



Each month the editor of *Newsline* selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. Although we routinely include briefs that focus on molecular imaging and therapy using radiolabeled agents, we have recently added a special section on molecular imaging with a selection of articles that goes beyond the traditional bounds of nuclear medicine.

## THERAPY

### Antivascular Enhancements to $^{131}\text{I}$ RIT

In an article published in the February issue of the *International Journal of Oncology* (2007;30:453–460), Lankester et al. from the Royal Sussex Cancer Centre and County Hospital (Brighton, UK) reported on a study designed to assess the magnitude of the antivascular effect of various doses of combrestatin A-4-phosphate (CA-4-P), a vascular disrupting agent, in SW1222 colorectal xenografts in a mouse model. Previously, radioimmunotherapy using  $^{131}\text{I}$ -A5B7, an anti-CEA antibody, has been combined with CA-4-P with positive results in xenografts, and the authors point to the feasibility of monitoring such results using dynamic contrast-enhanced (DCE) MR imaging. The tumor vascular effects of 30, 100, and 200 mg/kg of CA-4-P were assessed using DCE MR imaging, tumor vascular volume metrics, and conventional histology for necrosis at 4 and 24 hours after treatment. In

addition, the effects of CA-4-P on retention of  $^{131}\text{I}$ -A5B7 in tumor and normal tissue were assessed. Results indicated a significant reduction in tumor imaging kinetics at 4 hours after CA-4-P for all dose levels, an effect that persisted for at least 24 hours in the highest dosage group but not for the lower dosage groups. A similar pattern was noted for vascular volume and necrosis. Tumor retention of the radiolabeled antibody was seen to a similar degree at all 3 dose levels. The authors concluded that “these results demonstrate that moderate tumor blood flow reduction following antibody administration is sufficient to improve tumor antibody retention,” a finding that supports additional studies of this combined  $^{131}\text{I}$ -labeled antibody and vascular disrupting agent.

*International Journal of Oncology*

### PET and CT in Planning Target Volumes

In an article e-published ahead of print in the December 28 issue of the *International Journal of Radiation Oncology, Biology, Physics*, Grills et al. from the William Beaumont Hospital (Royal Oak, MI) reported on a study comparing planning target volume (PTV) definitions derived by CT, PET, and a combination of PET and CT in non-small cell lung cancer (NSCLC). The study included 21 patients with NSCLC scheduled for 3-dimensional (3D) conformal radiotherapy (RT) planning. All underwent staging PET imaging and CT treatment simulation imaging as well as a separate planning PET scan. From these scans 3 sets of PTVs were defined and compared: (1) CT volumes (CT tumor + staging PET nodal disease); (2) PET volumes (planning PET tumor); and (3) composite CT-PET volumes (fused CT-PET tumor). Set 1 volumes were used to create 3D

conformal RT plans, and relative coverages of the volumes were evaluated. Set 1 primary tumor gross tumor volumes were larger than those in set 2 in 48%, smaller in 33%, and equal in 19% of patients. The set 3 (composite) volume was larger than either CT or PET alone in 62%, smaller in 24%, and equal in 14%. Small portions of the set 3 partial tumor volume were significantly underdosed in 40% of patients when CT-only planning was used. These results led the authors to conclude that CT and PET are complementary and “should be obtained in the treatment position and fused” to define gross tumor volume in NSCLC. They noted that although the quantitative target volumes are sometimes similar to those with fused results, CT planning alone can miss qualitative differences in target locations, leading to underdosage of the target.

*International Journal of Radiation Oncology, Biology, Physics*

### Multimodality Approach to RIT in Pancreatic Cancer

In an article published in the January 1 issue of *Clinical Cancer Research* (2007;13:299–306), Baranowska-Kortylewicz et al. from the University of Nebraska Medical Center (Omaha) reported on a multimodality approach to radioimmunotherapy (RIT) of pancreatic cancer in a mouse model. The study included NCr-nu/nu mice bearing subcutaneous xenografts of SW1990 pancreatic adenocarcinoma. The authors initiated RIT with  $^{131}\text{I}$ -CC49, a TAG-72-targeting monoclonal antibody, augmented with imatinib, a potent inhibitor of platelet-derived growth factor receptor- $\beta$ . Biodistribution results indicated a 50% increase in  $^{131}\text{I}$ -CC49 tumor uptake in mice treated with imatinib, with tumor development slowed almost entirely for 3 weeks and no side effects noted. Treatment with either the radiolabeled antibody alone

or imatinib alone also delayed tumor growth but not as effectively as the combination of the 2. They concluded that “improved responses of pancreatic cancer xenografts to the multimodality treatment comprising RIT and platelet-derived growth factor receptor- $\beta$  inhibition suggest that this approach to therapy of pancreatic cancer may also be successful in patients.”

