Each month the editor of Newsline selects article on diagnostic, therapeutic, research, and practice issues from a range of international publications. Many selections come from outside the standard canon of nuclear medicine and radiology journals. This month the literature contained a remarkable number of articles on the utility of sentinel lymph node biopsy and associated techniques in the management of patients with breast and colorectal cancers. Several of these are included in this review. Note that although we have divided the articles into diagnostic and therapeutic categories, these lines are increasingly blurred as nuclear medicine capabilities expand. Many diagnostic capabilities are now enlisted in direct support of and, often, in real-time conjunction with therapies. 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.

Diagnosis

^{18}F-FES PET Predicts Response to Endocrine Treatment

In an article e-published ahead of print on May 8 in the *Journal of Clinical Oncology*, Linden et al. from the University of Washington (Seattle) reported on the ability of ^{18}F-fluorestradiol (^{18}F-FES) PET to predict response to salvage hormonal treatment in women with heavily pretreated metastatic breast cancer. The study included 47 women with estrogen receptor–positive tumors. Most patients had bone-dominant disease and previous tamoxifen treatment. Initial quantitative ^{18}F-FES uptake on PET in each patient was correlated with subsequent qualitative and quantitative tumor response after 6 months of hormonal therapy. An objective response was observed in 11 patients (23%). Although qualitative ^{18}F-FES PET results were not predictive of subsequent response, quantitiative ^{18}F-FES uptake and response were significantly associated. None of the 15 patients with initial standardized uptake values (SUVs) <1.5 responded to hormonal therapy, but 11 of 32 patients (34%) with SUVs >1.5 showed responses. All 11 of these patients were in the 24-member subset of participants whose tumors did not overexpress HER2/neu. The authors noted that treatment selection using quantitative ^{18}F-FES in this patient series would have increased the response rate from 23% to 34% overall and from 29% to 46% among patients lacking HER2/neu overexpression. They concluded that "quantitative ^{18}F-FES can predict response to hormonal therapy and may help guide treatment selection."

Journal of Clinical Oncology

Three-Node Sampling as Predictor in Breast Cancer

Motomura et al. from the Osaka Medical Center for Cancer and Cardiovascular Diseases (Japan) described on May 18 ahead of print in the *Annals of Surgical Oncology* a study designed to assess whether sampling of 3 axillary lymph nodes after sentinel node biopsy predicts the status of nonsentinel nodes in women with sentinel node breast cancer metastases. The study included 47 women who underwent sentinel node biopsy with a radioisotope and dye procedure and whose sentinel nodes were found on intraoperative print cytology to be metastasis positive. On each of these women, 3 axillary lymph node sampling was performed, followed by axillary lymph node dissection. Forty-three (91%) women were diagnosed as metastasis positive on final histologic examination of sentinel nodes. The status of the 3-sampled nodes was found to be significantly associated with the status of nonsentinel nodes. Six (43%) of 14 patients with positive 3-sampled nodes had at least 1 positive remaining node. Only 2 (7%) of 29 patients whose 3-sampled nodes were negative were found to have additional nodal metastases. The sensitivity, specificity, and accuracy of the 3 sampled nodes for the prediction of nonsentinel node metastases were 87.5%, 100%, and 95.3%, respectively. The authors concluded that 3-node sampling "may be useful for predicting the status of nonsentinel nodes and avoiding axillary lymph node dissection in patients with only sentinel node metastases."

Annals of Surgical Oncology

SLN Biopsy After Chemotherapy

In an article e-published ahead of print in the May 24 issue of the *Annals of Surgical Oncology*, Tausch et al. from the Institute for Risk Assessment and Prevention of Breast Diseases (Linz, Austria) reported on the findings of the Austrian Sentinel Node Study Group on the utility of sentinel lymph node (SLN) biopsy after preoperative chemotherapy for breast cancer. The study included 167 patients with clinically negative axilla after 3–6 courses of preoperative chemotherapy who underwent SLN biopsy and axillary lymph node dissection. Blue dye was used in 29 patients (17%), radioisotopes in 20 patients (12%), and a combination of these methods in the remaining 120 patients (72%). Biopsies revealed at least 1 SLN in each of 144 patients. Blue dye alone identified 86% of SLNs, tracers alone identified 65%, and the combined methods identified 88%. The SLN was positive in 70 women (42%), and in 39 of these

individuals was the only positive node with otherwise negative axillary nodes. At least 62 patients (37%) were free of tumor cells in the SLN and in the axillary nodes. The authors concluded that the results of SLN biopsy after preoperative chemotherapy are comparable to the results of SLN biopsy without such treatment and called for additional studies to confirm these "promising results."

