PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU
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March 27, 2009

For immediate release:

In this month's edition

Editors note: Research, new techniques and improved facilities by Philadelphia International Medicine hospitals and physicians may lead to new ways to treat some of our most challenging diseases. Below are just some examples from our hospitals.

Fox Chase Surgeon Performs the World's First Successful ViKY® Robot Assisted Surgery to Treat Pancreatic Tumors

Philadelphia – This month Fox Chase Cancer Center performed the world's first successful minimally invasive distal pancreatectomy using the ViKY® system's robotic laparoscope holder. The technology, developed in France and tested on thousands of patients in Europe, made its debut in a cancer setting in the United States at Fox Chase.

"Fox Chase is among only a handful of institutions worldwide using robotics or laparoscopy to treat patients with nearly all types of cancer," says Robert G. Uzzo, MD, FACS, chairman of the department of surgery at Fox Chase. "The use of technology, like the ViKY system, reinforces our hospital's commitment to excellence in minimally invasive surgical techniques for the care of patients with both benign and cancerous conditions."

Fox Chase surgeon Andrew A. Gumbs, MD, who specializes in minimally invasive hepato-pancreatic and biliary (HPB) surgery, explains, "This system is so versatile that surgeons like me are able to use it for many different laparoscopic procedures, including those in the gastrointestinal, urologic, thoracic and gynecologic regions."

Typically with minimally invasive procedures, like a laparoscopic distal pancreatectomy, surgeons use both hands to manipulate the surgical tools and need an assistant to manipulate the endoscope—a thin, lighted tube equipped with a camera that allows the surgeon to view the surgical field. Gumbs performed this first ever ViKY assisted minimally invasive distal pancreatectomy on a 65-year-

old man who was diagnosed with two pancreatic cysts, one of which is potentially cancerous.

Standard treatment for pancreatic cancer is surgery to remove the head or tail of the pancreas. When patients present with pancreatic cancer localized to the tail of the pancreas (instead of the head), they undergo a distal pancreatectomy, in which the surgeon removes the tail of the pancreas and leaves the head attached. The remaining portion can function normally by producing and releasing digestive enzymes and hormones. Patients with pancreatic cancer are typically treated with surgery followed by radiation therapy and/or chemotherapy to reduce the risk of recurrence.

"The new ViKY robotic laparoscope holder acts as an extra hand during surgery, giving me stability and steadiness," said Dr. Gumbs.

The ViKY system gave Dr. Gumbs precise control of the laparoscope while he performed the distal pancreatectomy. The endoscope moves according to the surgeon's orders, either through voice recognition or footswitch control.

Before the ViKY technology was available patients might have undergone open abdominal surgery, which requires a large incision and a lengthy recovery. Minimally invasive surgical techniques, like the surgery Dr. Gumbs performed, benefit patients in many ways, including a shorter hospital stay, faster recovery, quicker return to daily activity, less risk of infection and less scarring and bleeding.

Dr. Gumbs was the first American surgeon to complete a minimally invasive HPB fellowship at the Institut Mutualiste Montsouris in Paris, France. This is the hospital where the first published case of a single incision laparoscopic cholecystectomy in the world was done using the ViKY system. Dr. Gumbs is responsible for bringing the ViKY system to Fox Chase and will be training fellow surgeons on this technology.

Jefferson Research Offers New Diagnostic Tool for Women Suffering from Abnormal Vaginal Bleeding and Severe Uterine and Pelvic Pain

New research from the Department of Radiology at Thomas Jefferson University Hospital suggests sonohysterography (SHG), a simple ultrasound technique commonly used to evaluate the uterine cavity, improves the diagnostic capability of transvaginal ultrasound in detecting adenomyosis (a common benign condition of the uterus that causes dysmenorrhea, abnormal vaginal bleeding and pelvic pain). The study—set to be published in the April issue of the *American Journal of Roentgenology*—reveals an effective method to diagnose adenomyosis; it is a safe alternative to immediate biopsy for women who present with abnormal vaginal bleeding and severe uterine and pelvic pain.

