Innovations in Therapeutic Endoscopy for Pancreatic Disease: Confocal Laser Endomicroscopy

CLE allows early detection of cancer at the cellular level.

Pancreatic cysts are abnormal fluid-filled growths on or in the pancreas. Although many are benign, some become cancerous. Therefore it is very important that all pancreatic cysts are detected, evaluated, monitored, and if necessary, removed. Until recently, the only way to be vigilant about potentially cancerous cysts was to check on a regular basis (usually every six months to one year) using a form of imaging such as MRI or endoscopic ultrasound.

What if there were a way to know—early on, definitively and easily—whether the cyst should be removed or if it were harmless?

Thanks to confocal laser endomicroscopy, that capability is well on its way to reality. CLE is a laser-powered device that allows doctors to view cells in high definition, much like one would view them under a microscope, but from inside the body. According to Frank Gress, MD, Clinical Division Chief and Chief of Interventional Endoscopy in the Division of Digestive Disease and Liver Disease, “This technology is very exciting because it allows us to detect early...”

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Heart Safety for Breast Cancer Patients
Innovative approaches limit the radiation-related risk for developing heart disease.

A growing body of evidence has been demonstrating that certain women undergoing radiation therapy for early-stage breast cancer may have an elevated risk of developing cardiovascular disease. In a study published in *JAMA Internal Medicine* in October 2013, NewYork-Presbyterian/Columbia University Medical Center researcher David J. Brenner, PhD, DSc and colleagues published their findings that certain treatment factors increased the risk of heart attack and ischemic heart disease.

In their study, Dr. Brenner’s team analyzed the effect of four factors:
- Radiation dose – The amount of radiation absorbed by the body during treatment.
- Baseline cardiac risk – Whether the patient had existing cardiac risk factors, such as elevated cholesterol levels or high blood pressure.
- Treatment side – Whether treatment was performed on the left or right side.
- Body position – Whether the patient was in a supine or prone position during treatment.

The data revealed that women who had left-sided radiotherapy in a supine position had the highest measured cardiac dose.

“Because the effects of radiation exposure on cardiac disease risk seem to be multiplicative, the highest radiation exposure risks correspond to the highest baseline cardiac risk,” wrote Dr. Brenner in the study. That means that women who already have several underlying cardiac risk factors such as smoking, high cholesterol or high blood pressure, need more careful treatment.

Daniel S. O’Connor, MD, PhD, Assistant Professor of Clinical Medicine and Co-director of the Center for CardioOncology, emphasizes the need to treat underlying cardiac risk factors in patients undergoing radiation therapy.

“Cardiovascular health is an important component of long-term breast cancer survivorship. The current successes of early detection, early treatment and high cure rates have changed the patient-physician discussion about the prognosis of breast cancer. Results from Dr. Brenner’s study add to the framework of this discussion, including aggressive treatment of high blood pressure, high cholesterol, and smoking cessation to ensure long-term cardiovascular health to breast cancer survivors.”

**Advances in reducing cardiovascular risk during breast cancer treatment**

Breast cancer patients should also be aware of the advances made in radiation oncology during the last decade. At NewYork-Presbyterian/Columbia, numerous strategies have been instituted to minimize cardiovascular effects from breast cancer treatments. “We’ve made some important advances since Dr. Brenner’s study began in 2005,” says K.S. Clifford Chao, MD, Chair, Department of Radiation Oncology at NewYork-Presbyterian/Columbia.

Today patients at NewYork-Presbyterian/Columbia have access to innovative approaches which limit the radiation-related risk for developing heart disease, including:

- During radiation therapy, a patient can lie on her stomach with her breast suspended downward. Therapy is then targeted at the affected area with no beams directed toward the heart.
- With newer, more sophisticated imaging systems, radiation oncologists can now adjust for variations in the patient’s anatomy, tumor size, weight, and internal motion, as well as changes in tumor biology and function. This approach, called Adaptive Radiotherapy (ART), enables physicians to create a highly personalized treatment plan for every patient, while also limiting the amount of radiation exposure within the treatment field.
- A novel imaging technology called CTVision also helps to reduce radiation to critical body structures. The CT scanner pivots around the patient, taking a series of pictures that pinpoint the exact location to receive radiation therapy.
- Partial breast irradiation allows physicians to hone in on the actual field of cancer, delivering a larger dose directly to the affected site.
- A technique called hypofractionation allows physicians to give patients higher doses of radiation in fewer treatments, thereby limiting the number of exposures.

**Intraoperative Radiation Therapy**

Partial breast irradiation allows physicians to hone in on the actual field of cancer, delivering a larger dose directly to the affected site.

For more information about advances in treating Breast Cancer, please visit breastmd.org.
Patients with certain “orphan” or rare diseases face the unfortunate reality that research dollars and interest toward their disease are limited, which translates into stagnated progress in finding better treatments. But for children with lymphatic malformations (LMs), there is now good reason for hope. Thanks to a recent serendipitous discovery, an exciting treatment option is now available, and physicians are eagerly forging ahead with a promising new avenue of research.

