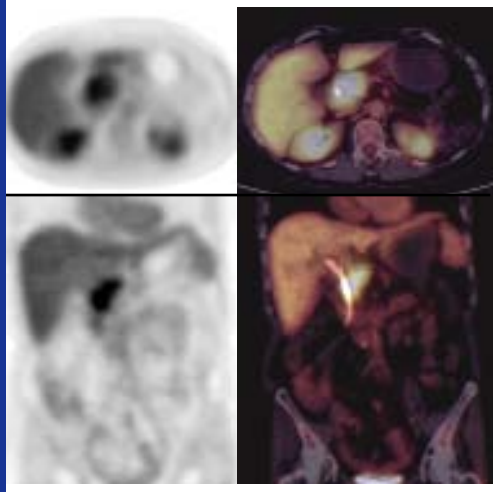
Pet Imaging Guides Treatment for Pancreatic Cancer Patients

Pancreatic cancer is the fourth leading cause of cancer death in the U.S. Each year, approximately 33,000 Americans develop cancer of the pancreas. If it is confined to the pancreas and hasn't spread to surrounding organs or lymph nodes, the cancer can sometimes be cured through surgery. But because it is difficult to diagnose, the disease is frequently undetected in its earliest stage, and has already spread, or metastasized, by the time it is diagnosed. Once pancreatic cancer has spread to the liver, median survival for patients is five to six months. At NewYork-Presbyterian/Columbia, new treatments developed in the laboratory have doubled this survival period in initial studies.

The Columbia University Pancreas Center, nationally known for its superior surgical procedures, innovative chemotherapy treatment, and pioneering prevention program, routinely relies on PET imaging (positron emission tomography), to guide treatment decisions. For tracking pancreatic cancer and its metastases to other organs, say Columbia faculty, PET's sensitivity is often superior to any other type of imaging procedure.

PET FOR POST-CHEMOTHERAPY EVALUATION

Columbia's **Robert Fine, MD,** *Herbert Irving Associate Professor of Medicine and Director of the Experimental Therapeutics Program,* is an oncologist who works with the Pancreas Center to treat its patients. Dr. Fine says PET is able to identify changes that are not detectable with CT *(computed tomography)*, the routine imaging method for observing tumors. While CT scans show anatomical structures including tumors, PET visualizes the chemical activity of cells (their metabolism). Cancer cells, which metabolize more sugars than normal cells, appear on a PET scan as bright "hot spots." Dr. Fine says that when chemotherapy has begun to work, the tumor does not physically shrink right away, and improvement cannot therefore be detected by a CT scan. "But PET can detect a response two or three months earlier than a CT scan, by indicating that the tumor's metabolic activity has



Top (cross-sectional view): PET and fused PET/CT show a "hot spot" in the pancreas of a patient with obstructive jaundice. The kidneys also appear as hot spots because of their high metabolic activity, although they are not cancerous. Bottom (frontal view): PET and fused PET/CT show stents placed in the patient's bile ducts (to relieve the obstruction) and the tumor, with no evidence that it has spread beyond the pancreas.

Pancreatic cancer is known to resist chemotherapy, forcing oncologists to use second and third lines of defense. To meet this challenge, Dr. Fine has developed several multiple-drug chemotherapy regimens.

➤ Developed by Dr. Fine's laboratory, the GTX chemotherapy regimen consists of three drugs — Gemzar, Taxatere, and Xeloda — and is currently in Phase II clinical trials. As a first-line therapy for advanced pancreatic cancer, GTX is routinely combined with radiation to shrink tumors so that they are operable. Dr. Fine calls GTX a "smart" regimen because it circumvents mechanisms of drug resistance by specifically inhibiting pathways active in pancreatic cancer. Of all the options available today, GTX has produced the highest response rates (40%) and rates of survival in the U.S. and Europe in early studies.

➤ Dr. Fine's laboratory found that pancreatic cancer cells can become resistant to GTX by activation of specific signaling pathways called MAPK. In response, the team developed a specific sequence of the drugs that inhibits this activation and leads to the death of cancer cells. Clinical studies to date show that approximately 40% of GTX failures can be salvaged by this chemotherapy regimen.

➤ The team has also created and perfected two novel therapies in their laboratory that will enter testing in pancreatic cancer patients in the near future. One is a gene therapy approach which selectively targets cells with mutations that occur in many pancreatic cancers. The other is a peptide that selectively binds to mutated proteins found in pancreatic cancer cells and then restores them back to a normal state, resulting in cell death. If the peptide is delivered endoscopically into the pancreatic duct, where 95% of all pancreatic cancers develop, it may be possible to eradicate pre-malignant pancreatic growths which contain this mutation (approximately 75%). Both novel therapies will be tested in patients with PET and CT scans.

