European Cancer Centers Announce Initiative

On September 5, the European Comprehensive Cancer Centre Alliance (ECCCA) formally launched a cooperative effort by 3 cancer centers to develop and implement innovative strategies to improve cancer cure and reduce treatment-related side effects. The Institut Gustave Roussy (IGR; Paris, France), the Netherlands Cancer Institute (NKI; Amsterdam), and the Karolinska Institute (Stockholm, Sweden) will bring together powerful technological platforms of genomics, proteomics, and preclinical evaluation tools to identify promising agents for combined cancer therapies in early clinical radiotherapy trials. The launch began with an inaugural symposium, organized at the NKI, where ECCCA participants presented a strategic plan and announced the first 3 clinical translational trials that will be activated in the participating centers. Each institute has submitted a trial that will be carried out in all 3 institutes. In these trials, findings from preclinical investigations will be transitioned directly into the clinic to evaluate efficacy. All 3 trials combine innovative radiation techniques with translational research.

The NKI-originated trial focuses on CT image-guided radiotherapy in breast-conserving treatment. Tumor response to treatment will be measured with PET and MR spectrometry. Genetic analyses will be performed on tumor tissue to evaluate the suitability of this limited treatment approach as well as to assess the effectiveness of different chemotherapeutics.

The Karolinska Institute–originated study will investigate stereotactic body radiotherapy in advanced lung cancer as an adjunct to pharmaceutical treatment. This therapy will be directed at both primary tumors and metastases, followed by conventional chemotherapy, with PET/CT used both to identify the location of these metastases and to assess treatment effectiveness. The goal is to reduce tumor burden and thereby enhance the effectiveness of chemotherapy.

The IGR-originated study will explore inhibition of the PI3-kinase/AKT/mTOR axis during radiotherapy. This trial will combine radiotherapy for locally advanced nonmetastatic non–small cell lung cancer with sequential radiochemotherapy and everolimus (a derivative of rapamycin that acts as an mTOR inhibitor) treatment. Functional and metabolic imaging, including PET, will be used to monitor tumor response, and histologic studies will be performed to define molecular characteristics of responding tumors.

More information on this cooperative effort is available at www.eccca.eu.

European Comprehensive Cancer Centre Alliance

ICD-10 Code Sets and Updated Transaction Standards

The U.S. Department of Health and Human Services (HHS) announced on August 15 a proposed regulation that would replace the International Classification of Disease (ICD)-9-CM code sets now used to report health care diagnoses and procedures with greatly expanded ICD-10 code sets, effective October 1, 2011. In a separate proposed regulation, HHS has proposed adopting the updated X12 standard, Version 5010, and the National Council for Prescription Drug Programs standard, Version D.0, for electronic transactions such as health care claims. Version 5010 is an essential element in using ICD-10 codes.

"We are taking a giant step forward toward developing a health care system that focuses on quality and affordability through the implementation of health information technology," HHS Secretary Mike Leavitt said. "The greatly expanded ICD-10 code sets will enable HHS to fully support quality reporting, pay-for-performance, biosurveillance, and other critical activities. Conversion to ICD-10 is essential to development of a nationwide electronic health information environment, and the updated X12 transaction standards are a critical step in the implementation of these new codes."

In 2000, the ICD-9-CM code sets were adopted for use in administrative transactions by both the public and private sectors to report diagnoses and inpatient hospital procedures. Covered entities required to use the ICD-9-CM code sets include health plans, health care clearinghouses, and health care providers who transmit any electronic health information in connection with a transaction for which a standard has been adopted by HHS. Developed almost 30 y ago, ICD-9 is now widely viewed as outdated because of its limited ability to accommodate new procedures and diagnoses. ICD-9 contains only 17,000 codes and is expected to begin to run out of available codes next year. The ICD-10 code sets contain more than 155,000 codes and accommodate a host of new diagnoses and procedures. The additional codes will facilitate implementation of electronic health records by supplying more detail.

"Now is the right time to move forward with the transition from ICD-9 to ICD-10," said Center for Medicare & Medicaid Services Acting Administrator Kerry Weems. "We recognize that the transition to ICD-10 will require some upfront costs, but each year of delay would create additional costs, both because of the limitations of ICD-9 and because of the need to employ the greater precision that ICD-10 codes provide to support value-based purchasing of health care and other initiatives. We will continue to work collaboratively across the health care system to ensure a smooth transition to use of the updated transaction standards and ICD-10."

Comments on the updated transaction standards proposed are due on October 21. Fact sheets describing both proposed rules and the comments process are available at www.cms.hhs.gov/apps/media/fact_sheets.asp.