Annals of Surgical Oncology

ALMANAC Trial Reports on SLN

R.E. Mansel from Cardiff University and researchers from across the United Kingdom reported in the May 3 issue of the *Journal of the National Cancer Institute* (2006;98:599–609) on a multicenter randomized trial to compare quality-of-life outcomes in patients with clinically node-negative invasive breast cancer who underwent sentinel lymph node (SLN) biopsy and outcomes in those who received standard axillary treatment. The Axillary Lymphatic Mapping Against Nodal Axillary Clearance (ALMANAC) trial is funded by the UK Medical Research Council. The study included 1,031 women randomly assigned to undergo SLN biopsy (555 patients) or standard axillary surgery (516 patients). Those with SLN metastases proceeded to delayed axillary clearance or received axillary radiotherapy, depending on the protocol at each participating institution. The relative risks of any lymphedema and sensory loss for the SLN biopsy group were equal to those of the standard axillary treatment group after 12 months. Axillary operative time, drain usage, length of hospital stay, and time to resumption of normal activities after surgery were reduced in the SLN biopsy group. Subjective quality-of-life reports and arm function scores were significantly better in the SLN biopsy group, with no differences in levels of anxiety. The study group concluded that SLN biopsy is "associated with reduced arm morbidity and better quality of life than standard axillary treatment and should be the treatment of choice for patients who have early-stage breast cancer with clinically negative nodes."

Journal of the National Cancer Institute

Predictive Power of PET in Breast Cancer

In an article e-published ahead of print in the May 22 issue of the *Journal of Clinical Oncology*, Cachin and colleagues from Australia and France reported on an investigation of the prognostic abilities of ^{18}F-FDG PET in patients treated with high-dose chemotherapy (HDC) with autologous stem cell transplantation for metastatic breast cancer. The study included 47 patients with metastatic breast cancer who were treated with ≤3 cycles of HDC. After the last cycle, all patents underwent CT and ^{18}F-FDG PET imaging, and some patients underwent ultrasound, mammography, and/or bone scanning, depending on the clinical indication. The conventional imaging techniques indicated complete responses in 16 (37%) patients, whereas ^{18}F-FDG PET indicated complete responses in 34 (72%) patients. Of the various factors assessed in the study, ^{18}F-FDG PET results were the most powerful and independent predictors of survival. Patients with negative posttreatment PET results had a median survival of 24 months, compared with only 10 months for those with positive PET results. The authors concluded that a single^{18}F-FDG PET study "performed after completion of HDC for metastatic breast cancer can powerfully stratify for survival." They noted that these findings may have significant implications for the ways in which outcomes are assessed after conventional-dose therapy for metastatic breast cancer.

Journal of Clinical Oncology

Ultrasound and PET in Lung Cancer Staging

Sawhney et al. from the Minneapolis Veterans Affairs Medical Center (MN) reported on May 5 ahead of print in *Clinical Gastroenterology and Hepatology* on a study comparing the utility of endoscopic ultrasound (EUS)–guided fine-needle aspiration with that of PET for staging mediastinal lymph nodes. The study included 72 patients with lung cancer who were suitable candidates for surgery and who underwent both PET and EUS. Imaging results were correlated with surgery results or follow-up with serial imaging. Complete data were available for analysis in only 65 patients, with final diagnosis based on histology in 59 and 1-year radiologic follow-up in 6 patients. PET accurately diagnosed mediastinal lymph node status in 77% of patients, whereas EUS fine-needle aspiration was correct in 94% of patients. The overall sensitivity, specificity, and accuracy of PET and EUS were 61%, 91%, and 77% and 87%, 100%, and 94%, respectively. The authors estimated that EUS obviated surgical procedures in 55% of patients with radiologic evidence of mediastinal metastasis and in 22% of patients without radiologic evidence of mediastinal metastasis. They concluded that "EUS fine-needle aspiration was more accurate than PET in staging mediastinal lymph nodes in lung cancer patients and resulted in a substantial reduction in mediastinoscopy and thoracotomy."

