a way for these high-impact projects to be pursued," said NIH Director Francis S. Collins, MD, PhD.

NIH expects to make awards of $12.8 million for new T-R01 projects in fiscal year 2010. Many of the announced awards focus on molecular medicine and include the planned use of molecular imaging techniques. More information on the Transformative R01 Award is at http://commonfund.nih.gov/T-R01. For descriptions of the 2010 recipients' research plans, see http://commonfund.nih.gov/T-R01/Recipients10.asp.

National Institutes of Health

Home-Built Cyclotrons

The Newsline editor noted with interest an article appearing in the latest issue of *symmetry: Dimensions of Particle Physics* (2010;7[4]), a publication of the Fermi National Accelerator Laboratory and SLAC National Accelerator Laboratory, on "The Do-It-Yourself Cyclotron." Contributed by staff writer Calla Cofield, the article traced the history of amateur cyclotron building and focused on an April 2010 conference that brought together a diverse group of individuals who have put together their own working cyclotrons. The complete article is available at: www.symmetrymagazine.org/cms/?pid=1000831.

symmetry: Dimensions of Particle Physics

Erratum

Academic degrees for 3 authors of "PET utilization under Taiwan's Universal Health Insurance program" (2010;51[10]:14N–16N) were in error. Corrected names and degrees include: Chih-Hsin Muo, MS; Fung-Chang Sung, PhD, MS, MPH; and Shih-Ni Chang, MS.

FROM THE LITERATURE

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. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

MOLECULAR IMAGING/THERAPY

Cerenkov Radiation Energy Transfer Imaging

Dothager et al. from the Washington University School of Medicine (St. Louis, MO) reported on October 11 in the online publication *PLoS One* (2010;5[10]:e13300) on studies of optical imaging of Cerenkov radiation in biological systems. Cerenkov radiation is electromagnetic radiation emitted when a charged particle (such as an electron) passes through an insulator at a constant speed greater than that of the speed of light in the same medium. Cerenkov radiation can be emitted in PET imaging with some β-emitting radionuclides. This study was designed to improve optical imaging of Cerenkov radiation by showing that such radiation from decay of ^{64}Cu and ^{18}F can be spectrally coupled by energy transfer to high Stokes-shift quantum nanoparticles that facilitate a variety of novel optical imaging applications and activation strategies for PET radiopharmaceuticals. Optical imaging of solutions containing the nanoparticles and ^{18}F-FDG showed Cerenkov radiation energy transfer ratios as high as 8.8 ± 1.1, and in vivo imaging in mice with subcutaneous pseudotumors injected with the nanoparticles after intravenous injection of ^{18}F-FDG showed corresponding ratios as high as 3.5 ± 0.3. In addition to the science presented, the article serves as a concise introduction to this rapidly expanding field of investigation.

PLoS One

Near-Infrared/PET Imaging

In an article in the October 1 issue of *Translational Oncology* (2010;3:307–317), Sampath et al. from the University of Texas Health Sciences Center (Houston) described a study investigating detection of cancer metastases with a dual-labeled near-infrared (NIR)/PET agent that can provide both intraoperative guidance and noninvasive imaging. The study was conducted in an immunoincompetent mouse model of human epidermal growth factor receptor 2 (HER-2)–positive cancer metastases. The authors detailed synthesis and initial studies of (^{64}Cu-DOTA)$_n$-trastuzumab-(IRDye800)$_m$. The agent was injected in mice at 2 and 6 wk after breast cancer cell implantation, and PET/CT and NIR fluorescence imaging were performed 1 d after injection. Results were compared with ^{18}F-FDG PET imaging. Resulting images with both ^{18}F-FDG alone and the new agent showed primary tumors, but metastases were visualized only with the dual-labeled agent. ^{64}Cu PET imaging showed lung metastases, and ex vivo NIR fluorescence imaging showed uptake in lung, skin, skeletal muscle, and lymph nodes, with histologic confirmation of corresponding cancer cells. Of note, the high signal-to-noise ratio from

NIR fluorescence imaging revealed "channels" of fluorescence between the primary tumor and axillary lymph nodes, "suggesting a lymphatic route for trafficking cancer cells." The authors concluded that $(^{64}Cu\text{-}DOTA)_n$-trastuzumab-$(IRDye800)_m$ may be an effective diagnostic imaging agent for staging HER-2-positive breast cancer patients and intraoperative resection."

