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For immediate release:

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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.

Prashant C. Shah, MD, Joins Fox Chase's Department of Surgical Oncology

Philadelphia—Prashant C. Shah, MD, has joined Fox Chase Cancer Center's Department of Surgical Oncology as an attending surgeon in the Division of Thoracic Oncology. He specializes in complex thoracic cancer cases, minimally invasive foregut/esophageal surgery, video assisted thoracoscopic surgery (VATS) lung and mediastinal surgery, and the surgical management of mesothelioma. He also has specialized training in treating patients with many types of benign thoracic surgical problems, such as GERD, hyperhidrosis, Barrett's esophagus, and achalasia.

"With a strong training background in VATS and minimally invasive techniques, I hope to work with the Fox Chase team to discover new ways of broadening the applications of minimally invasive thoracic surgery," Dr. Shah says.

Dr. Shah comes to Fox Chase from Brigham and Women's Hospital in Boston, where he completed Harvard fellowships in advanced minimally invasive thoracic surgery and advanced thoracic oncology. During his time in Boston, Dr. Shah was featured on "Boston Med," an ABC News series about hospitals in Boston.

"I chose Fox Chase for a number of reasons," Dr. Shah explains. "As a highly-ranked comprehensive cancer center, Fox Chase not only stays on the cutting edge of cancer treatment, but also

pioneers the newest, most advanced techniques. The clinical team's multidisciplinary approach gives patients access to a variety of experts who work together to offer the most effective treatment strategies.”

After earning his medical degree at St. George's University School of Medicine in Grenada, Dr. Shah completed his residency in general surgery at Maimonides Medical Center in Brooklyn. He also completed a cardiothoracic surgery fellowship at SUNY Downstate Health Science Center and Maimonides Medical Center after finishing his residency. He is a member of the New York Society of Thoracic Surgeons.

Jefferson Robot to Have First Clinical Trial Test in Prostate Cancer Patients

In the first-of-a-kind clinical trial, a robot will be used to place therapeutic radioactive seeds in prostate cancer patients. The National Cancer Institute-supported study, which will enroll 14 patients, has just opened at Thomas Jefferson University Hospital.

The robot has been designed by Thomas Jefferson University scientists to provide the steadiest and most precise method possible to implant scores of the seeds directly at the site of a cancerous tumor in the prostate gland, eliminating the possibility of human error, says Adam Dicker, MD, PhD, professor and chairman of the Department of Radiation Oncology at Jefferson.

This will be the first test in the U.S. and worldwide of robot-assisted brachytherapy for treating prostate cancer. The federal Food and Drug Administration has approved Thomas Jefferson University's application to test the device in patients.

Prostate brachytherapy, which requires accurate insertion of some 60–120 radioactive seeds in very specific places in the prostate, involves a high degree of clinical skill and attention to detail. “When performed with good quality, brachytherapy offers excellent cure rates compared to surgery, external radiation and proton therapy,” Dr. Dicker says. “However, poorly placed seeds may lead to urinary and rectal toxicities.”

Currently, physicians use a plastic or metal template with holes in which to insert 15-20 needles that contain radioactive seeds into the prostate gland. But because this grid is thin, it is difficult for a person guiding it to push it smoothly and straightly through glandular tissue. “The template forms a pivot point of sort, so the needles, which are unsupported, can twist ever so slightly,” he says. “Getting the seeds to the right place is very important because of the side effects that can occur from the radiation they emit.”

“With its motorized controls and imaging feedback, the robot can systemically place the seeds in a way we believe is more consistently accurate than a human can be,” says Yan Yu, PhD, professor and director of the Medical Physics Division in the Department of Radiation Oncology.

Dr. Yu led a team of medical physicists, engineers, radiation oncologists, radiologists and urologists who spent seven years developing the robotic system, which is called EUCLIDIAN. It incorporates high-resolution ultrasound image processing, dose planning using genetic algorithms, 3D visualization, smart needle rotation for reducing tissue deformation and prostate displacement, and force feedback from nano-sensors installed at various points on the robot. Needle insertion and seed delivery are fully automatic.

“The robot is controlled by a physician via a handheld controller and a computer interface,” he says. “It is capable of reverting to manual needle and seed insertion any time the physician desires.”

Dr. Yu says the robot has been described in 30 scientific papers by the Jefferson team, and the intraoperative software that operates the robot has been under development for more than 15 years and has been reported in 20 scientific papers.

