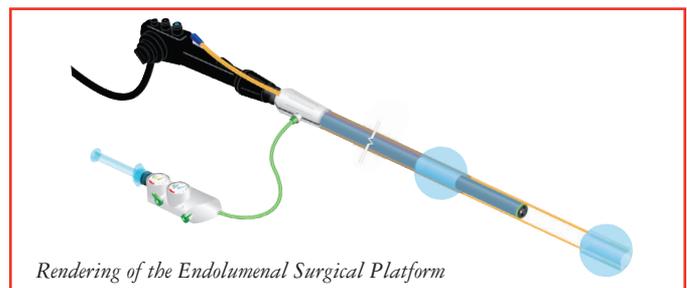
“You can liken this to the profound transformation in the care of cardiac patients when treatment for blocked arteries evolved from coronary artery bypass surgery to an outpatient procedure with angioplasty,” says Dr. Milsom. “We are at the dawning of a similar revolution in the care of GI patients.”



Dr. Jeffrey W. Milsom

Material Gains

In addition to targeting devices and imaging technology for innovation, MINT is also highly focused on capitalizing on the use of new biomaterials. “Our goal is to develop and apply new biomaterials, such as substances that can be injected or placed inside the body, to allow intestinal diseases to be treated in a new and dramatic way,” says Dr. Milsom. “We are now working to develop stents that could function to alleviate a blockage and then be absorbed by the body. For example, in Crohn’s disease, strictures or fistulas would be treated with a bioabsorbable stent that will dissolve. Current commercially available stents are made of a hard metal and can only be used under very limited circumstances, for example, with very sick cancer patients in whom you are trying to relieve a blockage prior to undergoing surgery. These current stents, when left in the body for an extended time, will erode through the wall of the intestine.”



Rendering of the Endolumenal Surgical Platform

The mission of Dr. Milsom and MINT is very clear. “We are now moving forward with a program that is going to minimize trauma for patients and allow them to have outpatient rather than inpatient treatment,” says Dr. Milsom. “Care will also be much safer and provided at a fraction of the cost. With new technologies, we believe in the possibilities...of being able to say, ‘When surgery is needed, you don’t have to cut out a piece of the intestine to cure an intestinal disease.’”

Recently, when asked by *AARP Magazine* as one of 11 doctors from around the country representing divergent specialties what he would do to improve the American health care system, Dr. Milsom suggested, “We need to continue to draw in extremely talented people from all over the world. If we are going to drastically lower the cost and the morbidity of surgical procedures and improve outcomes – which I think we can do in my lifetime – that’s going to take innovation.”

Reference Article

Nakajima K, Sharma SK, Lee SW, Milsom JW. Avoiding colorectal resection for polyps: is CELS the best method? *Surgical Endoscopy*. 2015 Jun 20. [Epub ahead of print]

For More Information

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The Center for Liver Disease and Transplantation Expands Program to NewYork-Presbyterian/Weill Cornell

The Center for Liver Disease and Transplantation (CLDT) at NewYork-Presbyterian Hospital recently has expanded its liver transplantation program to NewYork-Presbyterian/Weill Cornell Medical Center. Like its counterpart at NewYork-Presbyterian/Columbia University Medical Center, the Weill Cornell program brings together an outstanding team of hepatologists and transplant surgeons whose experience and expertise provide exceptional outcomes for patients.



Dr. Robert S. Brown, Jr.



Dr. Benjamin Samstein

The Center for Liver Disease and Transplantation at NewYork-Presbyterian/Weill Cornell is led by **Robert S. Brown, Jr., MD, MPH**, Interim Chief, Gastroenterology and Hepatology, and the Center’s Medical Director, and **Benjamin Samstein, MD**, Chief, Liver Transplantation and Hepatobiliary Surgery, and Surgical Director, The Center for Liver Disease and Transplantation.

“The Center is a full-service program for patients with liver disease that provides multidisciplinary, patient-focused care with seamless integration of hepatology, surgery, oncology, and radiology,” says Dr. Brown, an internationally known expert in liver disease and liver transplantation and a leading researcher on the clinical and cost outcomes of liver disease.

“Our program offers innovative and advanced technical procedures that lead to some of the best outcomes in the region,” says Dr. Samstein, a nationally recognized expert in living donor liver transplantation and laparoscopic liver surgery. Dr. Samstein specializes in advanced laparoscopic procedures for liver cancer, benign liver tumors, and hepatobiliary and pancreas disease, with additional expertise in hepatic adenoma, hepatic hemangioma, cholangiocarcinoma, colorectal metastasis, live donor nephrectomy,

laparoscopic living donor nephrectomy, and pediatric liver and organ transplant.

Other specialists in The Center for Liver Disease and Transplantation at Weill Cornell include:

- **Karim Halazun, MD**, a liver transplant and hepatobiliary surgeon whose main areas of expertise are in the surgical treatment of hepatic and pancreatic malignancies, namely HCC, cholangiocarcinoma, and colorectal liver metastasis
- **Arun B. Jesudian, MD**, a transplant hepatologist who specializes in the medical management of all types of liver disease, including viral hepatitis B and C, alcoholic and nonalcoholic fatty liver disease, autoimmune liver disease, inherited and metabolic liver disorders, cirrhosis, and hepatocellular carcinoma
- **Catherine Lucero, MD**, a hepatologist who specializes in liver diseases, including viral hepatitis B and C, fatty liver disease, autoimmune liver disease, metabolic liver disease, and hepatocellular cancer

Physicians in The Center for Liver Disease and Transplantation collaborate with referring gastroenterologists and hepatologists to facilitate access for their patients to the most current liver disease therapies and surgical approaches, including transplantation, communicating directly with the referring physician throughout the care process.

For More Information

(646) 962-5483 | nyp.org/livertransplant



Dr. Karim Halazun



Dr. Catherine Lucero



Dr. Arun B. Jesudian

Advances in Gastroenterology and GI Surgery

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