



## Highlights of Radiological Society of North America 92nd Scientific Assembly and Annual Meeting **CME**

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### Target Audience

This activity is intended for radiologists, cardiologists, oncologists, nuclear medicine specialists, and other relevant specialty physicians on Medscape with an interest in integrating advanced imaging techniques, such as PET scanning, CT scanning, magnetic resonance imaging (MRI), and molecular imaging, into their practice to facilitate the early detection and efficient clinical management of cancer, heart disease, and cardiac function.

### Goal

The objective of this activity is to spotlight the expanding roles of advanced imaging studies, such as PET scanning, PET/CT fusion imaging, CT scanning, magnetic resonance imaging (MRI), and molecular imaging, in the detection, assessment, and treatment of cancer and heart disease; to define appropriate settings for the use of these technologies; and to offer a venue for key opinion leaders in imaging to detail the benefit of these technologies for the radiology, oncology, cardiology, and other relevant clinical audiences on Medscape.

### Learning Objectives

Upon completion of this activity, participants will be able to:

1. Define the role of PET scanning and PET/CT scanning in the assessment and management of cancer
2. Outline recent innovations in molecular imaging of malignancies
3. Discuss the clinical merits of fast CT scanning in the assessment of coronary artery disease and cardiac anatomy and function
4. Detail the expanding role of MRI in evaluating cardiac anatomy and function and coronary artery disease

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#### Cardiac MRI: Still Vying With CT for Supremacy

Research on cardiac magnetic resonance imaging (MRI) continues as it evolves into a common clinical imaging tool. However, with the rapid technical developments in computed tomography (CT), including coronary CT angiography (CTA), it remains to be seen in what exact clinical situations either or both techniques may be the most appropriate and cost-effective approach. At the Radiological Society of North America (RSNA) 92nd Scientific Assembly and Annual Meeting; November 26-December 1, 2006; Chicago, Illinois, there were several scientific sessions, educational exhibits, invited presentations, refresher courses, and special focus sessions highlighting cardiac MRI techniques and clinical applications. Here we review the research that was presented on this topic.

#### Cardiac Function

MRI is able to provide important functional information, such as left ventricular ejection fraction and myocardial contractility. A study from Germany investigated the impact of endurance sports on cardiac function in elderly marathon runners.<sup>[1]</sup> This study

demonstrated that the mean left ventricular mass was significantly higher than that published for the "nonathlete" group ( $141 \pm 27$  g vs  $77.5 \pm 13$  g, respectively), although there was no significant difference in the left ventricular volumes. Therefore, it was concluded that endurance sports result in cardiac hypertrophy without dilatation.

### Cardiac Arrhythmia

Identification of the substrate for cardiac arrhythmia can have an important treatment implication. The Italian researchers assessed the cardiac MR-detected prevalence of myocardial structure and functional abnormalities in patients with arrhythmias.<sup>[2]</sup> The study included 43 patients with nonischemic ventricular arrhythmias. It was determined that in patients with primary ventricular arrhythmias, there is a high prevalence (87%) of morphologic, signal-intensity, and wall motion abnormalities even in the setting of negative echocardiograms. Although this study provided important correlative imaging substrates for ventricular arrhythmias, the clinical impact of such MRI findings on individual patients will need to be established.

### Cardiac Pacemakers

There have been concerns about the effects of switching magnetic field during an MRI examination on the cardiac pacemaker and its leads. Helfer and colleagues<sup>[3]</sup> evaluated the heating induced in the pacing leads during an MRI procedure. In this simulation study with realistic phantoms, it was determined that the MR-induced heating varied with the position of the pacing system in the scanner's bore. In one position the measured temperature increase was as high as  $31^{\circ}\text{C}$ , but at the center of the bore the temperature rise was more typically at about  $6^{\circ}\text{C}$ . In a related study from Germany, the researchers evaluated a strategy for safe performance of extrathoracic MRI studies in patients with cardiac pacemakers who are not pacemaker-dependent.<sup>[4]</sup> In this study that included 82 patients, although inhibition of the pacemaker was not observed, the pacing capture threshold increased significantly from the pre-MRI stage to the post-MRI period. In 3.5% of examinations, the serum troponin level increased in the post-MRI period indicating MRI-induced thermal myocardial injury. This study excluded pacemaker-dependent patients and thoracic MRI examinations. Therefore, the findings may not be generalizable to cardiac MRI studies in all patients with cardiac pacemakers.

### Cardiomyopathy

A Japanese study evaluated the diagnostic utility of MRI in detecting myocardial fibrosis, which may be predictive of fatal arrhythmias, in 74 patients with hypertrophic cardiomyopathy.<sup>[5]</sup> Cine, myocardial perfusion, and delayed enhanced (DE) scans were obtained with a 1.5T MRI system. A percentage of delayed enhancement was calculated according to the following: %DE = delayed enhancement area/total myocardial area. DE was found in 76% of patients. The left ventricular ejection fraction in patients with DE was significantly smaller than those without DE ( $59.7\% \pm 8.8\%$  vs  $63.2\% \pm 16\%$ , respectively;  $P < .05$ ). During follow-up ( $1256 \pm 193$  days), 8 patients experienced adverse cardiac events, and 7 of these patients had shown DE and 5 had myocardial perfusion defects. The study authors concluded that myocardial perfusion and DE on MRI are useful in identifying high-risk hypertrophic cardiomyopathic patients for early diagnosis of myocardial fibrosis as a potential substrate for fatal arrhythmias.

