

Heart WATCH FALL 2004

A NEWSLETTER PRODUCED BY THE TEXAS HEART INSTITUTE



 TEXAS HEART[®] INSTITUTE
at St. Luke's Episcopal Hospital

Recent THI Study Suggests That Preoperative Statin Use Is Associated with Reduced Postoperative Mortality

Abstract: In a recent study at THI, preoperative statin use was associated with reduced mortality after primary on-pump coronary artery bypass graft surgery.

In the last decade, the clinical benefits of statins have become clear. As trials involving more than 50,000 adults have demonstrated, these cholesterol-lowering drugs can reduce the mortality associated with coronary heart disease, as well as the incidence of myocardial infarction, stroke, and peripheral vascular disease. More recently, intensive lipid-lowering statin regimens have been shown to provide greater protection than standard statin regimens do against death and major adverse cardiovascular events in patients with acute coronary syndromes.

to target levels substantially below those it previously recommended. The new guidelines advise using statins to reduce LDL cholesterol levels to <100 mg/dL in those individuals at highest risk for adverse cardiovascular events, a reduction from the previous target of 130 mg/dL.

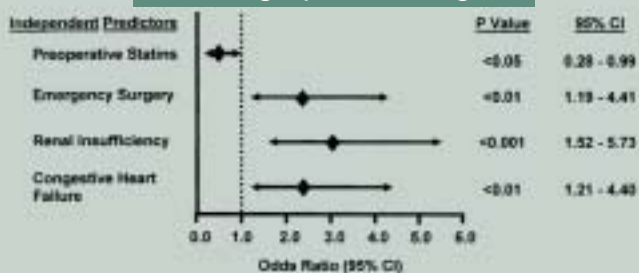
“Interestingly, the overwhelming majority of the data establishing the benefits of statins has come from ambulatory patient populations,” notes Charles D. Collard, MD, a cardiovascular anesthesiologist at the Texas Heart Institute at St. Luke’s Episcopal Hospital

in the risk of early death after primary CABG surgery with CPB, even after we had controlled for patient demographics, medical history, and concomitant preoperative medications,” says Dr. Collard. “In addition, mortality did not appear to be differentially affected by which commercially available statin preparation was used.”

Yet, despite the implications of the findings for patients undergoing cardiac surgery, Dr. Collard urges caution.

“It is important to recognize that we identified only an association between preoperative

Click graph to enlarge



Independent predictors of early mortality in patients who underwent primary on-pump coronary artery bypass graft surgery at THI in 2000–2001, along with associated odds ratios and 95% confidence intervals (CI). (From *Circulation* 2004;110 (11 Suppl 1):II45–II49, with permission.)

Although there is a risk of myopathy when statins are used in combination with certain other medications such as fibrates, statins are generally considered safe and effective.

The benefits do not appear to stop there, either. Accumulating evidence, including a recent Harvard study (*Circulation* 2004;109 [21 Suppl 1]:II18–II26), suggests that statins may also exert multiple anti-inflammatory effects independently of their effect on LDL cholesterol. Statins have been shown to reduce serum inflammatory markers in patients with acute coronary syndromes or idiopathic dilated cardiomyopathy, suggesting that the protection they offer against adverse cardiovascular events may be due in part to their ability to decrease systemic inflammation.

Moreover, the National Cholesterol Education Program recently revised its statin guidelines to declare that further benefit may be gained from early and continued lowering of low-density lipoprotein (LDL) cholesterol

(THI/SLEH). “Meanwhile, the role of statins in the acute perioperative period has not been adequately researched.”

Prompted by a recent Dutch study indicating a link between statin therapy and reduced postoperative mortality in patients undergoing major noncardiac vascular surgery (*Circulation* 2003;107:1848–1851), Dr. Collard gathered a team to investigate the effects of statins in an acute cardiac surgical setting. The research team identified more than 1,600 patients who underwent primary coronary artery bypass graft (CABG) surgery with cardiopulmonary bypass (CPB) at THI/SLEH between January 1, 2000, and December 31, 2001, and retrospectively reviewed the clinical data. The patients were divided into 2 groups: those who received preoperative statin therapy and those who received no preoperative anti-hyperlipidemic therapy.