The study included 26 women who underwent sonohysterography and MRI of the pelvis and in whom either modality suggested adenomyosis. Of these 26 women, 23 (88 percent) had SHG findings suggestive of adenomyosis. Three remaining women (12 percent) had adenomyosis identified on MRI

performed after sonohysterography. MRI confirmed adenomyosis in 22/23 patients (96 percent).

"This study describes the presence of ill-defined areas of fluid intravasation extending from the uterine cavity into the myometrium known as fluid containing tracks or so called 'myometrial cracks' on SHG," said Sachit Verma, MD, lead author of the study. "Myometrial cracks have not been described previously as a sign of adenomyosis. The tracks, seen in 26 percent of our cases, become conspicuous as saline seeps through the 'myometrial cracks'. They are difficult to characterize on standard transvaginal ultrasound. This peculiar appearance was seen in one of our patients on MRI as well," said Dr. Verma.

Patients often present with symptoms of abnormal bleeding, pelvic pain and infertility which may be due to a uterine fibroid, a polyp, tumor or adenomyosis. MR imaging is expensive and is not always available as a first line investigation to evaluate abnormal bleeding. In addition it is difficult to distinguish lesions in the uterus (myometrium and endometrium) using transvaginal ultrasound alone. SHG then has a role to play in managing these patients.

"Knowledge of 'myometrial cracks' will decrease the errors in interpretation and improve patient care so that specific treatment can be instituted," he said. "This additional information for the referring physician can possibly decrease the number of endometrial biopsies—reducing costs in patient management—in cases where SHG shows no uterine abnormality and adenomyosis is the sole cause of abnormal bleeding," said Dr. Verma.

Lab-Grown Nerves Promote Nerve Regeneration After Injury, Penn Study Finds

Researchers at the University of Pennsylvania School of Medicine have engineered transplantable living nerve tissue that encourages and guides regeneration in an animal model. Results were published this month in *Tissue Engineering*.

Hundreds of thousands of patients suffer peripheral nerve injuries every year, in many cases resulting in permanent loss of motor function, sensory function, or both. These injuries are a common consequence of trauma or surgery, but there are insufficient means for repair, according to neurosurgeons. In particular, surgeons need improved methods to coax nerve fibers known as axons to regrow across major nerve injuries to reconnect healthy targets, for instance muscle or skin.

"We have created a three-dimensional neural network, a living conduit in culture, which can be transplanted *en masse* to an injury site," explains senior author Douglas H. Smith, MD, professor, Department of Neurosurgery and director of the Center for Brain Injury and Repair at Penn. Dr. Smith and colleagues have successfully grown, transplanted and integrated axon bundles that act as 'jumper cables' to the host tissue in order to bridge a damaged section of nerve."

Previously, Dr. Smith and colleagues have "stretch-grown" axons by placing neurons from rat dorsal root ganglia (clusters of nerves just outside the spinal cord) on nutrient-filled plastic plates. Axons

sprouted from the neurons on each plate and connected with neurons on the other plate. The plates were then slowly pulled apart over a series of days, aided by a precise computer-controlled motor system.

These nerves were elongated to over 1 cm over seven days, after which they were embedded in a protein matrix (with growth factors), rolled into a tube, and then implanted to bridge a section of nerve that was removed in a rat.

"That creates what we call a 'nervous-tissue construct'," says Dr. Smith. "We have designed a cylinder that looks similar to the longitudinal arrangement of the nerve axon bundles before it was damaged. The long bundles of axons span two populations of neurons, and these neurons can have axons growing in two directions —toward each other and into the host tissue at each side.

The constructs were transplanted to bridge an excised segment of the sciatic nerve in rats. Up to 16 weeks post-transplantation, the constructs still had their pre-transplant shape, with surviving transplanted neurons at the extremities of the constructs spanned by tracts of axons.