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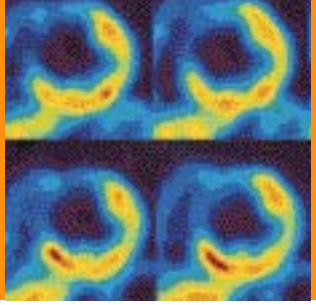

PET scan showing blood-flow in the heart (cardiac perfusion)

been slowed by treatment, or that the tumor is dying or dead." The opposite is true as well, he says. "PET can detect relapse months before it appears on a CT scan."

PET FOR POSTOPERATIVE EVALUATION

Beth Schrope, MD, PhD, *Assistant Professor of Surgery,* who performs pancreatic surgery, also relies on PET in her treatment of pancreatic cancer. For many patients, she uses PET imaging post-operatively to find out if a pancreatic cancer has recurred, or if it has metastasized. "We first follow up surgery with periodic blood testing. If tumor markers are elevated in the tests, we move to imaging, including PET," she says. Any kind of previous surgery leaves behind scar and fibrosis that are difficult to distinguish from cancer with a CT scan, she says. "But unlike cancer, a scar is not metabolically active, so on a PET scan we can tell if it's cancer or not."

Dr. Schrope also uses PET to determine whether to operate or not. The presence of metastasis is a key factor in deciding whether a patient is a candidate for surgery. A dilated bile duct in the liver can look like a metastasis on a CT scan. "A dilated bile duct viewed on a PET scan won't light up, whereas a metastasis in the liver will," she says. If the cancer has metastasized to other organs, surgery is not indicated — surgical resection has not been shown to have a survival benefit under these circumstances. "Pancreas operations are complex, so we really want to make sure there's no metastasis before we operate," she says.

"PET/CT imaging is adding a new dimension to the care and treatment of patients with pancreatic cancer," says **Ronald L. Van Heertum, MD,** *Professor of Radiology and Director, Columbia Kreitchman PET Center.* "We are very pleased with the additional information that this technology offers our patients and physicians."

If you are a physician and would like to refer a patient for an oncology PET scan, please call the Columbia Kreitchman PET Center at 212-923-1555.

If you are a patient and would like to get a PET scan, please discuss a referral with your physician.

A Shorter Cardiac Perfusion Test

A cardiac perfusion test enables the physician to detect coronary artery disease by revealing how well blood flows to the heart. The test is actually two consecutive images: a "rest" image at resting heart rate, and a "stress" image at peak heart rate. While PET is among the most accurate non-invasive techniques for perfusion testing because of its high resolution, it is also the best choice for certain patients:

- It is ideal for obese patients or women with large breasts, because soft tissue does not distort PET images.
- It is the test of choice for patients with certain heart conditions.

With multiple image tests, the *halflife* of the tracer (the drug that is tracked by the scanner) is decisive to the length of the test. For its perfusion scans, the Kreitchman PET Center is now using Rubidium, a tracer with an extremely short halflife—75 seconds. The result is a very quick scan, enabling patients to complete the PET perfusion test in only 30 minutes.

PET IMAGING FOR CANCER: MEDICARE COVERAGE

The good news for patients: through participation in the National Oncologic PET Registry (NOPR), patients can receive Medicare coverage of PET scans for many cancers — including pancreatic cancer — that were not previously covered. With the information obtained through this confidential research study, Medicare will evaluate PET's effectiveness as a part of cancer treatment planning.

Medicare routinely covers PET scans for the following cancers: colorectal, esophageal, head and neck, non small-cell lung, lymphoma, melanoma, and thyroid. As long as the patient's doctor provides a referral for the PET scan, neither the patient nor the physician will need to take any further steps to obtain Medicare coverage.

However, Medicare coverage for a PET scan of a cancer not listed above requires enrollment in the NOPR. Participation in this confidential study requires the patient's physician to fill out and submit two check-box forms. Staff at the Columbia Kreitchman PET Center routinely work with physicians to complete the process of enrolling the patient in NOPR. To read more about the NOPR, go to www.cancerPETregistry.org.

In addition, PET/PET CT is covered by many private insurers, which reimburse for PET on a case-by-case basis. Staff at the Columbia Kreitchman PET Center can work with physicians and patients to verify benefits and submit claims as needed.