The theme for the 55th Annual Meeting of the Society of Nuclear Medicine (SNM) was "Molecular Imaging: Build on the Past, Define the Future." The SNM meeting was organized according to eight councils, or tracks. This report focuses on the scientific events, presentations, and CME activities in the "Cardiovascular Council/Track." There were two predominant themes in the Cardiovascular Council: the value and integration of nuclear perfusion studies with other imaging modalities (including dual imaging capabilities such as computed tomography [CT] angiography/single photon-emission computed tomography [SPECT]); and the development of novel "molecular" tracers.

**Sunday, June 15**

The first scientific session in the cardiovascular track was the Cardiovascular Young Investigator Award Symposium. The session was divided into preclinical and clinical studies. In the preclinical section, the first place abstract was "Imaging of $\alpha\beta_3$ in human carotid plaques by $^{18}$Fgalacto-RGD PET/CT," which was presented by Dr Ambros J Beer et al (Technical University of Munich, Germany) [1]. While the abstract was a preclinical study, their report will likely spur further research and is a good example of many of the novel tracer techniques that were highlighted at this meeting. Beer and colleagues attempted to identify neovascularization in carotid plaques, which has been identified as an important step in the development of "vulnerable" plaque. By using $^{18}$Fgalacto-RDG, the authors attempted to identify integrin $\alpha\beta_3$ in carotid plaques. Integrin $\alpha\beta_3$ is a key player in angiogenesis. The authors identified nine patients who were found to have carotid stenosis and were scheduled to undergo carotid endarterectomy. These nine patients underwent PET/CT imaging. The authors found increased $^{18}$Fgalacto-RGD tracer uptake in stenotic sites (standardized uptake value [SUV] 1.5±0.2;
range 1.2–1.9) compared with blood pool (mean standardized uptake value [SUV] 1.2±0.2; range 0.7–1.7). While [18F] galacto-RGD tracer uptake was greater in sites with greater flow velocity, they could not discriminate between symptomatic and asymptomatic plaques. The authors validated their findings by using immunohistochemistry on the resected plaques and demonstrating evidence of neovascularization in areas with high [18F]galacto-RGD tracer uptake. The authors concluded that [18F]galacto-RGD PET/CT can identify elevated levels of αvβ3 in highly vascularized, inflammatory carotid plaques in patients. However, this study demonstrated proof of concept, and future studies will need to prospectively address whether [18F]galacto-RGD PET/CT can identify vulnerable carotid plaque and patients who are high risk of developing symptomatic carotid disease and neurologic events (eg, impending transient ischemic attacks).

The study by Beer et al was one of many vulnerable-plaque imaging feasibility or proof-of-concept studies. Ironically, the death of Tim Russert was frequently referred to during these sessions as a prime example of why vulnerable plaque imaging is so critical. Russert, like many patients with known and unknown coronary artery disease, had an unremarkable stress test in the months before his death. While not emphasized by physicians when discussing stress testing with their patients, stress testing does not identify vulnerable plaques, since more than 70% of these AHA stage 4 plaques are not flow-limiting and therefore do not provoke reversible ischemia during demand testing. Perhaps the greatest promise of vulnerable-plaque imaging is that it may provide not just a good defense but a potent offense against plaque rupture, the leading cause of sudden cardiac death (SCD) in the US.

