Molecular Imaging Device Market

According to a report released in July by health care market research publisher Kalorama Information (Rockville, MD), the market for molecular imaging devices will increase in the near term by an average of 5.8%/y, reaching $6.6 billion in 2014. Key reasons for this increase will be "cost savings associated with early disease detection and clinicians' demand for better, more accurate diagnostic tools." The study noted that this rise accompanies a continued quest by physicians for minimal invasiveness, rapid imaging processing time, low imaging cost, low radiation dose, and optimal resolution and contrast. "Meeting the growing demand for a better molecular imaging device is a big driver for companies seeking to break into this market," said Bruce Carlson, publisher of Kalorama Information. "The market could even grow further if physicians' demands are met and we see a rise in patient confidence, as this could translate into more individuals opting in for these services."

The report looked not only at PET and SPECT but at MR, ultrasound, and CT imaging as well as at hybrid modalities and combined techniques. Novel research areas and their corresponding device development potential were explored, including: heart failure, sentinel node biopsies, thyroid cancer, nanoparticle platforms, circulating progenitor cells, molecular-level tumor activity, brain cell inflammatory responses, motion-frozen technology, recurring prostate cancer, and a range of radiopharmaceuticals and novel tracers.

The proprietary report, *Molecular Imaging Markets (Market Intelligence Analysis of Market Opportunities in Molecular Imaging),* contains information on forecasts, company profiles, and trends in the molecular imaging market and is available at www.kalorama information.com/Medical-Imaging-Molecular-2613825/.

Kalorama Information

NRU Production Resumed

On August 17, the National Research Universal (NRU) reactor at the Atomic Energy of Canada Limited (AECL) Chalk River (Ontario) Laboratories was safely returned to operation. As of Newsline press time in September, all of the operating systems were in service and the reactor was once again producing medical isotopes. An AECL press release noted that with repairs complete and several additional enhancements made to the reactor during the outage, the NRU will return to its regular 28-d operating cycle, running at high power for 23 d, followed by a 5-d shutdown for routine maintenance.

The reactor reached high power operation on August 17, and the first ^{99}Mo was harvested and delivered to MDS Nordion on August 18. One planned shutdown on August 20 to remove specialized start-up equipment and an unplanned shutdown on August 30 did not interrupt ^{99}Mo production.

The reactor had been shut since May 19, 2009, resulting in an estimated US$70 million loss in repair costs and lost isotope sales. In addition to isotope production for medical purposes across North America, the NRU is the main research reactor providing materials and radiochemistry testing for the Canadian nuclear industry. It also produces neutrons for the National Research Council, an organization that is onsite at Chalk River Laboratories to perform neutron scattering experiments.

Although nuclear medicine specialists welcomed the return of isotope production at the reactor, several warned against overconfidence. "We are cautiously optimistic that NRU going back online will alleviate some of the most pressing concerns facing the nuclear medicine community," said Robert W. Atcher, PhD, MBA, chair of the SNM Domestic Isotope Availability Work Group. "However, this is not a magic bullet, and NRU coming back online will not solve this crisis. As the Canadian Nuclear Safety Commission staff are reported to have observed, gaps in the assessment of the reactor could have a serious impact on the reliability of the reactor's operation in the future." Atcher also pointed to the Canadian government's previous statement that they intend to permanently shut down isotope production at the NRU in 2016. Atcher and others continue to call for exploration of U.S. sources of ^{99}Mo and other isotopes used routinely in molecular imaging and therapy.

In an unrelated but positive note for international isotope supplies, the High Flux Reactor (Petten, The Netherlands) was successfully repowered on schedule on September 9, after more than 6 mo downtime for routine maintenance and repairs to corroded lines. When at full operation, the High Flux Reactor meets approximately 60% of Europe's medical isotope needs.

Atomic Energy of Canada Limited
Society of Nuclear Medicine

New ACMUI Members

The Nuclear Regulatory Commission (NRC) announced on August 17 the selection of Christopher J. Palestro, MD, as the nuclear medicine physician, and Milton J. Guiberteau, MD, as the diagnostic radiologist representative on the Advisory Committee on the Medical Uses of Isotopes (ACMUI). The ACMUI was established in 1958 and advises the NRC on policy and technical issues related to the regulation of the medical uses of radioactive material.

Dr. Palestro is chief of the division of nuclear medicine and molecular imaging of the North Shore Long Island (NY) Jewish Health System and is a professor of radiology at the Hofstra University School of Medicine. He is an internationally recognized authority on nuclear medicine imaging of infection and an active participant in SNM activities. He serves as chair of the Infection Section of the SNM Procedure Guidelines Task Force and vice-chair of the hematopoietic and

musculoskeletal sections of SNM's Lifelong Learning and Self-Assessment Programs.