Lymphatic malformations, or LMs, which are a form of vascular anomaly, are abnormally formed lymphatic vessels that can occur anywhere on the body. They may be localized or widespread. Localized LMs manifest as collections of abnormal swelling or cystic masses that contain clear lymphatic fluid; others are more diffuse and can cause lymphedema (swelling) of a limb or another part of the body. Some LMs affect the skin, while others can affect essential internal organs such as the respiratory system and intestinal tract. All LM patients are at risk of infection or bleeding and experience significant pain and discomfort. LMs involving the skin can drain or leak lymphatic fluid, while deeper LMs can cause overgrowth of affected structures, resulting in disfigurement and functional impairments. As June K. Wu, MD, Assistant Professor of Surgery, Division of Plastic and Reconstructive Surgery and Co-director of the Vascular Anomalies Group explains, children may suffer badly with these disfiguring and debilitating symptoms; some are even bed-bound due to pain and constant drainage from their skin.

Difficult to identify

Moreover, many suffer the compounded misfortune of misdiagnosis because of the complexity and variation among different LM clinical presentations. These conditions are sometimes complicated by the presence of additional arterial or venous disease (or both), in what is called mixed malformations. LMs can also be part of many different conditions such as Gorham Stout disease, which affects the bone, or Klippel-Trenaunay syndrome, which causes severe lymphedema of the affected extremity. In short, they can be very challenging to properly identify.

Difficult to treat

Because the lymphatic system extends throughout the body, LMs may not have well-defined borders, but rather infiltrate tissue planes. It may therefore be very difficult or impossible to surgically remove many vascular malformations, according to Angela Kadenhe-Chiweshe, MD, Assistant Professor of Surgery and the primary pediatric surgeon in the Vascular Anomalies Group. Sometimes sclerotherapy (injection of medicine that destroys the abnormal cells lining the lymphatic vessels in an attempt to collapse these channels) can be used to treat a finite area, but the malformed vessels often grow back after sclerotherapy or surgery. The chemotherapy agent rapamycin has been used to treat lymphatic malformations, but its immune-suppressing effects can be too dangerous for patients to tolerate. See a related story on vascular malformations in the Winter 2012 issue of healthpoints, at www.columbiasurgery.org/news/healthpoints/2012_winter/p2.html
children, especially those who are already losing immune-rich lymph fluid, according to Dr. Kadenhe-Chiweshe. As she explains, “LMs are difficult to treat and there is no real cure. The goals of our therapies are to reduce the risk of these lesions to our patients and allow them to live functional lives.”

**Breakthrough discovery**

Thanks to an unexpected observation by Dr. Wu and Carrie Shawber, PhD, a developmental biologist in the Department of Obstetrics and Gynecology, it was discovered that cells they isolated from LMs were sensitive to a common blood pressure medication called propranolol. In the laboratory setting, propranolol caused rapid death of these LM cells.

“Having observed the effects of propranolol on these LM cells, we began testing it in select patients beginning in 2012,” explains Dr. Wu. “Over 70% of our patients had some positive response, meaning that swelling, pain, or other symptoms improved.” In one case, a ten-year old boy had long been bed-bound; he was so sick that he had to have monthly blood transfusions because of continuous leakage through the skin of his buttocks. He suffered life-threatening sepsis, requiring multiple stays in the Intensive Care Unit. But after two weeks on propranolol, he was out of bed and walking on his own, says Dr. Wu. “He is not cured, and he still has residual LMs, but he is so much better.”

Developed in the 1960s to treat hypertension (high blood pressure), propranolol is an extremely well-studied beta blocker, so its safety profile is well known. Propranolol has been an accepted treatment for problematic hemangioma, a common vascular tumor, since 2008.

**Research and testing**

The doctors at the Vascular Anomalies group are optimistic and eagerly beginning the process of learning how propranolol may help children with LMs. Based on the positive responses they have observed, Drs. Wu and Shawber are developing clinical studies to systematically study the mechanisms of the drug and how it may be integrated into their standard armamentarium in treating LMs. They are also screening additional medicines that have the potential to work as well or even better.

Although the team has not yet fully identified the mechanism by which the drug acts to improve symptoms, its ability to reduce or eliminate patients’ LM symptoms represents an encouraging glimmer of hope. Animal studies to date suggest that propranolol may reduce abnormal lymphatic vascular development associated with LMs, although research is needed to confirm that hypothesis.

According to Dr. Kadenhe-Chiweshe, “The way to optimize a treatment is to understand how it works, how to dose it, to establish safe doses, and perhaps even to know who will benefit most from it. Drs. Wu and Shawber are doing a fantastic job of systematically studying the effect of propranolol on lymphatic tissue.” Dr. Wu cites the importance of having basic scientists working hand in hand with expert subspecialists in every field needed to effectively care for patients with these complex conditions. “Our goal is to continue to grow our multidisciplinary center to treat children with lymphatic malformations,” she says.