The winning abstract in the clinical category of the Cardiovascular Council Young Investigators' Competition was Dr Jonathan P Piccini et al's "SPECT myocardial perfusion imaging is a strong predictor of sudden cardiac death in patients with coronary artery disease." Under direction of Dr Salvador Borges-Neto (the senior investigator), Piccini et al examined the relationship between SPECT myocardial perfusion imaging (MPI) defects and the risk of SCD. Previously, Borges-Neto's group had shown that SPECT perfusion imaging is a strong predictor of cardiovascular and all-cause death [2]. Currently, LVEF determination is the gold standard for the risk stratification of SCD. Unfortunately, LVEF-based risk stratification is limited, especially since the majority of SCD events occur in patients with preserved LV
function. Previously, SPECT MPI has been shown to identify patients at increased risk for all-cause mortality and cardiovascular death; however, there are no data regarding SPECT MPI and the risk of de novo SCD in patients with CAD. The authors found that the summed stress score (which is a measure of perfusion defects during stress imaging) was highly associated with SCD in unadjusted and adjusted analyses (HR per three units 1.16 [95% CI 1.08–1.25]; p<0.0001). Furthermore, and perhaps more important, the authors found that the summed stress score identifies patients at risk for SCD across all LVEFs. Using serial Cox models, the authors also demonstrated that the summed stress score has independent and incremental prognostic power, even after the LVEF is taken into account. Again, while not a definitive study, the authors’ analyses raise the possibility that SPECT MPI, which evaluates both LV function and perfusion, may provide a more effective means of risk stratification for SCD (when compared with solitary LVEF determination).

Risk stratification for SCD was a frequent topic of discussion at this meeting. In other sessions focusing on new applications of SPECT imaging in cardiovascular disease, risk stratification for SCD was identified as an area of priority for further research. SPECT imaging has a proven track record in guiding therapy and prognosis in CAD, yet there is a paucity of data with respect to SCD. In addition, there is great interest in the development of novel tracers for cardiac sympathetic innervation and activity—which may also identify patients at risk for SCD. [123I]metaiodobenzylguanidine (MIBG) has been shown to tag cardiac sympathetic fibers, and its uptake reflects cardiac autonomic tone and dysregulation of cardiac sympathetic innervation in several small studies. Many physicians are already familiar with [123I]MIBG, since it has an established use in the evaluation of patients with pheochromocytoma and neuroblastoma. Patients with cardiomyopathy have exaggerated heart-to-mediastinum-[123I]MIBG tracer uptake and prolonged washout. Increased heart-to-mediastinum activity and delayed washout have been associated with increased cardiovascular death in patients with ischemic and nonischemic cardiomyopathy. GE Healthcare is sponsoring several studies examining the use of this tracer to identify patients with heart failure who may be at increased risk of SCD.
Monday, June 16

The main event in the cardiovascular track on Monday was the poster sessions. A large number of abstracts focused on multimodality imaging (eg, SPECT/CT, PET/CT, etc). There were also a considerable number of abstracts focused on dyssynchrony imaging and software development.

The abstract by Dr DW Cook et al (University of Lausanne, Switzerland), "Incidental findings at dedicated cardiac PET/CT," sought to assess the burden of extracardiac findings on dual imaging PET/CT studies performed for the evaluation of patients with suspect cardiovascular disease. They analyzed 49 PET/CT studies from 28 referral patients (mean age 61) and 21 healthy volunteers (mean age 27). They classified extracardiac findings in three categories: benign (eg, degenerative disk disease); possibly relevant (eg, signs of pulmonary hypertension); and suspicious (eg, pulmonary nodule >5 mm). They identified possibly relevant extracardiac findings in 54% of the referred patients and 19% in the healthy volunteers. Suspicious findings (which mandated further evaluation) were found in 36% of the referral patients but were absent from the 21 volunteers. The authors concluded that it is imperative to systematically review the low-dose CT portion of all hybrid studies in their entirety.

In the era of turf battles between cardiologist and noncardiologist readers, the issue of extracardiac findings is very important, timely, and relevant. The findings from this study suggest that extracardiac "overreading" is very important so as not to miss abnormalities that require further evaluation.

In the abstract by Dr Lucia Rampin et al (Santa Maria della Misericordia Hospital, Rovigo, Italy), "Direct His-bundle pacing preserves perfusion compared with right ventricular apical pacing," the authors conducted a prospective study of 12 consecutive patients who required standard pacemaker implantation. Each patient was implanted with two ventricular leads, one placed for direct His bundle pacing and the other in the conventional right ventricular apical location. After three months of direct His bundle pacing, the patients underwent right ventricular apex pacing. SPECT imaging, echocardiography, tissue Doppler imaging, and BNP determination were captured and compared after each pacing trial. In summary, direct His bundle pacing was associated with better perfusion scores.
(0.44±0.5 vs 0.71±0.53), less mitral regurgitation, and less dyssynchrony than right ventricular apical pacing.

