field of molecular imaging and nuclear medicine, including research funding, reimbursement, and Consistency, Accuracy, Responsibility, and Excellence (CARE) in Medical Imaging and Radiation Therapy legislation. Representatives from the Nuclear Regulatory Commission, FDA, and NIH attended or gave presentations to our attendees, and the society honored specific legislators for their outstanding support of the profession. SNM remains the lead champion on Capitol Hill for the basic sciences related to nuclear medicine and molecular imaging and therapy; the society is a staunch supporter of funding for clinical research at NIH and domestic medical isotope production enhancement for medical applications and scientific research.

The **Technologist Section** continues to advocate strongly to provide opportunities for those interested in extending their professional education to the graduate level and upgrade minimum educational requirements for nuclear medicine technology certification to a bachelor's degree at entry level. SNMTS emphasizes promoting standardized, legislated legal scope of practice and augmenting the knowledge base and skill sets to include fusion imaging with the latest technologies.

SNM continues to expand valuable educational and training opportunities at our **Mid-Winter Educational Symposium** and **Annual Meeting.** The 2008 Annual Meeting will host the second MI Gateway area, offer abstracts from a new MI track, and feature related continuing education programs. SNM took a leadership role in **maintenance of certification** and offers nearly 30 Lifelong Learning and Self-Assessment Program modules. The society continually debuts new educational activities, ensuring that members remain abreast of rapidly occurring advances, best practices in patient care, and proven practice-management techniques. Our **diagnostic CT and PET/CT cases**—a new component of SNM's practice improvement program—enable nuclear medicine physicians and radiologists to meet the PET/CT and diagnostic CT training and credentialing recommendations as published by SNM. SNM supports and trains nuclear medicine **residents and fellows,** offering comprehensive educational programs to meet Accreditation Council for Graduate Medical Education (ACGME) and American Board of Nuclear Medicine (ABNM) requirements. SNM plans to conduct educational forums with imaging advocacy coalitions, patient groups, pharmaceutical companies, and NIH advisory councils.

MICOE and PET centers of excellence, along with the multidisciplinary research offered in our journals, continue to promote the work of our scientists. ***JNM*** and the ***Journal of Nuclear Medicine Technology*** are now published online in advance of print publication to bring new research to readers at the earliest possible date. New **awards, grants, and fellowships** in the areas of multimodality molecular imaging are being offered. Nearly 100 million people have read or heard about SNM efforts this past year in online and print publications and on radio and television broadcasts. SNM has been recognized as *the* number one mover and shaker in the field of radiology from a publication covering the profession.

SNM's leaders, volunteers, and staff are passionate about expanding services to members and improving the practice of nuclear medicine and advancing molecular imaging and therapy. If you have any questions about SNM programs or services, please contact headquarters staff members, who are committed to providing you with high-quality assistance.

Virginia Pappas, CAE
Chief Executive Officer, SNM

Physics Applications in Nuclear Medicine: 2007

The past year saw some revolutionary changes in methods and resources available for internal dose assessment, as well as excellent progress in instrumentation. Significant advances were seen in detector development and image analysis methods, and new tools and information for dosimetry became available. Electronic resources continued to play a significant role in these essential areas of investigation.

Radiation Dose Assessment

RAdiation Dose Assessment Resource (RADAR) Task Group and Web Site: Standardized dose estimates are needed regularly by SNM members for new and existing diagnostic agents, to gain U.S. Food and Drug Administration (FDA) approval, to allow use in research institutions and medical centers, for quick reference for pregnant and breastfeeding women, and other applications. Basic data and models underlying these dose estimates are also regularly needed by the scientific community. The RADAR group established an information Web site (www.doseinfo-radar.com) in 2002 that has been regularly updated. This site has provided dose calculational tools and data to SNM members and others, averaging 20,000−25,000 page visits per month. In 2007, RADAR was given official task group status within SNM.

