THE NATIONAL ACADEMIES

REPORT IN BRIEF

Advancing Nuclear Medicine Through Innovation

The variety of technologies and procedures that comprise nuclear medicine are now a routine and vital part of diagnosing cancers, cardiovascular disease, and certain neurological disorders, as well as treating some cancers. There are a number of exciting emerging opportunities in nuclear medicine, including the ability to understand addictions and depression, to better assess the effectiveness of drugs, and to individualize cancer therapies. However, to realize these promises will require continued federal support for nuclear medicine research and parallel efforts to address such issues as the shortage of clinical and research personnel, an inadequate supply of radionuclides for research, and cumbersome regulatory requirements.

Nuclear medicine—which uses radioactive chemical elements called radionuclides to diagnose or treat diseases—has grown tremendously as a result of research investments over the past 50 years. It now plays an essential role in medical specialties from cardiology to oncology to neurology and psychiatry. Nearly 20 million nuclear medicine procedures are carried out each year in the United States alone.

Nuclear medicine encompasses a variety of imaging devices and therapeutics that use radionuclides. Nuclear imaging devices, such as PET and SPECT scans, work by tracking radioactive chemicals that are swallowed, inhaled, or injected into the body, where they accumulate in the organ or tissue of interest and reveal biochemical changes. Such imaging devices enable physicians to diagnose diseases including cancer, cardiovascular disease, and neurological disorders (e.g., Alzheimer's and Parkinson's diseases) in their initial stages. These techniques allow doctors to obtain medical information that would otherwise require more costly and invasive procedures like surgery or biopsy. Nuclear imaging devices are also valuable for conducting research on the biology of human diseases and for developing and testing new treatment approaches.

PET/CT scan. Photo courtesy of the Department of Radiology, MSKCC.

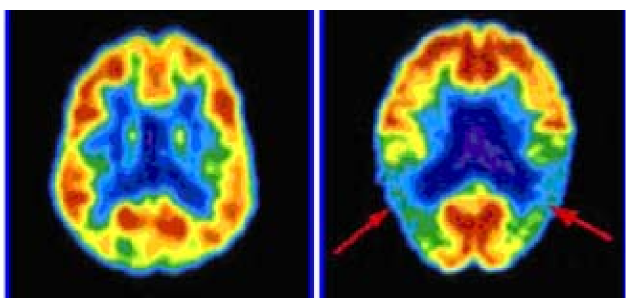
Highly targeted radionuclides can also be used to deliver lethal doses of radiation to tumor cells. This approach has enabled physicians to treat thyroid cancer and lymphoma, and could become an important tool in the arsenal to fight other diseases.

Although nuclear medicine has already made enormous contributions to biomedical research and disease management, its promise is only beginning to be realized in such areas as drug development, preventive health care, and personalized medicine. However, aging facilities and equipment, a shortage of trained nuclear medicine scientists, and loss of federal research support are jeopardizing the advancement of the field. At the request of the Department of Energy (DOE) and the National Institutes of Health (NIH), the National Research Council assembled a committee to review the current state of the science in nuclear medicine, identify future opportunities in nuclear medicine research, and recommend ways to reduce impediments to advancing the field.

Current Applications of Nuclear Medicine

Extensive research and technological advances over the past 50 years have resulted in an array of nuclear medicine applications that have improved patient care considerably. Nuclear medicine has grown to a $1.7 billion industry as nuclear medicine devices and therapies have become essential to a variety of medical specialties. Nuclear medicine procedures are now routinely used to non-invasively diagnose and monitor diseases and offer an effective approach to delivering targeted treatments for some cancers and endocrine disorders. Current clinical applications of nuclear medicine include the ability to:

- diagnose diseases such as cancer, neurological disorders (e.g., Alzheimer's and Parkinson's diseases), and cardiovascular disease in their initial stages through use of imaging devices including PET/CT (positron emission tomography/computed tomography) and SPECT/CT (single photon emission computed tomography/computed tomography);



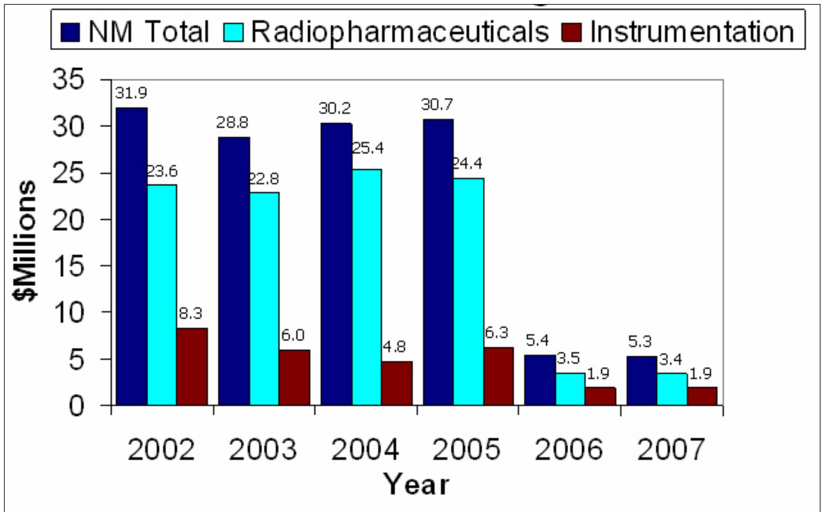
PET scan of a normal volunteer (left) and a patient with Alzheimer's disease (right). Nuclear imaging devices help doctors diagnose such diseases in their initial stages. SOURCE: Daniel Silverman, UCLA.