Translational Oncology

PET Brain Imaging with Liposomes

Oku et al. from the University of Shizuoka (Japan) reported on October 8 ahead of print in the *International Journal of Pharmaceutics* on a preclinical study of PET imaging of brain cancer with labeled liposomes. The researchers described the preparation of ^{18}F-labeled 100-nm liposomes also labeled with DiI fluorescence dye. The tracer was injected into rats, where it accumulated in implanted gliomas 1 h after the injection. The tracer did not accumulate in normal brain tissue. The smallest implanted tumor (1-mm diameter) was successfully imaged with the liposomes. The authors concluded that these results provide support for the hypothesis that "nanocarrier-based imaging of brain tumors is promising for the diagnosis of brain cancer therapy."

International Journal of Pharmaceutics

Proteome-Based Plasma Markers of Amyloid-β

In an article e-published on October 7 ahead of print in the *Journal of Alzheimer's Disease*, Thambisetty et al. from the National Institute on Aging (Baltimore, MD) reported on a study of plasma proteins associated with brain amyloid-β burden in nondemented older individuals as a step toward identifying blood-based markers reflecting core pathologic features of Alzheimer disease (AD) in presymptomatic individuals. The article described discovery-phase experiments using 2D gel electrophoresis and mass spectrometry–based proteomic analysis of plasma in brain samples obtained 10 y before ^{11}C-PiB PET brain imaging. A panel of 18 2D gel electrophoresis plasma protein spots effectively discriminated between individuals with high and low brain amyloid-β. Validation-phase studies found a strong association between plasma apolipoprotein E (ApoE) concentration and amyloid-β burden in the medial temporal lobe, localized to the hippocampus and entorhinal cortex. APOE ϵ4 carriers also showed greater amyloid-β levels than noncarriers in several brain regions. The authors noted that these results "suggest that both peripheral concentration of ApoE protein and APOE genotype are related to early neuropathological changes in brain regions vulnerable to AD pathology even in the nondemented elderly" and that the technique holds promise "for discovery of biologically relevant peripheral markers in those at risk for AD."

Journal of Alzheimer's Disease

Stem Cell Repair of Bone Defects

Chen et al. from the Third Military Medical University (Chongqing, China) reported in the October issue of *Cytotherapy* (2010;12:831–840) on a study using transplantation of genetically modified adipose-derived stem cells and acellular bone matrix to repair bone defects. The study was conducted in minipigs, and the authors described development of the bone matrix material and isolation, culture, and transfection of adipose-derived stem cells with recombinant human bone morphogenetic protein-2 recombinant human vascular endothelial growth factor (rhVEGF) plasmids. The resulting compounds were used to repair bone defects of the ulna in minipigs. Conventional radiography, radionuclide bone imaging, and SPECT monitored the therapeutic effects at 2, 4, 8, and 12 wk after transplantation/operation. Imaging indicated that the compound had better treatment effects than did control substances, and no adverse effects were noted. The authors concluded that the research indicated that acellular bone matrix is a good biologic material for tissue repair, and the novel compound "can accelerate bone formation significantly."

Cytotherapy

STEM-AMI Trial Results

In a study published in the October issue of the *European Journal of Heart Failure* (2010;12:1111–1121), Achilli, from the A. Manzoni Hospital (Lecco, Italy) and the Stem Cell Mobilization in Acute Myocardial Infarction (STEM-AMI) investigators group reported on results of an ongoing study to assess the effect of granulocyte colony-stimulating factor (G-CSF) on left ventricular (LV) function and volumes in patients with anterior ST-elevation myocardial infarction and depressed LV ejection fraction (EF). The study included 49 such patients undergoing primary angioplasty percutaneous coronary intervention (PCI), with symptom-to-reperfusion times of 2–12 h and EF ≤45% after PCI. One group (n = 24) was administered G-CSF and another group (n = 25) received a placebo, each beginning <12 h after PCI and continuing for 5 d. Patients underwent MR imaging at baseline and after 6 mo to determine effects on LVEF. Infarct size and perfusion were evaluated with late gadolinium enhancement and gated ^{99m}Tc-sestamibi SPECT. LV end-diastolic and -systolic volumes increased from baseline to 6 mo in the placebo group but were unchanged in the G-CSF–administered group. No significant differences in EF or perfusion were noted at 6 mo between the 2 groups. Significant reduction in transmural late gadolinium enhancement segments on MR imaging was seen at 6 mo in the G-CSF group but not the placebo group. The authors concluded that "early G-CSF administration attenuates ventricular

remodeling in patients with anterior ST-elevation myocardial infarction and EF ≤45% after successful PCI."

