

PHILADELPHIA INTERNATIONAL MEDICINE® NEWS BUREAU

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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.

Jefferson Offers Robotic Assisted Minimally Invasive Esophagectomy

Philadelphia – Thomas Jefferson University Hospital is the first in Philadelphia to offer robotic esophageal mobilization surgery, using the da Vinci® Robotic System. This procedure is ideal for esophageal cancer patients who require surgery to remove all or part of their esophagus. It is a safer alternative to traditional invasive ‘open’ surgery and will allow the patient to recover faster and leave the hospital sooner. It improves on conventional minimally-invasive techniques by decreasing the number of incisions required to perform the procedure.

“It’s exciting to be able to offer this type of procedure to domestic and international patients,” says Benny Weksler, MD, assistant professor, Department of Surgery. “Utilizing this technology not only reduces healing time and hospital stay, it also is significantly less painful, causes less scarring, reduces blood loss and in many cases, provides better clinical outcomes.”

During the procedure, the Jefferson surgeon uses the da Vinci system as part of the minimally invasive esophagectomy. Robotic arms, with tiny cameras, are placed in the patient at the right chest. Four small incisions are used. Once that is complete, the surgeon utilizes the articulated robotics instruments to guide the arms to the esophagus for its removal. The surgeon is then able to completely dissect the thoracic esophagus with four small incisions, allowing it to be successfully separated from the pericardium, the airway, the aorta and the thoracic duct. The procedure takes about two hours to perform.

Prior to this type of minimally invasive surgery, patients would have to undergo the more traditional and painful, open surgery where the surgery is performed through an incision in the right chest, using a rib spreader and occasionally removing a part of a rib. Patients will suffer significant postoperative pain and

many times this will lead to prolonged hospital stay and even complications. The minimally invasive-robotic approach decreases pain, complications and hospital stay and will not affect upper limb range of motion.

University of Pennsylvania School of Medicine Ranked #3 in Nation by *U.S. News & World Report*

The University of Pennsylvania School of Medicine is among the top three research-oriented medical schools in the nation, according to an annual survey of graduate schools by *U.S. News & World Report*. Penn is ranked #3 in the prestigious survey, with Harvard University and John Hopkins University ranked first and second, respectively.

Penn's Medical School was also ranked in the top ten in four specialty education programs including Internal Medicine (#4), Drug/Alcohol Abuse (#6), Women's Health (#6) and Pediatrics (#2). Two of Penn Medicine's doctoral specialty programs also ranked among the top ten in the nation: immunology and infectious disease (#7), and microbiology (#8). The School of Medicine was also ranked #12 among the top 50 medical schools for students going into primary care.

"Penn's ranking in the survey reflects the continued dedication and commitment to excellence among our faculty and staff. We are proud to continue our national leadership in medical education, patient care and research," said Dr. Arthur Rubenstein, Dean of the University of Pennsylvania School of Medicine and executive vice president of the University of Pennsylvania for the Health System.

The criteria to determine the top research-oriented medical schools included quality assessment, research activity, faculty resources and student selectivity.

Fox Chase Cancer Center's Robotic Assisted Kidney Cancer Surgery Proves to be Beneficial to Patients

Fox Chase Cancer Center researchers find that outcomes of robotic assisted kidney cancer surgery, when performed by experienced surgeons at high volume centers, prove more beneficial to patients when compared to open surgery. The study, authored by Fox Chase robotic surgeon Rosalia Viterbo, MD, was presented at the American Urological Association's Annual Meeting,

The standard treatment for kidney cancer is to surgically remove the entire or a portion of the kidney. This is known as nephron-sparing surgery, or partial nephrectomy, and is commonly performed using traditional open surgery. Recently, there has been interest in applying a laparoscopic approach for this procedure; however it has proven to be technically challenging to many surgeons.