The treatment of lymphatic malformations requires collaboration among multiple specialists. At NewYork-Presbyterian/Columbia, the Vascular Anomalies group includes specialists from pediatric dermatology, pediatric surgery, pediatric plastic surgery, interventional radiology, genetics, neurology, and pediatric orthopedics who work together as a team to care for each patient.
cancer and changes suggestive of early cancer such as dysplasia at the cellular level.” Physicians at NewYork-Presbyterian/ Columbia University Medical Center already use CLE in patients with Barrett’s Esophagus, and it is used elsewhere for gastric lesions (to check for stomach cancer) and in the colon to evaluate polyps.

At the Pancreas Center, Dr. Gress and colleagues may insert CLE through an endoscope in order to view abnormal tissue in the bile duct or pancreatic duct lining. They may also use CLE during endoscopic ultrasound (EUS) to determine whether pancreatic cysts warrant further treatment or not.

According to Dr. Gress, the ability to characterize cells with CLE is “a game changer” in the management of challenging conditions such as chronic pancreatitis, pancreatic cysts, pancreatic and bile duct strictures, and intraductal papillary mucinous neoplasm (IPMN, an early form of pancreatic cancer). “Until now, we have not had an endoscopic tool that could provide such fine detailed information about a pancreatic or bile duct stricture, or to know whether a pancreatic cyst is benign or malignant,” he explains.

Optical biopsies
CLE may be placed on a probe (probe-based CLE, or pCLE) and used to perform what is called an optical biopsy to determine whether cells are malignant or not by looking at them rather than extracting samples of tissue. It is also very helpful for targeting specific areas to biopsy. Some studies suggest that it may eventually replace the need for biopsies, although physicians at the Pancreas Center are still taking tissue biopsies and using CLE to validate their findings.

Researching CLE and its applications
To gain experience with CLE and to independently verify the positive outcomes that others have experienced with pCLE, Dr. Gress and his colleagues are collecting patient data and comparing that data to the images collected during probe-based CLE procedures. The team is also investigating the use of EUS-guided fine needle aspiration (FNA) CLE, also known as nCLE, in patients with pancreatic cysts. This work is part of a multicenter study in which the doctors insert an EUS needle into the pancreatic cyst, put the CLE probe through the needle, and examine the cells lining the walls of cysts. According to Dr. Gress, “We are hoping that nCLE will be able to provide high detailed and accurate characterization of pancreatic cysts such that pancreatic cysts can be more accurately differentiated into benign and malignant cysts.”

For more information about advances in treating pancreatic disease, please visit pancreasmd.org.

Frank Gress, MD
Clinical Division Chief and Chief of Interventional Endoscopy in the Division of Digestive Disease and Liver Disease
An expert in therapeutic endoscopy, he specializes in performing minimally invasive procedures to diagnose and treat disorders of the gastrointestinal tract, bile ducts, and pancreas.
New Faculty
Meet the newest physicians and surgeons in the Department of Surgery.

Paul Kurlansky, MD
Assistant Professor of Clinical Surgery, NewYork-Presbyterian/ Columbia University Medical Center
Director of Research, Recruitment and Continuous Quality Improvement, Columbia HeartSource

Paul Kurlansky, MD, returns to the home of his post-graduate training for a dual role at Columbia HeartSource and the Center for Innovations and Outcomes Research (CIOR).

While serving as Director of Research at the Florida Heart Research Institute in Miami during the last decade, Dr. Kurlansky also began working with the Columbia HeartSource team. He has been instrumental in guiding every HeartSource affiliate site that has a surgical program, and has now relocated to New York to be full-time Director of Research, Recruitment and Continuous Quality Improvement for the program.

In his role at CIOR, Dr. Kurlansky looks forward to helping NewYork-Presbyterian/Columbia surgeons to increase and improve the quality of their clinical and translational research.

Koji Takeda, MD, PhD
Assistant Professor of Surgery, Columbia University Medical Center
Assistant Attending Surgeon, NewYork-Presbyterian

The Section of Cardiac Surgery warmly welcomes Koji Takeda, MD, PhD, as a faculty member in the Section of Cardiac Surgery as of January 1, 2014. Dr. Takeda has been a fellow at NewYork-Presbyterian/Columbia specializing in heart failure surgery, LVAD implantation, and heart transplantation since January 2013. As a dual fellow and full attending surgeon this year, he will continue to focus on the management of heart failure as part of his transition toward leadership of these clinical specialties in the Section of Cardiac Surgery. In addition to his clinical practice, Dr. Takeda has research interests in mechanical circulatory support, heart transplantation, and cardiac regeneration therapy.

Dr. Takeda completed his medical training, post-graduate training, residency and fellowship in Osaka, Japan, after which he completed an advanced cardiovascular surgery fellowship at Northwestern University, Chicago.

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