

sary those services would be reported with the appropriate CT procedure code from the CPT radiology section.

The final change made to the nuclear medicine section of the AMA CPT book is in the introductory paragraphs. These changes are minor and consistent with many other changes in the CPT book this year to eliminate the word “physician” to make clear that other qualified individuals who are licensed will be able to report the services with these codes. SNMMI has created a detailed table outlining changes in codes and highlighting wording with significant implications for performance. The table is available at: [www.snmmi.org/index.cfm?PageID=12159](http://www.snmmi.org/index.cfm?PageID=12159).

SNMMI

## GAO Imaging Self-Referral Report

The Government Accountability Office (GAO) on October 31 released a report titled “Higher Use of Advanced Imaging Services by Providers Who Self-Refer Costing Medicare Millions,” which found that physician self-referral of medical imaging exams is driving up imaging utilization and exposing patients to unnecessary health risks while increasing Medicare costs. GAO specifically investigated the role of self-referral in MR imaging and CT services from 2004 to 2010. The agency found that the number of self-referred MR services increased by more than 80%, compared with a 12% increase for non-self-referred MR services. For CT services, the growth of self-referred services more than doubled, whereas non-self-referred CT services increased by about 30%. The report also documented the serious financial impact of

self-referral-driven overutilization on America’s health care system. GAO estimated that Medicare spent approximately \$109 million more in 2010 than it would have without self-referral incentives.

GAO’s analysis showed that providers’ referrals of MR and CT services substantially increased the year after they began to self-refer; that is, the year in which they purchased or leased imaging equipment or joined a group practice that already self-referred. Providers that began self-referring in 2009 (referred to as switchers) increased MR and CT referrals on average by about 67% in 2010 compared to 2008. In the case of MR imaging, the average number of referrals each switcher made increased from 25.1 in 2008 to 42.0 in 2010. In contrast, the average number of referrals made by providers who remained self-referrers or non-self-referrers declined during this period. This comparison suggests that the increase in the average number of referrals for switchers was not the result of any general increase in the use of imaging services among all providers. GAO’s examination of all providers that referred an MR or CT service in 2010 showed that self-referring providers referred about twice as many of these services as providers who did not self-refer. Differences persisted after accounting for practice size, specialty, geography, or patient characteristics. These 2 analyses suggest that financial incentives for self-referring providers were likely a major factor driving the increase in referrals.

Overall, medical imaging use and associated costs are down significantly since 2006. Medicare spends the same

amount on imaging scans now as in 2003. Only self-referred imaging grew significantly since the middle of the last decade. The complete report is available at [www.gao.gov/products/GAO-12-966](http://www.gao.gov/products/GAO-12-966).

Government Accountability Office

## Microwave Ablation and Thyroid Nodules

MedWaves, Inc. announced on November 26 that physicians at the Department of Nuclear Medicine at the Frankfurt (Germany) University Hospital had become the first group in a European hospital to use microwaves to ablate thyroid nodules. The technique has been reported in numerous pre-clinical studies and in clinical studies from South Korea and China, among others.

The success of the new treatment is especially relevant in Germany, where 20% of the population have 1 or more thyroid nodules and nearly 1 in 2 individuals older than 65 y is affected by a thyroid disorder. Microwave ablation offers a number of advantages over surgery, radiotherapy, or other forms of ablation, according to MedWaves and the Frankfurt medical team. The procedure is fast, lasting between 10 and 15 min, depending on the number of nodules. “The microwave ablation also causes significantly fewer side effects because no anesthesia is required. This makes it a very promising alternative to the established procedures,” said Hudayi Korkusuz, MD, who performed the microwave treatment.

MedWaves, Inc.

## 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. 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 in a Memory Clinic

