Heart WATCH

WINTER 2012

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Texas Heart® Institute

at St. Luke's Episcopal Hospital

Reporter Gene Imaging Can be Used for Long-term Monitoring of Transplanted Cells in the Pig Heart

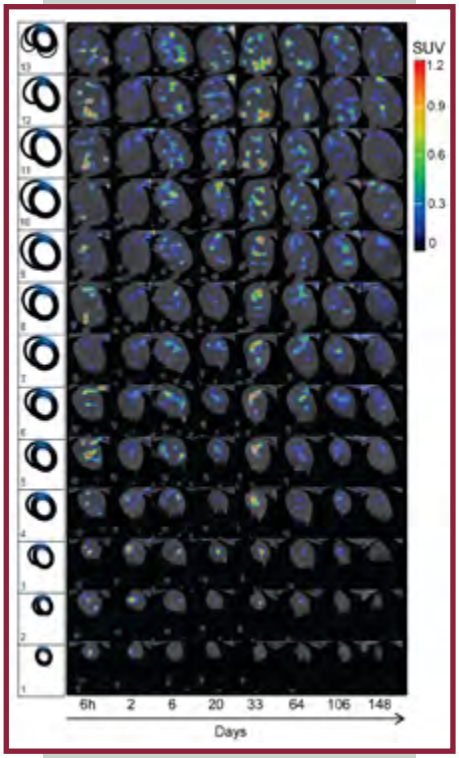
Abstract: Repetitive imaging studies show a biphasic distribution of transplanted mesenchymal stem cells expressing a reporter gene in pigs with acute myocardial infarction.

Although stem cell therapy holds promise for patients with heart disease, the long-term fate of transplanted cells after their delivery into the heart is unknown. If cells could be monitored in vivo for an extended period, researchers would be better able to identify the mechanisms underlying cell therapy and develop methods to improve the benefits of this novel treatment approach.

Researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) recently published results of a study of reporter gene imaging for long-term monitoring of transplanted mesenchymal stem cells (MSCs) in pigs with acute myocardial infarction (AMI) (*PLoS One* 2011;6:e22949). The study, conducted in collaboration with investigators at The University of Texas MD Anderson Cancer Center, examined the use of repetitive [^{18}F]FEAU positron emission tomography (PET)/computed tomography (CT) imaging to track the long-term fate of transendocardially injected MSCs that expressed a reporter gene.

The investigators transduced MSCs with the gene for herpes virus type 1 thymidine kinase, which is an enzyme that phosphorylates radiolabeled nucleoside analogues trapped inside transduced cells. To monitor these cells after transendocardial injection, the researchers performed PET/CT imaging after intravenously administering a radiotracer. "Our goal was to determine the feasibility of using repetitive [^{18}F]FEAU PET/CT imaging for up to 5 months to examine the biodistribution, survival, and long-term engraftment of transduced MSCs delivered via NOGA-guided transendocardial injections in pigs with AMI," states Emerson C. Perin, MD, PhD, Director of THI's Stem Cell Center and lead investigator of the study at THI at St. Luke's.

"Current imaging modalities for monitoring cardiac cell therapy involve direct radionuclide labeling of cells, which is complicated by a high false-positive rate and a limited duration of monitoring because of decay and clearance of the radionuclide," says James T. Willerson, MD, President and Medical Director of THI at St. Luke's and a study investigator. "In our approach, the reporter gene is expressed only in living cells and is passed on to daughter cells. This allows long-term imaging and makes radiolabel decay a non-issue."



[^{18}F]FEAU PET/CT images of the pig heart at various time points after transendocardial delivery of transduced MSCs. The left column shows a representation of the ventricles (thick ovals), the atria (thin ovals), and the infarct area (blue). (Reprinted from *PLoS One* 2011;6:e22949.)

