Journal of Nuclear Medicine, published on May 8, 2020 as doi:10.2967/jnumed.120.249219

Time for a Next-Generation Nuclear Medicine Gamma Camera?

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Hal Anger invented the gamma camera in 1957, and it is fair to say that the basic geometry and components of his camera design have remained substantially the same, while its use in general clinical applications has been optimized for imaging 140-keV gamma rays. The past 60 years have seen some improvements in NaI scintillators, readout electronics, collimators, reconstruction algorithms, and image analysis. During a short period in the late 1990s and early 2000s, opposing Anger cameras were used for clinically acquiring positron-emitting isotopes, and some camera components were reengineered for imaging 511-keV coincident photons. Not surprisingly, dedicated PET cameras proved to be the better choice for imaging PET radiotracers.

One clinical application, however, generated substantial camera variations. The highly successful use of cardiac imaging in the United States has spurred interesting new camera designs and novel radiopharmaceuticals. Nuclear cardiology currently represents more than 50% of all U.S. nuclear medicine scans. Dedicated cardiac cameras have implemented 7-, 9-, and 19-pinhole collimators, early use of new detectors (CsI and CZT), L-shaped camera configurations, and chair-based imaging. Given this important and well-recognized clinical application, camera designs morphed into a variety of geometries, detector materials, and associated reconstruction methods. Whole-body (bone scans) and brain-imaging cameras have evolved over these same years, but current whole-body scanners employ a standard Anger camera translated along the patient bed. Dedicated brain cameras have not yet achieved broad acceptance and, perhaps, are awaiting new breakthroughs in theranostic applications for brain imaging.

Recent developments in unsealed source therapies using electron- and α-emitting radiopharmaceuticals would benefit from improvements in patient-specific dosimetry estimates. ^{177}Lu, ^{90}Y, and ^{223}Ra are the most common isotopes currently used to deliver high doses to the targeted cancer and to spare healthy tissue. Because of the high radiation doses delivered locally by these radiotherapeutic agents, it is important to know the patient-specific uptake distribution of these ligands. Analogs of these ligands have been developed to assess uptakes. By imaging the analog (labeled with ^{68}Ga, for example), one assumes that the analog has the same pharmacodynamics and pharmacokinetics as the ^{90}Y- or ^{177}Lu-labeled therapy ligand. Such an assumption becomes complicated with ^{223}Ra, where such a process would be ignoring the doses to healthy tissues delivered by ^{223}Ra daughters.

Imaging of these radiotherapy ligands has been investigated. Two of the 6 photopeaks (113 and 208 keV) of ^{177}Lu were imaged with additional energy windows set to subtract scatter from higher energy emissions (*1*). An array of bremsstrahlung emissions, together with internal pair-production annihilation radiation, was used to produce ^{90}Y images (*2*). Images of ^{223}Ra (and its daughter ^{219}Rn) were acquired using 3 photopeaks (85, 154, and 270 keV) with 3 additional windows to deal with scattered events (*3*). Imaging protocols become more complicated for other α emitters, including ^{225}Ac, ^{211}At, ^{212}Pb, and others yet to be considered for therapy. These isotopes pose a challenge to nuclear medicine camera systems because the radiations lie outside current clinical imaging protocols. New camera designs could lead to improved image quantitation.

Is it time to reconsider the instrumentation we use for theranostic methods for these α-emitting unsealed sources? If nuclear cardiology could develop an array of specialized camera designs and acquisition methods to specifically image the heart, can we consider new instrumentation and image analysis methods that would give us

improved insights into targeted cancer therapy? The next phases of therapy outcomes that use these new ligands will speak to this question. A dedicated therapy camera could help to maximize dose to the cancer and minimize dose to healthy tissues. It seems axiomatic that by improving methods for imaging these new ligands, we would improve the success of the clinical therapy outcomes. This tandem step forward appears reasonable.

To which ideas can we turn for meeting this imaging challenge? The gamma emissions of these new therapy isotopes are often low yield. Can previous work on high-sensitivity coded apertures or Compton cameras be reinvestigated for some of the higher energy emissions? Can gas electron multiplication detectors be used to measure gamma rays and their incident angles without the use of collimators (*4,5*)? New detector systems have been and are being developed by PET instrumentation investigators, with some promising coincidence timing approaching 1 picosecond. Can any of these detectors be reapplied for single-photon imaging? Because some of the α emitters (despite the low yield of individual gamma emissions) emit many 10s of gammas at various energies (e.g., ^{225}Ac), could very high-energy resolution detectors be used to acquire the various gammas by picking out these photopeaks (and rejecting most other scattered photons) to assemble an image of unscattered multienergy gammas? Can recent advances in deep learning play an important role in imaging and estimating patient dose?

These and other questions will be considered and discussed at a National Institute of Biomedical Imaging and Bioengineering (NIBIB) workshop on "Engineering New Instrumentation for Imaging Unsealed Source Radiotherapy Agents," to be held August 17 and 18 at the Natcher Center on the main National Institutes of Health (NIH) campus in Bethesda, MD. We believe that such discussions are timely for moving hand-in-hand into the testing and use of α-emitting therapy trials.

The mission of NIH's NIBIB is to improve health by leading the development and accelerating the application of biomedical technologies. Among the many technologies supported, NIBIB researchers believe the challenge of considering cameras that would deliver improved dosimetry measurements for optimizing the outcome of α-emitting radiotherapy ligands is one that merits a serious look. For more information on the workshop, see https://www.imagingtherapy.nibib.nih.gov/.

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