In an article e-published on November 17 ahead of print in *Alzheimer's & Dementia*, Ossenkoppele et al. from the VU University Medical Center (Amsterdam, The Netherlands) reported on results from molecular imaging studies with PET in a memory clinic setting. The study included 154 patients who underwent both dynamic  $^{11}\text{C}$ -Pittsburgh ( $^{11}\text{C}$ -PiB) and static  $^{18}\text{F}$ -FDG PET imaging soon after completion of standard dementia screening in the clinic.  $^{11}\text{C}$ -PiB scans were positive for  $\beta$ -amyloid load in 40 of 66 (61%) patients with clinical diagnoses of Alzheimer disease, 5 of 18 (28%) with frontotemporal dementia, 4 of 5 (80%) with Lewy body dementia, and 3 of 10 (30%) with other dementias.  $^{18}\text{F}$ -FDG uptake patterns matched clinical diagnoses in 38 of 66 (58%) of Alzheimer patients and 6 of 18 (33%) patients with frontotemporal dementia. Combined, the PET results led to a change in diagnosis in 35 (23%) patients, in each of whom previous diagnostic certainty was <90%. PET also increased diagnostic confidence from  $71\% \pm 17\%$  to  $87\% \pm 16\%$ . A 2-y follow-up was completed in 39 patients and showed that  $^{11}\text{C}$ -PiB and  $^{18}\text{F}$ -FDG accurately predicted progression to Alzheimer disease for patients with mild cognitive impairment. Over the 2-y period, the dementia diagnosis established after PET remained unchanged in 96% of patients. The authors concluded that "In a memory clinic setting, combined  $^{11}\text{C}$ -PiB and  $^{18}\text{F}$ -FDG are of additional value on top of the standard diagnostic work-up, especially when prior diagnostic confidence is low."

*Alzheimer's & Dementia*

## PET/CT in HPV-Related SCC

Chan et al. from the Johns Hopkins Medical Institute (Baltimore, MD) reported in the November 1 issue of the *Archives of Otolaryngology:*

*Head & Neck Surgery* (2012;138:1040–1046) on a retrospective review of PET with contrast-enhanced CT in posttreatment management of human papillomavirus (HPV)-associated oropharyngeal squamous cell carcinoma (SCC). The study included the records of 67 patients with diagnoses of HPV-related SCC who were treated with radiotherapy as the primary treatment. All had undergone both pre- and posttreatment imaging with contrast-enhanced CT and PET, with an average of 90.5 d between completion of radiotherapy and follow-up PET/CT imaging. Records were evaluated for both pathologic and radiologic rate of persistence of nodal metastasis on CT, PET, and PET/CT. The radiologic rate on PET was assessed at standardized uptake value (SUV) thresholds of 2.0 and 2.5. After completion of radiotherapy, 20 patients underwent neck dissection. Of these, 4 had persistent tumors and 16 had no viable tumors. Final pathology reports were correlated with imaging responses to determine that for those who underwent neck dissection, negative predictive values were: 85.7% for CT, 91.7% for PET with an SUV threshold of 2, 85.7% for PET with an SUV threshold of 2.5, 100% for PET/CT with an SUV of 2, and 85.7% for PET/CT with an SUV of 2.5. Over a median follow-up of 26 mo, none of the 47 patients who did not undergo neck dissection experienced an isolated neck failure. Analysis of all 67 patients determined that negative predictive values were: 95.7% for CT, 98.2% for PET with an SUV threshold of 2, 95.0% for PET with an SUV of 2.5, 100% for PET/CT with an SUV of 2, and 95.7% for PET/CT with an SUV threshold of 2.5. The authors concluded that PET combined with contrast-enhanced CT has better predictive value than either imaging modality alone in patients with HPV-associated oropharyngeal SCC and that "PET/CT with an SUV threshold of 2 used in patients with HPV-related SCC offers an imaging modality with high negative predictive values that may obviate the

need for unnecessary neck dissection."

*Archives of Otolaryngology: Head & Neck Surgery*

## Bone Marrow Biopsy and PET/CT in Hodgkin Lymphoma

In an article e-published on November 13 in the *Journal of Clinical Oncology*, El-Galaly et al. from Aarhus University, Aalborg University, Odense University Hospital, and Copenhagen University Hospital (all in Denmark) reported on a study designed to determine whether a bone marrow biopsy (BMB) adds useful information to  $^{18}\text{F}$ -FDG PET/CT staging in patients with Hodgkin lymphoma. The study included a total of 454 such patients who were newly diagnosed and undergoing pretherapeutic staging that included both PET/CT and BMB. Patterns of tracer uptake on PET were categorized as uni-, bi-, or multifocal ( $\geq 3$  lesions). Clinical stage, risk assessment, and treatment plan were assessed with and without knowledge contributed by BMB results. Of the total patient population, 82 (18%) had focal skeletal PET/CT lesions and 27 (6%) had positive BMBs. None of the patients with positive BMBs were assessed by PET/CT as having stage I to II disease. Although BMB upstaged 5 patients who were assessed as stage III before biopsy, neither these nor any of the 454 patients would have been assigned to another treatment on the basis of BMB results. Focal skeletal PET/CT lesions identified positive and negative BMBs with a sensitivity and specificity of 85% and 86%, respectively. PET/CT results had positive and negative predictive values for BMB results of 28% and 99%, respectively. The authors concluded that the absence of positive BMBs in PET/CT-assessed stage I to II disease indicated that "the omission of staging BMB would not have changed the risk assessment or treatment strategy in this cohort of 454 newly diagnosed patients with Hodgkin leukemia."