*Clinical Cancer Research*

## PET and MR Track T Cells

Agger et al. from the University of Aarhus (Denmark) reported in the January issue of the *Journal of Immunotherapy* (2007;30:29–39) on a novel technique for tracking  $^{124}\text{I}$ -labeled cells in situ in a mouse model, combining the spatial resolution of MR imaging with the sensitivity and spatial accuracy of PET. The authors described the use of this technique, together with determination of tissue radioactivity, flow cytometry, and microscopy, to characterize and quantify the specific accumulation of transferred CD8+ T cells in tumor tissue in mice. Their combined PET/MR imaging technique was able to accurately determine the position of transferred  $^{124}\text{I}$ -labeled SIINFEKL-specific T cells in 3 dimensions in recipient mice as well as demonstrate a significant accumulation of the  $^{124}\text{I}$  label in and around subcutaneous tumors compared with normal tissue. The combination of PET and MR, they concluded, could become a routine technique for providing detailed knowledge about the fate of transferred cells within the bodies of recipients.

*Journal of Immunotherapy*

## Bone Marrow Cells After Acute MI

Nyolczas and other members of the Myocardial Stem Cell Administration After Acute Myocardial Infarction (MYSTAR) study reported in the February issue of the *American Heart Journal* (2007;153:212.e1–e7) on the structure and organization of a multicenter trial comparing early and later

intracoronary or combined percutaneous intramyocardial and intracoronary administration of nonselected autologous bone marrow-derived stem cells to patients after acute myocardial infarction (MI). The ongoing study includes 360 patients randomly assigned to 1 of 4 study groups: (A) early treatment with intracoronary injection (21–42 days after MI); (B) early treatment with the combined approach; (C) late treatment with intracoronary injection (3 months after MI); and (4) late treatment with the combined approach. The primary end points are changes in resting myocardial perfusion defect size and left ventricular (LV) ejection fraction as measured by gated SPECT at 3 months after therapy. The researchers will also evaluate the safety and feasibility of the application modes, changes in LV wall motion score index, myocardial voltage and segmental wall motion, LV end-diastolic and end-systolic volumes, and clinical symptoms. The MYSTAR trial is currently recruiting patients. Additional information is available through the National Institutes of Health Clinical Trials Web site at: <http://clinicaltrials.gov/show/NCT00384982>.

*American Heart Journal*

## Routine $\beta$ -Radiation Exposure

Rimpler and Barth, from the Federal Office for Radiation Protection (Berlin, Germany) reported ahead of print on January 12 in *Radiation Protection and Dosimetry* on precautions and monitoring associated with the increased use of sealed and unsealed  $\beta$ -radiation sources for radiation therapy, radioimmunotherapy (RIT), and brachytherapy. Because many of these techniques require handling high activities at short distances from the skin, the authors explored the range of exposure risks to medical staff. They studied extremity exposure in several workplaces and different types of treatment. Although focusing mainly on radiation therapy applications, their results are germane to nuclear medicine technologists and physicians working

with RIT. Local skin doses were measured with thin-layer thermoluminescent dosimetry (TLD) chips on the fingers of technologists and other staff. Recorded exposures exceeded the annual dose limit of 500 mSv. Although the authors recommended the use of ring dosimeters appropriate for  $\beta$  radiation, they noted that these dosimeters do not provide a reliable estimation of annual exposure when compared with the local skin dose results indicated by the TLD chips. They discussed the implications of these findings and provided additional suggestions for safe handling and adequate monitoring of exposure.

*Radiation Protection and Dosimetry*

## $^{131}\text{I}$ Therapy in Patients on Dialysis

Modarresifar et al. from the University of Alabama at Birmingham reported in the February issue of *Health Physics* (2007;92[2 suppl 1]:S45–S49) on a case study pointing to the radiation safety challenges involved in  $^{131}\text{I}$  ablation therapy for thyroid cancer in patients receiving hemodialysis. The case involved a 53-year-old man with thyroid papillary carcinoma, who was scheduled for high-dose (3,607.5 MBq) ablative therapy but at the same time was on alternate-day hemodialysis for chronic renal failure. The patient received treatment just after dialysis, and dialysis was repeated at 48–96 hours (per routine schedule) to remove excess  $^{131}\text{I}$  and reduce radiation exposure. The authors implemented new radiation safety measures to ensure that the patient received an optimal treatment dose with as-low-as-possible radiation to the critical organs and whole body and that dialysis staff was adequately protected. Two lead shields were placed between the patient and the dialysis nurses, with 2 nurses alternating patient contact roles to reduce radiation exposure. Nursing staff also wore film badges for monitoring of exposure, and these indicated that the shielding arrangement was effective in protecting staff against radiation.