The results of the repetitive imaging studies showed a biphasic distribution of MSCs after transendocardial delivery. At 6 hours, MSCs were clearly identified at the injection site and surrounding infarct sites, and some cells had migrated through the cardiac lymphatic vessels (*see Figure*). The [^{18}F]FEAU signal rapidly decreased 2 to 6 days after injection but then gradually increased at the injection and peri-infarct sites from day 6 to day 33, peaking at 34 days. At 64 days, the intensity of the [^{18}F]FEAU signal decreased substantially in many cardiac areas but was still detectable at the injection site and some peri-infarct sites, including the periaortic lymph nodes and the lymphatic sinus; the signal remained stable or decreased minimally for up to 5 months.

"Histologic analysis of cardiac tissues obtained 35 and 150 days after cell injection confirmed the presence of MSCs in regions corresponding to sites of [^{18}F]FEAU accumulation in PET/CT images," says Dr. Perin. "Furthermore, our studies showed that transplanted cells may integrate into the developing fibrovascular tissue and lymphatic vasculature and that several types of cells express the reporter gene, including fibromyoblasts, lymphovascular cells, and microvascular and arterial endothelial cells."

The finding that progeny derived from the transplanted cells persisted long-term supports the hypothesis that cell therapy provides benefits through a paracrine mechanism. Moreover, the novel finding that MSCs may engraft into the cardiolymphatic system suggests that transplanted cells may contribute to cardiac repair by participating in lymphatic aspects of the healing process.

"We have shown the feasibility of noninvasive, repetitive [^{18}F]FEAU PET/CT imaging for long-term monitoring of MSCs transduced with a reporter gene in pigs with AMI," says Dr. Perin. "Furthermore, we have provided important preliminary evidence that these cells may integrate as lymphatic endothelium, indicating a need for further study into the role of lymphatics in cardiac repair." ●

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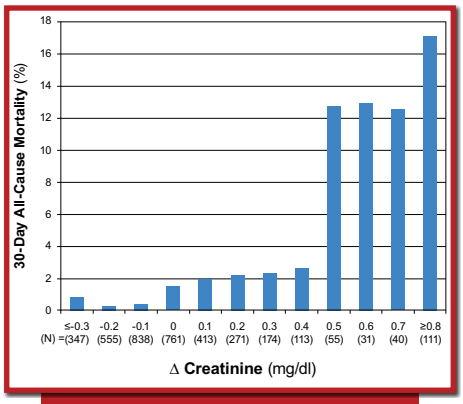
Postoperative Serum Creatinine May Be a Biomarker for Mortality After Coronary Artery Bypass Surgery

Abstract: Subclinical increases in postoperative serum creatinine predict mortality in patients with no more than moderate preoperative renal insufficiency who undergo on-pump CABG surgery.

Serum creatinine levels (SCr) are used both as a biomarker for renal function and as a means of preoperative risk stratification. However, few data exist regarding whether a postoperative change in SCr is independently associated with mortality in patients undergoing coronary artery bypass graft surgery (CABG) with cardiopulmonary bypass (CPB) who have normal preoperative renal function or varying degrees of preoperative renal insufficiency. It is also unclear whether outcomes after CABG surgery are affected by subclinical changes in postoperative SCr that do not meet the Acute Kidney Injury Network (AKIN) criteria or the Risk, Injury, Failure, Loss, and End-stage (RIFLE) kidney disease criteria for renal insufficiency. For these reasons, researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) initiated a study (*J Thorac Cardiovasc Surg 2011*; Epub ahead of print) in which multivariate logistic regression analysis was performed in a retrospective cohort of 3914 consecutive patients who underwent CABG surgery with the aid of CPB. Data were obtained from the THI Cardiovascular Research Database, and statistical analyses were performed by the Department of Biostatistics and Epidemiology, led by Dr. MacArthur Elayda. The researchers wanted to determine whether a change in postoperative SCr is an independent predictor of 30-day all-cause mortality in patients with normal renal function or varying levels of preoperative renal insufficiency. To control for selection bias, they also performed multivariate logistic regression analysis in a propensity-matched cohort of 2042 patients.

"Few data exist as to whether *postoperative* changes in SCr can be used as an independent biomarker for mortality after CABG aided by CPB in patients who have varying degrees of *preoperative* renal insufficiency," says Wei Pan, MD, Director of Cardiovascular Anesthesiology Research at THI at St. Luke's and the senior author of the study. "We wanted to assess SCr changes to see if they are a sensitive biomarker across the spectrum of preoperative renal function."