This small but carefully designed and well-conducted study confirms the results of other studies that have shown that septal or direct His bundle pacing preserves intrinsic electromechanical activation and is associated with improved hemodynamic parameters, including measures of myocardial perfusion. This abstract was one of several presentations that focused on the use of SPECT imaging to evaluate ventricular activation and mechanics, as opposed to its more traditional applications in the diagnosis and risk stratification of patients with CAD.

**Dr Mehrbod S Javadi** (Johns Hopkins University, Baltimore, MD) et al presented "Lowering radiation dose for integrated assessment of coronary morphology and its functional consequences: First experience with step-and-shoot CT angiography in the PET/CT environment." The combined use of CT angiography and PET myocardial perfusion imaging represents a powerful diagnostic technique in the evaluation of patients with suspected CAD. However, incremental radiation exposure is a significant limitation to the use of this hybrid imaging modality. Previous work in CT angiography has shown that prospective electrocardiographic gating can minimize radiation exposure by limiting scanning to diastole. The authors sought to demonstrate that this technique could be used in the PET/CT environment to limit radiation exposure. By using metoprolol to achieve a heart rate of less than 65 beats per minute, the authors were able to use ECG gating and limit scanning to the later portion of the RR interval. By so doing, the authors decreased the radiation exposure (n=15 patients) from 20.5±3.6 mSv to 5.5±0.1 mSv, a 70% reduction.

Hybrid imaging technologies hold great promise, and step-and-shoot techniques should minimize radiation exposure and encourage more liberal use of CT/PET imaging.

The abstract by **Dr Ludovic Le Meunier** et al (Cedars-Sinai Medical Center, Los Angeles, CA), "Feasibility of coronary plaque imaging with FDG high-definition PET: A Phantom Study," from **Dr Daniel Berman**'s laboratory, was another vulnerable plaque feasibility study. However, unlike some of the other physiology-based analyses, this abstract focused on the technical challenges of field of view and target image resolution. [18F]fluorodeoxyglucose (FDG) has been shown to...
label vulnerable plaque; however, the small size of coronary lesions has to date been a major limitation. The authors took advantage of new high-definition PET technology from Siemens and attempted to demonstrate improved resolution using a phantom study. The high-definition PET uses an innovative image reconstruction technique that improves resolution. The authors used computed tomography angiography (CTA) scans from 15 consecutive patients and analyzed the proximal coronary segments (the usual location for vulnerable plaque). These images were used to create coronary stenoses within a phantom thorax with 2:1 and 4:1 lesion/myocardial activity ratios. These mocked-up lesions were scanned using the high-definition PET scanner. The authors found significantly improved spatial resolution and control of noise and improved the partial volume effect.

The authors concluded that the new high-definition PET technology has an appropriate resolution and appears capable of coronary plaque mapping.

**Joint session on cardiotoxicity of chemotherapy**

On the second day of the meeting there was a joint meeting on the cardiotoxicity of chemotherapy sponsored by both the Cardiovascular Council and the Oncology Council of the SNM. This CME symposium focused on both the mechanisms and management of chemotherapy-associated LV dysfunction as well as strategies for prevention and monitoring patients receiving chemotherapy.