*Health Physics*

## DIAGNOSIS

## Optimal Imaging in Multiple Myeloma

In the January issue of *Haematologica* (2007;92:50–55), Zamagni et al. from the University of Bologna reported on a study comparing the utility of  $^{18}\text{F}$ -FDG PET/CT, MR imaging, and whole-body planar radiography in baseline assessment of bone disease in patients with newly diagnosed multiple myeloma. The study included 46 patients with newly diagnosed multiple myeloma, each of whom underwent imaging with all 3 techniques. Twenty-three of the patients received immediate autologous transplantation, and in these patients posttreatment PET/CT images were compared with MR images of the spine and pelvis. The authors found that PET/CT was superior to planar radiography in baseline assessment in 46% of patients, including 19% with negative radiography findings. PET/CT scans of the spine and pelvis in 30% of patients failed to show abnormal findings in areas in which MR imaging showed abnormal patterns of bone marrow involvement. However, PET/CT enabled the detection of myelomatous lesions in 35% of patients in areas that were outside the MR fields of view. When the results of PET/CT and MR imaging were combined, the ability to detect active sites of disease was as high as 92%. In the 23 patients imaged after transplantation, 15 had negative PET/CT scans (including 13 with excellent partial or near complete responses), but only 8 of these patients had negative MR scans, raising the question of whether PET/CT or MR imaging after transplantation will prove to be the better predictor of outcomes. The authors concluded that although MR imaging of the spine and pelvis remains the “gold standard” imaging approach for detection of bone marrow involvement in multiple myeloma, PET/CT provides “additional and valuable information for the assessment of myeloma bone disease in areas not covered by MR imaging.”

*Haematologica*

## PET/CT and MR in Advanced Melanoma

Pfannenbergl et al. from the Eberhard-Karls University (Tuebingen, Germany) reported on January 13 ahead of print in the *European Journal of Cancer* on a comparison of  $^{18}\text{F}$ -FDG PET/CT and whole-body MR imaging in staging of advanced melanoma, with a focus on comparative overall and site-specific accuracy and effects on patient management. The prospective study included 64 patients with stage III/IV melanoma who underwent both  $^{18}\text{F}$ -FDG PET and whole-body MR imaging for evaluation of a total of 420 lesions. PET/CT was found to have a greater overall accuracy than MR imaging (86.7% and 78.8%, respectively) and was significantly more accurate in N-staging and detection of skin and subcutaneous metastases. MR imaging, however, was more sensitive in detecting liver, bone, and brain metastases and more specific in classifying pulmonary lesions (although less sensitive). The authors found that whole-body imaging with either PET/CT or MR changed management strategies in 41 patients (64%). They concluded that “whole-body staging of patients with advanced melanoma is most accurate by combining whole-body PET/CT and organ-specific whole body MR imaging, including a brain, liver, and bone marrow protocol.”

*European Journal of Cancer*

## PET and Carcinoid Tumors

In the January issue of *Chest* (2007; 131:255–260), Daniels et al. from the Mayo Clinic (Rochester, MN) reported on the ability of  $^{18}\text{F}$ -FDG PET to detect carcinoid tumors presenting as questionable pulmonary nodules. The retrospective study included a review of institutional results that yielded a group of 16 patients (PET image study sets) with a pathologic diagnosis of bronchial carcinoid (typical in 11, atypical in 5) who had undergone antecedent  $^{18}\text{F}$ -FDG PET imaging. Fifteen of these patients had presented with pulmonary nodule(s). The mean greatest patho-

logic dimension of these carcinoids was 2.08 cm (range, 1.0–8.3 cm). In evaluating the imaging results, the authors found that PET’s sensitivity was 75% (12 true-positives and 4 false-negatives), with mean sizes of false-negative and true-positive carcinoids not significantly different. Fifteen of the patients were staged pathologically, and positive nodes were found in 2 of these patients. In 1 of these 2 patients, PET findings were true-positive but were false negative in the other. The authors concluded that  $^{18}\text{F}$ -FDG PET imaging is “useful for evaluation of typical and atypical thoracic carcinoid tumors.” They noted that although overall PET sensitivity for detection of carcinoid tumors is not as great as that seen in other applications, such as in non-small cell lung cancer, the capabilities are “much higher than prior reports suggest.”

