By the time Bill Beatty made it to the Emergency Department in Howard County, he was already several hours into a major heart attack. His physicians performed a series of emergency treatments that included an intra-aortic balloon pump, but the 57-year-old engineer’s blood pressure remained dangerously low. The cardiologist called for a helicopter to transfer him to Johns Hopkins.

It was fortuitous timing: Beatty was an ideal candidate for a clinical trial and soon received an infusion of stem cells derived from his own heart tissue, making him the second patient in the world to undergo the procedure.

Of all the attempts to harness the promise of stem cell therapy, few have garnered more hope than the bid to repair damaged hearts. Previous trials with other stem cells have shown conflicting results. But this new trial, conducted jointly with cardiologist Eduardo Marbán at Cedars-Sinai Medical Center in Los Angeles, is the first time stem cells come from the patient’s own heart.

Cardiologist Jeffrey Brinker, a member of the Hopkins team, thinks the new protocol could be a game-changer. That’s based partly on recent animal studies in which scientists at both institutions isolated stem cells from the injured animals’ hearts and infused them back into the hearts of those same animals. The stem cells formed new heart muscle and blood vessel cells. In fact, says Brinker, the new cells have a predetermined cardiac fate. “Even in the culture dish,” he says, “they’re a beating mass of cells.”

What’s more, says Hopkins lead investigator Gary Gerstenblith, the animals in these studies showed “a significant decrease in relative infarct size,” which shrank by about 25 percent. Based on those and earlier findings, investigators were cleared by the FDA and Hopkins’ Institutional Review Board to move forward with a human trial.

In Beatty’s case, Hopkins heart failure chief Stuart Russell extracted a small sample of heart tissue and shipped it to Cedars Sinai, where stem cells were isolated, cultured and expanded to large numbers. Hopkins cardiologist Peter Johnston says cardiac tissue is robust in its ability to generate stem cells, typically yielding several million transplantable cells within two months.

When ready, the cells were returned to Baltimore and infused back into Beatty through a balloon catheter placed in his damaged artery, ensuring target-specific delivery. Then the watching and waiting began. For the Hopkins team, Beatty’s infarct size will be tracked by imaging chief Joao Lima and his associates using MRI scans.

Now back home and still struggling with episodes of compromised stamina and shortness of breath, Beatty says his Hopkins cardiologists were “fairly cautious” in their prognosis, but he’ll be happy for any improvement.

Nurse coordinator Elayne Breton says Beatty is scheduled for follow-up visits at six months and 12 months, when they hope to find an improvement in his heart’s function. But at least one member of the Hopkins team was willing to acknowledge a certain optimism. “The excitement here,” says Brinker, “is huge.”

The trial is expected to be completed within one to two years.

**CADUCEUS Trial Eligibility**

To be considered a candidate for the study of cardiosphere-derived autologous stem cells to improve ventricular function following a myocardial infarction (CADUCEUS), patients must have had a myocardial infarction within the prior four weeks and been treated with successful coronary angioplasty and stent placement. In addition, the left ventricular ejection fraction must be between 25 percent and 45 percent. To refer a patient for consideration for the study, call Dr. Gary Gerstenblith at 410-955-6834 or Dr. Peter Johnston at 410-550-5966.
These studies are enrolling patients.

**Aortoiliac Disease**

Elizabeth Ratchford is the principal investigator of the CLEVER study, a prospective, randomized multicenter clinical trial comparing the benefits of supervised exercise, endovascular revascularization and optimal medical care in adults age 40 and older with intermittent claudication due to aortoiliac peripheral arterial disease. Info: Elizabeth Ratchford, 410-502-0517, erobin26@jhmi.edu

**Atrial Fibrillation**

Hugh Calkins is the principal investigator of a study investigating the safety and efficacy of the BARD Magellan atrial fibrillation ablation system in the treatment of paroxysmal AF. Info: Elizabeth Robinson, 410-502-0517, erobin26@jhmi.edu