Thirty-day all-cause mortality associated with each degree of change in serum creatinine level in a combined group of patients with normal preoperative renal function or with mild or moderate preoperative renal insufficiency. (Reprinted from *J Thorac Cardiovasc Surg* 2011; Epub ahead of print, with permission).

The researchers found that decreases in SCr were associated with reduced 30-day all-cause mortality. In comparison, subclinical increases in SCr were associated with increased mortality ($P<0.01$), even after propensity matching ($P=0.01$). Patients with a decrease in postoperative SCr accounted for approximately 50% of the patients who had the lowest mortality—these patients represented the baseline group. For statistical analyses, patients with no change in SCr were grouped with patients who had slight increases (0.1 and 0.2 mg/dL) compared with baseline levels.

"Our results show that in patients who undergo CABG with CPB, a postoperative change in SCr is an independent predictor of 30-day all-cause mortality if the patients had normal renal function or mild or moderate renal insufficiency in the preoperative period," says C. David Collard, MD, Chief of the Division of Cardiovascular Anesthesiology at THI at St. Luke's and a coauthor of the study (*see Figure*).

"Moreover, we found that a decrease in SCr after CABG with CPB is associated with the lowest mortality; conversely, even small increases in SCr that do not meet AKIN or RIFLE criteria are associated with a 3.9-fold increase in 30-day all-cause mortality."

"Our findings suggest that irrespective of the use of SCr as a marker for acute changes in renal function, changes in SCr during the perioperative period may be a sensitive and reliable early biomarker for predicting 30-day all-cause mortality in patients who undergo CABG with CPB," adds Dr. Pan. "This is important because subclinical SCr changes may be useful for post-CABG outcome management by providing early warning that clinical intervention is necessary." ●

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Contents

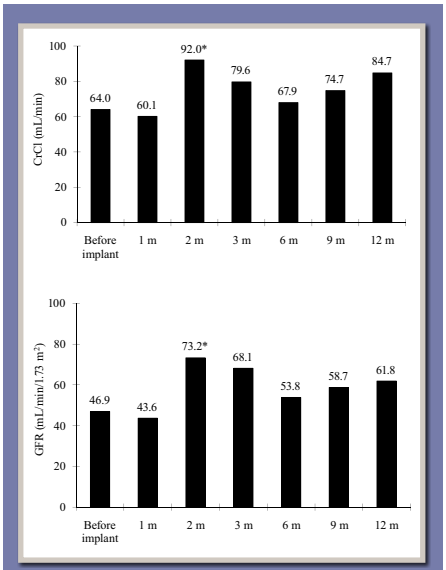
Renal Function Can Improve in Left Ventricular Assist Device Recipients Requiring Renal Replacement Therapy

Abstract: In HeartMate II patients requiring perioperative renal replacement therapy, those who clinically recover after the implantation procedure can recover renal function.

In patients with end-stage heart failure, left ventricular assist device (LVAD) implantation can provide effective hemodynamic support and improve quality of life. However, renal failure can adversely affect outcomes in LVAD patients with impaired renal function that requires renal replacement therapy (RRT). Additionally, many centers require that heart transplant candidates have a creatinine clearance (CrCl) of at least 50 mL/min. Physicians use inotropic agents and intraaortic balloon pumps (IABPs) in these patients to improve their hemodynamic status and renal function. However, surgeons at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) have found that LVAD implantation may be another option.

In a recent study (*J Heart Lung Transplant* 2011;30:182–7), O. H. Frazier, MD, Chief of the Center for Cardiac Support at THI at St. Luke's, and his team reviewed their experience with end-stage heart failure patients who required RRT by means of continuous venovenous hemofiltration dialysis (CVVHD), hemodialysis, or both, after receiving the HeartMate II (Thoratec Corporation, Pleasanton, CA) continuous-flow LVAD. Of 107 consecutive HeartMate II patients who survived implantation for more than 30 days, 15 required RRT because they had severe acidemia, volume overload, and a urine output of less than 400 mL/day that was unresponsive to diuretic therapy for more than 24 hours (with a serum creatinine [SCr] level greater than 2.0 mg/dL or 1.5 times the preimplant level). Of these 15 patients, 3 underwent CVVHD, and 12 had CVVHD plus hemodialysis.