Clinical Gastroenterology and Hepatology

SPECT or PET for Solitary Pulmonary Nodules

Naalsund and Maublant from the Rikshospitalet (Oslo, Norway) reported on May 5 ahead of print in *Respiration* on a multicenter study assessing the diagnostic performance of ^{99m}Tc-depreotide SPECT in differentiating benign from malignant solitary pulmonary nodules and comparing this performance with that of ^{18}F-FDG PET in a subset of patients. The study included 118 patients found on CT to have single pulmonary nodules ≤3 cm in size. All patients underwent ^{99m}Tc-depreotide SPECT imaging, and a subset of 29 patients also underwent ^{18}F-FDG PET imaging. Images were interpreted without additional information and later correlated with histopathology

results. ^{99m}Tc-depreotide SPECT was positive in 65 of 73 patients with a malignant lesion and negative in 30 of 45 patients with a benign lesion (sensitivity, specificity, and diagnostic accuracy were 89%, 67%, and 81%, respectively). For the 40 patients whose nodules were ≤1.5 cm, sensitivity was 75%, specificity was 96%, and diagnostic accuracy was 88%. In the subset of 29 patients imaged with both PET and SPECT, the sensitivity, specificity, and diagnostic accuracy of the 2 modalities were identical at 90%, 67%, and 83%, respectively. The authors concluded that the diagnostic accuracy of ^{99m}Tc-depreotide SPECT is good and comparable with ^{18}F-FDG PET imaging in single pulmonary nodules of indeterminate origin.

Respiration

Benign Disease in Pulmonary Lesion Resection

Smith et al. from the Washington University School of Medicine (St. Louis, MO) also focused on the differentiation of benign from malignant lesions in the lung in a report in the May issue of the *Annals of Thoracic Surgery* (2006;81:1824–1828). Their retrospective study reviewed institutional experience with focal pulmonary lesions suggestive of lung cancer and subsequently proven benign on surgical resection. The study included the records of 1,560 patients who underwent resection for focal pulmonary lesions. All patients underwent CT before resection, and a subset of 43 patients also underwent PET imaging. The surgical and perioperative course of patients found to have benign lesions was followed and compared with imaging results. Pathology indicated that lesions were benign in 9% (140 patients) of the study group. Of these patients, 103 (74%) underwent thoracotomy, 36 (26%) underwent video-assisted thoracoscopy, and 1 (0.7%) underwent sternotomy. One death occurred in the perioperative environment in this group. Half of the group found to have benign lesions (70 patients, 50%) also underwent mediastinoscopy before resection. Pathology after resection in this group indicated granulomatous inflammation in 91 patients (65%), hamartoma in 17 patients (12%), pneumonia or pneumonitis in 14 patients (10%), fibrosis in 5 patients (4%), and a miscellany of other causes in the remaining 13 patients (9%). Tracer uptake on PET had suggested malignancy in 22 of 43 patients and benign lesions in 20 of 43 patients (with 1 study not interpreted). Among this group of 43 patients, all of whom proceeded to resection, 38 also underwent needle biopsy before surgery, with 29 nondiagnostic, 5 negative, and 4 positive results. The authors concluded that this retrospective analysis indicates that even with "thorough clinical assessment, advanced imaging technology, and needle biopsy, many patients continue to undergo surgery for benign disease." They suggested that treatment approaches to early stage lung cancer should take this fact into consideration.

Annals of Thoracic Surgery

Colorectal Liver Metastasis Diagnosis and Treatment

In an article published in the May issue of the *Netherlands Journal of Medicine* (2006;64:147–151), Bipat et al. from the University of Amsterdam (The Netherlands) reported on the results of a survey sent to 107 chairs of hospital oncology committees on current practices in diagnosis and treatment of patients with colorectal liver metastases. Questions covered a wide range of topics, including choice of imaging modality and technique, types of specialists involved, existence of institutional guidelines, decision-making processes, types of surgery and chemotherapy, ablation approaches, and others. Seventy-three responses were received, showing substantial variation in almost all aspects of diagnosis and therapy. The 3 factors that the responding chairs felt needed most improvement were adequate general diagnostic and treatment guidelines, better registration of patients, and more precise guidelines for radiofrequency ablations. Surgeons (70), medical oncologists (66), and radiologists (42) were cited as key decision makers. Synchronous liver metastases were routinely assessed with ultrasound in 69 hospitals and CT in 2 (2 did not report). For metachronous liver metastases, ultrasound and CT were more evenly divided as the initial work-up modalities. As a second or additional imaging approach, CT was most often used (71), followed by MR imaging (38) and PET (22). Respondents reported that the choice of imaging modality was mainly influenced by the literature and to a lesser extent by availability, costs, personnel, and waiting lists. Substantial variation was also noted in the techniques used for each imaging modality. The authors found even greater variability in surgical approaches, chemotherapy regimens, and other treatment strategies. They concluded that "this variation reflects either under- or over-utilization of diagnosis and treatment options" and recommended the development of evidence-based guidelines to resolve these variations and develop optimal approaches.