European Journal of Heart Failure

DIAGNOSIS

Long-Term Outcomes with Prostascint

Ellis et al. from the Case Medical Center and Case Western Reserve School of Medicine (Cleveland, OH) and the Northeastern Ohio Universities College of Medicine (Rootstown) reported on October 18 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics* on an evaluation of the clinical utility of capromab pendetide imaging with SPECT/CT in primary prostate cancer for pretreatment prognostic staging and localization of biologic target volumes for individualized image-guided radiotherapy dose escalation (IGRT-DE). The study included 239 patients with clinical diagnoses of localized primary prostate cancer who were scheduled for primary radiotherapy over a period from 1997 to 2002 and who were evaluated at that time for tumor stage with conventional staging and capromab pendetide SPECT/CT. SPECT/CT identified distant metastatic uptake in 22 patients (9.2%), although none could be clinically confirmed. SPECT/CT pelvic images defined biologic target volumes for IGRT-DE (+150% brachytherapy dose) without (n = 150) or with (n = 89) external radiation. Risk groups were assigned according to National Comprehensive Cancer Network criteria. Median survivor follow-up was 7 y; at 10-y analysis, overall survival was 84.8% and biochemical disease-free survival was 84.6%. With stratification by RG, SPECT/CT findings were significantly in accord with 10-y results. The authors concluded that capromab pendetide SPECT/CT imaging in primary prostate cancer has statistically significant predictive value for both biochemical disease-free and disease-specific survival and has dual clinical utility in defining biologic target volumes and individualized IGRT-DEs.

International Journal of Radiation Oncology, Biology, Physics

CT Attenuation Correction and SPECT/PET

In an article e-published on October 8 ahead of print in the *International Journal of Cardiovascular Imaging*, Nkoulou et al. from University Hospital Zurich (Switzerland) reported on the effect of CT attenuation correction on myocardial viability pattern assessment by ^{99m}Tc-tetrofosmin SPECT/^{18}F-FDG PET. The authors studied differences in scan interpretation introduced by CT attenuation correction of SPECT myocardial perfusion imaging in patients undergoing cardiac viability assessment by SPECT/PET imaging. The study included 46 patients (mean age, 64 y; range, 36–83 y) with dysfunctional myocardium. SPECT/PET scans with and without CT attenuation correction were evaluated. Results were classified by FDG uptake, using the segment with maximum tracer in SPECT perfusion uptake as reference, and as normal, mismatch, mild match, and scar visual patterns by relative comparison of SPECT and PET. The researchers found that CT attenuation correction introduced a different reference segment for the normalization of the PET study in 57% of cases, changing flow–metabolism patterns in 28% of segments (normal, mismatch, mild match, and scar pattern in 462, 150, 123, and 47 segments, respectively, without attenuation correction, and 553, 86, 108, and 35, respectively, with CT attenuation correction). The use of CT attenuation correction for SPECT myocardial perfusion imaging resulted in 25% of segments originally classified as scar being reclassified, increased the number of normal segments by 20%, and decreased by 54% the number of patients with possible indications for revascularization.

International Journal of Cardiovascular Imaging

Vascular Inflammation and Multimodal Imaging

Jarrett et al. from the University of California, Davis reported on October 11 in the online journal *PLoS One* (2010;5[10]:e13254) on a study of in vivo mapping of vascular inflammation using both PET and MR imaging. The authors described the development of macromolecular and nanoparticle contrast agents targeted to macrophages and initial experiments in 3 mouse and rat models of atherosclerosis with inflamed vascular plaques formed spontaneously and/or induced by injury. Tracers contained gadolinium for T1 MR imaging or iron oxide for T2 MR imaging and ^{64}Cu for PET imaging. PET successfully identified regions of macrophage accumulation, and MR imaging visualized macrophage distribution at high resolution in these areas. For both modalities, contrast was enhanced in areas of inflammation but not in normal tissues. The authors concluded that this "multimodal imaging approach allowed high-sensitivity and high-resolution mapping of biomarker distribution and may lead to a clinical method to predict plaque probability to rupture."

PLoS One

Predicting Outcomes in Cervical Carcinoma

In an article e-published on September 30 ahead of print in the *International Journal of Radiation Oncology, Biology, Physics*, Olsen et al. from the Washington University School of Medicine (St. Louis, MO) reported on the prognostic significance of levels of squamous cell carcinoma (SCC) antigen, a serum biomarker for SCC of the cervix, before and after chemoradiotherapy and compared these results with pre- and posttreatment ^{18}F-FDG PET/CT. The retrospective study included the records of 63 women who underwent definitive chemoradiotherapy

for SCC of the cervix. Patients were divided into 2 groups on the basis of pretreatment SCC antigen levels (>30 ng/mL and ≤30 ng/mL). Pre- and 3-mo posttreatment PET/CT results and progression-free survival data were assessed in the 2 groups over the median follow-up period of 12 mo. Women with SCC antigen levels >30 ng/mL at baseline had more advanced lymph node disease on pretreatment PET/CT than those with lower levels. When these levels had normalized after chemoradiotherapy, patients were more likely to have a complete metabolic response on posttreatment PET/CT. Two-y progression-free survival was 73% for patients with SCC antigen levels ≤30 ng/mL at diagnosis and was 0% for those with higher levels. Two-y progression-free survival was 62% for patients whose levels normalized by completion of chemoradiotherapy and 0% for those whose levels did not normalize. These results led the authors to conclude that "Elevated SCC antigen at diagnosis and failure of the SCC antigen to normalize at the completion of treatment are associated with incomplete metabolic response and decreased progression-free survival" in SCC of the cervix.