“We found that preoperative statin therapy was associated with an almost 50% reduction

statin use and postoperative mortality, not a causative link,” he says. “Further, our study was limited in being retrospective by design, not controlling for the length of time patients were on statins before cardiac surgery, and not asking whether discontinuing statins increased the risk of postoperative mortality.”

The next step for Dr. Collard and his team will be to initiate a large, prospective, randomized trial to explore whether preoperative statin therapy significantly reduces the risk of early postoperative cardiac surgical morbidity and mortality. ●

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Potentially Cardiotoxic Cancer Treatments Pose Special Cardiac Challenges

Abstract: The potential cardiotoxicity of drugs, radiation, and surgery used to treat cancer poses special cardiac challenges for the oncologist and cardiologist.

In the United States, cancer is a leading cause of death, second only to cardiovascular disease. More than 1.3 million new cases of cancer are diagnosed each year. Like cardiovascular disease, cancer becomes more prevalent with age. Yet, cancer is becoming increasingly manageable, even in elderly patients, through the use of various combinations of surgical, radiation, and drug therapies.

Nevertheless, these treatments often pose unwanted cardiovascular risks for cancer patients. The anesthesia and extensive surgical trauma associated with curative surgery may lead to depressed myocardial function, adverse changes in blood pressure and blood volume, release of vasoactive molecules from the tumor, and arterial and venous thromboembolic events related to the hypercoagulable state known to be induced by many tumors.

“In addition, drug- and radiation-based treatments are often cardiotoxic,” says Sayed Feghali, MD, an interventional cardiologist at the Texas Heart Institute at St. Luke’s Episcopal Hospital (THI/SLEH), consulting cardiologist at the Texas Cancer Institute at SLEH, and clinical specialist at The University of Texas M. D. Anderson Cancer Center (UTMDACC) in Houston. “For this reason, primary and secondary cardiac tumors, which are relatively rare, are treated mainly by surgery. Drug and radiation-based treatments (often combined with surgery) are used mainly for patients with noncardiac cancers.”

“Anticancer drugs can induce a wide range of cardiotoxic effects, including myocardial depression, ischemia, blood pressure fluctuations, and arrhythmias,” says Edward T.H. Yeh, MD, a staff cardiologist at THI/SLEH and chairman of the department of Cardiology at UTMDACC. “The well-studied and widely used anthracyclines doxorubicin, daunorubicin, and epirubicin, which are used to treat many hematologic and solid tumors, may cause arrhythmias in the short term and congestive heart failure and left ventricular dysfunction in the long term, especially when

SOME POTENTIAL CARDIOTOXIC EFFECTS OF CANCER THERAPY

Drug-related

Myocardial depression
Ischemia
Hypotension
Hypertension
Arrhythmia

Radiation-related

Vascular injury
Thickening of myocardium, pericardium, or valves

given in high doses. These drugs are particularly toxic in patients with coronary artery disease, but they have also been known to cause damage in patients with no known history of this disease.”

Adds Dr. Feghali, “Radiation to the chest may directly injure the coronary arteries and cause fibrous thickening of the myocardium, pericardium, and cardiac valves. This may lead in turn to progressive loss of cardiac function, leading to ischemia, angina, and myocardial infarction.”

“In some cases, complications may not appear until many years later,” says Dr. Yeh. “For example, platinum drugs used to treat metastatic testicular cancer may cause ischemic complications up to 20 years down the road, and radiation may cause coronary artery disease 6 years later. Thus, the cardiologist plays an extremely influential role in determining the ultimate outcome of cancer treatment.”

“The cardiologist may enhance the effectiveness of cancer therapies by watching for treatment-induced damage and identifying it early enough to counteract it,” says Dr. Yeh. “This is done by periodic echocardiography to evaluate treatment effects on cardiac function and by laboratory tests to detect the presence of myocardial-injury markers troponin I and T. The cardiotoxic effects of most chemothera-

peutic agents may also be lessened, reversed, or even prevented by adjusting the strength and schedule of drug administration. If drug-induced heart failure does occur, optimal heart failure management then becomes essential.”

“Meanwhile,” adds Dr. Feghali, “radiation and surgical techniques are continually being refined to spare healthy tissue whenever possible.”