The German investigators compared histologic findings (specifically viral myocardial inflammation) with the presence of DE in contrast-enhanced MRI of 22 patients with dilated cardiomyopathy.<sup>[6]</sup> The results of the analysis showed that DE does not correlate with viral myocarditis in patients with dilated cardiomyopathy. This might have been due to the sample size or true biological unrelatedness between viral-induced myocarditis and depiction on MRI as DE. Other related research from France evaluated cardiac MRI in patients with clinical and biological myocarditis.<sup>[7]</sup> MRI was able to establish the diagnosis of myocarditis (through delayed gadolinium myocardial enhancement) in 49% of cases and allowed the differential diagnosis from myocardial infarction.

MR spectroscopy (MRS) was also evaluated for its ability in detecting alterations of energy metabolism in secondary cardiomyopathies. A manifestation of Fabry's disease, which is a lysosomal storage disease, is cardiac hypertrophy. German investigators used MRS to determine possible changes of energy metabolism in patients with Fabry cardiomyopathy receiving enzyme replacement therapy.<sup>[8]</sup> The research included 27 patients with genetically proven Fabry's disease who were examined before the onset of therapy and at 12 months during the follow-up period. Findings were compared with healthy individuals as controls. There were significant energetic alterations in Fabry cardiomyopathy with a trend toward biochemical improvement and a decline in the mean left ventricular mass during enzyme replacement therapy. The investigators indicated that larger sample size and more follow-up data would be necessary for definitive assessment of MRS in predicting treatment response in this clinical setting. The same group of German investigators also reported on the effect of enzyme replacement therapy on right ventricular function in patients with Fabry cardiomyopathy.<sup>[9]</sup> This study included 59 patients, and the procedure for data collection was similar to the latter study from the same laboratory. During 1 year of enzyme replacement therapy, MRI could detect right ventricular ejection fraction improvement from a baseline of  $55\% \pm 6\%$  to  $59\% \pm 6\%$  while depicting a decline in the right ventricular mass.

### Coronary Artery Disease

Researches from Beijing, China, compared the diagnostic accuracy of navigator-gated 3-dimensional (3D) magnetic resonance angiography (MRA) with 64-slice CT in evaluating coronary artery lumen with calcified atherosclerotic plaque.<sup>[10]</sup> Twenty-four patients with various extents of calcified atherosclerotic plaques on CTA were selected for coronary MRA, and conventional angiography was performed within 1 week of both studies for validation. The sensitivity and specificity of CTA were 89% and 33%, and those for MRA were 83% and 89%, respectively. The study concluded that navigator-gated 3D MRA had higher specificity than 64-slice CTA for detecting significant coronary artery disease ( $> 50\%$  diameter stenosis) in the setting of calcified plaque.

An investigation from Germany compared MR perfusion imaging and single-photon emission tomography (SPECT) for detection of

flow-limiting coronary stenosis compared with conventional coronary angiography and fractional flow reserve as a standard of reference.<sup>[11]</sup> The study included 43 patients with suspected coronary artery disease who received MRI and SPECT within 2 weeks of angiography. MRI displayed a sensitivity and specificity of 88% and 90%, respectively. The sensitivity and specificity of SPECT were 71% and 91%, respectively. This study suggested that MRI may be more sensitive than SPECT in detecting significant coronary disease at a comparable specificity. Another German report compared the visual and quantitative analyses of myocardial perfusion in order to determine the most accurate method in the clinic.<sup>[12]</sup> Thirty-two patients with suspected myocardial ischemia underwent MRI at 1.5T (turbo FLASH 2D sequence) at rest and after cardiac stress (140 micrograms [mcg] of adenosine per kilogram of body weight per minute). Visual image analysis was obtained through qualitative consensus interpretation of 2 experienced observers who were blinded to the clinical data. For the diagnosis of ischemia, stress perfusion deficit cutoff values of myocardial perfusion reserve indexes of 1.1, 1.2, 1.5, 1.7, 0.8, and 0.9 times the median were used. Invasive coronary angiography with luminal narrowing greater than 75% was used as a reference. The accuracy of visual assessment was 78%. On the basis of a maximum slope of signal intensity over time curves, the diagnostic accuracy was highest at 81% for the 0.8 times the median myocardial perfusion reserve index cutoff value. The study authors concluded that visual consensus provides comparable accuracy to the more laborious quantitative data analysis.

Another investigation from German researchers evaluated whether coronary flow reserve is reduced in nonstenosed bypass grafts supplying nonviable myocardium with the DE concept and measurements of MR phase-contrast flow.<sup>[13]</sup> This research showed that on the basis of DE evaluation, flow reserve was almost twice as high in the group of bypass grafts supplying viable myocardium compared with those grafts supplying nonviable myocardium ( $2.9 \pm 0.9$  vs  $1.5 \pm 0.7$ , respectively). The study concluded that flow reserve is reduced in nonstenosed bypass grafts supplying nonviable myocardium, which the investigators presumed might be due to altered microcirculation.