- provide molecularly targeted treatment of cancer, and certain endocrine disorders (including thyroid disease and neuroendocrine tumors);
- non-invasively assess a patient's response to therapies, reducing the patient's exposure to the toxicity of ineffective treatments, and allowing alternative treatments to be started earlier.

Emerging Opportunities and Future Applications

Advances are on the horizon in nuclear medicine that could substantially accelerate, simplify, and reduce the cost of delivering and improving health care. Collaboration among academic institutions, industry, and federal agencies could lead to a plethora of new applications of nuclear technologies to improve disease diagnosis, treatment approaches, drug development, and basic research. Emerging opportunities in nuclear medicine include the ability to:

- facilitate the practical implementation of personalized medicine, an approach in which physicians detect and treat diseases based on a patient's genetic profile. Nuclear imaging devices, for example, could aid the growth of personalized medicine by providing a way to track biochemical changes in the body, illuminating normal and pathological processes and the mechanisms by which individual diseases and disease subtypes arise.
- individualize treatment for cancer patients by employing targeted radionuclide therapeutics, which deliver doses of radiation using targeting vehicles—molecules that seek out certain cells, such as those in a malignant tumor. Investments in nuclear medicine could further develop techniques to tailor the properties of radionuclides and targeting vehicles to treat specific patients or types of cancer.
- understand the relationship between brain chemistry and behavior (such as addictions, eating disorders, depression) by using nuclear imaging devices to view biochemical changes in the brain. Such applications of nuclear imaging devices would enable precise, non-invasive assessment of a patient's brain functions.
- assess the efficacy of new drugs and other forms of treatments using nuclear imaging devices to observe the effects of drugs in the body, speeding the introduction of new drugs into clinical practice. It has been estimated that the use of PET during Phase I clinical studies could save upward of $235 million in research and drug development costs for each successful drug.
- understand the mechanisms by which new drugs are absorbed and take effect in the body by using radionuclides to visually track the uptake of drugs. Such an application would enhance the ability to find optimal dosage regimens for new drugs.
- develop new automated screening technologies that would accelerate and lower the cost of discovering and testing new imaging devices and drugs.



Funding for nuclear medicine research, 2002–2007 from the U.S. Department of Energy's Office of Biological & Environmental Research. SOURCE: Department of Energy.

- develop higher resolution, more sensitive imaging instruments to detect and quantify disease faster and more accurately. It is likely that nuclear medicine procedures can be developed that pinpoint the location of diseases before they can be clinically diagnosed, or offer insights about specific disease subtypes to enable doctors to target treatments to a patient's individual situation.
- further develop and exploit hybrid imaging instruments, such as PET/MRI (positron emission tomography/magnetic resonance imaging), to improve disease diagnosis and treatment. Theses hybrid imaging devices merge anatomical and functional information together to help pinpoint abnormal activity in specific organs or regions of the body.
- improve the ability to produce radionuclides to lower the cost and increase the availability of nuclear medicine treatments. Increasing access to radionuclides, miniaturizing the chemical processes to produce multiple radiopharmaceuticals for pre-clinical testing, and increasing the speed and resolution of nuclear imaging devices would enable nuclear medicine research and applications to advance more rapidly.

Challenges to Advancing Nuclear Medicine

The report identifies several specific challenges facing nuclear medicine, including the loss of federal support, a shortage of trained scientists, inadequate supply of radionuclides available for research, cumbersome regulatory requirements, and challenges associated with technology development and transfer. Addressing these challenges will help to achieve the full potential of the field.

Loss of Federal Commitment

Historically, the bulk of the support for nuclear medicine research in the United States has come from the DOE, which focuses on supporting research and development of next-generation technology and radiopharmaceuticals, and the NIH, which focuses on applying nuclear technologies to medical applications. However, the report concludes that nuclear medicine research is not currently sufficiently supported, particularly in the physical sciences. Funding for nuclear medicine research has been dramatically reduced in recent years: DOE funding for nuclear medicine research dropped 85 percent from 2005 to 2006 and remained low in 2007 (see figure above). There is currently no specific programmatic long-term commitment by any federal agency for maintaining high-technology infrastructure or centers.

Recommendation: Federal commitment to nuclear medicine research should be enhanced. To this end, DOE and NIH should coordinate a national nuclear medicine research program.