The focus of the RADAR task group is to:

- Provide accurate and up-to-date information on input data (radionuclide decay, absorbed fractions, standard organ masses, and other data) needed for radiation dosimetry to the scientific community on a timely basis;
- Perform research and develop new models and techniques to improve the state of the art in internal and external dosimetry;
- Publish information on dosimetry models and methods, in the form of journal articles, books, book chapters, conference proceeding articles, and others;
- Develop and publish software tools that facilitate calculation of standardized internal dose calculations; and
- Assess and disseminate standardized dose estimates for new radiopharmaceuticals.

The RADAR site holds:

- Tables of decay data for more than 800 radionuclides of interest in diagnostic and therapeutic nuclear medicine and radiation safety. The entire dataset may be downloaded as a Microsoft Word document or Excel spreadsheet, or data for individual nuclides may be viewed online at http://hps.org/publicinformation/radardecaydata.cfm. With the release of updated decay data (*1*) for these and more radionuclides, the RADAR group plans a revision and release of new data in 2008.
- Kinetic data and standard dose estimates for adults and children for more than 70 radiopharmaceuticals (www.doseinfo-radar.com/NMdoses.xls), for the most part as recommended by the Task Group on Dose to Patients from Radiopharmaceuticals of the International Commission on Radiological Protection (ICRP) (*2*).
- Kinetic data and standard dose estimates for the adult female at 4 stages of pregnancy for more than 80 radiopharmaceuticals (www.doseinfo-radar.com/pregtables.doc).
- Dose estimates for several unique dosimetry situations involving ^{131}I administration to pregnant or potentially pregnant women (www.doseinfo-radar.com/RADAR-INT-NM.html).
- Recommendations for management of breastfeeding nuclear medicine patients for more than 2 dozen radiopharmaceuticals per an article published in *The Journal of Nuclear Medicine* (*JNM*) in 2000 (*3*).
- Absorbed fractions and dose factors for all of the 800 radionuclides described in the previous bulleted items for 6 phantoms representing standardized adults and children and 4 phantoms representing standardized pregnant females. The RADAR group has also just finished a project updating ALL of these standardized phantoms, from the geometrical phantom model types of the 1980s (*4,5*) to highly realistic models based on medical image data (*6*). New absorbed fractions and dose factors for these realistic phantoms are scheduled for release in early 2008. Figure 1 is an example image; additional details are available at www.doseinfo-radar.com/RADARphan.html.

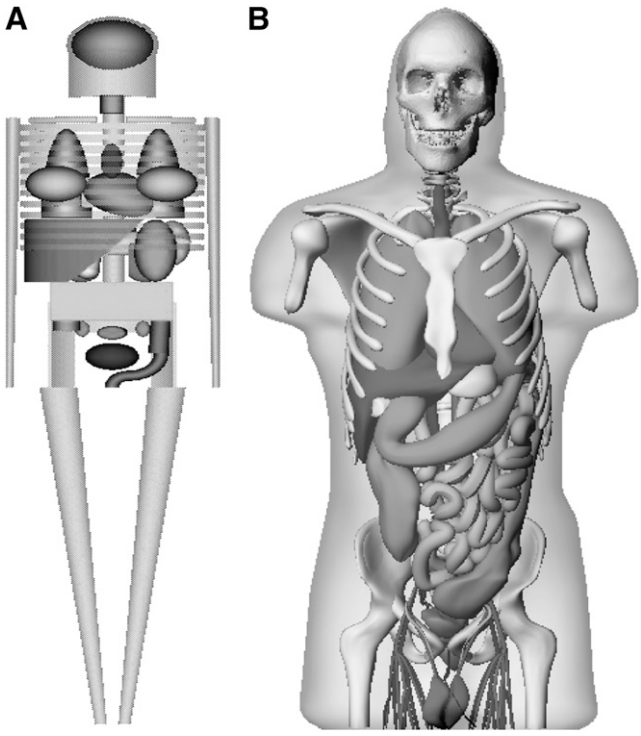

FIGURE 1. Stylized adult male model (A) and realistic human phantom (B) for internal dosimetry calculations.