The first speaker was **Dr Diwakar Jain** (Drexel University, Philadelphia, PA). His presentation focused on anthracyclines. Doxorubicin, the most commonly used cardiotoxic agent in clinical oncology, is associated with an incidence of CHF ranging from 2% to 20%. The lifetime cumulative dose of doxorubicin is the best predictor of the development of doxorubicin-related cardiomyopathy. The incidence of CHF is only 3% for those who have received a lifetime total dose of 300 mg/m² but increases to as high as 20% in those who have received 600 mg/m². Risk factors include age, the presence of prior cardiovascular disease, concomitant thoracic irradiation, and concomitant cardiotoxic agents. The mechanisms postulated vary but include oxidative damage and direct topoisomerase injury. Close monitoring of LVEF and discontinuation of chemotherapy with any substantial decline in LVEF is the only approach that has been found to be effective in preventing symptomatic heart failure in these patients.
Jain reviewed the data behind the current recommendations for serial multigated acquisition (MUGA) scans at baseline, after 250 to 300 mg/m², ≥450 mg/m², and after each subsequent dose. Gated-SPECT LVEF quantification is not as precise and should not be used as a substitute for MUGA. A fall in LVEF by 10% identifies patients at risk for CHF.

Some of the new data presented suggest that subclinical iron overload may be a risk factor for anthracycline-associated cardiomyopathy. Heterozygosity for the hemochromatosis genes (HFE⁺⁻ or HD⁺⁻) and receipt of blood transfusions (due to Fe content) [3] may prove to be potent risk factors and are currently being investigated. The first session closed with the observation that there are over 10 000 papers related to anthracycline cardiotoxicity spanning three decades, but in many respects the risks have not changed despite our significant research efforts.

Following Jain, Dr Gurusher Panjrath (Columbia University, New York) presented a CME talk on tyrosine-kinase-inhibitor (TKI)–related cardiotoxicity, a subject that has received considerable attention of late [4,5]. Cardiotoxicity is not a class effect with these medications, since only specific TKIs have been associated with cardiotoxicity. Trastuzumab, a humanized monoclonal antibody that targets the HER2B receptor, which is used in the treatment of breast cancer (adjuvant and for metastatic disease) has been associated with cardiotoxicity. It carries a 4% to 7% incidence of LV dysfunction when used alone, with a 1% to 3% risk of heart failure; however, when used in combination with other cardiotoxic agents, this risk is greater than 20%. A recent meta-analysis presented by the speaker demonstrated an RR of 2.45 for the development of cardiomyopathy. The risk factors are similar to those for doxorubicin cardiomyopathy. Some have postulated that the agent interferes with cardioprotective TKI signaling (through ERBB2) in the ventricular myocardium. The cardiomyopathy is partially reversible with cessation of trastuzumab therapy. Consensus expert opinion suggests that serial MUGA acquisition and BNP determination is likely the best approach to monitoring these patients.

Patients in the cardiovascular clinics are frequently the same patients seen in the oncology clinic. The subject of chemotherapy-related cardiotoxicity, while fairly prominent in the medical literature, is only going to become more important. Many of the newer
chemotherapeutic agents associated with cardiotoxicity are less well-known to practicing cardiologists and may represent an important area for continuing education.

**Abstract session continued**

The abstract by **Dr Mouaz Al-Mallah** (Brigham and Women's Hospital, Boston, MA) et al, "Do the ACCF/ASNC appropriateness criteria predict outcomes in patients with known coronary artery disease?" (Dr Marcelo DiCarli, the editor of *Circulation Imaging*, was the senior author) attracted a lot of attention. The appropriateness criteria, while only formally discussed in one session, were alluded to many times throughout the conference and were a frequent topic of informal discussion. This is a common theme from many imaging disciplines, including coronary angiography, CT, nuclear imaging, and echocardiography.

Al-Mallah et al et al tested the hypothesis that patients classified as appropriate imaging candidates would have better outcomes when compared with patients who underwent SPECT for inappropriate indications as reflected by the ACCF/ASNC criteria. In order to test this hypothesis, the authors studied the outcomes of 5943 patients without known CAD who underwent SPECT MPI (with sestamibi) for the investigation of possible cardiovascular disease between March 2002 and October 2006. Notably, 45.6% of the patients were asymptomatic. The indication for each test was labeled appropriate, uncertain, or inappropriate. Over a median follow-up of 2.6 years, the highest diagnostic yield and worst outcomes were in the "uncertain" group, prompting the authors to conclude that the appropriateness criteria should be reconsidered. Interestingly, nearly a third of the "inappropriate" patients went on to undergo revascularization, compared with 25% in the "appropriate" group.