Remarkably, the host axons appeared to use the transplanted axons as a living scaffold to regenerate across the injury. The authors found host and graft axons intertwined throughout the transplant region, suggesting a new form of axon-mediated axonal regeneration. "Regenerating axons grew across the transplant bridge and became totally intertwined with the transplanted axons," says Smith

Axons throughout the transplant region showed extensive myelination, the fatty layer surrounding axons. What's more, graft neurons had extended axons beyond the margins of the transplanted region, penetrating deep into the host nerve. Remarkably, the constructs survived and integrated without the use of immunosuppressive drugs, challenging the conventional wisdom regarding immune tolerance in the peripheral nervous system.

The researchers suspect that the living nerve-tissue construct encourages the survival of the supporting cells left in the nerve sheath away from the injury site. These are cells that further guide regeneration and provide the overall structure of the nerve.

"This may be a new way to promote nerve regeneration where it may not have been possible before," says co-first author D. Kacy Cullen, PhD, a post doctoral fellow in the Smith lab. "It's a race against time - if nerve regeneration happens too slowly, as may be the case for major injuries, the support cells in the extremities can degenerate, blunting complete repair. Because our living axonal constructs actually grow into the host nerve sheath, they may 'babysit' these support cells to give the host more time to regenerate."

New Jefferson Research Suggests Common Anti-Seizure Medications May Increase Risk of Cardiovascular Problems

An important clinical repercussion in the treatment of epilepsy has been discovered by a research team led by Scott Mintzer, MD, assistant professor in the Department of Neurology at Jefferson Medical College of Thomas Jefferson University. The team has determined that two of the most commonly prescribed anti-seizure medications may lead to significantly increased levels of cholesterol, C-reactive protein and other markers of cardiovascular disease risk. The finding – set to appear in the April issue of Annals *of Neurology* – may help doctors manage the care of patients with seizures more effectively by prescribing different anti-seizure medications that will not adversely affect cardiovascular health.

The study involved two of the most widely-prescribed anticonvulsants – phenytoin (Dilantin®) and carbamazepine (Tegretol®, Carbatrol®) – which have potent effects on many enzymes in the body involved in different areas of metabolism. The researchers recruited 34 epilepsy patients taking either one of those two drugs who were being switched over to one of two newer anti-seizure drugs which do not widely affect enzymes – lamotrigine (Lamictal®) or levetiracetam (Keppra®). The goal was to determine if the change affected the patients' cholesterol levels and other key markers of cardiovascular disease.

Just 6 weeks after the patients' drugs were switched, there were significant declines in total cholesterol, non-high-density lipoprotein (commonly referred to as 'bad') cholesterol, triglycerides and C-reactive protein, suggesting the older, commonly-used drugs might substantially increase the risk of cardiovascular disease.

"The epilepsy patients in this study saw a rapid and clinically significant improvement in several markers related to cardiovascular disease, including a decrease in total cholesterol that averaged 26 points. This is almost certainly not due to some positive effect from the new drugs. It's a consequence of being taken off the older ones, which were causing the cholesterol and other markers to be elevated in the first place," said Dr. Mintzer. "While more investigation is needed, these results may help physicians better understand the risks of these drugs and choose the most appropriate treatment for their epilepsy patients, especially those who are already at risk for cardiovascular disease or have a family history of it."

According to the Epilepsy Foundation, which also funded this study, there are almost three million people living with epilepsy with an additional 200,000 new diagnoses being made each year. Dilantin is the most commonly prescribed anticonvulsant in this country, and has been since its discovery in 1938. Throughout the industrialized world, Tegretol has been the most commonly prescribed anticonvulsant for more than 20 years. The results of this study could have far-reaching effects on how the millions of current, and future patients are, or will be, treated.

Philadelphia International Medicine is an organization that provides medical and patient support services to international patients. It also provides continuing medical education and health care training and education to international physicians, administrators and other practitioners. As the international department of several Philadelphia-area hospitals, international patients gain access to physicians and hospitals rated among the best in the world through one telephone call to PIM. You can reach PIM by calling 1-215-563-4733; fax, 1-215-563-2777; or e-mail, physicians@philadelphiamedicine.com. You can find out more about PIM through its Website at www.philadelphiamedicine.com.