*Journal of Clinical Oncology*

## Postchemotherapeutic Imaging in Hodgkin Lymphoma

Hartridge-Lambert et al. from the Memorial Sloan-Kettering Cancer Center (New York, NY) reported on November 6 online ahead of print in *Cancer* on a study evaluating the risk of disease recurrence and the value of radiologic surveillance in patients with early-stage nonbulky classic Hodgkin lymphoma treated with the chemotherapeutic combination of doxorubicin, bleomycin, vinblastine, and dacarbazine (ABVD) alone and who achieved a complete remission as assessed on posttreatment PET. The study included 47 patients (35 female, 12 male; age range 17–65 y, median = 28 y) who underwent 6 planned cycles of ABVD therapy with interim and/or posttreatment PET scans during a  $\geq 24$ -mo follow-up. The nodular sclerosing subtype was the most common in the study group ( $n = 41$ ). Patients were staged with IIA disease ( $n = 34$ ), IA disease ( $n = 6$ ), IIB disease ( $n = 6$ ), and IIEA disease (lung;  $n = 1$ ). All achieved complete remission. Only 2 patients had positive PET scans (1 at interim scanning and 1 at posttreatment); both were shown at biopsy to be sarcoidosis. Two other patients developed disease recurrence at 7 and 24 mos, respectively, although their interim and posttreatment PET findings were negative. A total of 45 patients experienced durable complete remissions, with 21 undergoing additional unscheduled imaging/workup during follow-up to investigate symptoms or imaging signs of concern. The authors concluded that because of the low risk of disease recurrence, posttreatment radiologic surveillance “appears to be unnecessary in patients with early-stage, nonbulky (CD20 negative) classic Hodgkin lymphoma who achieve a PET-detected complete remission with the ABVD combination alone.” They noted that foregoing posttreatment radiologic surveillance will reduce cumulative radiation exposure and health care costs in this predominantly young patient population.

*Cancer*

## PET and Recurrent Glioma

In an article e-published on November 1 ahead of print in *AJNR. American Journal of Neuroradiology*, Nihashi et al. from Nagoya University Graduate School of Medicine (Japan), Tufts Medical School (Boston, MA), Brown University (Providence, RI), Fujita Health University School of Medicine (Japan), and National Hospital Organization Nagoya Medical Center (Japan) provided a meta-analysis of reports on the diagnostic accuracy of PET in recurrent glioma. The authors searched in both the PubMed and Scopus databases, as well as in resulting review articles and their bibliographies, and 26 studies met the criteria for the meta-analysis. In these studies a diversity of treatment strategies and diagnostic criteria for PET were used, and recurrence was usually indicated for follow-up on the basis of CT or MR imaging. The diagnostic accuracies of both  $^{18}\text{F}$ -FDG and  $^{11}\text{C}$ -methionine ( $^{11}\text{C}$ -MET) PET varied widely as well.  $^{18}\text{F}$ -FDG PET showed a pooled summary sensitivity of 0.77 (range, 0.66–0.85) and specificity of 0.78 (range, 0.54–0.91) for any glioma histology.  $^{11}\text{C}$ -methionine PET showed a summary sensitivity of 0.70 (range, 0.50–0.84) and specificity of 0.93 (range, 0.44–1.0) for high-grade glioma. Data were available but limited on  $^{18}\text{F}$ -FET,  $^{18}\text{F}$ -FLT, and  $^{18}\text{F}$ -boronophenylalanine. Few studies performed direct comparisons of PET tracers or comparisons of PET and other imaging modalities. The authors concluded that  $^{18}\text{F}$ -FDG and  $^{11}\text{C}$ -MET PET “appear to have moderately good accuracy as add-on tests for diagnosing recurrent glioma suspected by CT or MR imaging,” but added that studies comparing different PET tracers and assessing the utility of other modalities are needed.