- A page devoted to the issue of nuclear medicine patient release criteria, developed in 2007 (www.doseinfo-radar.com/RADAR-INT-NM-Release.html).
- Dose information for external sources of radiation, point sources, sources on the skin, and sources in air or on contaminated ground surfaces, including freely downloadable computer codes for skin dose calculations or external dose calculations using voxel phantoms (www.doseinfo-radar.com/RADAR-EXT.html).
- A dose and risk consent language calculator that provides standard dose estimates and suggested consent language, based on individual dose calculations, for dozens of standard nuclear medicine as well as general radiology exams, including 2006 data for CT exam doses (www.doseinfo-radar.com/RADARDoseRiskCalc.html).
- Tutorials on internal dose calculations, kinetic modeling, uses of phantoms, risk models, and other dosimetry topics.
- A compilation of dosimetry-related literature references from the Medical Internal Radiation Dose (MIRD), ICRP, and RADAR groups (www.doseinfo-radar.com/RADARLit.html).

Members of the RADAR group developed the OLINDA/EXM software, with its technical basis previously established in the literature (*1*). Vanderbilt University continues distribution of the code since receiving FDA approval through a 510(K) mechanism in 2004. An update of the code, including new decay data and realistic standardized

phantoms as described previously, is scheduled for 2008. The RADAR Web site is continually updated with new and useful information; any and all suggestions and requests for useful information that could be added to the site are always appreciated.

Other Electronic Resources: Many other Web sites, too numerous to describe in detail, with highly useful information can be found through the SNM links page (http://interactive.snm.org/index.cfm?PageID=944&RPID=10) or the University of Michigan health physics resource page (www.umich.edu/~radinfo/).

A number of interesting e-mail lists (NucMed, RadPharm, PET-mail, Medical Imaging [Archive-Comm-L], Radsafe, Dose-Net, and others) facilitate active information exchange by e-mail. Subscriptions are free, and digest versions (once-per-day summaries of all posts) are usually available. A large number of Yahoo groups (also too numerous to detail) with interests in this area of science use bulletin-board approaches to information exchange (http://hps.org/links.html).

New Dosimetry Literature

Patient-Individualized Dose Calculations: Standardized dose calculations for reference adults and children have been well documented by the RADAR group and implemented in standard software (*7*), so that standard dose calculations can be performed by almost anyone with a reasonable understanding of dosimetry fundamentals. In therapeutic uses of radiopharmaceuticals, however, individualized dose calculations should be performed to safely deliver the highest possible dose to malignant tissues in each patient. Lassmann and Hänscheid (*8*) led off the year with an invited perspective discussing this important issue. DeNardo (*9*) finished off the year, in the December issue of *Cancer Biotherapy and Radiopharmaceuticals,* with an insightful overview of the subject of personalized cancer management, part of which involves individualized dosimetry. Konijnenberg et al. (*10*) demonstrated the importance of the study of regional dose distributions and dose–volume histogram information for heterogeneous radioactivity distributions in the kidneys for low-energy ß-emitters and electron emitters (e.g., ^{111}In or ^{177}Lu) of interest to radionuclide therapy. The use of advanced computing methods was demonstrated for individualized dose calculations of ^{131}I- and ^{90}Y/^{111}In-labeled therapeutic agents (*11,12*). Sgouros (*13*) provided a perspective on the prospects for performing cellular-level dosimetry for individual patients, in the same *JNM* issue with a scientific article by Watchman et al. (*14*) on theoretical dose calculations for low electron- or α-emitters in bone regions. Hindorf et al. (*15*) presented a method for single-cell dosimetry in radioimmunotherapy (RIT) in patients with B-cell lymphoma.