Dr. Guiberteau is academic chief of radiology, chief of nuclear medicine, and chief of women's imaging at St. Joseph Medical Center (Houston, TX) and is a professor of clinical diagnostic radiology and nuclear medicine at the University of Texas Medical School–Houston. In addition to many honors and distinctions, he has been president of the southwestern chapter of SNM.

All ACMUI member biographies are available on the NRC Web site at www.nrc.gov/about-nrc/regulatory/advisory/acmui/membership.html.

Nuclear Regulatory Commission

Federal Research Agenda for Breast Cancer

On August 16, a newly formed advisory committee was appointed to develop and coordinate a strategic federal research agenda on environmental and genetic factors related to breast cancer. The 19-member Interagency Breast Cancer and Environmental Research Coordinating Committee (IBCERCC) was established by the National Institute of Environmental Health Sciences (NIEHS), in collaboration with the National Cancer Institute (NCI), to review all breast cancer research efforts conducted or supported by federal agencies.

The committee will develop recommendations for the secretary of the U.S. Department of Health and Human Services, the National Institutes of Health, and other federal agencies, to improve existing research programs related to breast cancer research. In addition, the IBCERCC will create a comprehensive plan to expand opportunities for collaborative, multidisciplinary research and develop a summary of advances in federal breast cancer research. "The broad range of expertise and insight of these individuals will ensure the federal research portfolio continues to advance our understanding of the critical links between our environment, our genes, and our health," said Linda Birnbaum, PhD, director of NIEHS and the National Toxicology Program.

"The committee's focus on breast cancer and the environment research across federal agencies will be valuable in identifying scientific opportunities to better understand the impact of the environment on this disease," said Robert Croyle, PhD, director of the Division of Cancer Control and Population Sciences at NCI. IBCERCC members were scheduled to hold their first meeting on September 30 and October 1 in Washington, DC.

National Institute of Environmental Health Sciences

Medicare and Decision Support

The Centers for Medicare & Medicaid Services (CMS) announced on July 22 that it would open a relatively short window soliciting proposals for "conveners" to participate in the Medicare Imaging Demonstration (MID). The MID was authorized by section 135(b) of the Medicare Improvements for Patients and Providers Act of 2008 and will test whether the use of decision support systems (DSSs) can improve quality of care and reduce unnecessary radiation exposure and utilization by promoting appropriate ordering of advanced imaging services.

The 2-y demonstration will assess the impact that DSSs used by physician practices have on appropriateness and utilization of advanced medical imaging services ordered for the Medicare fee-for-service population. A DSS provides immediate feedback based on current medical specialty guidelines to the physician on the appropriateness of the test ordered for the patient. The demonstration is planned to focus on MR imaging, CT, and 1 nuclear medicine study.

All current Medicare coverage and payment policies are unaffected under this demonstration, and prior authorization processes are not part of the demonstration. CMS will use conveners to reach eligible physicians interested in participating in the demonstration. Conveners will be responsible for recruiting physician practices, deploying a DSS that incorporates medical specialty society guidelines for the selected procedures, ensuring that DSS remains current with those guidelines, collecting and transmitting data, and distributing payments to practices for reporting data. Conveners and physician practices will be paid for reporting complete data necessary to determine the appropriateness of the test. The deadline for application as a convener was September 21.

Eleven advanced imaging procedures—SPECT myocardial perfusion imaging; MR imaging of the lumbar spine, brain, knee, and shoulder; and CT of the brain, lumbar spine, sinus, thorax, abdomen, and pelvis—will be included in the demonstration. The 11 tests were selected based on high expenditures and utilization in the Medicare fee-for-service population and the availability of relevant medical specialty appropriateness guidelines. The law requires that the appropriateness criteria used in the demonstration be based on those developed or endorsed by medical specialty societies. CMS worked with medical specialty societies and other stakeholders to solicit their input and information on available appropriateness criteria.

Centers for Medicare & Medicaid Services

CMS Modifies "Only 1" PET Restriction

The Centers for Medicare & Medicaid Services (CMS) on August 4 issued a decision memo for PET for initial treatment strategy in solid tumors and myeloma amending 220.6.17 of the National Coverage Determinations (NCD) Manual. The memo stated that: "(1) The NCD will be changed to remove the current absolute restriction of coverage to 'only 1' FDG PET scan to determine the location and/or extent of the tumor for the therapeutic purposes related to the initial treatment strategy. . .; (2) CMS will continue to nationally cover 1 FDG PET scan to determine the location and/or extent of the tumor for the therapeutic purposes

related to the initial treatment strategy. . .; and (3) local Medicare administrative contractors will have discretion to cover (or not cover) within their jurisdictions any additional FDG PET scan for the therapeutic purposes related to the initial treatment strategy. . . .” The memo went on to state that “For any individual beneficiary the usefulness of any additional FDG PET scan for initial treatment planning might be affected by the beneficiary’s specific medical problem, the availability of results of other diagnostic tests, and the expertise of the interpreting physician. We believe in such situations that our local administrative contractors, who may more readily obtain this information, can make these determinations about any additional FDG PET scan for initial treatment planning within their jurisdictions. We do not believe that a national coverage determination is the most appropriate way to address coverage for any additional FDG PET scans for the therapeutic purposes related to the initial treatment strategy at this time.”