Many physicians (especially at this conference) seem somewhat unsure of the appropriateness criteria. While many agree that too many inappropriate studies are being done, there is a large degree of variation on what defines an appropriate exam. This controversy is further fueled by the fact that some appropriateness guidelines are at odds with the treatment guidelines published by the ACC/AHA. Finally, whereas cardiologists often just had one guideline to read, now they have to read an appropriateness guideline and the treatment guideline--certainly a daunting task for a busy, practicing cardiologist.
The appropriateness criteria, especially in the context of other guidelines, are an area ripe for continuing medical educational efforts--and lively academic debate.

The abstract by Dr Mark A Trimble (Duke University Medical Center, Durham, NC) et al, "Prevalence and predictors of dyssynchrony determined by gated SPECT perfusion imaging in patients with LV dysfunction," addressed a hot topic at these meetings. There were several presentations on the use of SPECT MPI to evaluate dyssynchrony. The group with the most experience in this emerging field is the Duke group and their collaborators from Emory and the University of Alabama. Previously, this group has shown that SPECT MPI can quantify dyssynchrony in an automated, reliable, and reproducible fashion. At this meeting, Trimble et al presented their findings from the use of this technique in 260 consecutive heart-failure patients referred for SPECT MPI. The authors found that dyssynchrony as identified by SPECT (phase standard deviation [SD] ≥43°) was present in 52% of the patients. The dyssynchrony measure (phase SD ≥43°) has been shown to predict a positive response to cardiac resynchronization therapy (CRT). The authors subsequently attempted to identify clinical predictors of a phase SD ≥43° and found that a low EF, wide QRS, and a high scar burden were all associated with dyssynchrony on SPECT. Surprisingly, one in five patients in this cohort who had nonischemic cardiomyopathy had dyssynchrony (as identified by SPECT), whereas more than half with ischemic cardiomyopathy had dyssynchrony. Historically, patients with nonischemic cardiomyopathy have a better response rate to CRT.

Following the PROSPECT study (randomized trial presented at HRS 2007) [6], which demonstrated that tissue Doppler imaging cannot reliably predict CRT response, there has been tremendous interest in the development of novel imaging techniques to identify dyssynchrony. Outside of nuclear cardiology, there has been a lot of promise surrounding strain imaging. Regardless of the specific technique, all of these tools have one thing in common: they are more sophisticated and complex than traditional imaging techniques and processing. Dyssynchrony imaging is a rapidly moving and increasingly complex field. While not yet widely used in clinical practice (or validated in prospective trials) these techniques are an important area for continuing research and physician education.
Tuesday, June 17

One of the most well-attended and prominent sessions on Tuesday was a CME symposium on novel tracer development. This session covered new tracer techniques across a broad range of development, including the basic science laboratory all the way to novel techniques being implemented in academic center nuclear labs. The first speaker in this session was Dr Lynne L Johnson (Columbia University). Her talk, "Novel tracers--will they change the field?" discussed new tracers as they relate to the holy grail of cardiovascular imaging: identification and localization of the vulnerable plaque. While her talk was almost completely restricted to animal work and basic studies, her presentation highlighted and reinforced much of the vulnerable plaque imaging studies presented at SNM. The final take-home message from Johnson was that techniques targeting extracellular matrix degradation (such as matrix metalloproteinase antibody tagging), neovascularization (such as integrin imaging, see Beer et al above), and FDG PET currently hold the most promise.