*Chest*

## CT and MR Image Fusion with PET in Prostate Cancer Recurrence

Wachter et al. from the Medical University of Vienna (Austria) reported in the January/February issue of *Urologic Oncology* (2007;25:90) on a study designed to assess the incremental value of CT and MR image fusion with  $^{11}\text{C}$ -acetate PET imaging for detection and localization of clinically occult recurrence of prostate cancer. The study included 50 patients who had previously undergone radical treatment for prostate cancer and presented with elevated/increasing serum prostate-specific antigen levels. Each underwent whole-body  $^{11}\text{C}$ -acetate PET. Uptake was interpreted as normal (10%), abnormal (64%), or equivocal (26%), and the 45 patients with abnormal and equivocal results underwent additional imaging with CT, MR, and/or bone scanning. Software-assisted image fusion of CT to PET and MR imaging to PET was performed and evaluated site-by-site in 51 abnormal ( $n = 37$ ) and equivocal ( $n = 14$ ) lesions. Image fusion changed characterization of equivocal lesions to

normal in 5 (10%) of these sites and abnormal in 9 (18%) and precisely defined the anatomic location of abnormal uptake in 37 (73%) of the 51 sites. PET findings changed patient management in 14 (28%) of the 50 patients. The authors concluded that retrospective fusion of  $^{11}\text{C}$ -acetate PET and CT or MR imaging is “feasible and seems to be essential for final diagnosis,” particularly in patients with PET tracer uptake in the prostate region.

*Urologic Oncology*

## Weight Index for $^{18}\text{F}$ -FDG SUVs

In an article e-published ahead of print on January 5 in *Molecular Imaging and Biology*, Thie et al. from the University of Tennessee Medical Center (Knoxville) reported on the creation of a weight index for standardized uptake values (SUVs) in  $^{18}\text{F}$ -FDG PET imaging designed to counter errors in SUVs caused by variations in patient weights. The authors used data from PET and PET/CT scans at their institution and from the literature to quantify sensitivity to weight and present a series of formulas devised to encourage SUV weight correction with an easily applied approach. They concluded that addressing weight sensitivity is appropriate where the coefficient of variation of SUVs is below about 1/3 and that the application of their resulting weight index is useful in reducing SUV variability and therefore error in routine PET imaging of diverse patient populations.

*Molecular Imaging and Biology*

## PET vs. PET/CT in Head and Neck Cancer

Fakhry et al. from La Timone University Hospital Center (Marseille, France) reported on January 4 ahead of print in the *European Archives of Otorhinolaryngology* on a comparison of PET and PET/CT imaging in patients with recurrent head and neck squamous cell carcinoma. The study included 32 patients who had undergone treatment for the disease, who presented for

evaluation of recurrent local disease, and who had undergone previous conventional workups with nasofiberscopy, CT, and/or MR imaging. All underwent  $^{18}\text{F}$ -FDG PET imaging, and resulting PET and PET/CT images were reviewed independently by 2 nuclear medicine physicians. Interpretation results were compared with biopsy and/or clinical follow-up for at least 8 months, which showed local recurrence in 18 (56%) patients. The sensitivity, specificity, and accuracy of PET were 94%, 36%–50%, and 69%–75%, respectively. The respective results for PET/CT were 94%, 57%, and 78%. These results indicated that PET/CT could have a direct impact on patient care, including the avoidance of unnecessary invasive procedures in 8 of 14 patients. The authors concluded that “combined PET/CT is more accurate than PET alone for detection of recurrent head and neck squamous cell cancer,” and that these findings were reinforced by the strong interobserver agreement on PET.