The prognostic value of MRI-identified microvascular obstruction (MVO) was also reported.<sup>[14]</sup> Specifically it was determined whether detection of MVO could predict improvement of the global left ventricular function by imaging perfusion and DE. The study included 36 patients with Q-wave myocardial infarction who underwent MRI at about 2 weeks and 12 weeks after infarction. This study showed that MR perfusion was superior to DE and could provide important prognostic information about global left ventricular functional recovery by assessing MVO in patients with myocardial infarction.

The researchers from New York compared 3 precontrast methods (muscle-nulled, fat-nulled, T1 quantification) for determining whether a myocardial infarction is older than 6 months.<sup>[15]</sup> Thirty-one patients with documented prior myocardial infarction participated in the study. Fat-nulled imaging (in which infarction is hypointense) performed best with a sensitivity of 75% and a specificity of 91% for discriminating infarctions older than 6 months. Precontrast T1 quantification at a cutoff of 613 ms had a sensitivity of 100% and a specificity of 82% for discriminating recent and chronic myocardial infarcts.

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### Milestones in Molecular Imaging

Molecular imaging continues to take great strides and generate excitement in radiology. In fact, at the Radiological Society of North America (RSNA) 92nd Scientific Assembly and Annual Meeting; November 26-December 1, 2006; Chicago, Illinois, there were newly established scientific sessions, educational exhibits, invited presentations, refresher courses, and special focus sessions dedicated to molecular imaging. A new "molecular imaging zone" located in the educational and scientific poster session area highlighted the research and education in this field. Here, we review the translational molecular imaging research that was presented emphasizing potential future clinical application.

#### Optical Imaging

A study from Philadelphia, Pennsylvania, evaluated the optical imaging methods that could be potentially used to distinguish between indolent and aggressive forms of human melanoma.<sup>[1]</sup> Human xenograft melanoma cell lines were implanted in athymic nude mice. Low-temperature NADH/Fp fluorescence imaging was employed. It was observed that more aggressive tumors had significantly higher Fp redox ratios (ie,  $Fp/[Fp + NADH]$ ) than the indolent ones. These findings suggested that the fluorescence imaging of the Fp redox ratio can potentially be a useful marker of human melanoma aggressiveness or metastatic potentiation, although the development of metastases also depends on other factors, such as tumor microenvironment and host immune system.

Another study determined whether multichannel near-infrared optical imaging can assess treatment-response susceptibility during trastuzumab treatment of breast cancer.<sup>[2]</sup> HER-2 probe showed expected increased binding to the HER-2-overexpressing tumors compared with HER-2 normal tumors. Also as hypothesized, trastuzumab treatment reduced the HER-2 probe binding in the HER-2-overexpressing tumors and inhibited tumor growth. The annexin probe was also developed to image apoptosis. This research showed that tumor response may be determined very early in treatment, allowing the opportunity to modify therapy, if necessary, to optimize response.

The clinical feasibility of a laser breast scanner was presented on pilot imaging data obtained from 24 normal control and 11 women with breast cancer.<sup>[3]</sup> The near-infrared diffuse optical spectroscopic properties of the breast tissues were compared. These properties depend on tissue concentrations of deoxy hemoglobin, oxyhemoglobin, water, and lipids. It was determined that very dense breasts have distinctly different optical characteristics compared with less dense breasts. Therefore, it was concluded that the laser breast scanner with diffuse optical spectroscopy may be a promising technique in the differential diagnosis of breast lesions. Another similar study from Austria evaluated the computed tomographic laser mammography (CTLM) system.<sup>[4]</sup> CTLM detects cancer through measurement of the tissue hemoglobin concentration as a surrogate marker for tumor angiogenesis. Increased absorption was seen significantly more in the malignant lesions (67%) than in the benign lesions (37%). The absorption increase was seen most by invasive ductal cancer (76%) followed by invasive lobular cancer (63%) and then ductal carcinoma in situ (48%). Of note, a number of ductal carcinoma in situ and grade 1 or 2 invasive cancers were missed. The exact underlying biological and/or technical reasons for the false-negative cases will need to be determined. Regardless of this, however, the study concluded that the CTLM system may be useful in the differential diagnosis of breast lesions.

#### Magnetic Resonance Imaging and Spectroscopy

The group from the Massachusetts General Hospital in Boston, Massachusetts, determined whether a novel, small, activatable magnetic resonance (MR) agent targeted to myeloperoxidase (MPO) can be used to detect active demyelinating lesions.<sup>[5]</sup> MPO is an enzyme secreted by the inflammatory cells in active demyelinating plaques in multiple sclerosis and in experimental autoimmune encephalomyelitis. Magnetic resonance imaging (MRI) of the mouse brain was performed with a 7T MRI scanner. In the presence of MPO, the targeted MR agent (bis-5HT-DTPA[Gd]) can be oligomerized and bind to protein causing a prolonged, increased T1-

weighted signal even up to 90 minutes, whereas a generic gadolinium (Gd) contrast agent only demonstrated short-time enhancement and fewer lesions. Immunohistochemical analysis confirmed that the new lesions detected with the targeted MPO-sensitive MR agent stained for the presence of MPO. This study demonstrated that targeting MPO allows differentiation of active from inactive (with only blood-brain barrier breakdown) demyelinating lesions.