Patient-specific adjustments can also be made to standardized dose estimates. Siegel and Stabin (*16*) outlined the correct method for mass scaling of standardized dose estimates to the red marrow. Cremonesi et al. (17) presented a well-developed methodology for patient-individualized adjustment of standardized dose calculations for several organs in high-dose RIT with ^{90}Y-ibritumomab tiuxetan using this approach. Following on the success of Shen et al. (*18*) in performing patient-individualized estimates of marrow mass for adjustment of standard doses, Pichardo et al. (*19*) presented a method for estimating spongiosa and marrow mass in individual subjects from CT data. An impressive paper was produced by Kobe et al. (*20*) evaluating the success of treatment of Graves disease in 571 subjects, using patient-individualized dose calculations. Relief from hyperthyroidism was achieved in 96% of patients who received >200 Gy, even for thyroid volumes >40 mL. Success rates with more traditional treatments (not using individually tailored dosimetry) are typically 60%−80% at best.

It remains an unfortunate situation that the nuclear medicine community in the United States has little interest in patient-individualized dose calculations for radiopharmaceutical therapy. Some in Europe, responding to the 1997 Euratom Directive (*21*), are appropriately improving patient care with these techniques, as clearly shown by Kobe et al. (*20*) and other researchers. Better rates of disease response and remission will ultimately be realized as this becomes more commonplace, but more widespread acceptance of dosimetry as a routine part of patient care is still needed, particularly in the United States. Although not involving a dosimetry regime, we recall that Press et al. (*22*) and Liu et al. (*23*) observed an overall response rate of 86% and complete response rate of 79% (with 39% of subjects surviving without recurrences for 5−10 y with no further therapies) using aggressive therapy with ^{131}I-labeled tositumomab in 29 patients with multiply relapsed B-cell lymphomas. Better patient outcomes can clearly be obtained with more aggressive approaches to therapy, and these approaches must include dosimetric analysis. Until this fact is more widely accepted and reimbursement schedules for approved therapies are increased, radionuclide therapy will continue to be suboptimal.

General Dosimetry Articles of Interest: An excellent practical guide to radiation safety considerations for individuals (including nursing infants) who are near patients who have received ^{90}Y-microsphere therapy was given by Gulec and Siegel (*24*). Many noteworthy papers on varied aspects of dosimetry from the 2nd International Symposium on Radionuclide Therapy and Radiopharmaceutical Dosimetry (October 2006, Athens, Greece) were presented as articles edited by Lassmann et al. (*25*) in *Cancer Biotherapy and Radiopharmaceuticals*.

Although not directly related to nuclear medicine practice (except as related to SPECT/CT and PET/CT), an article by Brenner and Hall (*26*) in the *New England Journal of Medicine* asserted that radiation doses delivered in CT examinations may be responsible for up to 2% of all cancer deaths in the United States. This is similar to their 2001 article suggesting that, based on the linear no-threshold model of radiation cancer induction, hundreds to thousands of cancer deaths would result from routine pediatric CT

examinations (*27*). In both cases, widespread alarm in the general public was addressed by responsible statements published by the American College of Radiology, SNM, and others. Reduction of unnecessary radiation exposure is always desirable; these articles, with follow-up exposure in the popular media, have had the unfortunate effect of also causing patients to avoid necessary medical examinations involving ionizing radiation.

Standard dose estimates were provided in 2007 for a number of new proposed agents, including the tachykinin NK1 antagonist radioligand ^{18}F-SPA-RQ (*28*), ^{11}C-PIB (*29*), ^{111}In-ChL6 bioprobes in a human breast cancer xenograft model (*30*), an^{18}F-labeled HSV-tk gene expression imaging agent (*31*), ^{18}F-FACBC (*32*), ^{11}C-PBR28 (a PET radioligand designed to image inflammation) (*33*), and ^{14}C-glycocholic acid and ^{14}C-xylose breath tests (*34*).

Radiobiology Aspects of Nuclear Medicine Studies

Many articles on radiobiology appeared in the literature in 2007, and a comprehensive review is not possible here. A few studies from *JNM* and related sources will be described as representative. Lundh et al. (*35*) studied the effects of ^{131}I irradiation on ^{125}I transport and cell proliferation at low absorbed doses in cultured porcine thyroid cells. They concluded that "radiation-induced thyroid stunning and cell cycle arrest may be independent phenomena." The issue of thyroid stunning by ^{131}I was also discussed in letters to the *JNM* editor by Hilditch et al. (*36*) and Sisson (*37*). However, Silberstein (*38*) noted in a group of 50 patients that when stunning did occur, its clinical impact was minimal.