Department of Health and Human Services

New FDA Advisory Committee Policies

The U.S. Food and Drug Administration (FDA) announced on August 4 several changes in policies and procedures affecting management of FDA advisory committees. These include stricter limits on financial conflicts of interest for committee members, amended voting procedures, and changes to the processes for disclosing information pertaining both to advisory committee members and to specific matters considered at advisory committee meetings. The policies and procedures are described in 4 final guidance documents, and proposed changes in policies are described in a draft guidance. Most of the changes in the final guidance documents went into effect immediately, and all were expected to be fully implemented by the end of the year.

"The FDA's regulatory decisions affect the health of millions of Americans, and we don't make those decisions in a vacuum," said Randall Lutter, PhD, deputy commissioner for policy. "It's imperative that we seek advice from independent experts and that we do so in a way that is public, open, and transparent. Today's announcement strengthens our processes." FDA advisory committees are panels of independent, outside experts who advise agency officials in considering regulatory decisions involving complex medical and scientific issues. In 2007, FDA convened 48 meetings of advisory committees on topics ranging from the safety of diabetes medications to the evaluation of new anticancer drugs for use in children.

Two of the guidance documents released address FDA processes for evaluating and disclosing information about potential conflicts of interest and FDA waivers allowing participation in advisory committee meetings. Before each meeting, advisory committee members are screened by FDA staff to identify any potential financial conflicts of interest, such as grants, stock holdings, or contracts with a company that would be affected by the committee's recommendations. FDA is instituting a cap of $50,000 as the maximum personal financial interest an advisor may have in all companies that may be affected by a specific meeting. If an advisor's personal financial interest is greater than $50,000, he or she will not be allowed to participate in that meeting. If less than $50,000, FDA officials may, in certain situations, grant a waiver but will do so only if they determine an essential need for the advisor's specific expertise. Waivers, which include a description of the advisor's personal financial interest and why the need for the expertise was essential, will be posted on the FDA's Web site in advance of each meeting. New templates for waivers and financial interest disclosure will be available.

Another prospective change will be in public availability of briefing materials, the background information provided to advisory committee members. FDA intends to post briefing materials given to advisory committee members on the FDA's Web site at least 48 h before the meeting is scheduled to occur. The guidance document provides details on preparing and submitting documents to FDA for inclusion in the briefing materials and also recommends a timetable that sponsors should follow when submitting such documents.

The agency also issued recommendations addressing the way that advisory committees will vote on questions. It was recommended that advisory committees use a process of simultaneous voting in which all members vote at once. In the past, advisory committees sometimes voted sequentially, with the committee chair calling on each member to announce his or her vote aloud. Simultaneous voting avoids "voting momentum" in which some voters may be influenced, even subconsciously, by the votes of those who precede them. The agency also recommended that the results of votes be announced immediately in the meeting, and FDA intends to post on the FDA Web site a list indicating how each member voted.

FDA also proposed new criteria to clarify when the agency should refer a matter to an advisory committee. In some instances FDA is required by law to refer a matter to an advisory committee; in other instances, FDA would consider these new criteria when deciding whether to refer a matter to an advisory committee.

The agency also has made improvements to the advisory committee Web site. For more information on these and other changes, see the FDA Advisory Committee home page at www.fda.gov/oc/advisory/.

Food and Drug Administration

Recurring Isotope Shortages

The Netherlands Nuclear Research and Consultancy Group (NRG) announced on August 26 that an inspection of its High Flux Reactor in Petten had revealed gas bubbles escaping from a pipe wall into the primary cooling system and, as a result, that the next irradiation cycle would not begin. Press releases indicated that NRG would not produce any medical isotopes for at least 2 mo. The NRG provides more than 60% of European radioisotopes and also supplies users in Canada and the United States. The shutdown at the High Flux Reactor came after a similar shutdown in 2007 of the National Research Universal reactor in Chalk River, Canada, by Atomic Energy of Canada Limited (AECL). Moreover, the unexpected NRG shutdown came during a week when 4 other major reactors around the world (including the Chalk River facility) were scheduled to be down for routine maintenance or inspection.

Professional groups expressed concern about the effects of the latest series of shutdowns on routine delivery of medical imaging and treatment services. "SNM has serious concerns about this most recent outage," said

SNM President Robert W. Atcher, PhD, MBA. "A combination of anticipated outages at other production reactors, coupled with unanticipated shutdowns, is simply devastating. The impact on the patients who are in need of diagnostic tests using these radioisotopes is very serious. The United States and other countries are not prepared to adequately deal with the current situation—let alone anticipate other situations as they continue to arise. Following the shutdown of Canada's Chalk River facility late last year, we simply cannot afford to sit and wait as the situation continues to worsen."