*AJNR. American Journal of Neuroradiology*

## $^{11}\text{C}$ -Choline PET/CT in Recurrent Prostate Cancer

Mitchell et al. from the Mayo Clinic (Rochester, MN) reported on October 30 ahead of print in the *Journal*

*of Urology* on the ability of  $^{11}\text{C}$ -choline PET/CT to accurately identify prostate cancer distribution and extent after primary treatment failure. The study included the records of 176 men who underwent  $^{11}\text{C}$ -choline PET/CT with biochemical recurrence after treatment failure. PET showed an overall sensitivity, specificity, and positive and negative predictive values of 93%, 76%, 91%, and 81%, respectively. Out of the 176 PET/CT studies, 56 (32%) were rated as clinically useful (ie, they defined lesions not so clearly delineated by conventional imaging, leading to changes in clinical management). The optimal prostate-specific antigen (PSA) value for lesion detection was 2.0 ng/mL. PSA at the time of PET imaging and clinical stage at initial diagnosis of prostate cancer were significant predictors of positive  $^{11}\text{C}$ -choline PET/CT findings. In addition to concluding that  $^{11}\text{C}$ -choline PET/CT performs well in men with biochemical recurrence after primary treatment failure, the authors summarized their findings that “ $^{11}\text{C}$ -choline PET/CT substantially enhances the rate of prostate cancer lesion detection by approximately 32% beyond what can be garnered using conventional imaging techniques and at a lower PSA value.”

*Journal of Urology*

## PET/CT and Merkel Cell Carcinoma

In an article e-published on November 2 ahead of print in the *Journal of the American Academy of Dermatology*, Hawryluk et al. from the Harvard Medical School (Boston, MA) reported on the utility of  $^{18}\text{F}$ -FDG PET/CT in the management of Merkel cell carcinoma (MCC). The study included analysis of 270 PET/CT studies performed in 97 patients with pathology-proven MCC. The imaging studies were performed as part of initial (61 scans, 61 patients) and later (209 scans, 79 patients) treatment strategy decision making. MCCs were tracer avid with a mean maximum standardized uptake value (SUV) in primary lesions of 6.5 (range, 1.3–12.9) and a mean maximum SUV in regional and distant metastases of 7.2 (range, 1.5–9.9).

PET/CT upstaged 16% of patients who underwent baseline scans and indicated that bone and bone marrow metastases were more common than previously reported and often undetected by CT. PET/CT performed as part of the initial management strategy tended to upstage patients with more advanced disease. When performed as part of the subsequent treatment strategy, PET/CT identified metastatic disease, particularly in bone or bone marrow, not seen on CT. The authors concluded that “<sup>18</sup>F-FDG PET/CT imaging is a valuable staging and restaging tool in MCC management.”

*Journal of the American Academy of Dermatology*

### RIT in Follicular Lymphoma

Rose et al. from Emory University (Atlanta, GA) reported in the December issue of *Clinical Lymphoma, Myeloma, and Leukemia* (2012;12:393–399) on a systematic review and meta-analysis of radioimmunotherapy (RIT) (<sup>131</sup>I or <sup>90</sup>Y) consolidation in patients with untreated follicular lymphoma. The authors searched the CENTRAL and MEDLINE databases, as well as conference abstracts for relevant phase II/III clinical trial reports. Eight studies with a total of 783 patients were included in the final analyses. Data points included pretreatment disease status, patient characteristics, treatment regimen, response rates, progression-free survival (PFS), and overall survival (OS). Complete response rates after RIT ranged from 69.0% to 96.5%, 2-y PFS rates ranged from 64.8% to 86.1%, and 5-y PFS rates ranged from 47.0% to 67.3%. Estimates of pooled complete and overall response rates were 82.7% (range, 67.4%–91.7%) and 96.2% (range, 90.4%–98.6%), respectively. Estimates for 5-y PFS and OS were 57.6% (range, 47.8%–66.9%) and 90.1% (range, 83.9%–94.1%), respectively. The authors suggested that the data acquired in this meta-analysis “can further the discussion on RIT as a consolidation therapy and inform decisions on future study designs,” but added that additional studies are needed to

compare the benefits of RIT consolidation with those of maintenance therapy with rituximab.