*European Archives of Otorhinolaryngology*

## Guidelines for PET in Lymphoma Response Assessment

An international team of physicians and other scientists reported on January 22 ahead of print in the *Journal of Clinical Oncology* on a set of consensus guidelines created to provide clinicians and clinical trials researchers with uniform criteria with which to compare and interpret the use of PET for response assessment in lymphoma. The report by Juweid et al. was part of a larger set of clinical trial parameters addressed by the International Harmonization Project to standardize clinical approaches in lymphoma. These guidelines build on criteria for treatment response assessment of non-Hodgkin’s lymphoma published in 1999 and now revised to reflect the increased use of PET, immunohistochemistry, and flow cytometry. The new PET guidelines were based on data from the recent litera-

ture and on the collective expertise of panel members in the use of PET in lymphoma. Among the recommendations were: (1) posttreatment PET should be performed at least 3 weeks and preferably at 6–8 weeks after chemotherapy or chemoimmunotherapy and 8–12 weeks after radiation or chemoradiotherapy; (2) visual assessment alone is adequate for interpreting PET findings when assessing response after completion of therapy; (3) mediastinal blood pool activity is recommended as the reference background activity to define PET positivity for a residual mass  $\geq 2$  cm in greatest transverse diameter, regardless of location; and (4) a smaller residual mass or normal-size lymph node ( $\leq 1$  cm<sup>2</sup>) should be considered positive if its activity is above that of the surrounding background. In addition, the group also proposed specific criteria for defining PET positivity in the liver, spleen, lung, and bone marrow and encouraged use of attenuation-corrected PET. They also recommended that PET be performed for treatment monitoring during the course of therapy *only* in a clinical trial or as part of a submission to a prospective registry. In a separate article in the same journal introducing the release of the guidelines, Cheson et al. noted, “We hope that these guidelines will be adopted widely by study groups, pharmaceutical and biotechnology companies, and regulatory agencies to facilitate the development of new and more effective therapies to improve the outcome of patients with lymphoma.”

*Journal of Clinical Oncology*

## MOLECULAR IMAGING ———

### Microbubbles to Monitor Antitumor Therapy

Korpanty et al. from the University of Texas Southwestern Medical Center (Dallas) reported in the January 1 issue of *Clinical Cancer Research* (2007;13:323–330) on a study investigating the use of contrast ultrasound imaging of targeted microbubbles to

monitor vascular response to therapy in a mouse model of pancreatic adenocarcinoma. The researchers used microbubbles conjugated to monoclonal antibodies to image and quantify the vascular effects of 2 different antitumor therapies (antivascular endothelial growth factor [VEGF] monoclonal antibodies and/or gemcitabine) in subcutaneous and orthotopic pancreatic tumors in mice. Ultrasound was used to localize microbubbles to endoglin (CD105), VEGF receptor 2, or VEGF-activated blood vessels. Targeted microbubbles significantly enhanced imaging of tumor vasculature when compared with untargeted or control IgG-targeted microbubbles. The intensity of targeted microbubbles on ultrasound correlated with the level of expression of the targets and with microvessel density in tumors under both the antiangiogenic and cytotoxic therapies. The authors concluded that “targeted microbubbles represent a novel and attractive tool for non-invasive, vascular-targeted molecular imaging of tumor angiogenesis and for monitoring vascular effects specific to antitumor therapy *in vivo*.”

*Clinical Cancer Research*

### Molecular MR Imaging and Angiostatic Therapy

In an article e-published on January 3 ahead of print in the *FASEB Journal*, Mulder et al. from universities in The Netherlands and the United States reported on the use of molecular MR imaging in early *in vivo* assessment of angiostatic therapy. The researchers used MR imaging of  $\alpha\beta 3$ -targeted bimodal liposomes to quantitate angiogenesis in a tumor mouse model and evaluate the therapeutic efficacy of angiogenesis inhibitors anginex and endostatin. MR findings correlated well with those from fluorescence microscopy. These findings indicate that RGD peptide liposomes can be used to increase the sensitivity of MR images in detecting changes in tumor angiogenesis *in vivo*.

*FASEB Journal*

### MR and Hyperthermic-Controlled Chemotherapeutic Release

Ponce et al. from Duke University (Durham, NC) reported in the January 3 issue of the *Journal of the National Cancer Institute* (2007;99:53–63) on the use of MR imaging to measure the temporal and spatial patterns of drug delivery in a rat fibrosarcoma model during treatment with lysolipid-based temperature-sensitive liposomes containing doxorubicin and an MR contrast agent administered in combination with local hyperthermia. The study was performed in rats bearing 10–12-mm fibrosarcomas that were treated with the “loaded” liposomes before and/or during 60 minutes of local tumor hyperthermia administered via a catheter inserted at the center of the tumor. Continuous MR imaging was used to monitor drug distribution and calculate intratumoral doxorubicin concentrations. End-points for tumor monitoring were 60 days past treatment or tumors reaching 5 times their original volumes. Results indicated that the doxorubicin accumulated more quickly and reached higher concentrations in tumor when the loaded liposomes were administered during rather than before hyperthermia. Liposomes administered during hyperthermia also yielded the greatest antitumor effect, with a median tumor-to-5-times volume of 34 days compared with only 18.5 days when liposomes were administered before hyperthermia and 22.5 days when administered before and during hyperthermia. The authors concluded that this simple approach using controlled and target-specific release of agents packed in liposomes was most effective when delivered during hyperthermia, resulting in a peripheral drug distribution.