A group from Philadelphia evaluated  $^1\text{H}$  (proton) and  $^{31}\text{P}$  magnetic resonance spectroscopy (MRS) for the detection of treatment response in xenograft tumor models of non-Hodgkin's lymphoma.<sup>[6]</sup> The treatment was multiple cycles of CHOP (cyclophosphamide, hydroxydoxorubicin, vincristine, prednisone). Bryostatins were also used to inhibit the expression of the multiple drug-resistant gene to enhance therapeutic effect. The tumor volumes in the treated group decreased by 60% of the pretreatment values, whereas those for the control group increased monotonically. MRS was able to show spectral changes consistent with decline in relevant metabolites 1 week after the first cycle of treatment, whereas the control group showed a slight increase in these same metabolites. A similar study was reported by Chinese investigators from Shanghai who studied the metabolites of pancreatic diseases and their *in vivo*  $^1\text{H}$  MRS characteristics for the purpose of differentiating benign from malignant pancreatic tumors.<sup>[7]</sup> The study authors found that the choline:lipid ratio in pancreatic carcinoma was significantly higher than that in an inflammatory pancreatic mass. Therefore, they suggested that *in vivo*  $^1\text{H}$  MRS may be used for the differential diagnosis of pancreatic masses.

A South Korean group of investigators determined whether supraparamagnetic iron oxide (SPIO)-labeled autologous white blood cell (WBC) MRI can differentiate soft-tissue abscess from necrotic tumor.<sup>[8]</sup> Experimental tumor and abscess models were employed in rabbits. The rabbits were imaged before and 4 hours after SPIO-labeled WBC administration. The 3T MRI findings were correlated with histopathology. The study authors observed the characteristic signal drop at abscess peripheries on SPIO-labeled autologous WBC MR images as a result of the presence of iron-containing monocytes. This study suggested that SPIO-labeled autologous WBC MRI can be a useful imaging tool in differentiating abscess from necrotic tumor.

Researchers from The Netherlands compared the contrast agents MS-325 (a Gd-based blood pool agent that binds to albumin) and Gd-DTPA in conjunction with MRI for detecting sites of atherosclerotic plaques in the vessel walls.<sup>[9]</sup> These studies were performed on New Zealand white rabbits. Plaque development was induced by balloon denudation, and the rabbits were fed a cholesterol-enriched diet. Mean enhancement for MS-325 was significantly higher for atherosclerotic plaque compared with the control nonatherosclerotic vessel wall ( $1.8 \pm 0.6$  vs  $1.2 \pm 0.3$ , respectively;  $P = .02$ ). Conversely, there was no statistically significant difference observed with Gd-DTPA. The study authors concluded that MS-325 may be useful in the imaging evaluation of atherosclerosis. A related study from New York used another new MR contrast agent, P947 (Guerbet), that is formed from a peptide with a high affinity for matrix metalloproteinases (MMPs), which are involved in atherosclerotic plaque growth and rupture.<sup>[10]</sup> The animal model and the experimental atherosclerosis were similar to the previous study from The Netherlands. Again, a statistically significant higher MR signal was seen in the atherosclerotic plaques than in the control with P947. No detectable changes were noted with the conventional Gd contrast agent. Immunohistochemistry showed that the highest signal with P947 was located in the MMP-rich areas. This study also demonstrated that it may be possible to detect early atherosclerosis with MRI with a suitable targeted contrast agent.

Investigators from San Francisco, California, compared 2 techniques for measuring tumor vascularity, *in vivo* contrast-enhanced MRI, and perfusion-dependent fluorescent microscopy in monitoring tumor microvessel response to angiogenesis inhibition.<sup>[11]</sup> Breast cancer xenografts were used as the tumor model in female nude rats. When the tumors reached 1 cm, the rats were either treated with anti-vascular endothelial growth factor (VEGF) antibody bevacizumab at 2 different dose levels (treated groups) or with saline (control group). MRI-assayed tumor vascularity was significantly higher in the control tumor than in both treated tumors. Microscopic measurement agreed with the MRI-assayed findings. The study authors concluded that dynamic albumin Gd-DTPA-enhanced MRI can measure the richness of the tumor vascularity and can be useful in evaluating treatment response with antiangiogenic agents.

A Belgian study evaluated dynamic contrast-enhanced MRI with a macromolecular Gd contrast agent (gadomelitol) for therapy assessment in a rat model of colorectal cancer.<sup>[12]</sup> Gadomelitol is a macromolecular blood pool agent with physicochemical properties suited for tumor microvascular imaging. The experimental groups included rats with control untreated tumor and rats treated with either erythropoietin or radiation therapy. It was noted that radiation therapy significantly reduces vascular permeability and microcirculatory flow and EP reduces neovascular permeability. The study authors concluded that gadomelitol allows *in vivo* assessment of altered neovascular permeability, which can be important in assessing response following antiangiogenic therapy.