Netherlands Journal of Medicine

Ex Vivo SLN Mapping in Colorectal Cancer

In an article e-published ahead of print on May 24 in the *International Journal of Colorectal Disease*, Yagci et al. from the Gulhane Military Medical Academy (Ankara, Turkey) reported on experience with sentinel lymph node (SLN) mapping for staging in colorectal cancer and detailed a mapping procedure to define skip metastasis. The study included 47 patients with colorectal cancer who underwent ex vivo SLN mapping. Immediately after resection, blue dye was injected around the tumor. Lymph nodes harvested from 15 patients were mapped in a standard SLN procedure. Lymph nodes harvested from 32 patients were also mapped separately according to their original anatomic location and classified as epicolic–paracolic, intermediate, or principal. Both SLNs and non-SLNs in this

group underwent additional staining and analyses. A total of 873 lymph nodes were confirmed on histolologic examination (mean = 18.6 ± 8.1 nodes per patient). SLNs were identified in all but 1 patient (97.8%). Immunohistochemical staining showed micrometastases in the lymph nodes of 4 patients, whose results were negative on conventional SLN studies. Anatomicl skip metastases were also noted in 4 of 32 patients (12.5%). The authors concluded that not only is ex vivo SLN mapping in colorectal cancer feasible and able to produce a high SLN identification rate, but that these data also suggest that occult skip metastases can occur in the apical lymph node group and may occur outside the resected area.

International Journal of Colorectal Disease

Accuracy of Ex Vivo SLN Mapping in Colon Cancer

Smith et al. from the University of British Columbia (Vancouver, Canada) also reported in May on the use of ex vivo sentinel lymph node (SLN) mapping in colon cancer. In the *American Journal of Surgery* (2006;191:665–668), they explored the question of whether ex vivo SLN mapping could be applied successfully to the identification of occult micrometastases in patients with colon cancer and thereby improve the accuracy of staging and appropriate management. The study included 17 patients with intraperitoneal colon tumors undergoing resection. SLNs were identified as the first blue stained node(s) after ex vivo peritumoral injection of blue dye. Additional lymph nodes were resected and processed by standard pathologic evaluation for colon cancer. After routine staining, SLNs that were negative were analyzed further by multilevel sectioning and immunohistochemistry staining. SLNs were identified in all but 1 individual (94%). In 3 patients, the SLN was the single positive node. The average number of nodes per patient was 16 (range, 4–54). The authors noted that SLNs accurately reflected the status of the entire lymph node basin in 16 (94%) patients. Two (12%) patients with negative nodes by initial staging were upstaged after additional SLN analyses. The authors concluded that with a negative predictive value of 89%, the SLN mapping technique is feasible and that SLN results were concordant with non-SLNs in the majority of patients.

American Journal of Surgery

PET/CT in Esophageal Cancer

In the May–June issue of *Molecular Imaging and Biology* (2006;8:193–200), Jadvar et al. from the University of Southern California (Los Angeles) evaluated the clinical utility of ^{18}F-FDG PET/CT in precise localization of pathologic foci and exclusion of normal variants in patients with esophageal carcinoma. The study included 60 patients who underwent PET/CT scans either at the time of initial diagnosis (14 patients) of esophageal cancer or at an appointment for surveillance and/or detection of recurrent and metastatic disease (46 patients). Prior treatment included esophagectomy with gastric pull-up (23), surgery and chemotherapy (3), surgery and chemoradiation therapy (10), chemotherapy (5), radiation therapy (2), and chemoradiation without surgery (3). Diagnostic validation was by histology (3 patients) and clinical/radiologic follow-up for up to 1.5 years (57 patients). Overall, the authors found that PET/CT image fusion provided relevant complementary diagnostic information in 14 patients with discordant findings (23% of total) and that these resulted in biopsy in 3 cases, initiation of chemotherapy in 4 cases, and a wait-and-watch strategy in 7 cases. The authors detailed these results for the 2 groups and concluded that these findings add to the current body of findings that suggest that PET/CT may improve the imaging evaluation of patients with esophageal cancer by providing complementary structural–metabolic information. They added that these findings indicate that "PET/CT may be the most appropriate imaging modality in the evaluation of patients of esophageal cancer that may impact patient management."