"Renal function improved within 2 months after the initiation of LVAD support," says Rajko Radovancevic, MD, Associate Director of the Center for Cardiac Support and a coauthor of the study. "In 10 patients, renal function improved to the extent that RRT could be discontinued. Afterward, 2 of these patients underwent heart transplantation, 1 underwent heart and kidney transplantation, and 2 died at home of conditions unrelated to renal function. The other 5 patients continue to have a good quality of life while awaiting heart transplantation."



Creatinine clearance (CrCl) and glomerular filtration rate (GFR) before implantation through 12 months' follow-up or at the last result before heart transplant or death (15 patients at 1, 2, and 3 months; 12 at 6 months; 9 at 9 months; and 6 at 12 months). *Average values reached statistical significance after 2 months' support (P=0.041 forCrCl and P=0.032 for GFR). (Reprinted from *J Heart Lung Transplant* 2011;30:182–7, with permission.)

Dr. Frazier and his team found that all renal function indicators for the 10 patients after RRT removal were significantly improved (P<0.05) compared with values obtained before HeartMate II implantation. Before implantation, the blood urea nitrogen (BUN) and SCr levels were 44±25 and 1.9±0.6 mg/dL, respectively. The CrCl was 64±39 mL/min, and the glomerular filtration rate (GFR) was 46.9±20.7 mL/min/1.73 m^2. In the 10 HeartMate II patients in whom RRT was discontinued, the BUN and SCr levels were 27±15 and 1.3±0.6 mg/dL, respectively, the CrCl was 96±57 mL/min, and the GFR was 78.4±47.6 mL/min/1.73 m^2.

"We were able to wean the 10 patients from RRT who recovered from the LVAD implantation procedure and improved to New York Heart Association class I status. Renal function began to normalize within the first month of LVAD support," says Dr. Frazier. "By the second month, BUN, SCr, GFR, and CrCl levels were all normal in these patients."

Regardless of whether RRT was continued or discontinued for the 15 patients requiring it, renal function normalized within the first month of LVAD support and remained within acceptable ranges throughout the entire year of follow-up for patients still receiving HeartMate II support or at the last result before heart transplant or death (*see Figure*).

"Our results show that renal dysfunction that necessitates RRT after implantation of a continuous-flow LVAD improved enough to allow discontinuation of renal support in patients who otherwise recovered clinically," says Dr. Frazier. "Our experience has shown that a left ventricular assist device does not have to provide pulsatility to maintain normal end-organ function, particularly renal function. On the basis of our results, continuous-flow pumps can provide acceptable survival rates even in patients with severely compromised renal function that requires RRT."●

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Endomyocardial Calcification Is Identified as a Cause of Heart Failure

Abstract: In an unusual case, extensive, unexplained cardiac calcification led to progressive heart failure in a young man.

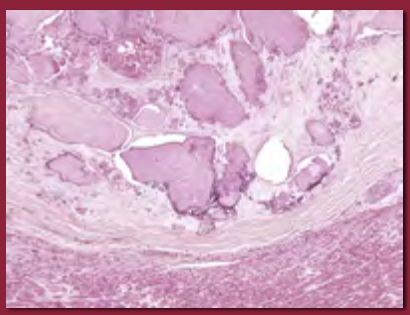
Massive myocardial calcification is rare. Calcium can be deposited into the myocardium as a result of altered calcium homeostasis or local pathologic processes. Significant myocardial calcification can cause dilated and restrictive cardiomyopathy, ultimately leading to intractable congestive heart failure.

Cardiovascular pathologists at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) recently encountered an unusual, unexplained case of massive cardiac calcification in a 20-year-old man with severe restrictive cardiomyopathy. Their findings have been published as a case report in *Cardiovascular Pathology* (2011; 20:e185-e188).