Accurate imaging assessment of the lymph nodes is important in staging and restaging cancer, which in turn can significantly affect clinical management. Researchers from Harvard Medical School, Boston, Massachusetts, evaluated lymphotropic magnetic nanoparticles (*Combidex*, Advanced Magnetix) to identify lymph node metastatic involvement in 18 men with a history of prostate cancer and a rising prostate-specific antigen (PSA) level who were candidates for salvage radiation therapy.<sup>[13]</sup> Mean PSA was 0.96 ng/mL (0.3-3.7). Two patients (11%) experienced adverse reactions (grade 1 allergic reaction) after injection of the magnetic nanoparticles. The MR images showed variable locations of suspicious nodes. Long-term validation data are currently pending for these MR findings. Another preliminary report from the same laboratory evaluated the signal-intensity characteristics of the prostate gland with ultrasmall supraparamagnetic iron oxide (USPIO)-enhanced MRI.<sup>[14]</sup> Sixty-nine patients participated in this study. It was noted that there was a trend for a higher uptake level in the central zone of the prostate gland than in the peripheral zone of the gland. The investigators are now assessing the utility of this observed differential gland uptake in correlation to the sites and pathologic grades of the primary prostate tumors.

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## Cardiac Imaging Update: Enhanced Role for 64-Slice CT

The use of computed tomographic (CT) scanning of the heart is expanding rapidly. With the development of the 64-slice CT scanner, it is now possible to obtain exquisite images of the coronary arteries in addition to assessment of myocardial perfusion and cardiac function. At the Radiological Society of North America (RSNA) 92nd Scientific Assembly and Annual Meeting; November 26-December 1, 2006; Chicago, Illinois, there were many scientific sessions, educational exhibits, invited presentations, refresher courses, and special focus sessions highlighting this important topic. In this overview, we review the new developments in cardiac CT, including coronary CT angiography (CTA).

The topic of the Annual Oration of Diagnostic Radiology was "Rise of Cardiac Imaging Forces Radiologic Reinvention." The Oration was delivered by Kerry M. Link, MD, Director of the Center for Biomolecular Imaging at Wake Forest University Health Sciences in Winston-Salem, North Carolina. Dr. Link stated that for long it has been thought that cardiac imaging belongs to cardiology, that it is not economically viable, and that there is lack of training among radiologists. However, he challenged radiology to a second chance in redefining our core services by delivering high-quality cardiac imaging. Regardless of the fast development of cardiac CT, Dr. Link cautioned that at this time, cardiac CT is most suited for evaluating coronary artery disease and structural abnormalities. Regardless of this, he added that with the imaging technologies advancing so rapidly, the current limitations will be overcome. By the same token, he suggested that radiology should make the adequate investments to succeed in cardiac imaging. This in part will require changes in radiology training, in having radiologists be more responsible for monitoring patients during the imaging session and by investing in cardiac imaging research. He concluded that at this critical time, the response of radiology to these challenges will dictate the outcome of our future involvement in cardiac imaging.

We now review some of the research and new developments that were presented as either scientific or educational presentations.

### Coronary Calcium

Rutten and colleagues,<sup>[1]</sup> from The Netherlands, determined the error that is induced when a predefined cardiac phase is used for calcium scoring by an electrocardiographic (ECG)-gated 64-slice CT compared with selection of the most motionless phase in the cardiac cycle. The study population included 50 subjects with known or suspected coronary artery disease. Beta blockers were used to reduce the heart rate. In each patient, calcium scoring (Agatston score [AS] and mass score [MS]) was performed on 10 data sets reconstructed at 10% intervals throughout the cardiac cycle. For each data set, cardiac motion was subjectively scored on a 3-point scale, and the most motionless phase was used as the reference. In 58% of patients, the most motionless phase was seen at 70% of the cardiac cycle. Using the motionless phase instead of a predetermined reference phase would have induced an average error of -4% (-59% to 15%) for AS and -3% (-62% to 10%) for MS.

Investigators from Israel evaluated the rate of unassessable segments due to heavy calcification in 30 patients with elevated calcium scores (700-2987 AS) undergoing coronary CTA with 64-slice CT.<sup>[2]</sup> This study demonstrated that the rate of unassessable segments due to heavy calcification was low (5%) and therefore concluded that an elevated calcium score should not be considered as an absolute contraindication for coronary CTA.

### Coronary Arteries

A vast number of coronary angiographies are performed for diagnosis without intervention. CTA can potentially be cost-effective in preselecting those patients who may benefit most from intervention in association with conventional angiography. The researchers from The Netherlands prospectively studied the diagnostic performance of the 64-slice coronary CTA for detecting significant coronary lesions (defined as  $\geq 50\%$  diameter stenosis) in 145 patients scheduled for valve surgery.<sup>[3]</sup> Of the 145 patients, 35 patients were excluded because of CT criteria (arrhythmia, impaired renal function, contrast allergy), and 13 patients were excluded because of other considerations. Of the remaining 97 patients, 27 patients denied written informed consent, and therefore the final study population included 70 patients (exclusion rate of 52%). The prevalence of significant coronary artery disease was 25.7%. On a per patient basis, sensitivity, specificity, and positive and negative predictive values were 100%, 92%, 82%, and 100%, respectively. Although these results are encouraging, the diagnostic performance of coronary CTA in this clinical setting is influenced by patient preselection in view of the relatively high exclusion rate. This same group of investigators compared 64-slice CTA with conventional coronary angiography in 180 patients with atypical chest pain, stable or unstable angina, or non-ST segment elevation myocardial infarction.<sup>[4]</sup> Patients who had undergone bypass surgery or percutaneous coronary intervention were excluded. Lesions with  $\geq 50\%$  luminal narrowing were considered significant stenoses. With the conventional coronary angiography as the standard of reference, 64-slice CT demonstrated a sensitivity of 93%, specificity of 96%, and positive and negative predictive values of 78% and 98%, respectively, for detecting significant coronary stenosis on a segment-by-segment basis. This study therefore showed that in a relatively diverse group of symptomatic patients, 64-slice CT can reliably detect significant coronary disease.

