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. 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.

Visually Estimated Coronary Artery Calcium and PET

Selvaraj, Khan, et al. from the University of Pennsylvania (Philadelphia), the Marshfield Clinic Health System (WI), and the Albert Einstein Medical Center (Philadelphia, PA) reported in the May issue of *Open Heart* (2021;8[1]:e001648) on a study designed to determine the prognostic value of visually estimated coronary artery calcium (VECAC) from chest CT or attenuation correction CT acquired during PET myocardial perfusion imaging (MPI). The goal was to compare these results with those for traditional risk factors and conventional PET imaging markers. The study included imaging from 609 patients (mean age, 58 ± 11 y; 65% women, 35% men; 67% black, 33% other) with no known coronary artery disease who underwent PET MPI with attenuation correction CT and/or chest CT imaging. VECAC score categories of ≤10, 11–400, and >400 Agatston units were seen in 68%, 12%, and 20%, respectively, of patients. Over a mean follow-up of 4.3 ± 1.8 y, the 2 higher categories were statistically associated with primary outcomes (all-cause death, acute coronary syndrome, or stroke) after adjusting for traditional risk factors, MPI findings, and coronary flow reserve. In a model that included PET MPI, coronary flow reserve, and clinical risk factors, the addition of VECAC improved prognostic value. The authors concluded that "VECAC is a potent predictor of events beyond traditional risk factors and PET imaging markers, including coronary flow reserve" and that these data point toward implementation of routine VECAC.

Open Heart

^{99m}Tc-Mebrofinate Distribution and Posthepatectomy Liver Failure

In an article e-published on April 27 ahead of print in *HPB (Oxford)*, Dasari et al. from the Queen Elizabeth Hospital (Birmingham, UK) and the University of Birmingham (UK) reported on an investigation of variations in anatomic (LV_{Rem}%) and functional (fLV_{Rem}%) remnant volumes in ^{99m}Tc-mebrofinate uptake on SPECT/CT in patients at high risk of posthepatectomy liver failure. The study included 92 scans, in which LV_{Rem}% and fLV_{Rem}% returned identical results in 15% of cases and varied by ±10 percentage points in 79% of cases. A difference of >10% was seen in more than a fifth of patients and was significant in those with primary liver cancers. Twenty-nine percent of patients underwent surgery as planned on ^{99m}Tc-mebrofinate uptake on SPECT/CT, and dynamic imaging was a strong predictor of posthepatectomy liver failure. The authors noted that ^{99m}Tc-mebrofinate SPECT/CT is emerging as a useful modality in preoperative assessment of patients scheduled for major liver resection, with significant individual variations in anatomic and functional distributions that must be considered in surgical planning. Reduced uptake on SPECT/CT, measured as the dynamic uptake in the future liver remnant, is a strong predictor of postoperative liver failure.

HPB (Oxford)

Phase 3 Trial: PSMA PET/CT and RT in Prostate Cancer

Calais, Zhu, Hirmas, et al. from the University of California Los Angeles, the University of Duisburg-Essen and German Cancer Consortium (DKTK)/University Hospital Essen (Germany), the Technical University Münich (Germany), and the Veterans Affairs Greater Los Angeles Healthcare System (CA) reported on May 7 in *BMC Cancer* (2021;21[1]:512) on the study protocol for a multicenter randomized phase 3 trial (NCT04457245) assessing prostate-specific membrane antigen (PSMA) PET/CT prior to definitive radiation treatment for unfavorable intermediate- or high-risk prostate cancer. In the trial, 312 patients will be randomized to proceed with standard definitive radiation treatment (control arm, 150 patients) or to undergo a PSMA PET/CT scan (either ^{18}F-DCFPyL or ^{68}Ga-PSMA-11) prior to definitive radiation treatment planning (intervention arm, 162 patients). In the intervention arm, the treating radiation oncologist can incorporate PSMA PET/CT findings into radiation treatment planning. Patients with M1 disease on PET will be excluded from the intervention arm, because treatments alternative to definitive radiation therapy may be more appropriate. The primary endpoint will be the success rate for patients with unfavorable intermediate- and high-risk prostate cancer after standard definitive radiation therapy compared with that for PSMA PET–based radiation treatment. Secondary endpoints for all study participants will include progression-free survival, metastasis-free survival after initiation of radiation, overall survival, percent change in initial treatment intent, and safety. This will be the first randomized phase 3 prospective trial intended to

determine whether PSMA PET/CT can improve outcomes in patients with prostate cancer who receive definitive radiation therapy, both by optimizing patient selection and personalizing the radiotherapy plan.