Reske et al. (*39*) evaluated the effects of Auger emitter–delivered dose to the DNA of leukemia cells. Several authors from The Netherlands involved in the patient-specific dose evaluation described above also performed an interesting investigation into regional renal tubule damage after internal emitter therapy (*40*). Prideaux et al. (*41*) provided some preliminary investigations into the importance of the use of derived radiobiological quantities (i.e., the biologically effective dose rather than the cumulative absorbed dose) in the evaluation of patient-individualized dose calculations. A summary of the MIRD continuing education meeting on several current radiobiology issues was presented in the October issue of *JNM* in an article titled "Bystander and low–dose-rate effects: are these relevant to radionuclide therapy?" (*42*). Few issues could be resolved definitively at this time, but an excellent overview of the current literature was provided. Murray and McEwan (*43*) also provided an excellent literature overview of this subject earlier in the year.

Instrumentation and Analysis Innovations

Rapid instrumentation imaging technology advancement continued unabated in 2007. Technology developments come from many disciplines. Much comes from the high-energy physics laboratories and from the electronics and computing industries. Strong support for the development of homeland security applications has been a significant factor, especially given lagging support from the National Institutes of Health and Department of Energy. Rapid developments in molecular biology have led to the need for higher resolution, higher sensitivity imaging systems to track labeled molecules and labeled cells in small animal tests for both scientific and technique development before use in human subjects. Improved systems for external and internal imaging applications continue to enter clinical practice.

Advances in nuclear imaging technology proceed at a rapid pace, fueled by computing innovations (new low-cost components for faster acquisition, processing, transfer, and display) and novel materials with promise for improved image capture ($LaBr_3$ is high on this list, as well as the achievement of better yields of quality cadmium zinc telluride). A new generation of solid-state MR imaging–compatible photomultiplier tubes is being incorporated into PET/MR imaging systems, and these systems show promise for having clinical impact comparable with that experienced with PET/CT and SPECT/CT (*44*). Commercial PET/MR systems are now being evaluated in selected clinical centers. Fast scintillators are now used to advantage in time-of-flight PET, with improved imaging results in large patients. The use of adaptive imaging shows benefits in cardiac applications, where arrays of detectors focus on the known region of interest. Extensions of these ideas to allow for dynamic changes in aperture spacing and openings are under development.

Much discussion and elaboration of the technical issues and examples of tests using new technologies were presented at the fall 2007 IEEE Medical Imaging Conference in Hawaii, chaired by Ronald Jaszczak, PhD, and Benjamin Tsui, PhD. In addition to the many scientific talks and posters, the meeting featured short courses on physics and design of detectors for PET and SPECT, molecular biology for imaging scientists, and programming and medical applications using graphics hardware. The meeting included refresher courses on digital design with field-programmable gate arrays; GEANT 4, a simulation tool for multidisciplinary applications; and advances in X-ray CT, photon detectors and scintillators for medical imaging applications, and advances in analytic tomographic reconstruction.

Registration of external images of nuclear tracers with anatomic information from MR and/or CT provides information on pharmacokinetics in regions of interest and in the whole body. When ligands are coupled to fluorescent molecules, optical images can be obtained at greatly enhanced resolution (cellular dimensions). When taken to the operating room, external probes provide information that guides the surgeon in locating and removing residual tumor, the margins of which are not easily perceived without such probes. Henry Wagner, Jr., MD, highlighted a number of intraoperative probes used in these studies in his 2007 SNM Highlights Lecture (*45*).