The nuclear facility at Petten is a principal supplier of ^{99}Mo, the most widely used isotope in nuclear medicine. "This could be described as a perfect storm in isotope availability," said Atcher. "This is a cumulative situation where we cannot maintain a patchwork approach to isotope production and supply. It also highlights the vulnerability of having no domestic source of clinically used isotopes in the United States."

In Canada, where the issue of radioisotope availability remains a hot-button issue after the Chalk River shutdown, controversial restart, and recent government decision not to go ahead with the twin MAPLE reactors that would have provided isotope production backup, initial reactions to the Petten shutdown were mixed. On August 28, the Toronto Sun carried an article indicating that supplies would be "OK" and quoting an AECL official indicating that "if a shortfall occurs, the Chalk River facility can ramp up to meet Canadian needs." On the same day, the media service CanWest News carried a more gloomy assessment from the same official, who cautioned that while the facility might meet Canadian needs, it certainly could not supply the rest of the world with isotopes to bridge the gap during NRG repairs.

SNM is working with partners from other molecular imaging and health care organizations to identify and implement both immediate and long-term solutions. In June, SNM's Isotope Availability Taskforce published a draft report examining potential solutions for creating a domestic supply of medical isotopes in the United States. Reactor outages, coupled with recent efforts to curtail the use of highly enriched uranium in radioisotope production as a nonproliferation strategy and to deter terrorism, now pose a significant threat to ^{99}Mo availability within the United States.

"This is a serious problem requiring a quick response and in-depth solution," said Michael Graham, MD, PhD, SNM president-elect. "Now, more than ever, it is critical that the United States, along with other countries, take the lead on recommending alternatives to ensure consistent access to mission-critical isotopes, which are essential to hospitals and their ability to provide patient care."

One immediate challenge is for the world's radioisotope producers to work together to coordinate routine downtime. "Perhaps in the future you wouldn't want to have all of (the world's) reactors, or most of them, shut down for maintenance," said Christopher O'Brien, MD, president of the Ontario Association of Nuclear Medicine. "What this documents is that medical isotope production is not unique to any specific country and should be viewed as a world resource."

These events are developing as Newsline goes to press, and updates will be included in future issues.

SNM

Medicare Panel Questions NOPR Data

A U.S. Medicare advisory panel meeting on August 20 expressed doubts that industry-sponsored data on the use of PET imaging to diagnose and evaluate 9 cancers could apply more widely to other cancers. The panel of outside experts also said it did not have confidence that patient data gathered from the National Oncologic PET Registry (NOPR) provided convincing evidence that PET could help physicians make better decisions or improve outcomes. Despite evidence presented by numerous professional and industry groups (see additional Newsline coverage, p. 24N), including recent data indicating that PET provides information that positively affects management decisions for one-third of patients, panel members expressed skepticism about the applicability of these data in the broad range of cancers being considered for expanded Medicare coverage of PET.

SNM was among a number of groups that petitioned Medicare in 2005 to provide reimbursement for PET imaging in brain, cervical, bladder, small-cell lung, ovarian, testicular, prostate, kidney, and pancreatic cancers. Medicare's response was agreement to cover PET imaging in these conditions provided that patients were enrolled in a nationwide registry designed to gather additional data to support later reimbursement considerations. Recent results from the NOPR data prompted SNM and a coalition of industry and professional groups to petition for expedited review of expanded reimbursement.

To the surprise of many molecular imaging specialists, the Medicare panel questioned the available data's relevance across the range of 9 cancers. "I don't see how you make the leap," panel member Linda Bergthold, PhD, a sociologist and research associate at Stanford University (CA) specializing in health care financing, told the press. "The quality of the data. . .was really stunningly poor." Medicare is expected to make a draft decision in January and a final ruling in April.

SNM sources

Status of Canadian Medical Imaging Reviewed

Medical Imaging in Canada, 2007, a report released on August 21 by the Canadian Institute for Health Information (CIHI), contained some positive news but other more discouraging data on the status of advanced imaging techniques in that country. Although the numbers of MR and CT scanners increased significantly over the last 4 y, with corresponding rises in the numbers of examinations, the supply of

these scanners fell well below the recommendations of the Organisation for Economic Co-operation and Development (OECD) and far below comparable data in the United States. The numbers for PET and PET/CT were even more discouraging: as of January 1, 2007, the entire country was served by a total of 18 PET/CT and 13 PET scanners.