*Clinical Lymphoma, Myeloma, and Leukemia*

### PET/CT in CIED Infection

In a study e-published on November 12 ahead of print in *Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology*, Cautela et al. from CHU La Timone (Marseille, France) assessed the diagnostic yield of <sup>18</sup>F-FDG PET/CT in patients with cardiac implantable electronic device (CIED) infections. The prospective study included 21 patients with CIED, diagnosed using conventional criteria. Infections were classified as: superficial skin infection, pocket-site infection, or cardiac device–related infective endocarditis (CDRIE). All patients underwent PET/CT imaging. Conventional diagnosis showed superficial skin infection in 1 patient, pocket-site infection in 15, and CDRIE in 13 (definite = 7; possible = 6). PET/CT sensitivity and specificity in patients with pocket-site infections were 86.7% (range, 59.5%–98.3%) and 100% (range, 42.1%–100%), respectively. PET/CT accurately identified the only patient with superficial skin infection. PET/CT sensitivity and specificity for CDRIE were 30.8% (range, 9.1%–61.4%) and 62.5% (range, 24.5%–91.5%), respectively. Most false-negatives were seen in patients who had undergone antimicrobial treatment. The authors concluded that <sup>18</sup>F-FDG PET/CT is “highly accurate for the diagnosis of skin and pocket CIED infection but low for infective endocarditis,” implying that the reliability of PET/CT in management decision making varies according to the type of CIED infection.

*Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology*

### Video Gaming and CBF

Chou et al. from Taipei Veterans General Hospital and National Yang Ming University (Taipei, Taiwan) reported on November 5 ahead of print in *Psychiatry Research* on a SPECT

study designed to assess the effects of video game playing on cerebral blood flow (CBF) in young adults. The study included 30 healthy young adults (18 men, 12 women) who were already familiar with video game playing. Each underwent 3 sessions of <sup>99m</sup>Tc-ECD SPECT to measure CBF. The imaging sessions included a baseline acquisition and 2 acquisitions after playing 1 of 2 video games (1 violent role-playing game, 1 nonviolent) for 30 min each. CBF was found to be significantly decreased in the prefrontal cortex and significantly increased in the temporal and occipital cortices after playing each video game. After playing the violent game, decreased CBF in the anterior cingulate cortex was significantly correlated with the number of characters killed. The finding of hypoperfusion in prefrontal regions after video game playing is consistent with a previous study showing reduced or abnormal prefrontal cortex functions after video game playing. The authors concluded that the finding of decreased CBF after playing the violent video game provides support for a previous hypothesis that the anterior cingulate cortex might play a role in regulating violent behavior.

*Psychiatry Research*

### PET in Endometrial Cancer Follow-Up

In an article e-published on October 26 ahead of print in *Gynecologic Oncology*, Kadkhodayan et al. from the Ghaem Hospital (Mashhad, Iran) reported on a meta-analysis of published literature on the accuracy of <sup>18</sup>F-FDG PET in the follow-up of endometrial cancer patients. A range of databases was searched, and provided 11 studies (541 patients) that met inclusion criteria. Pooled results indicated that for detection of overall recurrence, PET sensitivity, specificity, positive and negative likelihood ratios, and diagnostic odds ratio were: 95.8%, 92.5%, 9.53, 0.075, and 204, respectively. PET/CT provided better results than PET alone. PET contributed to treatment changes in 22%–35% of patients. The authors concluded that

$^{18}\text{F}$ -FDG PET “is an accurate method for detection and localization of recurrence in posttherapy follow up of endometrial carcinoma.”

*Gynecologic Oncology*

## 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 accessioned into the PubMed database in November. In an article e-published on November 23 ahead of print in *Critical Reviews in Biochemistry and Molecular Biology*, Tomasi and Volkow from the Nation-

al Institute on Alcohol Abuse and Alcoholism (Bethesda, MD) described “Striatocortical pathway dysfunction in addiction and obesity: differences and similarities.” Timmer and Knaapen from the VU University Medical Center (Amsterdam, The Netherlands) provided an overview of “Coronary microvascular function, myocardial metabolism, and energetics in hypertrophic cardiomyopathy: insights from positron emission tomography” on November 14 ahead of print in the *European Heart Journal Cardiovascular Imaging*. In an article appearing on November 15 ahead of print in *Pharmacology & Therapeutics*, Upadhyay et al. from the Indian Institute of Technology Delhi (New Delhi, India)

reported on “The Warburg effect: insights from the past decade.” On November 13 ahead of print in *Current Medicinal Chemistry*, Catafau and Bullich from the Barcelona Imaging Group (Spain) summarized: “Molecular imaging PET and SPECT approaches for improving productivity of antipsychotic drug discovery and development.” Treglia et al. from the Catholic University of the Sacred Heart (Rome, Italy) on November 5 ahead of print in *Rheumatology International* published “Emerging role of fluorine-18-fluorodeoxyglucose positron emission tomography in patients with retroperitoneal fibrosis: a systematic review.”