Although the latter study excluded the postbypass graft surgery patients, a Canadian investigation reported on the use of 64-slice CTA in symptomatic patients after coronary artery bypass graft (CABG) surgery.<sup>[5]</sup> The study authors evaluated 24 symptomatic post-CABG patients with invasive conventional coronary angiography as the standard of reference. The mean interval from CABG surgery to the imaging evaluation was  $9 \pm 6.5$  years. On a per vessel basis, CTA showed a sensitivity of 100% and specificity of 95% for detecting occlusion or stenosis in grafts. The study concluded that 64-slice CTA is a sensitive and specific tool for comprehensive detection of new disease in grafts and native coronary arteries in symptomatic post-CABG patients. A similar report from Austria examined 39 patients with 64-slice CTA.<sup>[6]</sup> The sensitivity and specificity for detecting bypass graft stenosis in the range 50% to 90% were 80% and 100%, respectively. The report noted that distal anastomosis stenosis may be missed due to spatial resolution limitation.

The use of 64-slice CTA in the assessment of coronary artery stent patency and restenosis was reported in a German investigation.<sup>[7]</sup> A total of 46 stents were evaluated, of which 45 (98%) had sufficient diagnostic image quality. The standard of reference for the findings of the CTA was quantitative conventional coronary angiography. The sensitivity and specificity of the 64-slice CTA were as follows: proximal stent stenosis (75% and 95%, respectively), in-stent disease (75% and 92%, respectively), and distal stent stenosis (67% and 85%, respectively). The study concluded that the improved spatiotemporal resolution of the 64-slice CT is also beneficial for the assessment of coronary stents. A similar topic was studied by another German group that noted out of 13 stents smaller than 3 mm in diameter, only 1 (8%) was evaluable, whereas 65% of those stents with a diameter greater than 3 mm could be assessed.<sup>[8]</sup> Per artery basis, assessment was possible in 69% of the left main/left anterior descending artery stents, 42% of the left circumflex artery stents, and 43% of the right coronary artery stents. The sensitivity and specificity for detecting in-stent restenosis were 86% and 98%, respectively.

In another study, the clinical outcome of abnormal coronary CTA studies was evaluated.<sup>[9]</sup> Eighty-nine consecutive CTA studies (16- and 64-slice) were analyzed in patients considered candidates for invasive coronary angiography. The mean calcium score was  $290 \pm 569$  (range, 0-3518). Subsequent catheterization was performed in only about 15% of the CTA studies (13 patients). Calcium score and biological sex did not influence the decision for subsequent catheterization, although the patients who underwent catheterization were older than those who did not ( $61 \pm 8.5$  years vs  $54 \pm 15.1$  years, respectively;  $P < .05$ ).

A study from Israel reviewed the perception of the hospital- and community-based cardiologists in regard to the use of 64-slice CTA.<sup>[10]</sup> A 2-page questionnaire was sent to 35 cardiologists with a 100% response rate. The survey found that only a minority of cardiologists (11%) would use CTA as a screening tool in asymptomatic patients; 50% to 60% believed that CTA will replace conventional coronary angiography; and 75% stated that CTA findings affected their management of individual patients. A related



investigation assessed the cost-effectiveness and diagnostic utility of 64-slice CTA in patients with an intermediate Framingham risk profile (atypical chest pain and asymptomatic individuals).<sup>[11]</sup> The sensitivity and specificity of CTA in detecting significant coronary stenosis were 100% and 78%, respectively, on a per patient basis. CTA was also found to be cost-effective as a second-line noninvasive gatekeeper test if used prior to the decision for conventional angiography in cases of positive exercise ECG.

A Chinese report also indicated that due to its higher spatiotemporal resolution, 64-slice CTA provides improved image quality and visibility of small coronary branches when compared with 16-slice CTA.<sup>[12]</sup>

### Congenital Heart Disease

The group from San Diego, California, evaluated 64-slice CT for the diagnosis and management of patients with congenital heart disease.<sup>[13]</sup> They reviewed their findings from 107 studies in 104 patients in whom all had prior 2-dimensional ECG. The 64-slice CT was found to be a viable imaging modality for examining a large variety of congenital heart conditions (eg, septal defects, tetralogy of Fallot, transpositions, aortic coarctation, truncus arteriosus, double outlet right ventricle, etc) for determining ventricular systolic function, as well as for evaluating the lungs and the airways. Of importance, the CT findings affected clinical management in 45% of patients.

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### Expanding Applications for PET and PET/CT Scanning

The use of hybrid imaging, particularly positron emission tomography/computed tomography (PET/CT), is expanding rapidly. At the

Radiological Society of North America (RSNA) 92nd Scientific Assembly and Annual Meeting; November 26-December 1, 2006; Chicago, Illinois, there were many scientific sessions, educational exhibits, invited presentations, refresher courses, and special focus sessions highlighting this important topic. Here we review the research that was presented on the clinical applications of PET and PET/CT with an emphasis on oncologic applications.