“Robotic brachytherapy combines the expertise of a multi-disciplinary clinical team led by radiation oncologists, with the most sophisticated robot technologies available today, to aim for the ultimate goal of delivering the best possible dose distribution each time for every patient, and verifying this before the patient leaves the procedure,” said Dr. Dicker, who is the principal investigator of the EUCLIDIAN clinical trial at Jefferson.

Temple researcher collaborates on national study to improve lung function

Each year in the United States, about 100,000 people die from complications related to emphysema, a condition in which the air sacs in the lungs are no longer able to expand and contract properly. Michael Hollingsworth lived with severe emphysema for years. He was on oxygen therapy, which required him to wear a nose tube and get the oxygen for which his lungs were laboring through a tube. It did little for his quality of life, and eventually his condition worsened.

“I was in the hospital twice, both times because I stopped breathing,” he said. “It got to the point where the oxygen wasn’t working anymore.”

After that, his doctor suggested he come to Temple University Hospital, to enroll in a clinical trial that was studying less invasive ways to treat chronic emphysema. Hollingsworth had a procedure in which tiny one-way valves were inserted into the airways leading to the most severely damaged part of his lung. The valves block air entry but enable air exit, thereby deflating the most diseased region and shifting ventilation to more healthy areas of the lung. By reducing the size of the diseased parts, the procedure decreased his chest cavity size and improved the function of his chest wall, breathing muscles and heart.

Hollingsworth's procedure was part of VENT, or Endobronchial Valve for Emphysema Palliation Trial, a multi-center, national study that looked at whether endobronchial valves (EBVs) could be a viable alternative to surgery.

The study, which published in the online version of the New England Journal of Medicine on Sept. 23, followed the progress of 321 patients with emphysema – 220 of whom received EBVs, and 101 who received medical therapy. At six months, the patients who received the valves showed measurable improvements in standard tests of lung function. Among those with the most severe forms of emphysema, researchers saw an even more robust improvement in the patients' lung function and fewer symptoms.

For Hollingsworth, getting the EBVs meant no more oxygen tubes, and an additional four years of working as a crane operator before his retirement.

“This study suggests that endobronchial approaches to lung volume reduction can produce important improvements in physiological and functional outcomes in properly selected individuals with potentially less complications than lung volume reduction surgery,” said study co-author Gerard J. Criner, MD, chief of pulmonary and critical care medicine at Temple University Hospital, and professor of medicine at the School of Medicine.

Lung volume reduction surgery is the standard therapy that is used to treat hyperinflation in select severe emphysema patients for whom other treatments have not worked. The surgery essentially cuts out areas of hyperinflated lungs to make them work less hard so the patient can breathe easier. However, this procedure is costly and carries with it significant risk.

The ultimate goal of VENT was to provide data and information that will fuel more clinical trials with EBVs in the United States. Currently, the valves are only available clinically in Europe.

“Data from VENT should help to focus future prospective controlled trials in patients with sufficient heterogeneous emphysema and intact fissures to determine the effects of EBV on achieving clinically meaningful and durable improvements in lung function and functional status,” said Dr. Criner.

The Temple Lung Center and its director Dr. Criner have been highly commended for leadership in respiratory disease diagnosis, treatment and research. Temple University Hospital was recently named one of the nation's top hospitals for pulmonology by U.S. News & World Report.

In addition to VENT, the Temple Lung Center currently heads the mid-Atlantic consortium for the Long-Term Oxygen Treatment Trial (LOTT), an NIH-funded, six-year nationwide study of the effectiveness and safety of long-term home oxygen therapy for sufferers of COPD, and also conducts STATCOPE, a prospective study to determine if the drug simvastatin can reduce the frequency of COPD flare-ups or exacerbations and COPD Gene, a study examining the genotypic and phenotypic expressions of exposure to tobacco smoke and development of COPD.

In 2009, Dr. Criner authored a study in the American Journal of Respiratory and Critical Care Medicine, which looked at the use of biologic lung volume reduction in patients with emphysema. In this technique, rather than surgically removing the diseased parts of the lung, a medicated gel is inserted into the area, where it hardens, and over time, causes the area to wither and retract.

This study was funded by Emphasys Medical Inc. and Pulmonx Inc., in Redwood City Calif. Other authors on the study are Frank Sciruba at the University of Pittsburgh Medical Center, Armin Ernst at the Harvard University Medical School, Felix J.F. Herth at the University of Heidelberg, Charlie Strange at the Medical University of South Carolina, Charles H. Marquette at the University Hospital of Nice, Kevin L. Kovitz at the Tulane University Health Sciences Center, Richard P. Chiacchierini of Chiacchierini and Associates, Jonathan Goldin at the David Geffen School of Medicine at UCLA, and Geoffrey McLennan at the University of Iowa.