Shortage of Trained Nuclear Medicine Scientists

There is a critical shortage of clinical and research personnel in all nuclear medicine disciplines. Training, particularly of radiopharmaceutical chemists, has not kept up with current demands at universities, medical institutions, and industry, a problem that is exacerbated by a shortage of university faculty in nuclear chemistry and radiochemistry. There is a pressing need for additional training programs with the proper infrastructure to support interdisciplinary science, more doctoral students, and post-doctoral fellowship opportunities.

Recommendation: Train nuclear medicine scientists. NIH and DOE, in conjunction with specialty societies, should consider convening expert panels to identify the most critical national needs for training and determine how best to develop appropriate curricula to train the next generation of scientists and provide for their support.

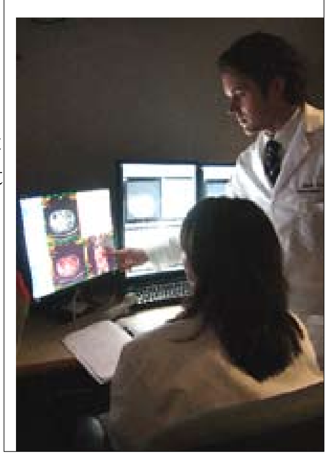


Photo courtesy of Dept. of Radiology, MSKCC.

Inadequate Domestic Supply of Medical Radionuclides for Research

There is no domestic source for most of the medical radionuclides used in day-to-day nuclear medicine practice. The lack of a dedicated domestic accelerator and reactor facilities for year-round uninterrupted production of medical radionuclides for research is discouraging the development and evaluation of new radiopharmaceuticals.

Recommendation: Improve domestic medical radionuclide production. To alleviate the shortage of accelerator- and nuclear reactor-produced medical radionuclides available for research, a dedicated accelerator and an appropriate upgrade to an existing research nuclear reactor should be considered.

Cumbersome Regulatory Requirements

The report identifies regulatory requirements that impede the efficiency with which new radiopharmaceuticals are brought into clinical feasibility studies. Complex U.S. Food and Drug Administration (FDA) toxicologic and other regulatory requirements, combined with a lack of guidelines on manufacturing nuclear imaging devices and radiopharmaceuticals, make translating nuclear medicine research into practical applications unnecessarily difficult. Additionally, there is a lack of consensus for standardized image acquisition in nuclear medicine imaging procedures, making it challenging to harmonize protocols for multi-institutional clinical trials.

Recommendation: Regulatory requirements should be clarified and simplified. FDA should provide clear guidelines specifically in the areas of toxicology (for evaluating when it is safe to conduct clinical trials on new radiopharmaceuticals) and good manufacturing practices. Members of the imaging community should work with federal agencies to develop standardized imaging protocols.

Need for Technology Development and Transfer

Transfer of technological discoveries from the laboratory to the clinic is critical for advancing nuclear medicine.

Improvements in detector technology, image reconstruction algorithms, and advanced data processing techniques, as well as development of lower cost radionuclide production technologies, are among the research areas that should be explored for effective translation into the clinic.

Recommendation: Encourage interdisciplinary collaboration. DOE's Office of Biological & Environmental Research should continue to facilitate collaborations between basic chemistry, physics, computer science, and imaging laboratories, as well as multi-disciplinary centers focused on nuclear medicine technology development and application.

Committee on State of the Science of Nuclear Medicine: Hedvig Hricak (*Chair*), Memorial Sloan-Kettering Cancer Center, New York; **S. James Adelstein**, Harvard Medical School, Boston, Massachusetts; **Peter S. Conti**, University of Southern California, Los Angeles; **Joanna Fowler**, Brookhaven National Laboratory, Upton, New York; **Joe Gray**, Lawrence Berkeley National Laboratory, California; **Lin-Wen Hu**, Massachusetts Institute of Technology, Cambridge; **Joel Karp**, University of Pennsylvania, Philadelphia; **Thomas Lewellen**, University of Washington, Seattle; **Roger Macklis**, Cleveland Clinic Foundation, Ohio; **C. Douglas Maynard**, Wake Forest University School of Medicine, Winston-Salem, North Carolina; **Thomas J. Ruth**, Tri-University Meson Facility, Vancouver, Canada; **Heinrich Schelbert**, University of California, Los Angeles; **Gustav Von Schulthess**, University Hospital of Zurich, Switzerland; **Michael R. Zalutsky**, Duke University, Durham, North Carolina; **Naoko Ishibe** *(Study Director)*, National Research Council.

This report brief was prepared by the National Research Council based on the committee's report. For more information, contact the Nuclear and Radiation Studies Board (202) 334-3066 or visit http://nationalacademies.org/nrsb. Copies of *Advancing Nuclear Medicine Through Innovation* are available from the National Academies Press, 500 Fifth Street, NW, Washington, D.C. 20001; (800) 624-6242; www.nap.edu.