Whatever the specifics of a particular case, the goal of collaboration between oncologist and cardiologist is to ensure that the cancer treatment targets the malignancy without producing unwanted cardiovascular side effects. These and other cardiac issues in cancer patients were recently discussed at THI’s *Fourth Symposium on Congestive Heart Failure*, on October 21–22, 2004, in Houston. ●

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Clinical Database Expansion to Foster Evidence-Based Cardiovascular Care

Abstract: Expansion of THI's clinical research database to include data from imaging and electrophysiology studies will foster more evidence-based cardiovascular care.

Since the early 1990s, evidence-based medicine has been establishing its foothold in clinical practice. The wide availability of computerized online databases and search software allows clinicians to guide therapeutic decision-making by quickly locating relevant evidence, weighing its strength and usefulness, and then putting useful findings into practice.

Over the same period, the Texas Heart Institute research database (THIRDBase) has grown into a comprehensive, longitudinal clinical registry of outcomes for over 150,000 patients treated for cardiovascular disease at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH). It has been used to study long-term outcomes of individuals and groups of patients after one-time and repeat cardiovascular procedures, and it is now being expanded to reflect more fully the THI/SLEH experience.

Maintained by the staff of the department of Biostatistics and Epidemiology, THIRDBase contains information dating back to THI's first coronary artery bypass graft operation in the late 1960s. In 1993, the database was redesigned to accommodate the increasing amount of patient information needed to support the research interests of THI and its professional staff, residents, and fellows. THIRDBase now includes a wide range of data on all patients admitted to THI/SLEH with a diagnosis of cardiovascular disease. These data include demographic data, cardiovascular risk factors for various outcomes, medical histories, physical findings, cardiac catheterization and clinical laboratory data, and information on surgical and percutaneous interventional procedures, complications, and follow-up.

"A special strength of the database is its detailed, yet flexible coding system," says MacArthur Elayda, MD, PhD, a clinical cardiologist by training who is now a cardiovascular epidemiologist in the department of Biostatistics and Epidemiology and the manager of THIRDBase. "The system conforms to data standard sets that have been established by the

"Incorporating existing imaging and electrophysiological data into THIRDBase will guarantee better evidence-based answers to our questions about cardiovascular care."

*—James M. Wilson, MD
Director
Cardiology Education*

American Heart Association, American College of Cardiology, and Society of Thoracic Surgeons to help standardize the language of cardiovascular care. This ensures that the data we collect are useful and appropriate and easily shared with databases outside our institution and with the cardiovascular community as a whole."

Yet, despite its size and comprehensiveness, THIRDBase has not yet reached its full potential.

"THIRDBase contains a wealth of unique data," says James M. Wilson, MD, assistant chief of Cardiology at THI/SLEH and director of Cardiology Education, "but it can be made even more valuable and useful by including important information on the magnetic resonance imaging, computed tomography, echocardiography, and electrophysiology studies done here every day. That information is currently spread out among several departmental databases."

Since October 2003, a committee of clinician-researchers, hospital administrators, and biostatisticians has been addressing this issue.

Dr. Wilson and representatives from the departments of Magnetic Resonance Imaging, Echocardiography, Electrophysiology, Cardiology, Cardiology Research, Cardiovascular Surgery, and Cardiac Catheterization have been meeting regularly with Dr. Elayda and SLEH administrators to iron out the logistics of incorporating the new data into the database.

"The expansion will require no new investment in computer hardware since the entire database easily fits on one server," says Dr. Elayda. "It will, however, require more in terms of the personnel needed to maintain and periodically update the database. But this will be a worthwhile investment because it will improve the quality of clinical care offered here."

The initial transfer of the imaging and electrophysiological data into THIRDBase will begin soon and take about 6 months to 1 year. An information technologist will download the information from computer servers in the various departments, and a specially trained abstractor in Dr. Elayda's area will identify and encode data of interest. Data analysts and biostatisticians will then analyze the database in response to particular treatment- and research-related questions posed by professional staff, residents, and fellows.