### Brain Tumor

Accurate detection of recurrent brain tumor after radiation and/or chemotherapy has important therapeutic and prognostic implications. One study assessed the complementary value of magnetic resonance spectroscopy (MRS) and positron emission tomography with <sup>18</sup>fluorodeoxyglucose (FDG-PET) for detection of recurrent/residual viable brain tumor after radiation and/or chemotherapy.<sup>[1]</sup> It was found that in high-grade tumors, postradiation tissue heterogeneity, cyst, necrosis, and gliosis may limit the accurate assessment of tumor viability by MRS. However, in cases of low-grade tumors MRS correctly determined the presence of viable tumor but did not accurately assess tumor to the same degree as it was possible with FDG-PET.

In another investigation from North Carolina, the study authors determined the prognostic significance of the size and magnitude of abnormal FDG uptake within areas of contrast enhancement on posttherapeutic MRI in patients with high-grade glioma.<sup>[2]</sup> Ten patients with grade 3 or 4 glioma were treated with resection followed by intracavitary radiation therapy with I-131 labeled antitenascin monoclonal antibody. Serial MRI and FDG-PET scans were performed within a 48-hour period. Contrast-enhancing MRI volumes of interest were defined and registered onto PET, and the corresponding activity was expressed as the ratio to the activity in the contralateral normal-appearing white matter. A lesion was defined as the portion of the metabolic activity of the volume of interest greater than 2 standard deviations above the mean in the contralateral normal-appearing white matter. Survival curves were also constructed. Enhancing lesions with a volume of more than 15 cc and with a mean activity ratio greater than 1.2 on PET were associated with decreased survival. It was concluded that the development of large contrast-enhancing lesions associated with high mean FDG accumulation suggests poor prognosis.

The Japanese investigators compared C-11 acetate, C-11 methionine, and FDG-PET in 20 patients with brain tumor (12 primary malignant tumor, 2 metastases, and 8 primary benign tumors).<sup>[3]</sup> Methionine uptake was observed in all 14, acetate in 12 of 14, and FDG in 5 of 14 malignant lesions. The study authors concluded that methionine is more sensitive than acetate or FDG for detecting brain tumors.

The investigators from the University of Pittsburgh, Pittsburgh, Pennsylvania, assessed the uptake characteristics of [F-18] fluorothymidine (FLT) in 3 patients with glioma through kinetic modeling and correlation to K<sub>67</sub> immunohistochemistry.<sup>[4]</sup> Their data in this very limited number of patients suggested that increased FLT uptake may be associated with tumor in subjects with untreated grade 2 oligodendrogliomas or with treated tumor despite a low-proliferation K<sub>67</sub> index, which in turn may be due to a combination of blood-brain barrier disruption, increased transport and/or net influx, and reactive inflammatory changes in the tumor and the surrounding brain tissue.

### Head and Neck Cancer

The investigators assessed the utility of performing additional body PET/CT in 172 patients with known head and neck cancer.<sup>[5]</sup> The body PET/CT identified previously unknown metastases in 16% of patients, which led to the conclusion that additional body PET/CT is warranted for all patients with head and neck cancer, even when no metastatic disease is expected.

Ghesani and colleagues<sup>[6]</sup> evaluated the predictive value of FDG-PET/CT in patients with surgically resectable oral cavity cancer. The positive and negative predictive values of FDG-PET/CT for detecting cervical lymph node metastases were 76% and 83%, respectively. These same values were 79% and 67% for CT and/or MRI alone, respectively. The conclusion was that the negative predictive value of PET/CT is superior to that of CT or MRI, and that a combination of PET/CT and CT/MRI was highly associated with pathologic findings when both studies agreed.

### Thyroid Cancer

Kim and colleagues<sup>[7]</sup> compared the diagnostic utility of FDG-PET and neck ultrasound in 25 patients with differentiated thyroid carcinoma and a negative diagnostic radioiodine scan and a rising thyroglobulin level. Combined FDG-PET and ultrasound yielded a detection rate of 60% for recurrent disease in this clinical setting. In another study from the same investigators, it was determined that diffuse increased FDG thyroidal uptake on PET scans is not predictive of an abnormal thyroid function test, and therefore routine thyroid function tests are not warranted in asymptomatic patients with diffuse thyroidal hypermetabolism.<sup>[8]</sup>

### Lung Cancer

Alkhalwaldeh and colleagues<sup>[9]</sup> assessed the diagnostic accuracy of dual-time-point FDG-PET imaging (60 and 110 minutes after tracer injection) of small pulmonary nodules (< 1.5 cm) compared with single-time-point imaging. Biopsy and follow-up revealed 39% of patients with malignant pulmonary nodules, whereas 61% of patients had benign nodules. Single-time-point imaging with a standard uptake value (SUV) threshold of 2.5 had a sensitivity and specificity of 39% and 91%, respectively. On dual-time-point imaging (with greater than 10% increase in SUV, from initial and delayed images as criterion for malignancy), the sensitivity and specificity were 69% and 97%, respectively. This study suggested that dual-time-point PET imaging has significantly higher accuracy in the characterization of small pulmonary nodules when compared with single-time-point evaluation. Conversely, another study

showed that dual-time-point (60 and 120 minutes post-FDG injection) PET scans do not improve the diagnostic performance measures of PET in differentiating radiation-induced inflammation structural changes from malignant lesions.<sup>[10]</sup> This may be due to the often observed relatively intense hypermetabolism that is associated with radiation therapy.