"The patient was referred to us to be evaluated for a heart transplant," says Ana Maria Segura, MD, MPH, a Research Scientist in Cardiovascular Pathology at THI at St. Luke's who was involved with the case. "Despite aggressive medical therapy, he had New York Heart Association [NYHA] functional class IV, stage D heart failure. On noncontrast computed tomography, his heart—especially the left atrium—was significantly enlarged, and the left ventricle and mitral valve annulus had extensive calcification. He had no significant elevation in his pulmonary resistance or transpulmonary gradient, indicating that he was a candidate for heart transplantation."

The patient's history included multiple hospitalizations between the ages of 6 and 8 years for respiratory infections and bronchial obstructions. When he was 8 years old, his left atrium was found to be dilated, and he had mitral valve insufficiency related to weakening of the connective tissue in the valve cusps. Subsequently, he experienced shortness of breath during aerobic exercise, and his condition progressively worsened. At age 15, he was diagnosed with a mild form of restrictive cardiomyopathy, which continued to worsen over the next 5 years.

After being evaluated at our center, the patient was listed for heart transplantation. Five months later, he underwent a successful orthotopic transplant. At that time, microscopic sections of his native heart showed multiple calcium nodules associated with necrosis and granulomatous inflammation (*see Figure*). The nodules were localized in the subendocardial area, extending focally into the myocardium. Special staining was negative for acid-fast bacilli and fungal microorganisms.



Histologic section showing multiple left ventricular calcified nodules in the native heart of a 20-year-old patient who underwent a heart transplant for restrictive cardiomyopathy and progressive heart failure (hematoxylin and eosin, ×10 magnification). (Reprinted from *Cardiovasc Pathol* 2011;20:e185-e188, with permission.)

"The massive calcification seen in this patient's heart was remarkable," says L. Maximilian Buja, MD, Chief of Cardiovascular Pathology Research at THI at St. Luke's, who reviewed the case. "We carefully examined the patient's history and clinical presentation for possible causes of the endomyocardial calcification."

The most common causes of myocardial calcification include previous myocardial infarction, endomyocardial fibrosis, infections such as tuberculosis, chronic renal failure, and hyperparathyroidism. Myocardial calcification can also occur in patients with underlying diseases, such as autoimmune disorders, that predispose the heart to calcification. In addition, myocardial tumors—especially myxomas, fibromas, and metastatic osteosarcomas—can contain foci of calcification.

"Surprisingly, our patient did not have a previous myocardial infarction or any other detectable condition that could explain the cause of the calcified nodules in his heart," says Dr. Buja. "Nineteen months after his transplant, he remains in NYHA class I. To our knowledge, this is the first reported instance of idiopathic endomyocardial nodular calcification as a cause of heart failure." ●

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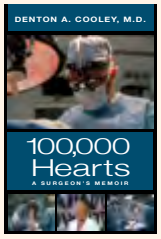
Denton A. Cooley, MD, Texas Heart Institute Founder, Publishes His Memoir



Denton A. Cooley, MD, founder, Surgeon-in-Chief, and President Emeritus of the Texas Heart Institute (THI), has written *100,000 Hearts: A Surgeon's Memoir*, which is now available online and in bookstores. The title refers to the number of open heart operations Dr. Cooley and his team performed at THI during his long, remarkable career. Best known for performing the first human implant of a total artificial heart in 1969, Dr. Cooley describes how a shy Houston boy evolved into a world-renowned surgeon. Beginning with his childhood memories, he goes on to recount his experiences as a basketball-scholarship recipient at The University of Texas. He describes his years as a trainee at the Johns Hopkins School of Medicine, where he took part in the famous 1944 blue-baby operation, which stimulated his interest in heart surgery, and at The Brompton Hospital for Chest Diseases in London. The book also covers his personal life and his feud and eventual reconciliation with rival heart surgeon Dr. Michael E. DeBakey. Because Dr. Cooley pioneered many cardiovascular operations that are now considered routine, he is uniquely qualified to describe the dawn and evolution of cardiovascular surgery.