Experienced laparoscopic surgeons at high volume centers, such as Fox Chase, are now using the da Vinci® robot assisted surgical system for patients with kidney cancer, or renal cell carcinoma. The advanced technology has enabled faster and greater technical proficiency allowing for completion of complex surgical procedures, facilitating a minimally-invasive approach for partial nephrectomy.

"Our patients have experienced many benefits from the robot assisted approach, including shorter

hospital stays (average 3 days), preserved kidney function (reduced need for dialysis), smaller scars with optimal cosmetic results, lower blood loss, and earlier return to normal activity,” says Dr. Viterbo.

As a result of the fast recovery, patients do not delay the next step in their treatment plan, chemotherapy or radiation therapy, stopping the disease from progressing as fast. Similarly, patients with disease on both kidneys benefit because there is less waiting time between surgeries and there is no delay on further treatment. Again, this provides less opportunity for the cancer to grow and spread.

William Krassan came to Fox Chase after learning he had renal cell carcinoma in the right kidney and cystic renal cell carcinoma in the left. Using the da Vinci robot, Dr. Viterbo performed a partial nephrectomy on each kidney, just 8 weeks apart. This laparoscopic approach allowed the surgeon to reach the kidney through 4 tiny holes in the patient’s abdomen. Open surgery would have required one large incision in his back and a longer time until the next surgery could have occurred.

“The procedure and recovery were fairly painless and easy,” says Krassan. “Dr. Viterbo did a wonderful job in an expeditious way. She was able to save 90 percent of my right kidney and two-thirds of my left kidney.” Viterbo added, “Results of the study show robot assisted partial nephrectomy to be a safe and technically feasible minimally invasive approach to kidney sparing surgery.”

Jefferson Study: Therapeutic Effect of Imatinib Improved with Addition of Chloroquine

The therapeutic effects of the blockbuster leukemia drug imatinib may be enhanced when given along with a drug that inhibits a cell process called autophagy, researchers from the Kimmel Cancer Center at Thomas Jefferson University reported in the *Journal of Clinical Investigation*.

The cell-death effect of imatinib (Gleevec) was potentiated when chloroquine, an autophagy inhibitor, was given with imatinib for the in vitro treatment of chronic myeloid leukemia (CML) cells including the CML stem cells, according to Bruno Calabretta, MD, PhD, professor of Cancer Biology at Jefferson Medical College of Thomas Jefferson University.

Autophagy is a process that allows cells to adapt to environmental stresses, and enables drug-treated CML cells to escape cell death. Imatinib is a tyrosine kinase inhibitor that suppresses proliferation and induces death of the malignant cells that cause CML. However, additional effects of the drug have not been studied in detail, according to Dr. Calabretta.

In this study, Dr. Calabretta’s team, along with Dr. Paolo Salomoni’s team from the MRC Toxicology Unit at the University of Leicester in the United Kingdom, found that imatinib induces autophagy in CML stem cells that overexpress a protein called p210^{BCR/ABL}. Stem cells that express this protein have been historically resistant to imatinib and also to second-generation tyrosine kinase inhibitors, including dasatinib, nilotinib and bosutinib.

The autophagy process allows stem cells to survive treatment with imatinib, and continue to survive.

The researchers used chloroquine to see if it would have an effect on imatinib treatment. The dual treatment with imatinib and chloroquine eliminated most CML stem cells. Also, imatinib-induced cell death was significantly increased in mice inoculated with p210^{BCR/ABL}-expressing cells.

“Imatinib’s primary effect is inhibiting the proliferation of CML cells, but the frequency of resistance increases in advanced stages of the disease,” Dr. Calabretta said. “There is a need to develop new therapeutic approaches that, in combination with tyrosine kinase inhibitors, eliminate CML stem cells that escape imatinib treatment. We show that imatinib induces autophagy, which enables these cells to survive and eventually resume proliferation. We also show that chloroquine, an autophagy inhibitor, combined with imatinib actually appears to potentiate imatinib-induced cell death.”

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.