"Incorporating existing imaging and electrophysiological data into THIRDBase will guarantee better evidence-based answers to our questions about cardiovascular care—how, for example, our patients fare on cardiac resynchronization therapy," says Dr. Wilson. "It will also allow us to translate our experience into more efficient and effective care for all our patients and into publications that will benefit many other clinicians and patients as well." ●

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Laboratory Researchers Seek to Harness Clinical Potential of Nanotechnology

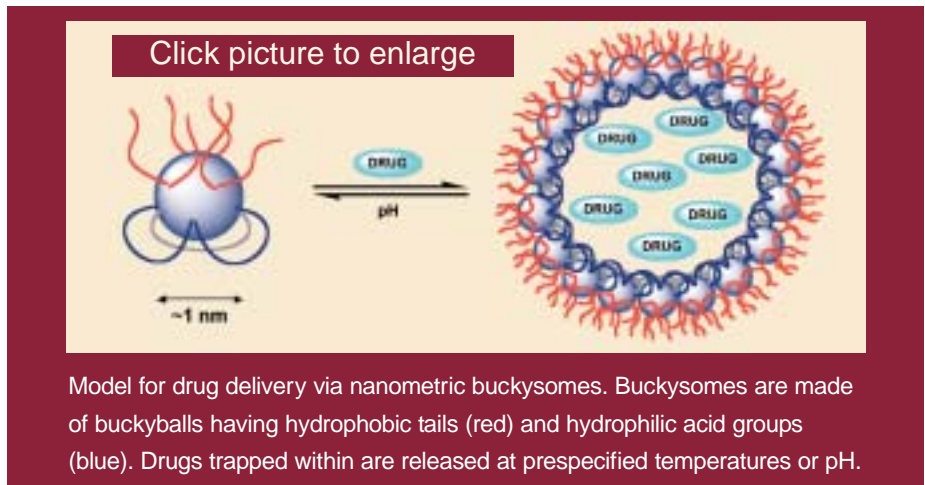
Abstract: Laboratory researchers at THI are studying ways to harness nanotechnology for drug delivery and diagnosis in cardiovascular medicine.

The Texas Medical Center (TMC) has become a hotbed for research and development in the rapidly evolving field of nanotechnology. Recent developments in the field include the establishment of a consortium involving several TMC institutions, Rice University, and the University of Houston; the creation of a National Heart, Lung, and Blood Institute Nanotechnology Working Group; the awarding of several government grants; and the start-up of several local nanotechnology companies. In this fertile environment, laboratory researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH) are working to harness the clinical potential of certain nanotechnologies.

Nanotechnology concerns materials, structures, and devices that exist on the extremely small nanometric (<100 nm) scale. Theoretically, nanoscale materials can be fashioned into minimally invasive, relatively benign, easily targeted, and extremely functional units such as nanosensors for real-time monitoring of biological signals, nanotubes for use in diagnostic testing, and nanospheres for drug delivery. Each of these structures would be considerably smaller than a single cell.

"Because nanotechnology has so much potential to enhance our ability to diagnose, treat, and prevent disease, the National Institutes of Health have set aside considerable resources to fund nanomedicine research through their new Roadmap initiative," says S. Ward Casscells III, MD, associate director of Basic Cardiology Research at THI/SLEH and vice president for Biotechnology at The University of Texas Health Science Center at Houston (UTHSCH).

In one approach, THI researchers are helping to develop a methodology for the controlled release of anesthetics from nanometric liposomes called "buckysomes." Developed by German chemist Andreas Hirsch, the bucky-some is a systematically arranged conglomeration of hollow, carbon-caged molecules called buckminsterfullerenes, or buckyballs, that has been chemically modified to resemble a lipid.



"Buckysomes are not easily soluble in water or other aqueous environments," says Jay Conyers, PhD, a senior research scientist overseeing nanotechnology research at THI/SLEH. "However, the integrity of their membranes is exquisitely sensitive to changes in pH and temperature, and they are amenable to labeling with antibodies to specific cellular receptors. This makes buckysomes ideal for targeted delivery of encapsulated drugs."

At THI/SLEH, buckysomes are being experimentally evaluated for their potential to release anesthesia drugs into blood cells and macrophages under controlled physiological conditions. Up to now, these studies have involved inert surrogates instead of drugs; drugs will be used in animal models in the near future.