Molecular Imaging and Biology

Therapy

PET and Boron Neutron Capture Therapy

In an article e-published on May 23 ahead of print in *Head and Neck*, Aihara et al. from the Kawasaki Medical School (Kurashiki, Japan) reported on what is described as the first clinical case of boron neutron capture therapy (BNCT) for head and neck malignancies using ^{18}F-*p*-boronophenylalanine (BPA) PET (^{18}F-BPA PET). The patient, a 48-year-old woman with recurrent submandibular cancer, was first evaluated with ^{18}F-BPA PET to verify the BPA-accumulating capacity of the tumor, with a calculated tumor-to-normal tissue boron concentration ratio of 2.9. Treatment planning was based on CT imaging and specialized therapy software. The tumor was irradiated at the Kyoto University Research Reactor for 90 minutes with epithermal neutrons (tumor dose, 20.0–25.2 Gy; normal tissue dose, 3.2–5.8 Gy). The authors reported that in the 1.5-year follow-up to this treatment, the patient has experienced continuous complete regression in the tumor, with no acute or chronic complications. They noted that these positive results in a single patient should be followed by additional research with this promising therapeutic approach.

Head and Neck

Long-Term Effects of ^{131}I in Thyroid Cancer

Durante et al. from the Institut Gustave Roussy (Villejuif, France) reported on May 9 ahead of print in the *Journal of Clinical Endocrinology and Metabolism* on a study of the long-term benefits and limits of radioiodine therapy in patients with distant metastases from papillary and follicular thyroid carcinoma. The study included

444 patients treated over a 40-year period (223 with lung metastases only, 115 with bone metastases only, 82 with both lung and bone metastases, and 24 with metastases at other sites). Routine treatment involved administration of 3.7 GBq ^{131}I after withdrawal of thyroid hormone treatment, every 3–9 months for 2 years and then once each year until complete disappearance of metastatic uptake. Thyroxine treatment was given at suppressive doses between courses of ^{131}I treatment. The authors found that negative imaging studies (negative total-body ^{131}I scans and conventional radiographs) were attained more frequently in those who were younger, had well differentiated tumors, and/or had limited disease. Most negative studies (96%) were obtained after administration of 3.7–22 GBq ^{131}I. Almost half of negative studies were not obtained until more than 5 years after initiation of treatment of metastases. Only 7% of patients who achieved a negative study experienced subsequent tumor recurrence. Among patients who achieved a negative study, overall survival at 10 years after initiation of therapy was 92% but was only 19% in those who did not achieve a negative study. The authors concluded that radioiodine treatment is "highly effective in younger patients with ^{131}I uptake and small metastases" and that these patients should be treated until the disappearance of any uptake or until a cumulative activity of 22 GBq has been administered.

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with patients; and (c) electronic registration and patient history information to replace the medical clipboard;

(2) The Certification Commission for Health Information Technology (CCHIT) incorporate HITSP standards as criteria for product certification on an ongoing basis, to ensure interoperability; and

(3) A subgroup be formed to frame privacy and security issues relevant to innovations in technology and medicine.

The AHIC also unanimously adopted all CCHIT criteria for certification of ambulatory electronic health records (EHRs). The Office of the National Coordinator for Health Information Technology entered into a $2.7 million contract with the CCHIT last year to develop and test criteria for certification of health information technology, which began in April of 2006. The CCHIT will expand certification to inpatient EHRs in 2007. Standards for transmission and security of images and associated patient information are covered under many of these recommendations and agreements. For information about the AHIC and its workgroups and the complete recommendations, visit www.hhs.gov/healthit/ahic.html.

U.S. Department of Health and Human Services

Last "Radium Girl" Marks 100th Birthday

On May 28 Mae Keane, the last surviving "radium girl," celebrated her 100th birthday in Middlebury, CT. She was among a number of young women in the 1920s who worked in factories and shops decorating watch and clock faces with radioluminescent paint. Keane began at the Waterbury (CT) Clock Company in 1924, earning $18 per week or 6 cents for each dial painted. There, like women in New York and Pennsylvania performing similar tasks, she routinely "pointed" her brush by moistening it with her lips before re-dipping it into the paint.

"I don't think the bosses even knew it was poison," Keane told a reporter from the *Waterbury Republican-American*. "The foreman would tell us it was very expensive and to be careful. We had no idea. But when they did find out, they hid it." Keane worked in the factory for only a few months, but during that period she began to experience dental, dermatologic, and ophthalmologic problems. Many of her colleagues who remained on the radium painting line at the factory died before 1928, and others lingered on with increasingly debilitating radiation-induced illnesses that have been chronicled in many articles and several historical books.

In response to the traditional query about the reasons for her longevity, Keane replied that she had never smoked, loved to walk and dance, and enjoys caramels, chocolates, and an occasional apricot sour or Bailey's Irish Cream.

Waterbury Republican-American