BMC Cancer

PET, Lateral Lymph Node Metastases, and Rectal Cancer

In an article in the May 8 issue of *BMC Cancer* (2021;21[1]:520), Yukimoto et al. from Osaka University and Jinsenkai MI Clinic (Osaka; both in Japan) reported on a study evaluating the efficacy of preoperative PET/CT in the diagnosis of lateral pelvic lymph node metastases in rectal cancer. The study included 84 patients with rectal cancer who underwent PET/CT to determine SUV_{max} in the primary tumor and lymph nodes before lateral pelvic lymph node dissection. Postoperative pathology identified the presence of metastases in the left (6 patients), right (7 patients), and both (2 patients) lateral pelvic lymph nodes. PET/CT had a sensitivity of 82%, specificity of 93%, positive predictive value of 58%, negative predictive value of 98%, false-positive value of 7%, and false-negative value of 18% when the cutoff value of the lateral pelvic lymph node SUV_{max} was set at 1.5. Although the cutoff value of the short axis set at 7 mm on CT was most useful in diagnosing lymph node metastases, SUV_{max} was more useful in specificity. The authors concluded that "the cutoff value of 1.5 for lymph node SUV_{max} in PET is a reasonable measure to predict the risk of preoperative lateral pelvic lymph node metastases in rectal cancer patients."

BMC Cancer

G Protein–Coupled Receptors in ^{131}I-Refractory Thyroid Cancer

In an article e-published on May 17 ahead of print in the *Journal of Clinical Endocrinology and Metabolism*, Suteau et al. from CHU Angers, Institut de Cancérologie de l'Ouest Service de Biométrie (Angers), Endo-ERN Centre for Rare Endocrine Diseases, Institut Curie (Paris), and the TUTHYREF Network (Villejuif; all in France) reported on the development of a specific atlas of G protein–coupled receptor (GPCR) expression in progressive and refractory thyroid cancer to identify potential targets aimed at "drug repositioning." The study included tumor and normal thyroid tissue samples from 17 patients with refractory thyroid cancer (12 papillary and 5 follicular). GPCR mRNA expression was analyzed with a custom panel of 371 GPCRs, with results compared with those from public repositories and pharmacologic databases to identify eligible drugs. Four receptors were identified as downregulated in follicular thyroid cancer and 24 in papillary thyroid cancer, 7 of which were identified also through analyses of publicly available datasets on primary thyroid cancers. Out of the many differentially expressed genes, 22 GPCRs were identified as targets of approved drugs. Some GPCRs were also associated with prognostic factors. The authors concluded that their approach to GPCR mRNA expression profiling provides "an opportunity to identify potential therapeutic targets for drug repositioning and precision medicine in radioiodine-refractory thyroid cancer."

Journal of Clinical Endocrinology and Metabolism

Reviews

Review articles provide an important way to stay up to date on the latest topics and approaches through valuable summaries of pertinent literature. The Newsline editor recommends several general reviews accessioned into the PubMed database in April. In an article e-published on April 14 ahead of print in *The American Journal of Medicine,* Li and Kronenberg from Vanderbilt University Medical Center (Nashville, TN) provided an overview of "Myocardial perfusion and viability imaging in coronary artery disease: Clinical value in diagnosis, prognosis, and therapeutic guidance." Berland et al. from the Dana-Farber Cancer Institute (Boston, MA), the Université Côte d'Azur (Nice, France), Harvard University (Cambridge, MA), Nice Center Hospital (France), and the Harvard Medical School (Boston, MA) published "Nanobodies for medical imaging: About ready for prime time?" in the April 26 issue of *Biomolecules* (2021;11[5]:637). In the April 11 issue of *Molecules* (2021;26[8]:2201), Liberini et al. from the University of Torino (Italy), the University of Messina (Italy), University Hospital Zürich (Switzerland), and the Kantonsspital Baden (Switzerland) described "The future of cancer diagnosis, treatment, and surveillance: A systemic review on immunotherapy and immune-PET radiotracers." Sier et al. from the Leiden University Medical Center (The Netherlands), Edinburgh Molecular Imaging Ltd. (UK), the University of Twente (Enschede, The Netherlands), the University of Wisconsin Madison, and Percuros BV (Leiden, The Netherlands) published "Endoglin/CD105-based imaging of cancer and cardiovascular diseases: A systematic review" in the April 30 issue of the *International Journal of Molecular Sciences* (2021;22[9]:4804). In the April 17 issue of *Current Oncology Reports* (2021;23[6]:68), Timmer et al. from Amsterdam UMC (The Netherlands) reviewed "Locally advanced pancreatic cancer: Percutaneous management using ablation, brachytherapy, intra-arterial chemotherapy, and intra-tumoral immunotherapy."