Promise of Outpatient Brain Gene Therapy is One Step Closer, Researchers Say

They say their findings potentially represent a major advance in the effort to treat brain disorders with therapeutic transgenes, or external genes – suggesting that gene therapy to the brain could be given to patients on an outpatient basis, simply by IV administration into the arm.

All other viral gene delivery vectors tested to date must be delivered directly into the brain and they may elicit immune responses that impair their effectiveness, the researchers say. The immune system may recognize and eliminate brain cells that have been genetically modified, and it can mount an antibody response against the virus vector itself that limits how often that therapy can be given.

“Our unique and simple method avoids these problems,” says the study senior investigator, David Strayer, MD, PhD, Professor of Pathology, Anatomy & Cell Biology at Jefferson Medical College of Thomas Jefferson University. “We don’t have to enter the skull and inject into the brain, and we see absolutely no immune response or any other side effects in our animal experiments.”

Using such a method, it may be possible, for example, to treat diseases thought to be due to excessive oxidative damage to neurons and neuron proteins, such as early Alzheimer’s disease or Parkinson’s disease, with extra genes that limit oxidative damage to brain neurons, he says. “This is theoretical of course, but through our method of delivering genes directly to neurons, we might be able to arrest or slow the progression of a number of neurodegenerative disorders, or potentially correct selected disorders that are due to one faulty gene,” Dr. Strayer says. “Our approach also allows us to offer gene therapy as often as needed – not just one or two times.”

The advance was made possible by two major discoveries. One was use of vectors derived from recombinant SV40 viruses, which have been extensively tested by Dr. Strayer, and the other is use of a

sugar alcohol, mannitol, that relaxes the blood-brain barrier so that the vector can pass through. The idea to combine these two approaches came from first author Jean-Pierre Louboutin, M.D., Ph.D., a research associate in the Department of Pathology at Jefferson.

“Mannitol is commonly used in a clinical setting to reduce intra-cranial pressure during head trauma,” he says. “It loosens the tight vascular barrier that only allows small molecules like oxygen to move from the blood into the brain. We thought it might help our viral vectors pass through – and it does.”

Using mannitol before delivery of the gene-laden SV40 viral vectors in mice also directs most of the viral particles into the brain, instead of to other parts of the body, for reasons that the researchers do not yet understand, Dr. Louboutin says. “It makes delivery of the genes into brain tissue very efficient.”

The SV40 virus, which has been known to researchers for 50 years, is a monkey virus that does not harm humans, says Dr. Strayer. He devised a method to take out all the viral genes leaving a small residual piece of virus DNA that allows the now-inert virus to reproduce and to attach to its coat proteins in very specific cells designed to package the vector. The researchers then inserted therapeutic genes into the viral vector. These genes are delivered by the vector to neurons in the brain, and insert themselves into the genome of those brain neurons to produce the beneficial protein.

While other scientists have worked with the SV40 virus as a gene transfer vector, Dr. Strayer and his team have investigated this gene therapy vehicle most extensively.

In this study, Dr. Strayer and Dr. Louboutin, as well as their co-authors, tested use of the SV40 viral vector and mannitol to deliver antioxidant enzymes to the central nervous system of mice. These genes have been used successfully in Dr. Strayer’s laboratory to treat some of the manifestations of HIV-related injury to neurons, which is a result of oxidative damage is important to loss of cells. “This kind of damage is also seen in Alzheimer’s and Parkinson’s disease,” says Dr. Louboutin.

The researchers delivered genes that produce two different anti-oxidant enzymes to the mice, and tested the effectiveness of gene delivery with and without prior administration of mannitol. They found that mannitol increased expression of the gene ten-fold in the brain and spinal cord. This team of researchers, furthermore, has found that gene delivery by SV40-derived vectors is very long-lived; in animal studies lasting up to 18 months, these vectors provide steady, enduring expression of the therapeutic genes that have been inserted into the vector.

Dr. Strayer cautions that there are many different settings in which gene delivery may be used and that no viral vector fits all of those needs. As promising as SV40-derived vectors are, they “prefer” to deliver their genetic payload to neurons and not to other brain cells, such as astrocytes. “That informs us as to how best to use this new gene delivery system,” he says.

The study was funded by the National Institutes of Health. Other co-authors include Alena Chekmasova, Ph.D., and Elena Marusich, Ph.D., from Thomas Jefferson University, and J. Roy Chowdhury, M.D., from the Albert Einstein College of Medicine. The authors declare no conflicts of interest.

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