In another study from South Korea, it was assessed whether FDG-PET/CT may be used to differentiate between inflammatory and malignant ground-glass opacities.<sup>[11]</sup> The maximum SUV of inflammatory ground-glass opacities was significantly higher than for malignancy ( $2.02 \pm 1.5$  vs  $1.07 \pm 0.6$ , respectively;  $P < .05$ ). The malignancies included adenocarcinoma, bronchioloalveolar carcinoma, metastases, and low-grade lymphoma. The optimal cutoff value for maximum SUV was 1.27, at which point the sensitivity and specificity were 72% and 65%, respectively, for detecting malignancy. At maximum SUV of 2.5, the positive predictive value for inflammatory ground-glass opacities was 100%.

Ahmed and colleagues<sup>[12]</sup> compared FDG-PET/CT and contrast-enhanced CT in the evaluation of lymph nodes in lung cancer with pathology results as the standard of reference. The criteria used for assigning pathology included an SUV maximum of greater than 2.5 for PET/CT and the typical size measurements for chest CT. The sensitivity and specificity of nodal involvement were 93% and 58% for PET/CT and 80% and 69% for contrast-enhanced CT, respectively. The study authors concluded that FDG-PET/CT is more sensitive than contrast-enhanced chest CT (albeit less specific) in the diagnosis of mediastinal lymph node involvement, and recommended that medianoscopy and biopsy should be considered in any patient with a PET/CT-positive mediastinal node, if the exact pathology would result in a change in the patient's clinical management.

In another prospective investigation from South Korea, the findings of PET/CT were compared with histologic nodal assessment in 568 patients with non-small-cell lung cancer.<sup>[13]</sup> The sensitivity and specificity for mediastinal nodal staging with PET/CT were 70% and 100% for T1 tumors, 60% and 95% for T2 tumors, 44% and 100% for T3 tumors, and 38% and 92% for T4 tumors, respectively. The study concluded that PET/CT provides high specificity regardless of T stage in mediastinal nodal staging, and is more efficient in lower T-stage tumors.

### Lymphoma

A group from Germany reported on the combined use of whole-body FDG-PET/CT colonography and optical colonoscopy in staging of patients with colon cancer.<sup>[14]</sup> The investigators found that a combination of whole-body PET/CT colonography and optical colonoscopy offers the most accurate tumor staging. However, it would be interesting to find whether in some cases this comprehensive staging procedure can be streamlined and simplified, which may have cost-benefit implications.

The investigators from the University of Southern California, Los Angeles, retrospectively correlated the metabolic activity and the CT appearance of metabolically active metastatic osseous lesions in patients with lymphoma.<sup>[15]</sup> This study showed that the metabolic activity of the osseous lymphomatous deposits does not correlate with lesion morphology on CT. Approximately one third of lesions on PET may not have morphologic correlate on CT (ie, marrow infiltration only). Similarly, a significant number of suspicious lesions on CT also did not display abnormal FDG uptake. This study suggested that both CT and PET provide important complementary diagnostic information in regard to osseous involvement in patients with lymphoma.

In another study from the United Kingdom, the investigators assessed whether a full "head-to-thighs" PET/CT scan is necessary in evaluation of first treatment in patients with lymphoma.<sup>[16]</sup> It was determined that in patients older than 45 years with lymphoma, there may be an increased incidence of unexpected second pathologies, which advocates a full head-to-thighs PET scan in these patients. In contrast, the investigators suggested that in younger patients, a PET/CT scan may be kept limited to the area of known disease without missing significant other pathology.

Hundt and colleagues<sup>[17]</sup> compared FDG-PET/CT with separately evaluated PET and contrast-enhanced CT. The sensitivity and specificity were 85% and 91% for CT alone, 98% and 99% for PET alone, and 98% and 99% for combined PET/CT, respectively. Therefore, these study authors found no statistically significant difference between PET/CT and separated PET and CT. The correlation between the lesions enhancement in Hounsfield Units (HU) and SUV on PET was statistically significant regardless of only a moderate correlation ( $r = 0.51$ ). The moderate correlation reflects the different aspects of the tumor assessed by contrast-enhanced CT (perfusion) and PET (glucose metabolism of viable tumor).

Researchers from Emory University in Atlanta, Georgia, examined the spectrum of FDG-PET/CT in Burkitt's lymphoma.<sup>[18]</sup> They found that non-African Burkitt's lymphoma is often located in the abdomen and is intensely hypermetabolic (maximum SUV range, 11-31). This series also showed that the standard chemotherapy regimen reduces the SUV in most patients (85%) and allows prediction of therapy response.

### Infection and Inflammation

A Swiss study evaluated the diagnostic value of FDG-PET/CT in a trauma patient suspected of having chronic osteomyelitis.<sup>[19]</sup> The sensitivity and specificity for detection of chronic osteomyelitis in 37 patients were 94% and 90%, respectively, for the whole group. The sensitivity and specificity for the axial skeleton were perfect at 100%, whereas those for the appendicular skeleton were 90% and 88%, respectively. The study authors concluded that FDG-PET/CT is a highly sensitive and specific method for the assessment of chronic infection in patients with trauma.

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