

Joint SNM/RSNA Molecular Imaging Summit Statement

The SNM and the Radiological Society of North America (RSNA) organized a 2-day Molecular Imaging Summit in April in Oak Brook, IL, that brought together physicians, scientists, and staff from 16 societies to begin long-term collaboration in areas of mutual interest. The following joint statement, issued by

summit co-chairs Brian C. Lentle, MD, and Mathew L. Thakur, MD, is being published by both *The Journal of Nuclear Medicine* and the official scientific journal of the RSNA, *Radiology*. The statement was prepared for publication by the staff of *Radiology* and is reproduced here in without change.

Report of a Summit on Molecular Imaging*

By Mathew L. Thakur, PhD, and Brian C. Lentle, MD

Medicine will change more in the next twenty years than it has in the past two thousand.

L. Turnberg (1)

The Radiological Society of North America (RSNA) and the Society of Nuclear Medicine (SNM) jointly convened a workshop on molecular imaging (MI) in April 2005. The purpose was to anticipate the changes in the imaging sciences that might result as molecular biology, nanotechnology, genomics, and proteomics increasingly impact upon everyday medical practice in general and upon imaging in particular (2–4).

The meeting was attended by physicians, scientists, and staff representing the Academy of Molecular Imaging (AMI), the American Association of Physicists in Medicine (AAPM), the American Board of Nuclear Medicine (ABNM), the American Board of Radiology (ABR), the American College of Radiology (ACR), the American Roentgen Ray Society (ARRS), the American Society of Nuclear Cardiology (ASNC), the Canadian Association of Radiologists (CAR), the Canadian Association/Society of Nuclear Medicine (CASNM), the European Congress of Radiology (ECR), the Federación Mexicana de Radiología e Imagen (FMRI), the International Society for Magnetic Resonance in Medicine (ISMRM), the RSNA, the Society for Molecular Imaging (SMI), the SNM, and the Society of Radiopharmaceutical Sciences (SRC).

MI is not new. Many speakers reflected that the one context in which the concept has already

reached the bedside is the use of fluorine 18 fluoro-deoxyglucose (FDG) positron emission tomography (PET), principally in cancer diagnosis. Nevertheless, on the horizon and in the laboratory are diagnostic and therapeutic techniques that will change medical practice and that represent a potentially important future for imaging scientists and physicians.

The focus of the meeting was to consider how to prepare the imaging community at large for that future and to begin to examine some of the implications of MI in terms of education and intersociety relations.

Round Table

To begin, speakers from each organization briefly reviewed the status quo in the body they represented. The specialty societies represented had all, in some way, moved to address what they saw as their future. This involved some or all of the following educational or developmental tools: (a) educational programs in the elements of MI; (b) plenary lectures at major meetings on related topics; (c) symposia or workshops addressing molecular biology, genomics, et cetera; (d) providing grant support to investigators addressing research questions relevant to the field of MI; (e) creation of “paper” institutes addressing MI within the structure of individual societies; and (f) participation in U.S. national initiatives to map and promote imaging research in general and MI research in particular.

Society representatives were able to briefly review and illustrate, based on their laboratory and clinical perspective, the status of MI both in animal research and in clinical applications. Discussion ranged over small-animal imaging devices for computed tomography (CT), magnetic resonance (MR) imaging, and optical imaging, as well as human-scale devices employing FDG PET, PET with other MI probes, MR spectroscopy and, perhaps, optical imaging.

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Dr Tom Miller, representing the ABNM, emphasized that the future involves not just MI but molecular and anatomic correlation. This reality will have implications for the education not only of nuclear physicians, but also of radiologists. The former will need to learn cross-sectional anatomy; the latter, the concepts of tracer techniques and functional imaging.

Entities such as the SNM Center of Excellence in Molecular Imaging represent potential foci around which broadly based programs might develop. Equally, the AMI has four institutes focused on clinical MI, MI technology, and imaging in drug development, as well as an industry forum for promoting MI technology.

Of the known hallmarks of cancer, molecular probes already have the potential to interrogate, for example, hypoxia (misonidazole), angiogenesis (AV β 3 integrin), glucose metabolism (labeled FDG), amino acid metabolism (labeled tyrosine, methionine), tumor cell proliferation (labeled thymidine), and others. Other potential applications will arise in the context of an improved understanding of genomics. In MI, combined technologies such as PET/MR imaging and MR imaging/ultrasound are likely to follow where PET/CT has led.