Centers for Medicare & Medicaid Services

FROM THE LITERATURE

Each month the editor of Newsline selects articles on diagnostic, therapeutic, research, and practice issues from a range of international publications. Most selections come from outside the standard canon of nuclear medicine and radiology journals. These briefs are offered as a monthly window on the broad arena of medical and scientific endeavor in which nuclear medicine now plays an essential role. We have added a special section on molecular imaging, including both radionuclide-based and other molecular imaging efforts, in recognition of the extraordinary activity and promise of diagnostic and therapeutic progress in this area. The lines between diagnosis and therapy are sometimes blurred, as radiolabels are increasingly used as adjuncts to therapy and/or as active agents in therapeutic regimens, and these shifting lines are reflected in the briefs presented here. We have also added a small section on noteworthy reviews of the literature.

MOLECULAR IMAGING/THERAPY

Imaging of Gene Therapy in NSCLC

Singh et al. from the University of Texas M.D. Anderson Cancer Center (Houston) reported on July 23 ahead of print in *Human Gene Therapy* on a study assessing whether a human somatostatin receptor subtype-2 (SSTR2)–based reporter gene can be used as a marker of gene transfer into non–small cell lung cancers (NSCLC), which account for 85% of lung cancer–related deaths in North America. In in vitro studies, SSTR subtype expression was assessed in 3 NSCLC cell lines using reverse transcription polymerase chain reaction. Lines were infected with an adenovirus containing hemagglutinin-A-tagged-SSTR2 (Ad-HA-SSTR2) or a control insert, and expression was assessed by immunologic techniques and binding to ^{111}In-octreotide. In in vivo studies, intrathoracic H460 tumors in mice were imaged at baseline with MR and, using ultrasound guidance, injected with Ad-HA-SSTR2 or a control virus. ^{111}In-octreotide was injected on d 2, and the mice underwent planar and SPECT imaging. Biodistribution was assessed with MR and γ-camera imaging as well as by assessment of excised organs/tumors. All 3 NSCLC cell lines expressed different SSTR subtypes, but none expressed SSTR2. However, after Ad-HA-SSTR2 infection, HA-SSTR2 expression was seen in all 3 cell lines using antibodies targeting the HA domain or ^{111}In-octreotide targeting the receptor domain. Intrathoracic tumors infected with Ad-HA-SSTR2 were clearly visible on γ-camera imaging, with expression quantified by biodistribution studies. Immunohistochemistry found that 78% of NSCLCs were negative for and 13% had low levels of SSTR2 expression. The authors concluded that “SSTR2-based reporters can serve as reporters of gene transfer into NSCLCs.” It is noteworthy that the study included the effective use of a combination of several nuclear techniques and MR imaging.

Human Gene Therapy

Peptides for Osteosarcoma Imaging

Sun et al. from the National Institutes of Health (Bethesda, MD), the Fourth Affiliated Hospital (Harbin Medical University, China), and the Jiangsu Institute of Nuclear Medicine (Wuxi, China) reported in the August 15 issue of *Clinical Cancer Research* (2010;16:4268–4277) on a study of phage display screening for peptides that bind specifically to osteosarcoma cells. From a phage display peptide library of 2.7×10^9 displayed peptides, 1 peptide was enriched after 4 rounds of in vitro selection in 143B osteosarcoma tumor cells. Both the peptide and a phage clone displaying the peptide were conjugated with fluorescent dyes for in vitro cell and ex vivo tumor tissue staining. The peptide was labeled with ^{18}F for PET imaging, and cell uptake and biodistributions studies were performed with an ^{18}F-labeled osteosarcoma-specific peptide. The dominant sequence isolated was ASGALSPSRLDT, which was named OSP-1. OSP-1 was found to have significant similarities to the heparinase II/III family protein, which binds and reacts with heparan sulfate proteoglycans. Fluorescence staining indicated that fluorescein isothiocyanate-OSP-1-phage or Cy5.5-OSP-1 had high binding with a panel of osteosarcoma cell lines, much greater than binding observed in several other experimental cell types. ^{18}F-OSP-1 had significantly higher ac-