

Written Testimony for the Record
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Subcommittee on Labor, Health and Human Services, Education and Related Agencies
Senate Appropriations Committee
In Support of FY2023 Appropriations for the National Institutes of Health

Chair Murray, Ranking Member Blunt, and members of the Subcommittee, I am Richard L. Wahl, MD, President of the Society of Nuclear Medicine and Molecular Imaging and the Elizabeth E. Mallinckrodt Professor and head of radiology at Washington University School of Medicine in St. Louis, MO.

The Society of Nuclear Medicine and Molecular Imaging (SNMMI) is a nonprofit scientific and professional organization that promotes the science, technology, and practical application of nuclear medicine and molecular imaging. Research in this field has led to breakthroughs for diagnosing and treating patients with deadly conditions such as cancer, heart disease, and Alzheimer's disease. SNMMI strives to be a leader in unifying, advancing, and optimizing molecular imaging, with the ultimate goal of improving human health through noninvasive procedures and therapeutic approaches utilizing internally-administered radiopharmaceuticals. With over 15,000 members worldwide, SNMMI represents nuclear medicine and molecular imaging professionals, including physicians, physicists, radiochemists, pharmacists, and technologists, all of whom are committed to the advancement of the field. It is my pleasure to submit this testimony on behalf of SNMMI.

We strongly support at least \$49.048 billion for the National Institutes of Health's base appropriation. This figure represents an increase of \$3.5 billion over FY2022 plus the release of the 21st Century Cures funds. SNMMI also supports a proportional increase to the National Institute of Biomedical Imaging and Bioengineering (NIBIB), resulting in at least \$458.5 million for FY2023—a \$33.6 million increase over the FY2022 enacted level. Further, should the Advanced Research Projects Agency for Health (ARPA-H) or pandemic preparedness efforts progress, funding should be designated separately from NIH's base and should supplement, not supplant, investment in basic research. Through consistent, strong funding for NIH and our national research infrastructure we can continue to make advancements that will improve the lives of patients with a wide spectrum of diseases and disorders. SNMMI is grateful for the Subcommittee's past support of NIH and encourages the Subcommittee to continue advancing discovery and innovation in nuclear medicine and molecular imaging.

Nuclear medicine, in particular, is undergoing a renaissance as a precision medicine specialty, with new radiopharmaceuticals, radiopharmaceutical therapies, and instrumentation to elucidate biology and benefit patients. Federal research funding allows our members, partners, and stakeholders to improve imaging tools and therapies, which, in turn, broadens the resources available to address many challenging conditions. As a physician/clinician-scientist, my work has been greatly impacted by NIH funding, resulting in 18 patents, over 450 peer-reviewed scientific manuscripts, and several FDA-approved theranostic (therapy + diagnostics) drugs and devices. I use state-of-the-art technologies like positron emission tomography (PET) combined with computer tomography (CT) and other advanced imaging modalities to improve the diagnosis and treatment of cancer types, including prostate, breast, neuroendocrine, and pancreatic, while also researching rare and orphan diseases.

Nuclear Medicine and Molecular Imaging: Precise and Personalized Medicine

Nuclear medicine and molecular imaging procedures are used in a wide array of diseases and disorders, including cancer, Alzheimer's and Parkinson's Diseases, and cardiac disease, among others¹. Congress's support of NIH has helped to advance the science and the researchers who make these discoveries. NIH support is often the foundation of the newest technologies that go on to help patients. This subcommittee's continued support of the NIH, especially the National Cancer Institute (NCI), NIBIB, National Institute on Aging (NIA), National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Mental Health (NIMH), and National Heart, Lung, and Blood Institute (NHLBI), will help scientists address many unmet medical needs. Some of the advances from the nuclear medicine and molecular imaging community in detecting and treating cancer and selecting the right patient for the right therapy are detailed below.

Improved Imaging and Therapy for Cancer using Molecularly Targeted Radiopharmaceuticals

Major nuclear medicine advances in the fight against prostate cancer have appeared in the news. In the past year, three cancer-targeted radioactive imaging agents (*Pylarify*[®], *Illuccix*[®], and *Locametz*[®]) received FDA approval and have entered commercial distribution for greatly improved detection of prostate cancer. These radiotracers seek out prostate cancer cells throughout the body, allowing the active foci of cancer to be seen on a PET/CT scan. This class of agents targeting prostate specific membrane antigen or PSMA, can identify cancer months or years ahead of standard imaging such as CT or MRI, allowing patients to receive appropriate treatment sooner when it can be more effective. The FDA has also recently approved a companion targeted radiotherapeutic, *Pluvicto*TM (¹⁷⁷Lu-PSMA-617), for men with late-stage castrate-resistant prostate cancer that had spread. The PSMA part of the drug makes it act like a guided missile or geotag to seek out prostate cancer cells. The attached lutetium-177 radioisotope destroys the cancer cells while leaving healthy tissue intact. Combined, the radiopharmaceutical therapy is in effect a “smart bomb” to selectively destroy foci of prostate cancer. The men treated with ¹⁷⁷Lu-PSMA had a four-month longer median survival than men receiving best standard of care alone. These results prompted FDA to label the treatment as a breakthrough therapy which accelerated its approval time and allow it to reach patients in need faster. None of this would have been possible without the early support of 13 NIH grants.²

Imaging and therapy molecule pairs, such as those using PSMA molecules as targeting agents, are often referred to as theranostics, a rapidly developing area of personalized medicine. If the diagnostic version of the molecule can find the cancer with a PET scan, then the same molecule with a therapeutic isotope can be used to attack the cancer. Further advancements in the theranostics space are anticipated. This treatment principle is being applied to cancer types for which we have no or few treatment options, such as pancreatic cancer. An exciting new class of theranostic molecules are those targeting fibroblast-activation-protein (FAP).³ This protein (FAP) is overexpressed in many cancer types including breast, pancreas, lung, kidney, and ovarian. The FAP molecule can be labeled as a diagnostic agent and then as a therapy. This treatment paradigm gives doctors a new tool in the fight against cancer. The NCI is currently supporting a phase 1 clinical trial ([NCT04457258](https://clinicaltrials.gov/ct2/show/study/NCT04457258)) on this promising new agent.