The applicability of MI is also not limited to cancer and its treatment. It already promises to change the diagnosis and understanding of Alzheimer disease, to cite but one example.

Importantly, MI is likely to lead to a further blurring of the distinction between diagnosis and treatment and to a paradigm shift to early diagnosis that leads to image-guided, individualized molecular therapy. Further, when in therapy, biomarkers will be able to be imaged and quantified to provide early evidence of the efficacy of the treatment.

The ubiquitous interest in MI was reflected in the presence of representatives from the ASNC and international imaging societies. The representatives from ASNC reported that their meetings have already featured symposia on MI. The ISMRM representatives reported the creation of a Study Group on Molecular and Cellular Imaging; the organization of an ISMRM workshop on MI in 2003, in addition to the fast growing attention to MI at the ISMRM annual meeting; and other ISMRM symposia.

The SNM had articulated a goal "to harness the power of MI and molecular therapeutics in search of better and more effective means to manage diseases and improve the quality of life for patients."

Of note, the ECR had emphasized MI in its courses over the most recent 2 years, while recognizing it as unlikely that European centers would enjoy the financial support available, at least until

now, in the United States. The response in Europe is to foster networks that link existing groups of physicians and physician-scientists instead of relying on "monolithic" advanced centers.

A Definition

A number of concise and elegant definitions of MI have been developed, notably by Weissleder and colleagues (5,6), Massoud and Gambhir (7), and Herschmann (8). Nevertheless, the group believed it should go beyond these.

A traditional distinction has been made between anatomic—or structural—imaging and functional—or physiologic—imaging. Simplistically, that distinction had, historically, been made between techniques such as CT and nuclear medicine methods as being, respectively, anatomic and functional. However, that simple distinction has increasingly become blurred by CT, MR imaging, and other techniques that provide both functional and structural information, while fusion techniques such as PET/CT represent a hybridization of diagnostic methods.

Most of functional imaging is also MI, but not all. BOLD (blood oxygen level-dependent) and diffusion-tensor sequences in MR and magnetoencephalography are some—far from exclusive—examples of functional imaging that do not address biologic events on the molecular scale. Given these considerations, the group developed the following definition of MI, successfully testing it against the existing variety of imaging tools available in humans and in animal experimental contexts:

MI techniques directly or indirectly monitor and record the spatiotemporal distribution of molecular or cellular processes for biochemical, biologic, diagnostic, or therapeutic applications.

Education

There was a broad consensus that no one single educational program would fit the range of scientists and clinicians involved in MI. Traditionally, the graduate student–postdoctoral stream addresses its educational needs on a point-of-need basis. The inherent diversity of research and development in MI makes this appropriate. There might be merit in making an inventory of institutes involved in MI, along with the core MI activities within each, to facilitate graduate and undergraduate studies. While basic science research is inherently self-sustaining in terms of intellectual content, there are disturbing signs of declining financial support for MI investigations as the United States realigns its research priorities.

Some of the skill sets involved in MI include appropriate elements of physics, chemistry, molecular biology, genomics, statistics, mathematical modeling, et cetera. Any attempt at development of a standardized curriculum might only be usefully directed to clinical imagers, in recognition of the diversity of the disciplines involved.

A further educational challenge consists in awareness raising among potential referring physicians and, not least, the public at large.

For the clinical application of MI, 1-year fellowships are desirable, with MI being promoted as a translational research tool. In the longer term, the basic science components of education in the radiologic sciences may need to be diversified beyond medical physics, radiopharmacology, and radiobiology. Above all, the present communication chasm between basic scientists and clinicians must be overcome for MI to realize its potential to reinvent radiologic science.

As clinical practice evolves, MI is inherently directed to disease processes (cancer, genetic disorders, neurodegenerative disease, etc) and does not readily align with the current paradigms of organ-based or machine-based imaging services. In the longer term, the radiologic sciences may need to evolve away from organ-based to disease-based subspecialization.

The group was of the opinion that it is not yet the time for board recognition of MI, even if that were practical or desirable. Nevertheless, to build toward the future, it is not too early for education in radiology and nuclear medicine to include content in molecular biology, genomics, and gene therapy, et cetera.

The realization is that radiochemists are becoming an endangered species. The United States has for decades been a net importer of chemists. However, in the post 9/11 world, abundant external sources of talent might no longer be available.