"Besides allowing regional or general drug targeting, this novel means of anesthesia delivery might also be made self-regulating," says Dr. Conyers. "It's conceivable that the buckysomes could be designed to stop releasing anesthetic agents once a patient is fully sedated, thus sparing the patient any adverse drug effects."

The potential of nanotechnology for diagnosing vulnerable plaques is also under investigation. In 2000, Dr. Casscells and colleagues discovered temperature variations in plaques excised from the occluded carotid arteries of rabbits. Since then, these researchers have been seeking ways to detect such "hot" plaques in

humans before they can rupture and become life-threatening. Several potential nanomaterial-based contrast agents for computed tomographic scanning are being studied in vitro, using monocytes as their targets; under physiological conditions, circulating monocytes are well known to infiltrate vulnerable plaques as part of the inflammatory response.

"The idea is that standard, commercially available contrast agents would ride 'piggyback' on the nanomaterials, which would seek out infiltrating monocytes in otherwise undetectable vulnerable plaques and render the plaques visible," says Dr. Casscells.

"We are about 6 months away from beginning in vivo studies of our drug-delivery nanotechnology in mouse and rabbit models," says Dr. Casscells. "Beyond that, the pace at which this and other nanotechnology applications migrate from laboratory to clinic will largely depend on how well we can control and manipulate the unique properties of nanostructures." ●

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New Approach to Monitoring for Cerebral Hyperthermia after Cardiopulmonary Bypass

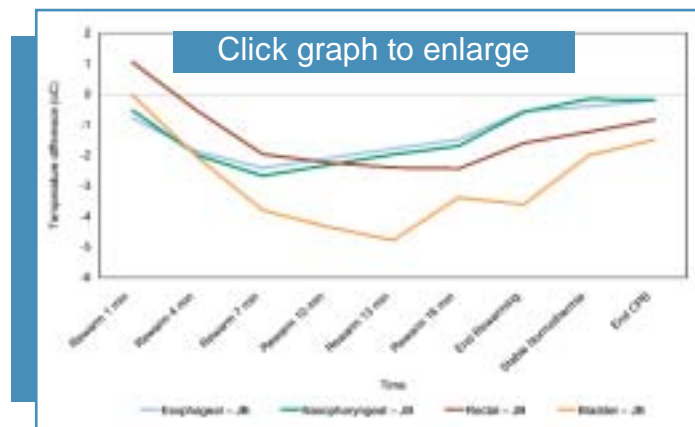
Abstract: THI anesthesiologists seek to make rewarming after cardiopulmonary bypass safer by monitoring brain temperature at novel sites.

In patients undergoing

coronary artery bypass grafting (CABG) surgery with cardiopulmonary bypass (CPB), inducing hypothermia may lower the risk and severity of postoperative cardiac and neurologic complications. However, this requires that the patient be gradually rewarmed afterwards until CPB is discontinued. Rewarming must be carefully controlled to prevent cerebral hyperthermia because overheating can damage the brain or aggravate neurologic injuries caused by intraoperative cerebral emboli. Therefore, rewarming is guided by body temperature readings taken continuously via temperature probes or temperature-monitoring catheters. These devices are most commonly placed in the nasopharynx, esophagus, bladder, or rectum.

Recently, however, a pair of studies conducted by Nancy A. Nussmeier, MD, director of Cardiovascular Anesthesiology Research, and colleagues at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH) revealed that temperatures measured at these sites may not adequately reflect cerebral temperatures and suggested a better way to monitor rewarming. In the first study, temperatures were monitored continuously at 5 different sites in each of 12 patients undergoing CABG with CPB. The sites included the 4 most commonly monitored ones as well as the jugular bulb, a naturally dilated portion of the internal jugular vein. Because blood flows through the jugular bulb almost immediately after exiting the brain, jugular bulb temperature is the best approximation of brain temperature that can be obtained outside the brain itself.

"We monitored temperatures at these sites the entire time the patients were on CPB," Dr. Nussmeier explains. "We found that, over most of the rewarming period, temperatures at all 4 of the commonly monitored sites were lower than the temperatures at the jugular bulb. Bladder temperatures were 2–5°C lower and rectal temperatures 1–2.5°C lower than jugular bulb temperatures for much of the rewarming period. So using rectal or bladder



Difference between temperature at each of 4 commonly monitored sites and temperature at the jugular bulb (JB).

temperature recordings means taking a bigger risk of exposing the patient to cerebral hyperthermia during rewarming. On the other hand, nasopharyngeal and esophageal temperatures were closer to, though still consistently lower than, jugular bulb temperature."