**Coronary Artery Disease**

Ronald Berger, principal investigator for the DETER-MINE study, is testing the hypothesis that ICD therapy in combination with medical therapy in post-MI patients with mild to moderate LV dysfunction improves long-term survival compared to medical therapy alone. Patients who do not meet the EF or infarct mass criteria as measured by CE-MRI may be placed in the study registry. Info: Elizabeth Robinson, 410-502-0517, erobin26@jhmi.edu

**Heart Failure**

Alan Cheng is the principal investigator of a randomized, double-blinded, nonsignificant risk, three-armed trial called SMART-AV to investigate the effects of optimizing AV delay timing in heart failure patients receiving Bi-V ICD therapy. Info: Elizabeth Robinson, 410-502-0517, erobin26@jhmi.edu

Charles Henrikson is the principal investigator of a study to determine if an algorithm can be developed based on pre-implant clinical variables to predict responses to cardiac resynchronization therapy. Info: Elizabeth Robinson, 410-502-0517, erobin26@jhmi.edu

**Ischemic Heart Disease**

Jon Resar is the principal investigator of the Spirit Small Vessel Registry Study evaluating the safety and effectiveness of the 2.15 mm XIENCE V Everolimus Eluting Coronary Scent System in improving coronary luminal diameter in subjects with ischemic heart disease due to a maximum of two de novo native coronary artery lesions, each in a different epicardial vessel. Info: Kathleen Carno, 410-955-7377, kcarno@jhmi.edu

**Marfan Syndrome**

Luca Vricella is the Johns Hopkins principal investigator of a multicenter study evaluating and comparing operative outcomes of the aortic valve-sparing and aortic valve-replacement surgical interventions in adult and pediatric patients with Marfan syndrome. Info: Kimberly Behrens, 410-502-1914, kbehren1@jhmi.edu

**Metabolic Syndrome**

Pamela Ouyang is the principal investigator of a placebo-controlled trial studying the effect of a range of doses of an oral antioxidant, alpha lipoic acid, on levels of oxidative stress and inflammation in patients with glucose intolerance/diabetes, hypertension, high lipids and moderate obesity. Info: Jeanne Wingo, 410-550-4278, jwingo@jhmi.edu

**Sudden Cardiac Death**

Gordon Tomaselli is the principal investigator of the PRO-ICD study examining the role of genetic, protein and electrocardiographic markers measured longitudinally in predicting the risk of SCD and overall mortality in patients with implantable defibrillators placed for primary prevention. Info: Barbara Butcher, 443-287-3427

To learn more about these and other studies, visit the Clinical Trials page at hopkinsmedicine.org/heart.

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**Practicum-ly Speaking**

If you asked any of the hundreds of clinicians and researchers who’ve participated in the Johns Hopkins CTA Practicum what was most memorable, you’d likely get a common response: intense and impassioned.

It’s hardly the testimonial you’d expect from a rigorous course teaching the interpretation of cardiac CT angiography results, but its co-directors, cardiologists Edward Shapiro and David Bush, aren’t interested in spewing dry data and performing lackluster lectures.

Rather the duo has designed and created an interactive experience that’s been attracting a broad mix of cardiologists, radiologists, researchers and academic fellows from across the country and around the world.

“I think the intensity of our excitement about cardiac CTA definitely comes across,” says Shapiro.

The technology itself—among the more difficult cardiac diagnostic tests to interpret—is still largely untapped, though its most common application is in ruling out coronary narrowing in patients with uncertain diagnoses. In those cases, CTA can definitively show whether or not a blockage is present—and avoid other unnecessary testing down the road.

But, where the bigger thrills lay for Shapiro and Bush are the various other applications for CTA that have yet to be widely used or understood.

“There are a dozen other niches for CTA that many haven’t caught on to yet,” Shapiro explains. “Once these are used to their full potential, CTA will dominate cardiac diagnostics.”