*Journal of the National Cancer Institute*

### MR Spectroscopy Detects Cervical Cancer Apoptosis

In the January 17 issue of *BMC Cancer* (2007;7:11), Lyng et al. from the Rikshospitalet-Radiumhospitalet Medical Center (Oslo, Norway) reported on the use of high-resolution

magic-angle spinning  $^1\text{H}$  MR spectroscopy for metabolic mapping and assessment of apoptosis in cervical carcinomas. The study sample consisted of 44 biopsies taken from 23 patients before and during radiotherapy for cervical cancer. Each specimen underwent the MR spectroscopy imaging, in which a standard pulse-acquire spectrum provided information about lipids and a spin-echo spectrum enabled detection of non-lipid metabolites in the lipid region of the spectra. Results were compared with subsequent histopathologic analysis, where the researchers found that apoptotic cell density correlated with the standard pulse-acquire spectra but not with the spin-echo spectra (indicating the significance of lipid metabolites). The spin-echo spectra contained the main information on tumor cell fraction and tumor cell density, in which cholines, creatine, taurine, glucose, and lactate were most important. Significant correlations were identified between tumor cell fraction and glucose concentration and between tumor cell density and glycerophosphocholine concentration and ratio of glycerophosphocholine to choline. The authors concluded that these findings indicate “the apoptotic activity of cervical cancers can be assessed from the lipid metabolites” using this MR spectroscopy technique and that the resulting data in HR “may reveal novel information on the metabolic changes characteristic of apoptosis.” Because the observed changes differed from those associated with tumor load and tumor cell density, the authors also suggested that this method could be useful in exploring the role of apoptosis in the course of the disease.

*BMC Cancer*

### Imaging Preclinical Changes in Valvular Function

In the January 23 issue of *Circulation* (2007;115:377–386), Aikawa et al. from the Massachusetts General Hospital (Boston, MA) reported on a study using multimodality molecular imaging

to visualize early changes in aortic valvular cell functions in vivo and to assess the utility of the resulting data in predicting future risk and identifying therapeutic targets for prevention of valvular stenosis. The authors used a panel of near-infrared fluorescence imaging agents to map endothelial cells, macrophages, proteolysis, and osteogenesis in vivo in the aortic valves of hypercholesterolemic apolipoprotein E-deficient mice. They found that the valves of apolipoprotein E-deficient mice contained macrophages, were thicker than those in wild-type mice,

and showed early dysfunction detected by MR imaging in vivo. Fluorescence imaging detected uptake of macrophage-targeted magnetofluorescent nanoparticles in apolipoprotein E-deficient valves but not in controls. Protease-activatable near-infrared fluorescence probes showed proteolytic activity in valvular macrophages, and ex vivo MR imaging enhanced with vascular cell adhesion molecule-1-targeted nanoparticles detected endothelial activation in the regions of highest mechanical stress in the valves. Osteogenic near-infrared fluorescence signals indicated ongoing

active processes of osteogenesis in inflamed valves in areas in which no calcium deposits were visibly evident. Quantitative image analysis correlated near-infrared fluorescence signals with immunoreactive vascular cell adhesion molecule-1, macrophages, and cathepsin-B. The authors concluded that this array of molecular imaging approaches can combine to “detect in vivo the key cellular events in early aortic valve disease, including endothelial cell and macrophage activation, proteolytic activity, and osteogenesis.”

*Circulation*

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*(Continued from page 19N)*

treatment monitoring, and detection of early recurrence. In the coming months, the journal will emphasize molecular imaging through a planned supplement, continuing education articles, Newsline’s literature briefs, and a monthly Newsline column (that debuted last month).

These actions—along with defining, delivering, and promoting positions on legislative and regulatory issues on

your behalf; fostering the collaborative nature of doctors, technologists, and scientists; and monitoring changes in federal and state rules and regulations that affect how you get paid—attest to how ably SNM takes care of the business at hand.

*Virginia Pappas*  
*Chief Executive Officer, SNM*