(Continued from page 17N)

Many reviews have been published on various aspects of  $^{18}\text{F}$  radiochemistry and biologic applications of radio-labeled compounds for PET imaging. However, neither reviews nor articles provide a deep view of development and studies focusing on  $^{18}\text{F}$  over the past 40 years. One of the reasons is certainly size limitations (more than 300 pages would be required) and the tedious task of complete classification of the large variety of  $^{18}\text{F}$ -labeled products. A review focusing on the development of  $^{18}\text{F}$  compounds and their biologic applications designed for the multidisciplinary community would be desirable.

These problems were overcome by setting up a database that can be updated on a regular basis and can host an unlimited number of compounds and their associated data (relevant biologic data and references). To the best of our knowledge, DIRAC is the most complete database on  $^{18}\text{F}$ -radiolabeled compounds available, covering the radiochemistry and biologic work performed with  $^{18}\text{F}$ -fluorinated products over the last 40 years. DIRAC can be used to highlight the importance of some specific receptors in a pathology, to associate chemical characteristics of compounds with a biologic target, or to identify the significance of chemical groups in  $^{18}\text{F}$  radiochemistry and biology and the impact of chemical features on PET imaging with  $^{18}\text{F}$ -labeled compounds.

In the future, tighter interconnection between databases already in use and electronically formatted scientific journals may enable automated or semiautomated Web-based search engines. It is clear that machine-readable data provided by authors or editors will lead to dramatically more accurate and complete databases that can be more easily interconnected and will strengthen online research and analyses of data (3,12). From this perspective, DIRAC

could also be used as a standard to evaluate the relevance and accuracy of results generated by Internet-based software and help in its development and optimization.

## REFERENCES

1. Ido T, Wan CN, Casella V, et al. Labelled 2-deoxy-D-glucose analogs.  $^{18}\text{F}$ -labeled 2-deoxy, 2-deoxy-2-fluoro-D-glucose, 2-deoxy-2-fluoro-D-mannose, and  $^{14}\text{C}$ -2-deoxy-2-fluoro-D-glucose. *J Label Compd Radiopharm*. 1978;14:175–183.
2. Reivich M, Kuhl DE, Wolf A, et al. The  $^{18}\text{F}$ -fluorodeoxyglucose method for the measurement of local cerebral glucose utilization in man. *Circ Res*. 1979;44:127–137.
3. Nicola G, Liu T, Gilson MK. Public domain databases for medicinal chemistry. *J Med Chem*. 2010;55:6987–7002.
4. Iwata R. Reference book 2004 for PET radiopharmaceuticals. 2004. Available at: <http://kakuyaku.cyril.tohoku.ac.jp/public/preface2004.html>. Accessed on September 21, 2012.
5. Chopra A, Shan L, Eckelman WC, et al. Molecular Imaging and Contrast Agent Database (MICAD): evolution and progress. *Mol Imaging Biol*. 2012;14:4–13.
6. Dirac PAM. Quantised singularities in the electromagnetic field. *Proc R Soc Lond A* 1931;133:60–72.
7. Smith TAD.  $^{18}\text{F}$ -fluoride labelling of macromolecules in aqueous conditions: silicon and boron-based  $^{18}\text{F}$ -fluorine acceptors,  $^{18}\text{F}$ -FDG conjugation and  $\text{Al}^{18}\text{F}$  chelation. *J Label Compd Radiopharm*. 2012;55:281–288.
8. Lee E, Kamlet AS, Powers DC, Neumann CN, et al. A fluoride-derived electrophilic late-stage fluorination reagent for PET imaging. *Science*. 2011;334:639–642.
9. Martarello L, Greenamyre JT, Goodman MM. Synthesis and evaluation of a new fluorine-18 labeled rotenoid as a potential PET probe of mitochondrial complex I activity. *J Label Compd Radiopharm*. 1999;42:1039–1051.
10. Wagner HN Jr. A brief history of positron emission tomography (PET). *Semin Nucl Med*. 1998;28:213–220.
11. Blasberg R. PET imaging of gene expression. *Eur J Cancer*. 2002;38:2137–2146.
12. Névél A, Wilbur JW, Lu Z. Improving links between literature and biological data with text mining: a case study with GEO, PDB and MEDLINE. *Database (Oxford)*. 2012. Available at: [www.ncbi.nlm.nih.gov/pmc/articles/PMC3371192](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3371192). Accessed on November 23, 2012.

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