Until then, the five-day practicum bests others like it and created an interactive experience that’s been attracting a broad mix of cardiologists, radiologists, researchers and academic fellows from across the country and around the world.

“We’re not just saying sit back, listen and watch what we do,” says Bush. “This is a completely hands-on encounter.”

And, the two aren’t opposed to bantering disagreements within the specialty, highlighting differing opinions on analysis and figuring out with participants the significance of their findings.

“We’re looking at everything from all angles,” says Shapiro. “That’s the best interpretation.”

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**Throughout the rest of 2009, the Cardiac CTA Practicum is offered on the following dates:**

- September 21-25
- October 19-23
- December 7-11

For dates in 2010, registration and location details and more: www.jhucardiacct.org or 410-550-0849.
When Heart-Device Patients Need MRI

Pacemakers and implantable cardioverter defibrillators have come a long way in the past two decades, yet the debate continues regarding the safety of performing MRI in patients who have the devices. Cardiologists Henry Halperin and Saman Nazarian say it may be time for a new perspective.

Millions of patients have had either pacemakers or ICDs implanted, and millions more will. The problem is that up to 75 percent of those patients will likely need an MRI in their lifetime.

“If you have an implanted cardiac device and you need an MRI, traditional concerns limit your options,” says Nazarian. Those concerns have included possible movement of the devices, programming changes and induced lead currents that result in heating and cardiac stimulation. Nazarian explains in a study published in Circulation that other problems have included strong electromagnetic fields that might cause asynchronous pacing, activate tachyarrhythmia therapies or inhibit a demand pacemaker.

But in that same study, Nazarian, Halperin and other colleagues concluded that MRI can be safely performed in patients with implanted cardiac devices.

What’s more, they were able to answer diagnostic questions in 95 percent of cases using MRI versus 20 percent using alternatives like CT scans and nuclear imaging. “The need to be able to use MRI in these situations is significant,” says Halperin.

To prevent inappropriate device behavior, they reprogram each device so its electronics won’t mistake the MRI radiofrequency for an arrhythmia. They also turn off a defibrillator’s shocking function for the 30 to 60 minutes needed to perform the imaging test. In addition, they limit the amount of energy used at peak scanning, reducing the strength of the electromagnetic field from as much as 4 watts per kilogram to 2 watts per kilogram per patient. And during the scan, they closely monitor every patient using electrocardiography, blood pressure and pulse oximetry.

There are caveats, though. Halperin notes special protocols for patient safety and emphasizes that the procedures need to be performed at centers that follow those protocols. Plus, patients who aren’t eligible include those with “abandoned” leads not connected to the implanted device or with leads on the outside of the heart.

Halperin, Nazarian and their team have made definitive diagnoses in more than 300 patients who have been scanned so far, helping plan artery-opening procedures, measuring tumor growth, detecting strokes and brain masses, and diagnosing a blood clot in the spine that had been missed by CT scanning. They also pinpointed the cause of one woman’s seizures, allowing surgical cure.

An Endo in Sight for Abdominal Aortic Aneurysms

Clarence Blackwell awoke one morning feeling fatigued and nauseated, and soon began vomiting. Over the past several years, the 77-year-old had had six vessel heart bypass procedures with 20 percent residual function of his heart (EF 20-25 percent). He had significant heart ischemia (positive stress test) but was not deemed a candidate for further coronary revascularization. He also had significant renal insufficiency (cr 2.6 and GFR 26 cc/min). Unwilling to take any chances, Blackwell’s wife insisted he go to an ER, though she thought he might only be having an appendix problem.

Her determination likely saved Blackwell’s life, says Mahmoud Malas, chief of endovascular surgery at Johns Hopkins Bayview Medical Center, where emergency department physicians quickly identified a large, leaking abdominal aortic aneurysm.