"Increases in the number of imaging scanners over the last few years mean that the majority currently installed and in use in Canada are less than 6 years old," said Francine Anne Roy, director of health resources information at CIHI. "These newer machines are using the latest technology to produce more detailed scans."

This generally positive spin on advances in imaging technology was countered by the release on the same day of a report with data suggesting that Canada is "slow to adopt the latest medical technology, forcing Canadian patients to rely on old and often outdated medical equipment for treatment." The peer-reviewed study, *Medical Technology in Canada*, was prepared by the Fraser Institute, an independent research organization based in Calgary, Canada. "Lack of access to cutting-edge medical technology has significant consequences; the most obvious is that a patient's survival or return to full health is compromised because of a later or less sophisticated diagnosis and more invasive treatment," said Nadeem Esmail, director of health system performance studies at The Fraser Institute and coauthor of the study.

The study evaluated the availability of medical technology in Canada compared with other nations within the OECD, measured the age and sophistication of medical technology, and measured the stock of available cutting-edge medical technology in Canada's 5 largest cities. The study focused on technologies in diagnostic imaging and laboratory diagnostic, surgical, and patient services areas and concluded that access to medical technology in Canada is well below average. One element cited as a "key indicator of Canada's performance on the medical technology front" was the availability of PET scanners. The study found that Canada ranked below average and ahead of only Finland, Spain, the United Kingdom, and The Netherlands among developed nations in the number of PET scanners per million people.

When examining the age and sophistication of medical technologies used in Canada, the study found that the Canadian heath care system relies heavily on an inventory of older and outdated medical technologies. Canada also often relies more on less-sophisticated forms of technology than is optimal. For example, at the beginning of 2006, 14.8% of Canada's hospital-based CT scanners, 29.3% of hospital-based MR units, 26.1% of hospital-based SPECT units, 35.7% of hospital-based gamma cameras, 47.4% of hospital-based angiography suites, and 40.2% of hospital-based cardiac catheterization labs were older than their respective Canadian Association of Radiologists–developed lifecycle guidelines.

The study also surveyed the availability of 50 cutting-edge medical technologies, including PET and PET/CT, at hospitals in the 5 largest cities and found that only 10 of these technologies were available in more than half the facilities. Of the remaining 40 technologies, 21 were present in 25%–50% of responding facilities, and 19 were present in less than 25% of responding facilities. "The results of our failure to invest in new medical technologies are exemplified by long waiting times, less efficient use of medical resources, and less timely and sophisticated diagnosis and treatment," Esmail said. "Canada's failure to invest in the latest medical technology cannot be explained by a lack of money. On the contrary, Canada's universal access health insurance program is among the developed world's most expensive such programs."

The CIHI and Fraser Institute reports can be downloaded from their respective Web sites at: http://secure.cihi.ca/cihiweb/splash.html and www.fraserinstitute.org.

Canadian Institute for Health Information
The Fraser Institute

Hanford B Reactor Designated as Historic Landmark

On August 25 U.S. Department of the Interior Deputy Secretary Lynn Scarlett and U.S. Department of Energy (DOE) Acting Deputy Secretary Jeffrey F. Kupfer announced the designation of the DOE B Reactor as a National Historic Landmark and unveiled DOE's plan for a new public access program to enable Americans to visit the reactor during the 2009 tourist season. The B Reactor at the DOE Hanford Site in southeast Washington State was the world's first industrial-scale nuclear reactor and produced plutonium for the atomic weapon dropped on Nagasaki, Japan, in World War II. The reactor produced fissionable material from 1944 to 1968, and its water-cooled, graphite-moderated design served as the model for all U.S. nuclear reactors until 1952.

"The men and women who worked on the B Reactor made their mark on history with an extraordinary technological and human achievement," said Kupfer. "Preservation of the B Reactor will ensure their groundbreaking role in American history remains visible for future generations to see. Their accomplishments will serve as inspiration to others as we continue to apply science and technology to address today's most pressing global challenges."

The designation of the B Reactor as a National Historic Landmark was formally signed by Secretary of the Interior Dirk Kempthorne on August 19. National Historic Landmarks can be significant districts, sites, buildings, structures, and/or objects that possess exceptional value or quality in illustrating or interpreting the heritage of the United States. Fewer than 2,500 historic places bear this national distinction. Four other Manhattan Project sites are already National Historic Landmarks: the Los Alamos (NM) Scientific Laboratory, the X-10 Graphite Reactor at Oak Ridge (TN), the Trinity Site (Socorro, NM), and the Chicago (IL) Pile I.

