~80 to 200 ms temporal resolution. The current state-of-the-art also includes a 16 (or more) slice CT, a rotation of less than 500 ms, the use of intravenous contrast and nitrates to improve image quality and can accommodate patients with heart rates less than 60 to 65 bpm. Dual source CT has a higher speed leading to higher resolution with good sensitivity and specificity. These machines have two x-ray sources and two detector arrays. Another advantage of dual source CT is that patients with a heart rate >65 bpm no longer need to be treated with beta blockers to slow the heart rate.

Multi-detector CT (MDCT) systems can take multiple x-rays simultaneously. Because of their speed, they are now being used for coronary artery imaging. Numerous publications have demonstrated that MDCT is comparable to cardiac catheterization in the detection of coronary stenosis with high sensitivity and specificity. There are, however, limitations associated with the technology. Severe calcification, for example, can make images difficult to interpret, and the motion of the heart causes some artifacts. Although cardiac CT can be utilized to visualize stent placement, the technology remains hindered by poor image quality in this applications. He also emphasized that this is a diagnostic tool only, and one cannot implement an intervention as in angiography.

Although limitations still exist, CT scans have their place in diagnosing certain classes of patients. The fact that CT scans have a high negative predictive value to rule out coronary stenosis means that cardiac catheterization can be avoided if a CT scan is negative. This is particularly helpful in patients that have a low probability of coronary blockages. "Do everything you can to have the highest quality imaging" in order to have reliable results, said Dr. Achenbach. He particularly stressed having adequate equipment, protocols, and staff training. Guidelines for the appropriate use of cardiac CT were recently published the *Journal of the American College of Cardiology* (Hendel et al. *JACC* 2006; 48(7):1475-1497).

CPR Guidelines and Hypothermia Improve Survival

Sudden cardiac arrest is a major public health concern, with more than 400,000 deaths annually in the United States alone. A patient's chance of survival drops by 7-10%/min when CPR is delayed after cardiac arrest. Widespread adherence to the new Advanced Cardiac Life Support/Emergency Cardiac Care guidelines for CPR and the increased use of therapeutic hypothermia may improve both of these statistics.

During cardiac arrest, spontaneous circulation ceases and the vital organs are not adequately perfused. If the patient is successfully resuscitated, circulation resumes, and reperfusion to the vital organs occurs. Reperfusion has been associated with free radical production which can lead to mitochondrial damage and programmed cell death. Mild hypothermia may suppress many of the chemical reactions associated with reperfusion injury.

In two prospective randomized trials comparing mild hypothermia (32-34°C) with normothermia in comatose survivors of out-of-hospital cardiac arrest favorable neurologic outcomes were observed. One study was conducted in five European countries and the other took place in four hospitals in Melbourne, Australia. The European study showed that cooling to 32-34°C for 24 hours decreased the chance of death (risk ratio, 0.74; 95% CI, 0.58-0.95) and increased the probability of good neurological outcome (risk ratio, 1.40; 95% CI, 1.08-1.81) (*NEJM* 2002; 346(8):549-556). The Australian study showed that cooling patients to 32-34°C for 12 hours increased the chance of good neurological recovery (risk ration 2.65; 95% CI,

1.02-6.88; p=0.046) (Bernard SA, et al. *NEJM* 2002; 346(8):557-563). Unlike in the studies of traumatic brain injury, no adverse outcomes were observed in cooled patients.

"Therapeutic hypothermia is one of the most exciting new therapies for cardiac arrest patients in the last decade," Raina M. Merchant, MD, from the University of Chicago, comments. "It has already begun to have a major impact on outcomes from cardiac arrest. It is only a matter of time before we see patients not only survive cardiac arrest, but survive it well."

Dr. Merchant says that American physicians are beginning to move forward with using this new therapy, especially in emergency rooms and intensive care units. In the next few years she predicts acceptance will improve and therapeutic hypothermia will be used frequently.

For more information on the therapy being practiced at the University of Chicago, please visit http://hypothermia.uchicago.edu.

Challenges and Issues in Developing Antithrombotic Therapies for ACS/PCI Use

"The glass is mostly full," stated assistant professor Robert P. Guigliano, MD, Harvard Medical School, in his presentation summary. The topic was "Challenges and Issues in Developing Antithrombotic Therapies for ACS/PCI Use," and he left little doubt that the difficulties are many. They are caused by the very complex physiological systems being addressed, by an array of pitfalls in drug testing and other practical issues. However, Dr. Giugliano affirmed that the future holds many promising new agents, and well-established testing methods can assess their value.

Robert P. Guigliano, MD

The path toward these new therapies is a challenging one. "We've skimmed off most of the cream. The bar for any new therapy is high," he said, "because we've been fairly successful in the past."

The history of physiologic complexity emerging to confound what seemed to be sound medical judgment is extensive. It was well represented by the case of the substantial success of intravenous GPIIb/IIIa inhibitors failing to persist in Phase III clinical trials of oral GPIIb/IIIa inhibitors. Mortality was higher versus aspirin across a range of major trials. "Our simplified view of platelet activation and anticoagulation isn't accurate enough and can sometimes mislead us," he said in an interview. "Also, drugs act in complex ways in more than one organ system and through more than one pathway."

On the novel antiplatelet horizon are more potent oral thienopyridines, intravenous PGY12 inhibitors, oral-reversible PGY12 inhibitors and thrombin receptor antagonists. Anticoagulants in development include oral direct thrombin inhibitors, oral factor Xa inhibitors and inhibitors of factors Va, VIIa, IXa. Noting that the possible combinations with already available agents (e.g., aspirin, dipyridamole, unfractionated and low-molecular-weight heparin, warfarin, thienopyridines, GPIIb/IIIa inhibitors, cilostazol, bivalirudin, fondaparinux, drug-eluting and bare metal stents) amount to 282 followed by 75 zeroes, Giugliano said that identifying optimal uses for future agents may seem to be dauntingly