In Dr. Nussmeier's second study, involving 31 CABG patients, temperatures were monitored at the same 5 sites as before, plus one other site: the arterial outlet of the membrane oxygenator, that portion of the CPB circuit in which blood temperature is controlled by the perfusionist. Because blood from the oxygenator flows into the ascending aorta and up into the brain, the temperature of blood exiting the oxygenator outlet is likely to be a good indicator of brain temperature.

"Again, we found substantial differences among all the sites in terms of temperature," says Dr. Nussmeier. "Temperature in the commonly monitored body sites lagged significantly behind blood temperature in the membrane oxygenator outlet and jugular bulb. In other words, temperatures were higher at the commonly monitored sites than in the membrane oxygenator while the patient was being cooled, and lower when the patient was being rewarmed. Once again, bladder and rectal temperatures were particularly inaccurate. Jugular bulb temperature, on the other hand, equilibrated with oxygenator outlet temperature within approximately 10 minutes of the start of CPB."

"In both studies, the temperature differences among all the sites varied substantially between patients," Dr. Nussmeier adds. "For example, in some patients, nasopharyngeal temperature was closer to jugular bulb temperature than temperature at any other body site, while in other patients, esophageal temperature was closest. So, neither of the 2 sites was consistently more reliable than the other in all patients."

On the basis of these findings by Dr. Nussmeier and her colleagues, the standard practice at THI/SLEH for rewarming CABG patients on CPB has changed.

"Our policy now is begin rewarming early and proceed gradually, keeping the temperature of the CPB perfusate at or below 37.0°C and discontinuing CPB when the nasopharyngeal temperature reaches 36.5°C. Temperature in the oxygenator outlet is monitored as the best indicator of brain temperature." ●

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Novel Integrated Approach to Microscopic Pathology Enhances Cardiovascular Device Research

Abstract: A new, more integrated program of microscopic pathology is enhancing laboratory and clinical research on implantable cardiovascular devices at THI.

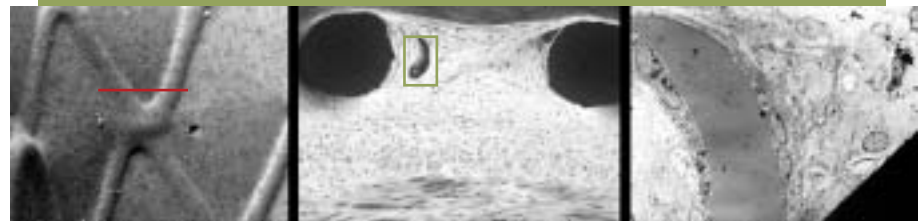
Implantable cardiovascular

devices have long been an important research focus at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI/SLEH). Catheters, cannulas, stents, pacing leads, left ventricular assist devices, and replacement heart valves that are excised during clinical procedures or experimental animal studies are routinely sent to THI's pathology department for evaluation. The findings are used to make diagnoses and to evaluate device safety and effectiveness. In recent years, this work has been enhanced by the development of a novel integrated approach to microscopic pathology.

"In 2001, when floodwaters from Tropical Storm Allison destroyed our basement laboratories," says Fred J. Clubb, Jr., DVM, PhD, director of Cardiovascular Pathology Research at THI, "one of our first tasks was to replace our lost electron microscopes. This offered us a unique chance to streamline our microscopy program and make it more useful to our clinical and research colleagues."

At the time of the flood, 3 complementary, state-of-the-art microscopy techniques were being used in the department: light microscopy (LM) and high-resolution transmission electron microscopy (TEM) to examine 2-dimensional details on cross-sectional specimens and high-resolution scanning electron microscopy (SEM) to examine 3-dimensional ultrastructural surfaces and shapes. However, an important shortcoming of using all 3 approaches was that specimens prepared for LM and TEM were rendered useless for SEM, and vice versa.