Goals to Be Met in Advancing MI

1. Educate imaging scientists and practitioners who may be involved, along with potential referring physicians and the public.
2. Identify key components of a noncertified fellowship in MI, possibly as a precursor to formal consideration of MI by the boards involved.
3. Assure the viability of MI through the development of techniques that meet a clinical need and that are reimbursable.
4. Collaborate across societies to develop a long-range plan for raising awareness of MI in the public arena.

5. Anticipate needs through (a) the funding of fellowships, grants, and travel awards to develop a cadre of appropriately educated individuals; (b) targeted support of translational research; and (c) creation of a multidisciplinary network to provide the infrastructure for multisite clinical trials.
6. Reach out to nonimaging specialists, since a lesson from achieving FDG PET reimbursement has been the support of the referral physician base.
7. Continue and expand MI research.
8. Advocate for replacing the Response Evaluation Criteria in Solid Tumors (RECIST) on the basis of existing evidence to apply MI techniques (FDG PET, at this time) as primary and not secondary markers of treatment response.
9. Develop a common listserv of those practically involved in MI to facilitate exchanges of information, such as announcements of funding opportunities.
10. Identify resources to initiate or expand MI programs.
11. Engage industry in the development of MI.
12. Identify and address key regulatory issues that might serve as roadblocks to MI, and, in particular, (a) restructure the Radioactive Drug Research Committee (RDRC); (b) lobby the Food and Drug Administration to rationalize the requirements for the testing of diagnostic, as compared with therapeutic, agents; and (c) seek ways to revisit or to update the RECIST criteria used in oncology trials on the basis of modern evidence to the effect that MI methods are used as primary and not secondary markers of treatment response.

Conclusions

A sense of common purpose among those attending emerged, together with the sense that the meeting was a timely one in historical terms. These considerations emboldened the group to move to a series of proactive recommendations, as follows:

1. That this position paper be developed by the RSNA and SNM conveners, be circulated for ratification, and be published in appropriate venues.
2. That each organization appoint, by means of a process appropriate to that organization, a representative volunteer and staff person to a committee charged with prioritizing, promoting, and advancing this MI agenda.

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3. That this committee effect its business largely by means of conference call, but that it meet at least once annually face-to-face at some appropriate venue.
4. That the committee seek ways to represent to the Food and Drug Administration the urgent need to make a distinction between diagnostic and therapeutic agents with respect to the regulatory approval process.
5. That the committee seek ways to replace the RECIST criteria used in oncology trials, on the basis of modern evidence.
6. That the committee work to achieve a restructuring of RDRC.
7. That the committee facilitate the development of multidisciplinary educational programs capable of being customized and presented at suitable venues to educate and inform both imaging and referring physicians.
8. That the committee seek ways to engage industry in advancing the development of MI.
9. That the committee identify the resources necessary to initiate or expand MI programs.
10. That the committee seek to engage other potential referring physicians and their organizations in seeking support for and development of MI.

Postscript

Dr Henry Wagner, in one of his archetypical, not to say renowned, program summations of the SNM annual meetings, once remarked about nuclear medicine as it reached one of its crossroads that "it is wrong to reach a turning point and not turn" (9). That remark may now be capable of being generalized in the evolution of all of the radiologic sciences. The sense of the meeting was that it proved a timely reminder that imaging techniques as a whole are at a crossroads with respect to MI. We owe it to our

successors to ensure that, at this particular turning point, we do indeed also turn.

Acknowledgments

List of participants (in alphabetical order): Dr Philip Alderson (ABR, ACR), Lynn Barnes (SNM), Dr Gary Becker (RSNA), Dr John Boone (AAPM), Dr Linda Bresolin (RSNA), Dr Steve Burrell (CAR), Dr Peter Conti (SNM), Dr Johannes Czernin (AMI), Dr Jeffrey Duerk (ISMRM), Dr William Eckelman (SRS), Dr Guillermo Elizondo-Riojas (FMRI), Dave Fellers (RSNA), Dr David Glover (ASNC), Dr Robert Gropler (ASNC), Becky Haines (ARRS), Dr Christian Herold (ECR), Dr Brian C. Lentle (RSNA), Dr Thomas Meade (SMI), Dr Tom Miller (ABNM), Dr Chrit Moonen (ISMRM), Virginia Pappas (SNM), Dr J. Anthony Parker (ABNM), Kim Pierce (AMI), Dr James Provenzale (ARRS), Dr E. Russell Ritenour (AAPM), Gregg Robinson (SNM), Dr Henry Royal (ABNM), Tracy Schmidt (RSNA), Dr Mathew Thakur (SNM), Dr Jean-Luc Urbain (CASNM).

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