Several years ago, the traditional open procedures done to repair an AAA, Malas says, “would’ve put significant stress on the heart of someone who’s had severe coronary disease.” If he survived the operation, he might face respiratory failure or pneumonia and ileus as complications.

Today, endovascular repair is performed routinely for these types of patients. But, says Malas, just because these repairs have become more common doesn’t make them less risky. People with heart problems are compromised already, he notes. When you have someone like Blackwell with kidney problems too, an endovascular procedure gets even dicier. “Like a lot of patients,” Malas says, “he also had a challenging anatomy, which makes it difficult to navigate the endograft devices.”

Malas performed the emergency endovascular repair using a CO2 angiogram to avoid the large amounts of contrast medium that would be required to show the anatomy of the aorta and iliac arteries. Though CO2 doesn’t offer as precise a visual as the usual contrast media, it’s safer for patients with compromised kidneys. Malas also uses the most recent generation of endografts, which, he explains, “have become much more flexible and, in skilled hands, make it safer for patients with tortuous anatomy.”

Blackwell’s operation required only a small incision through his groin and an overnight hospital stay. The next day he was walking around, and a short time later he was back to his regular routine.

Endovascular procedures, says Malas, are still evolving and improving, and Johns Hopkins is participating in a number of clinical trials that are looking at better devices that can improve outcomes.

One of the biggest challenges is that there often are anatomical difficulties like Blackwell’s that make navigation for endovascular procedures prohibitive. In one trial, Malas and others are working with the next generation of devices, flexible endografts that are designed to conform to a patient’s anatomy.

“We’re also performing endovascular repair of thoracic aortic aneurysm with remarkable results” he says.

Endovascular Surgery Clinical Trial

The Pythagoras trial is an FDA-approved study to evaluate the effectiveness of the AorFix endograft in treating abdominal aortic aneurysms in patients with tortuous anatomy not considered candidates for EVAR (EndoVascular Aneurysm Repair).

For details, call 410-550-4335.
Surgical Ventricular Reconstruction Does Work

For patients who survive a myocardial infarction, the aftermath is often left ventricular remodeling causing dilation of LV, congestive heart failure—and poor quality of life. When medications fail to adequately relieve ongoing symptoms, one alternative to heart transplant that cardiac surgeon John Conte has found effective in carefully selected patients is surgical ventricular reconstruction. When performed at the same time as coronary artery bypass grafting, the procedure to return the heart to its more normal size and elliptical shape, he says, can allow the heart to work more normally by lowering pressure build-up inside the heart cavity and reducing the amount of oxygen and energy the heart needs to keep pumping.

Although it’s been debated whether CABG plus SVR is more beneficial than CABG alone, at least year’s annual meeting of the Society of Thoracic Surgeons, Conte presented results of the first head-to-head comparison of the single and dual procedures that applied strict scientific controls. Patients in both groups were carefully matched for degree of heart failure and medical history, and outcomes were from the same team of surgeons to ensure that surgical quality was uniform.

What the study showed was that heart function improved for 57 percent of patients who had CABG only and for 80 percent who had the combination procedure. Improvements in ejection fraction were similar in both groups (34 percent and 32 percent, respectively), and there was no difference in intraoperative mortality (6.4 percent and 5.2 percent, respectively).

Given these findings and his own experience—he’s performed more than 150 of the dual procedures since 2000 and has trained more than 100 surgeons to perform the procedure—Conte was disconcerted by recent-ly reported conclusions of another study that also had set out to compare CABG alone to CABG plus SVR. Dubbed STICH (for Surgical Treatment for Ischemic Heart Failure), the study had originally called for more than 100 surgeons to participate—Conte was one of 95 surgeons who had been invited to participate but chose not to.

The study’s primary goal was to demonstrate nonviability. “Instead,” says Conte, “we estimate that about one in 20 CABG patients who have congestive heart failure might fit into this category.”

When it comes to SVR, says John Conte, choosing the right patients is key.