Recommendations

Participants in the Summit Clinical Issues session made several recommendations for action. Among these were recommendations to:

- Promote utilization of new radiopharmaceuticals through clearly defining critical areas of development, validating outcomes and efficiency, and enlisting patient advocacy.
- Reach out to the larger community that will be affected by the benefits of molecular imaging, including efforts to improve referring physician and clinician education, incorporate molecular imaging into clinical management algorithms, encourage patient advocacy groups, interact with clinical trial networks in oncology (perhaps by securing a seat at the decision-making tables), and provide specific educational information to other medical specialties, especially psychiatry and cardiology.
- Continue the SNM–industry coalition, including enhanced efforts at communication with the U.S. Food and Drug Administration (FDA) and other federal bodies. Participants suggested that the FDA might be invited to participate in coalition meetings.
- Encourage the formation of a national taskforce on molecular imaging by the National Academy of Sciences.
- Encourage the creation of multicenter clinical trials to evaluate response in targeted therapies, quantification of perfusion in cardiac studies, cost/benefit effectiveness of PET and other techniques, and explore a range of oncology, CNS, and other benefits.
- Ask the SNM Brain Imaging Council to investigate the question of the perceived "disconnect" between the availability of novel CNS probes and clinical applications.
- Encourage funding and regulatory bodies, as well as other disciplines, to accept changes in patient management resulting from imaging findings as review benchmarks.
- Encourage clinical trials for validation of dynamic PET for determination of absolute blood flow.
- Encourage standardization of acquisition and processing in all areas of clinical molecular imaging.

Summary Statement

Molecular imaging is already benefiting clinical care, but if its myriad potential benefits are to be realized in routine practice, the community must work together to define, demonstrate, and promote the value of molecular imaging for improvement in health care and lead the transition to personalized medicine. In the near term, this effort should involve the creation of a range of multicenter clinical trials to demonstrate benefits in outcomes and management change, enhanced cooperative efforts to streamline and make practical the development of new radiopharmaceuticals, and the creation of durable outreach channels to educate and advance in partnership with the public, referring physicians, specialists in other disciplines, and federal and regulatory bodies.

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PRESENTATIONS

Molecular Imaging Moves to the Clinic

A major advantage of nuclear imaging methodologies is the ability to rapidly translate from bench to bedside. As a basis for molecular imaging, radiotracer imaging methodologies are slowly being built up to image the following aspects of cancer biology:

(1) Cancer phenotype, especially the differences between malignant cells and their normal counterparts. Probes for altered metabolism, protein expression, and molecules associated with distinctive behavior, such as the tendency to metastasize, are being investigated (e.g., accelerated amino acid metabolism, such as ^{18}F-aminocyclobutane carboxylic acid; ^{11}C methionine [*1*] in castrate-resistant prostate cancer; ^{18}F-fluorodihydrotestosterone in prostate cancer [*2,3*]; and characterizing specific antigen expression with G250 in clear cell renal cancer).
(2) Tumor microenvironment. Hypoxia, neovasculature, alterations in the stroma of cancer cells, and the interaction of cells within the cancer mass (e.g., ^{18}F-misonidazole for hypoxia) are all under investigation.
(3) Imaging-guided targeted molecular radiotherapy. Targeted radiotherapy is a major advance in nuclear medicine that is being refined by advances in molecular imaging and used to measure dosimetry of tumor and normal tissues (e.g., ^{124}I-NaI for imaging of thyroid cancer [*4*]).

Currently, preclinical advances are occurring in areas such as:

(1) Cancer pharmacology, including drug-based tracers, multidrug resistance, pharmacokinetics and pharmacodynamics of important cancer drugs (e.g., targeting of Her 2 Fab'2 ^{68}Ga [*5,6*] and ^{124}I-HSP90 inhibitors to human tumors).
(2) Tumor immunology, including the interaction of antitumor antibodies, immune cells, and cancer cells within the tumor mass (e.g., targeting of immune cells in Epstein–Barr virus lymphoma [*7*]).
(3) Gene expression imaging, especially the ability to image key genes important to the altered phenotype of cancer, cancer pharmacology, and the interaction of cancer cells with the tumor microenvironment (*8*).

Topical Questions and Areas of Concern

In the laboratory, molecular imaging is multimodal, involving optical (fluorescent, bioluminescent), nuclear (PET and SPECT), and magnetic resonance imaging and spectroscopy. What are the advantages and disadvantages of nuclear imaging in terms of clinical applications, and what other types of imaging will be seen as "molecular?" What are some examples of nonnuclear molecular imaging?

Among the imaging disciplines, nuclear medicine has placed the greatest emphasis on physiology and biochemistry as part of the training process. It is natural to think in tracer terms, and this type of thought pattern lends itself well to applications of "molecular imaging." Another advantage is that nuclear imaging methods and review tracers scale up extremely well from bench to bedside. Imaging studies performed on intact animals with a microPET can be scaled up with virtually complete accuracy to human-sized animals. This is another major advantage of the review tracer approach and a key reason that nuclear medicine will play a major role in molecular imaging in the future. We have seen this already with the explosion in growth of ^{18}F-FDG imaging, which, in my mind, is *the* molecular imaging technique. It is only a matter of time before a continuous stream of new radiotracers enters clinical practice. These may initially be based on ^{18}F radiotracers but will soon extend to other positron-emitting forms.

Although PET has been a main focus, SPECT should be considered as well. The main advantage of SPECT is the ability to image more than a single isotope at once. The main disadvantage is the lack of quantification.

Molecular imaging will be performed with combined instruments at a clinical level. This has already been made obvious by the great added value of CT in PET/CT. The benefit is that molecular imaging is put in an anatomic context. It is likely that MR imaging will be combined with PET in the future to take advantage of some of the unique capabilities of MR for tissue imaging and characterization. The main advantage of the addition of MR will be in providing an anatomic context for the sensitive and specific molecular imaging offered by review tracer methodologies.

Molecular imaging has grown up as a multidisciplinary program with medical physicists. What training and background should be required for clinical molecular imagers, and how can we foster excellence in clinical imaging through training?

Molecular imaging will continue to require attention to a multidisciplinary approach that is going to include PhD scientists and MD clinicians working in harmony. SNM has a long tradition of cooperation between major disciplines, particularly nuclear medicine, radiology, cardiology, radiochemistry, and other areas of medical imaging. This trend will be strengthened in the future as molecular imaging expands our joint interests to molecular biologists and pharmacologists. The SNM can help in this role by identifying specific areas of need for interdisciplinary collaboration and encouraging the appropriate discipline-specific education that will be required for optimum interaction. In the training of clinical molecular imagers, additional knowledge will be critical to achieving excellence in performance. At the present time, no training programs combine all of the necessary elements of biology, physiology, and anatomy that will be required for molecular imaging. The SNM should encourage the American Board of Nuclear Medicine and the American Board of Radiology to consider developing joint programs to meet evolving needs in this area. Where there are gaps, the SNM should step in to provide leadership in creating educational materials, much as we have done with PET and PET/CT training.

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