"Preparing a sample for microscopy is essentially destructive," explains Dr. Clubb. "For example, a specimen containing biological tissue that is being prepared for conventional SEM must be completely dehydrated and coated with a molecular layer of a gold alloy before being evaluated in the electron microscope's high-vacuum environment. Otherwise, even the small amounts of water found in tissues and cells could seriously



Integrated microscopic examination of a coated stent, first topographically by low-vacuum SEM (original magnification $\times 70$) (left) and then cross-sectionally by LM (original magnification $\times 25$) (middle) and TEM (original magnification $\times 2500$) (right). Note how the last 2 techniques reveal a part of the stent coating that has torn away and become sequestered by cells.

damage the specimen, degrade the vacuum, and blur the image."

"Unfortunately, the drying and gold-coating rule out further processing for LM or TEM," Dr. Clubb says. "On the other hand, the embedding in plastic and slicing of specimens required for LM and TEM make processing for SEM impossible."

"Traditionally, we needed at least 2 and sometimes 3 different specimens to accomplish complete microscopic studies," he adds. "One week after the flood, however, a new approach suggested itself when I was shown a low-vacuum scanning electron microscope while visiting Medtronic, Inc., in Minneapolis, MN. This microscope allowed specimens to be observed at high resolution in a low vacuum, with no significant loss of image quality." (Dr. Clubb is a consultant for Medtronic, Inc.)

Two other attributes of the low-vacuum technology intrigued Dr. Clubb. First, water poses fewer operational hazards under low-vacuum conditions. Second, specimens to be viewed by low-vacuum SEM require neither excessive drying nor gold coating.

"Because the preparative technique for low-vacuum SEM allows the same sample to be processed later for LM and TEM, the low-vacuum device seemed a suitable replacement for our lost high-vacuum scanning electron

microscope and a way to streamline our work," says Dr. Clubb. "So, I and my colleagues here and at Medtronic, developed a protocol for integrative microscopy."

Today, the pathology department at THI houses a low-vacuum scanning electron microscope and transmission electron microscope, both of which are digitally linked with light microscopes into a core computer-image analysis system.

"This novel integration of microscopy techniques allows us to use and conserve our specimens more efficiently, complete our pathology studies more quickly, and correlate our different yet complementary microscopic findings for a single specimen much more precisely," notes Dr. Clubb. "In some cases, it may even reduce the number of animals needed to complete experimental studies. Consequently, we have become more efficient at evaluating implantable cardiovascular devices and better able to help our clinical and research partners improve safety and effectiveness." ●

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Cover: Ornamental pin donated by Zadok Jewelers of Houston 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

Texas Heart Institute Fourth Symposium on Congestive Heart Failure

October 21–22, 2004 • Houston, Texas
Program Director: Sayed Feghali, MD

Texas Heart Institute Stem Cells for Myocardial Regeneration: A New Chapter in Basic Science and Cardiology

October 22, 2004 • Houston, Texas
Program Director: Paolo Angelini, MD

Texas Heart Institute Heart Failure Summit for the Cardiologist, Cardiovascular Surgeon, and Clinical Researcher

November 4, 2004 • Houston, Texas
Program Director: James T. Willerson, MD

American Heart Association Satellite Symposia

November 6, 2004 • New Orleans, Louisiana

Advancing the Standard of Care

Program Directors: James J. Ferguson III, MD;
James T. Willerson, MD; R. David Fish, MD

Mechanical Support of the Failing Heart

Program Directors: Reynolds M. Delgado III, MD;
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For information about the CME activities listed above, please e-mail cme@heart.thi.tmc.edu or call 832.355.2157. To view selected CME presentations and other physician resources online, please visit www.texasheartinstitute.org/doctors1.html.

SELECTED UPCOMING NATIONAL AND INTERNATIONAL MEETINGS

American Heart Association Scientific Sessions 2004

November 7–10, 2004 • New Orleans, Louisiana

Society of Thoracic Surgeons 41st Annual Meeting

January 23–26, 2005 • Tampa, Florida

American College of Cardiology 54th Annual Scientific Session

March 6–9, 2005 • Orlando, Florida

International Society for Heart and Lung Transplantation 25th Annual Meeting and Scientific Sessions

April 6–9, 2005 • Philadelphia, Pennsylvania