International Journal of Radiation Oncology, Biology, Physics

Intraoperative PET Probe in DTC

Kim et al. from Kyungpook National University (Daegu, Korea) reported on October 20 ahead of print in *Surgery* on the use of an intraoperative PET probe for tumor localization and verification of complete resection in differentiated thyroid cancer. The study included 12 patients with differentiated thyroid cancer who required total thyroidectomy with a modified radical neck dissection (MRND) or who had recurrent thyroid cancer after thyroid surgery. Types of procedures in which the probe was used included total thyroidectomy with MRND, selective neck dissection, and excision of recurrent thyroid masses. ^{18}F-FDG was injected, and surgical exploration was performed 2–6 h later. The PET probe was a commercial high-energy γ probe seeking 511 keV photons. All tumors were localized precisely and in real time by the PET probe, and in 7 patients the probe identified lesions not seen on preoperative PET. The authors concluded that "Radioguided surgery using an intraoperative PET probe in thyroid cancer appears to be a useful method for real-time tumor localization, verification of complete excision, and minimization of the possibility of residual cancer," adding that an intraoperative PET probe in thyroid cancer may decrease unnecessary repeat surgeries and complications from persistent disease.

Surgery

PET/CT in TB-Associated Uveitis

In an article e-published on October 8 ahead of print in the *British Journal of Ophthalmology*, Doycheva et al. from the University of Tübingen (Germany) evaluated the clinical usefulness of ^{18}F-FDG PET/CT in detection of tuberculosis as the underlying disease in patients with uveitis and positive interferon-γ release assays. Ninety-five uveitis patients were screened, and positive release assays were found in 24 individuals, of whom 20 underwent PET/CT imaging. Resulting images were evaluated for presence, size, and metabolic activity of hilar and mediastinal lymph nodes and pulmonary lesions. PET/CT imaging showed increased tracer uptake in mediastinal or hilar lymph nodes in 9 patients (45%). After PET/CT–guided lymph node biopsy, mycobacterium tuberculosis was detected in culture in 2 patients (10%). In 7 patients (35%) with serpiginous choroiditis, partly calcified lymph nodes without tracer uptake were found. Nine of 11 (82%) antituberculosis–treated patients with progressive courses of uveitis experienced remission. The authors concluded that in interferon-γ release assay–positive patients with severe uveitis forms (such as serpiginous choroiditis and occlusive retinal vasculitis), "^{18}F-FDG PET/CT is useful to identify lesions appropriate for biopsy and helps to establish the diagnosis and appropriate therapy for presumed tuberculosis-induced intraocular inflammation."

British Journal of Ophthalmology

REVIEWS

Review articles provide an important way to stay up to date on the latest topics and approaches by providing valuable summaries of pertinent literature. The Newsline editor recommends several reviews on cardiac imaging and assessment accessioned into the PubMed database in October. In an article e-published on October 12 ahead of print in *Heart Failure Reviews*, Boogers et al. from Leiden University Medical Center (The Netherlands) provided an overview of "The role of nuclear imaging in the failing heart: myocardial blood flow, sympathetic innervation, and future applications." Ghosh et al. from the University of Ottawa Heart Institute (Ontario) described "Assessment of myocardial ischaemia and viability: role of positron emission tomography" on October 21 ahead of print in the *European Heart Journal*. In an article e-published on October 15 ahead of print in *Current Cardiology Reports*, Hiari and Rudd reviewed "FDG PET imaging and cardiovascular inflammation." A special issue of *Cancer Imaging* (2010;10) released in October carried a range of articles on cardiac molecular imaging, including but not limited to: Hicks, "Use of molecular targeted agents for the diagnosis, staging and therapy of neuroendocrine malignancy" (S83–S91); Rankin, "^{18}F-2-fluoro-2-deoxy-D-glucose PET/CT in mediastinal masses" (S156–S160); Hegarty and Collins, "PET/CT and breast cancer" (S59–S62); Anderson et al., "Tumour response evaluation with fluorodeoxyglucose positron emission tomography: research technique or clinical tool?" (S68–S72); and Bellomi, "Nonconventional imaging of lung cancer" (S161–S162).