None of these advances would be possible without the support of radiochemistry and isotope production research. The next generation of radioisotopes, alpha emitting therapeutic isotopes, which have much greater cancer killing power per radioactive decay, are in clinical trials and are expected to provide better patient outcomes. Support of that research is critical.

Quantitative Molecular Imaging

A PET scanner is often thought of as an imaging tool; however, it is inherently a highly specific measuring tool. Recent advances in PET technology such as PET/MRI and total-body PET, where the whole body can be imaged at once, have opened new research possibilities.⁴ To realize the full potential of these advances, quantitative analysis will be required to appreciate the sensitivity of the scanner and the tracers it measures. The NCI has supported the harmonization of PET/CT scanners through numerous grants including NIH R01CA169072, and for the last decade, the NCI, through their Cancer Imaging Program has developed and supported a consortium of academic sites called the Quantitative Imaging Network performing and advancing quantitative imaging mostly in support of clinical trials.

Imaging of the brain in Alzheimer Disease

About a year ago, the FDA approved an innovative antibody therapy for Alzheimer's disease which removes amyloid plaque from the brain. At present, PET scanning using radiotracers that target the amyloid protein or the abnormal tau protein seen in dementias of the Alzheimer type have been key to identifying patients who may be suitable candidates for such clinical trials and these emerging therapies. The support of the NIH was key to developing these brain imaging agents and continued NIH support is essential to allow PET to probe the earliest changes of dementia and to monitor the effects of emerging innovative therapies. There are now several FDA approved PET imaging agents to identify patients with amyloid or tau deposition, helping identify how to best target limited resources to patient groups most likely to benefit from such therapies. The ability to select patients most likely to respond to therapy is expected to save tens of billions in healthcare dollars per year.

Immuno-oncology Imaging

In 1980, the NCI added \$13.5M to their budget for new Biological Response Modifiers, this triggered a search for agents able to modify a body's response to tumor cells.⁵ That investment spawned the multi-billion-dollar drug class of immune checkpoint inhibitors (ICI), starting with the approval of Yervoy® (ipilimumab) in 2011. In the US in 2020, a year severely impacted by the COVID-19 pandemic, sales of the top three ICI topped \$17B. ICIs are generally considered to be safe and effective treatment options for numerous cancer types including lung cancers and melanoma, and some people like former US President Jimmy Carter had a remarkable response to ICI therapy. However, they do not work in all patients; indeed over half of patients treated with these agents die of their disease. New radiotracers are in development to image the immune system in conjunction with a PET or SPECT camera. Clinical trials with these tools have demonstrated the ability to predict response to ICI therapy after just one cycle of therapy. Future studies will aim to pre-select, with imaging, patients who are likely to respond to immune checkpoint inhibitors thus enabling effective therapy earlier and eliminating side effects of futile treatments. The ability to select patients likely to respond to therapy will also save billions in healthcare dollars.

Data Science and Workforce

The field of nuclear medicine and molecular imaging is rapidly expanding with new diagnostic imaging tracers, radiopharmaceutical therapies (RPT), and technologies. With new diagnostic tracers comes a need to properly interpret the innovative scans. Artificial intelligence (AI) algorithms can assist with the tedious components of image interpretation and even help with quality report generation. Development of well-credentialed registries of studies to train and validate such AI algorithms, reflecting diverse sets of patients will help advance this field. Radiopharmaceuticals therapies (RPTs), like other oncology therapies, are often studied in and approved for patients with late-stage disease, for example, after all other treatments have failed. To harness the full potential of RPTs, use earlier in the disease course may be advisable. Image and clinical data registries are needed to capture post-approval information on the use of RPTs and the patient outcomes to further guide their use. Recent imaging

and therapy FDA approvals in prostate cancer and Alzheimer's disease, two highly prevalent conditions, require that the highly specialized field of nuclear medicine and molecular imaging train a cadre of qualified individuals to diagnose and treat these patients. It is critical for the NIH to fund and expand training grants so that our brightest scientists have the skills to develop a sustainable career pathway. Funding for AI technologies and registries will improve patient care and outcomes.

Summary and Conclusion

Robust NIH funding is crucial to advancing our efforts to detect and treat serious medical conditions. NIH investments help to sustain both our local and national research institutions across every state in the nation. China is advancing rapidly in the high technology medical space notably in AI. Funding NIH's base program with at least \$49.048 billion will help researchers, scientist and physicians retain its competitive edge.

Thank you for your strong, continued support of NIH, NCI, NIMH, NIBIB and all the Institutes and Centers working to advance molecular imaging and radiopharmaceutical therapies to improve the lives of patients worldwide. On behalf of the Society of Nuclear Medicine and Molecular Imaging, I urge you to continue your strong support of our nation's research and innovation enterprise.

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