A Novel Bispecific Antibody May Improve Retention of Transplanted Stem Cells in Injured Myocardium

Abstract: A novel bispecific antibody promotes adhesion of bone-marrow–derived multipotent stromal cells to an antigen marker of injured myocardium.

Stem cell therapy shows promise for the treatment of patients with cardiovascular disease. However, the effectiveness of this therapy may be limited by low rates of stem cell retention and engraftment. One approach to improving retention is to target stem cells to damaged tissues by using a bispecific antibody that has dual specificity for the stem cell and the injured tissue. This method has been used to target CD34+ hematopoietic stem cells to infarcted myocardium in rodents.

Researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at St. Luke's) and The University of Texas MD Anderson Cancer Center have extended this technology by developing a bispecific antibody with specificity for another stem cell type: bone-marrow–derived multipotent stromal cells (BMMSCs) (*Bioconjug Chem* 2011;22:1706-14). BMMSCs are mesenchymal-type cells that offer multilineage differentiation potential. In preclinical studies, they have been shown to improve cardiac function after acute myocardial infarction.

"The objective of this study was to develop and test a novel bispecific antibody that would target BMMSCs to injured myocardium," states Darren G. Woodside, PhD, Assistant Director of the Wafic Said Molecular Cardiology Research Laboratory at THI at St. Luke's.

The bispecific antibody developed by Dr. Woodside and colleagues is composed of 2 antibodies that are covalently cross-linked (*see Figure*). The cardiac-tissue–targeting arm of the bispecific antibody uses a monoclonal antibody (mAb) specific for myosin light chain 1 (MLC1), which is found in the interstitial tissue of injured myocardium. The stem-cell–targeting arm uses a mAb that recognizes the phenotypic cell surface marker CD90, which is found on BMMSCs.

The investigators used a 2-step process to generate the anti-CD90 × anti-MLC1 bispecific antibody. First, each individual antibody was modified with one partner of a chemically reactive pair. Next, the 2 antibodies were cross-linked via these covalent modifications. The particular cross-linking chemistry used in this study has several advantages: it precludes the formation of homodimeric antibody products (which would bind only 1 of the antigens), allows the rapid quantification of antibody modifications, and enables real-time, non-destructive monitoring of bispecific antibody generation.

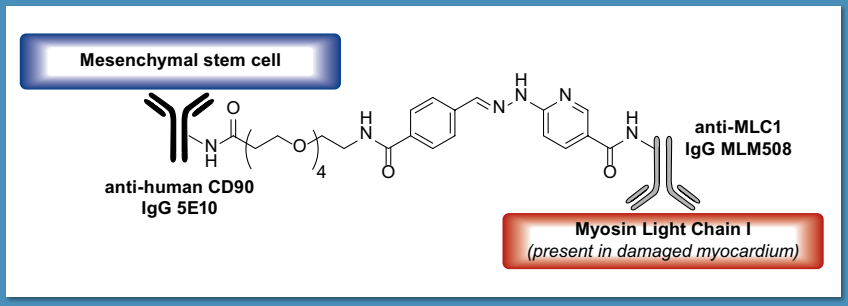


Diagram of the bispecific antibody. An antibody targeting CD90 (a phenotypic cell surface marker on bone-marrow–derived multipotent stromal cells) is covalently cross-linked to an antibody targeting myosin light chain 1 (a marker of injured myocardium). (Adapted from *Bioconjug Chem* 2011;22:1706-14, with permission. ©2011 American Chemical Society.)

"After generating the antibody, we had to ensure that each arm could bind its target antigen after being chemically modified," states Dr. Woodside. "Our in vitro studies showed that the immunoreactivity of each antibody was not reduced in the cross-linked species—the bispecific antibody was able to bind to pig BMMSCs and to purified recombinant MLC1."

"We also performed osteogenic, adipogenic, and chondrogenic differentiation assays in the presence of unmodified anti-CD90 antibody and confirmed that binding of the anti-CD90 antibody to BMMSCs does not impede their differentiation ability," states Dr. Woodside.