The DOE will also increase public access to the B Reactor, which is

currently limited to about 50 tours annually. Beginning in March 2009, individuals and families will be able to tour at least 3 d/wk through October 2009 by presenting identification at the Hanford Site. The DOE plan sets a timetable for more permanent decisions about the future preservation of B Reactor. Five of Hanford's 9 plutonium production reactors have been dismantled and "cocooned" as part of a closure contract covering cleanup of Hanford's Columbia River Corridor, and the B Reactor could have undergone this process as early as 2009. In March 2008, DOE announced a policy directive to support preservation of the B Reactor that required the reactor to be maintained in a state that preserves its historical significance.

U.S. Department of the Interior
U.S. Department of Energy

Tatum Named Associate Director of CIP

The National Cancer Institute (NCI) announced on August 1 that James L. Tatum, MD, has been selected for the position of associate director of its Cancer Imaging Program (CIP). He joined CIP in 1998 as a special assistant to the associate director and since that time has assumed increasing responsibilities. In 2006, he became the head of CIP's Molecular Imaging Branch. Since July 2007, he has used his expertise in the areas of molecular imaging and imaging drug development to guide CIP as its acting associate director.

Tatum serves as chair of the imaging drug group of the Joint Development Committee, where he plays a vital role in overseeing imaging agents in the NCI drug pipeline. He represents imaging from the NCI viewpoint on the steering committee for the Nanotechnology Characterization Laboratory (NCL), a joint effort of NCI, the Food and Drug Administration, and the National Institute of Standards and Technology. He is also a member of the NCL review panel and serves on the steering committee of the Small Animal Imaging Program at NCI–Frederick.

Early in his research career, Tatum focused on imaging alterations in the pulmonary capillary membrane associated with acute respiratory distress syndrome and the application of imaging techniques to evaluate drug interventions. Later, his research shifted to studies of myocardial ischemia, including acute coronary syndrome, with a focus that continues in his research today on the use of imaging in medical decision making.

Tatum received his undergraduate degree in biology from the College of William and Mary (Williamsburg, VA) and his MD from the Medical College of Virginia (MCV; Richmond). He completed his residency in medicine and radiology at MCV Hospitals, followed by a nuclear medicine fellowship at Duke University (Durham, NC). He is board certified in diagnostic radiology, nuclear medicine, and nuclear cardiology. In 1978, he joined the faculty of Virginia Commonwealth University (VCU), where he was later appointed professor of both radiology and medicine. During his tenure at VCU, he served as chair of the division of nuclear medicine, director of nuclear cardiology, chair of the department of radiology, associate vice president for health sciences, and director of the Molecular Imaging Center.

National Cancer Institute

(Continued from page 23N)

Mollura, MD, Johns Hopkins University; Karen Gulenchyn, MD, McMaster University (Ottawa, Canada); Wim Oyen, MD, PhD, Radboud University (Nijmegan Medical Center, The Netherlands); Matthias Benz, MD, University of California, Los Angeles; Andreas Buck, MD, The Children's Hospital of Philadelphia (PA); and Wengen Chen, MD, PhD, also from The Children's Hospital of Philadelphia.

"We are truly thrilled to offer these awards and deeply appreciative of the support of the donors who make this ground-breaking research a reality," said VanBrocklin.

Application deadlines for the 2009 SNM Research Grants will be in late winter 2009. More information about the awards, along with application forms, is available at www.snm.org/grants.

(Continued from page 27N)

curtail the use of highly enriched uranium in radioisotope production as a nonproliferation strategy and to deter terrorism, now poses a significant threat to ^{99}Mo availability within the United States. The subsequent cancellation in May 2008 of the MAPLE reactors at the Chalk River Laboratories has made the need for an alternative domestic source for ^{99}Mo production more acute. We will keep SNM members apprised of this developing situation.

There has been a tremendous amount of activity during the first 3 mo of my presidency. In addition to developments in the issues reviewed above, we will report on a major new thrust for SNM in the coming months. As I have noted to many audiences, many of SNM's activities are now multiyear projects that require teamwork and commitment to common goals. We are fortunate that Alexander McEwan, MD, immediate past president of SNM, established a solid framework and that Michael Graham, PhD, MD, president-elect, and Dominique Delbeke, MD, PhD, vice president-elect, have agreed to sustain many of these longer range activities.

Robert W. Atcher, PhD, MBA
SNM President