The second speaker in this series was Jain. He presented very impressive data regarding a novel rest-stress [18]FDG-99mTc-sestamibi imaging approach from his lab. While these data have been reported on previously, it certainly drew the most attention from the audience. While many cardiologists are familiar with the clinical presentation of myocardial ischemia during acute coronary syndromes, ischemia during provokable stress testing is usually a transient phenomenon and is not always associated with a wall-motion defect. Flow voids associated with impaired perfusion during ischemia can be challenging to detect (as reflected by the limited sensitivity for detection of single-vessel disease with SPECT MPI). During ischemia, myocardium utilizes considerably more glucose than during resting conditions (an 8- to 10-fold increase). The increased myocardial glucose uptake can easily be imaged with [18]FDG. Jain and colleagues used dual isotope imaging with FDG and sestamibi. In this new imaging technique, three series of images are produced: FDG stress images; sestamibi stress perfusion images; and sestamibi rest perfusion images. In traditional rest-stress SPECT imaging, areas of fixed defects signify infarct, and reversible defects (defect on stress but not resting images) correspond to ischemia. In FDG-sestamibi scanning, there is an additional set of FDG images. In the FDG stress images, areas of ischemia show bright signal intensity, and normal areas have no tracer activity. The speaker showed case after case
where the FDG images clarified what typically would have been a challenging traditional SPECT MPI study. For example, FDG ischemia images can help clarify attenuation vs ischemia, and they can identify "balanced" ischemia. In addition, the added FDG images increase the sensitivity of SPECT MPI considerably (sensitivity FDG-sestamibi 91% vs 82% for traditional SPECT-MPI). In conclusion, exercise FDG imaging is a powerful and highly promising technique. Concerns over radiation dose may be minimal, since in theory rest images could be eliminated altogether in a gated study.

The last presentation in the series was by Dr Markus Schwaiger (Technical University of Munich) on "How to integrate imaging for the work-up of coronary artery disease." While there is extensive debate over the optimal test for the screening and diagnosis of coronary artery disease, Schwaiger attempted to focus on the strengths and weaknesses of each imaging technique. The speaker highlighted the proven outcomes data with SPECT MPI as well as its wide availability. However, the primary limitation of SPECT MPI is its sensitivity of 89% and specificity of 78%. With respect to cardiac MRI, Schwaiger emphasized the tremendous dependence on complex protocols and operator experience. The principal advantage of cardiac MRI is its ability to provide scar patterns (via hyperenhancement, viability, good evaluation of the pericardium, and excellent structural definition [eg, in adult congenital heart disease]) [8]. The author stated that adenosine stress MRI should be considered an experimental technique; however, it is clearly used in centers of excellence with good results (eg, Northwestern, Duke, etc). Cardiac PET was lauded for its increased sensitivity, superior quantitative capabilities, and its promise of combined use in hybrid imaging platforms (eg, CT/PET). Of course the restricted availability of PET and the time-consuming nature of the exam and protocol have thus far limited its use to research centers.

The other major CME session on Tuesday was the "Challenging cases/read with the experts" session. Three leaders in the field reviewed several difficult cases and concluded each with a final angiographic determination. While there were several "pearls and pitfalls" discussed, none of them were particularly novel. Lung field uptake in patients with heart failure, subendocardial ischemia, and transient ischemic dilatation, advantages to monochromatic reading, and CT-based attenuation correction were among many topics discussed.

55th Annual Meeting of the Society of Nuclear Medicine (SNM)
Summary

The 55th annual SNM meeting cardiovascular track centered on several major themes and topics:

1. Hybrid imaging techniques,
2. Novel tracer development--especially with respect to the vulnerable plaque.
3. Novel applications of existing SPECT MPI techniques, including risk stratification of sudden cardiac death and dyssynchrony imaging.
4. Other health implications of nuclear techniques--including radiation dose and extracardiac findings.
5. Appropriateness criteria and outcomes.

All of these topics will continue to garner attention and continued research funding. Some technologies, including vulnerable plaque imaging and hybrid imaging, will require more time before they are ready or mature enough for routine clinical use. Other topics and technologies, such as appropriateness criteria and novel applications for SPECT MPI such as dyssynchrony imaging, are already affecting daily practice or will do so in the very near future. CME activities should especially focus on these later (and more controversial) areas.

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