Finally, to determine whether the bispecific antibody could increase the binding of BMMSCs to MLC1 (the marker of damaged myocardium), the investigators performed parallel-plate flow-chamber assays, in which pig BMMSCs pretreated with the bispecific antibody were perfused into a flow chamber containing immobilized MLC1. "These assays indicated that the bispecific antibody can tether BMMSCs to MLC1 in vitro, even under physiologic levels of shear stress exceeding that encountered by cells emigrating from the vasculature in an inflammatory environment," states Dr. Woodside.

"In summary, we have developed a novel anti-CD90 × anti-MLC1 bispecific antibody that has the potential to target BMMSCs to damaged heart tissue and to improve the benefits of stem cell therapy," states Dr. Woodside. "Each arm of the construct is functional, and the antibody can bind BMMSCs to MLC1 under stringent in vitro conditions. The next step is to test the bispecific antibody in a pig model and determine whether it increases the retention of transplanted stem cells in injured myocardium." ●

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Texas Heart Institute Involved in First Prospective, Multicenter Trial of Totally Percutaneous AAA Repair Technique

Abstract: The first prospective, multicenter trial of totally percutaneous abdominal aortic aneurysm repair with the "pre-close" technique has yielded promising initial results.

The most common type of aortic aneurysm is abdominal aortic aneurysm (AAA), which is often treated endovascularly. Typically, in endovascular repair, a catheter carrying a stent-graft is inserted through the femoral artery and advanced into the abdominal aorta, where the stent-graft is deployed to exclude the aneurysm from blood flow. This procedure involves far less surgical trauma than open AAA repair; totally percutaneous endovascular aortic repair (PEVAR) usually requires only 2 puncture wounds in the common femoral artery (CFA) for insertion of the cannulas. Nonetheless, for AAAs that require larger stent-grafts, the puncture wounds are sometimes large enough to warrant concern about wound-related complications.

To address this problem, some clinicians advocate using suture-mediated wound-closure devices during PEVAR procedures. These devices are used in the "pre-close" technique, in which suture needles are deployed into the CFA at the start of an endovascular procedure and are then used to close the wound at the end of the procedure (*see Figure*). This technique allows the interventionalist to close larger punctures than would be possible if the suture needles were not deployed until the end of the procedure.

Support for the pre-close technique has been based on the findings of single-center studies and on anecdotal evidence. To clarify the value of using the pre-close technique with suture-mediated wound-closure devices, Zvonimir Krajcer, MD, Co-Director of the Peripheral Vascular Disease Service at the Texas Heart Institute at St. Luke's Episcopal Hospital, and colleagues at 18 other centers around the United States are conducting the first randomized, prospective, multicenter clinical trial of PEVAR with established pre-close techniques.

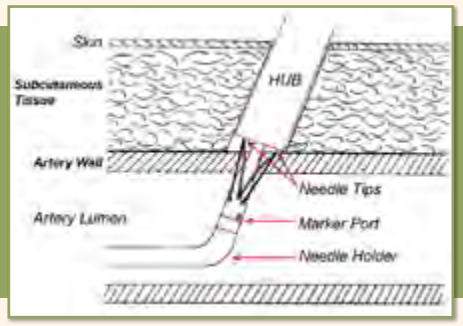
Before randomization began, each of the participating sites was required to perform 2 PEVAR procedures to demonstrate physician competence with the pre-close technique. As a result, preliminary data were obtained from 38 patients (2 each from 19 sites) between April 2010 and May 2011. These results were recently published in the *Journal of Cardiovascular Surgery* (2011;52:651-9); Dr. Krajcer was first author of the article.

All of the patients had an AAA that was either more than 5 cm in diameter or rapidly expanding—the standard indications for intervention in AAA cases. The other eligibility criteria included vascular anatomy amenable to endovascular exclusion of the AAA and to pre-close suturing of the access point in the CFA. In all cases, the pre-close technique was performed with 1 of 2 devices manufactured by Abbott Vascular (Redwood City, CA): the Perclose ProGlide Suture Mediated Closure System or the Prostar XL Percutaneous Vascular Surgical System.