Sensitivity and resolution are equally important for clinical imaging of patients, because dosimetry issues limit the amount of radioactivity that can be injected. During the 2007 SNM Annual Meeting, Townsend et al. demonstrated a 75% increase in SPECT sensitivity simply by the use of

larger imaging receptors. Patton et al., using the adaptive imaging approach of the DSPECT imaging system, demonstrated a 10-fold increase in effective cardiac imaging sensitivity.

Heinrich Schelbert, MD, PhD (*46*), provided an editorial introducing the new JNM feature "Focus on Molecular Imaging," pointing to the goal of visualizing and measuring fundamental biologic processes at the molecular, cellular, and subcellular levels. To do so requires high-specific-activity radiolabeled ligands targeted to site-specific receptors. Because many of the studies are performed in animals, this requires imaging systems that combine higher sensitivity and spatial resolution than needed for clinical studies. The development of multipinhole spherical collimators (USPECT) by the Utrecht group allows researchers to achieve very high resolution in small a priori defined regions. This has been demonstrated in brain studies using cocaine addiction models and is proposed for use in other areas of psychiatric research (*47,48*).

Collimator aperture designs for imaging static and dynamic processes are the focus of renewed interest. The use of novel pinhole and slit slat combinations is being explored for fast tomographic imaging. A vivid demonstration was provided by the Duke University group, which produced high-resolution gated cardiac images in mice (*49*). Other combinations of the slit slat approach are in the process of implementation by several commercial gamma camera companies for clinical imaging applications.

The Johns Hopkins University group (*50*) is exploring the use of rotating composite slant-hole collimators for reconstructing longitudinal tomographic images of the heart using the principle demonstrated earlier by Muehllehner.

It is often noted that very little is truly new and that much of what we do simply takes advantage of new materials or improved algorithms. That is true in the technology area, but the molecular revolution is actually changing things. We now know more about targets of interest. The last 2007 issue of *JNM* contained an article from China in which the authors used antisense technology to image a potential proliferation marker in tumor cells (*51*). They imaged a substantial increase in the localization of a ^{99m}Tc-labeled antisense probe of messenger RNA as a marker of the activity of a human telomerase gene in a nude mouse bearing an MCF-7 mammary tumor xenograft. We have adequate imaging tools now, and among the remaining important tasks is the need to identify and successfully target them. In that way, investigators (and patients) will be able to characterize and then successfully treat disease in patient- and disease-specific ways. The fact that work is going on all over the world is encouraging, because the challenges are many and will require much time, effort, and free exchange of information.

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Molecular Imaging: The State of the Science

We may not yet have reached a watershed, but 2007 was a significant year for molecular imaging. The concept of molecular imaging is percolating throughout the medical imaging community. We are seeing recognition of nuclear medicine as the original molecular imaging modality as well as a groundswell of interest in the possibilities of targeted ultrasound contrast media and hyperpolarized ^{13}C spectroscopy, along with cutting-edge approaches, such as fluorescent and bioluminescent imaging, optical imaging with quantum dots, and nanoparticle probes, that are still in development.

PET has become the most widely used clinical molecular imaging modality while also becoming increasingly useful as a research tool in drug discovery, psychiatric research, and clinical trial monitoring. Clinical use could expand exponentially with approval of some of the many PET tracers under development. PET offers the possibility of definitively diagnosing Alzheimer's disease in its earliest stages by directly imaging amyloid plaque (with ^{11}C-PIB and ^{18}F-FDDNP). Other research centers are looking at the chemical processes of addiction in the living brain using tracers such as ^{18}F-DOPA and ^{11}C-raclopride. SPECT and new single-photon probes, such as iodinated amyloid plaque agents, are emerging as tools for molecular imaging.

Nonnuclear molecular imaging continues to break new ground in the research lab. Multimodality imaging systems are in use in small animal imaging. Recent advances include simultaneous acquisition of MR spectroscopy and PET data. Optical tomography shows promise in bringing bioluminescent imaging into clinical practice—something that was considered impossible in the recent past. Tracers for tracking stem cells and lymphocytes in vivo are bringing the day closer when "personalized medicine" will be not only possible but accepted as standard practice. Imagine a pharmacologic