"The pre-close technique was performed successfully in all but 1 of the 38 patients," says Dr. Krajcer, "including all 6 patients in whom a second pre-close was performed in the opposite CFA. The average time to achieve hemostasis was just 6 minutes. Also, the 30-day outcomes were encouraging. Of the 37 patients who underwent successful pre-close, only 1 had any major postprocedural complications; this patient, who did not remain on bed rest during recovery, developed a CFA pseudoaneurysm and lower-limb occlusion and ischemia, which were treated successfully."

Other postoperative data also suggest that PEVAR with the pre-close technique is associated with rapid recovery. The average time from procedure to hospital discharge was 1.4 days. Moreover, upon discharge, patients were asked to rate their groin pain on a scale of 0 (no pain) to 10 (the worst imaginable pain); the mean rating was 1.6.

"These preliminary findings suggest that PEVAR with the pre-close technique is safe and effective," Dr. Krajcer concludes. "Of course, we expect to have much more conclusive data within the next year, when the randomized study is completed." ●



A suture-mediated wound-closure device deploying suture needles into the arterial lumen for later wound closure.

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Texas Heart Institute Launches Its First App

The Texas Heart Institute has launched its first application for iPhone, iPad, and Android. The app, called Auscultation Primer, is a tool that enables physicians, nurses, and medical students to practice listening to the sounds of the heart in order to diagnose cardiovascular disease. Auscultation Primer includes some of the most common heart sounds and murmurs, taken from live recordings; each recording is accompanied by a phonocardiogram and an electrocardiogram for timing the cardiac events. Dr. James M. Wilson, Director of Cardiology Education at THI, led the team that developed the app, which may be downloaded for free from numerous sites. In the first 10 days after its launch, more than 1100 downloads were made by users all over the world. The app has earned high ratings from reviewers. By providing a global reach, it is THI's latest tool for helping to reduce the toll of cardiovascular disease through research and education.

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Cover: Jewelry donated by Mariquita Masterson for the Celebration of Hearts display in the Wallace D. Wilson Museum of the Texas Heart Institute at St. Luke's Episcopal Hospital—The Denton A. Cooley Building.

Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Second Annual DERC Diabetes Symposium
Marriott Medical Center
January 28, 2012 • Houston, Texas
Program Co-Directors: Mandeep Bajaj, MD, and Lawrence Chan, MD

Thirteenth Symposium on Cardiac Arrhythmias: Practical Approach to Heart Rhythm Disorders
The Houstonian Hotel
February 18, 2012 • Houston, Texas
Program Director: Ali Massumi, MD

Future Direction of Stem Cells in Cardiovascular Disease
McCormick Place
March 23, 2012 • Chicago, Illinois
Program Director: James T. Willerson, MD

Houston Echo Review 2012: Echo for the Echo Board
Texas Heart Institute
April 13–14, 2012 • Houston, Texas
Program Director: Raymond Stainback, MD

Selected Upcoming Local, National, and International Meetings

Society of Thoracic Surgeons 48th Annual Meeting
January 28–February 1, 2012 • Fort Lauderdale, Florida
www.sts.org/education-meetings/sts-annual-meeting

International Society for Heart and Lung Transplantation 32nd Annual Meeting and Scientific Sessions
April 18–21, 2012 • Prague, Czech Republic
www.ishlt.org/meetings/annualMeeting.asp

American Association for Thoracic Surgery 92nd Annual Meeting
April 28–May 2, 2012 • San Francisco, California
www.aats.org/annualmeeting/

Heart Rhythm Society 33rd Annual Scientific Sessions
May 9–12, 2012 • Boston, Massachusetts
www.hrsonline.org/sessions/

For information about Texas Heart Institute CME activities, please e-mail cme@texasheart.org or call 713-218-2200.
To view or complete selected online CME courses (certificates are available online), please visit www.cme.texasheart.org.
New courses are added regularly.

For 21 consecutive years, the Texas Heart Institute at St. Luke's Episcopal Hospital has been ranked among the top 10 heart centers in the United States by *U.S. News & World Report*'s annual guide to "America's Best Hospitals."