

High Country Nuclear Medicine Conference, Vail, Colorado

FUTURE OF NUCLEAR MEDICINE DEBATED AT UNIQUE INTERDISCIPLINARY MEETING

“Our final determination of whether or how these techniques will be used in clinical practice depends on a mixture of scientific and economic factors. Too often in recent years, though, we’ve seen investigators get distracted by socioeconomic and political aspects. If we compromise the scientific evaluation because we’re concerned about cost, then we never really know the true value of an idea.”

One of the characteristics that makes the nuclear medicine field so fascinating — the diversity of scientific and clinical disciplines that converge to pursue the medical use of radioactive tracers— also makes it difficult for a professional in this field to interact at length with colleagues who are not peers or collaborators.

At large scientific meetings with several parallel sessions, attendees are drawn to papers given by peers. Communication at small meetings, for the most part, flows one way— from speaker to audience. One annual event, however, brings together some of the leading investigators in nuclear medicine to explore the current directions of the field and to be challenged by their audience.

The High Country Nuclear Medicine Conference, held each spring in Vail, Colorado, combines an intensive week-long scientific program with winter sports to promote camaraderie among participants. “We patterned the High Country Nuclear Medicine Conference after the traditional Gordon Conferences held for biologists, chemists, and physicists,” said Harold A. O’Brien, PhD, of Los Alamos National Laboratory, New Mexico, and chairman of the organiz-



The village of Vail, Colorado, site of the annual High Country Nuclear Medicine Conference, held this year March 13-18, 1988.
(David Lokey)

ing/program committee. (Universities in New England and California annually hold more than 100 Gordon Research Conferences, which bring scientists together for a week of morning and evening scientific sessions with the midday hours free for hiking, sailing, jogging, or sight-seeing. These “Frontiers of Science” meetings began in 1931.)

“This meeting is not a workshop or a course. The talks range from re-

views to new developments. We want the audience to feel free—at any time during a presentation—to shout out questions, challenge statements, and ask for clarifications. We encourage participants to ask speakers, ‘What relevance does this information have to my practice, my research, or my company?’ It’s this type of interchange that makes the High Country Conference unique,” explained
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COMMENTARY

How to Strengthen Nuclear Medicine:

BUILD MORE BRIDGES TO REFERRAL BASE AND STOP PURSUING "GOLD STANDARDS"

There are many clinical collaborators who are very enthusiastic about making use of our nuclear medicine technology. We need to know enough about their specialties to understand the needs of their patients. We also need to work in true cooperation with other physicians to maintain their interest in nuclear medicine research and clinical studies. As long as we can bridge the gap between diagnostic medicine and other specialties, the field of nuclear medicine will hold its own in the health care world.



Dean F. Wong, MD

It's important that we strengthen our training and our self-image, and that we try harder to promote ourselves as a unified group. It's also important for our nuclear medicine colleagues to remain open-minded in pursuing seemingly competitive procedures. Skepticism toward new procedures still in the research stage is reflected in the commonly heard pessimistic statements predicting that these procedures will never become practical enough for routine clinical applications.

As an example, for several years only a small minority within the nuclear medicine field extolled the clinical possibilities of brain imaging with positron emission tomography (PET). While most members of the nuclear medicine community were dismissing those possibilities as "pie in the sky," excitement about PET brain imaging was being sparked in the neurology, neuroscience, and psychiatry communities. Many active investigators in PET brain imaging feel they receive more recognition from the above specialties than from their colleagues in nuclear medicine. I'm convinced that nuclear medicine professionals who concentrate on other specialties—cardiology, endocrinology, or oncology, to name a few—have experienced that same irony. The nuclear medicine community needs to start supporting its own people much more than it currently does if we are to survive as a strong and independent specialty.

We need to start thinking more in truly interdisciplinary terms, and we must work very carefully to keep up with the literature in other medical disciplines. During discussions with referring physicians, it's imperative that we ask questions and press for more simplified explanations of things that we don't understand. When psychiatrists consult with our department about PET procedures, for example, I always try to obtain some piece of information

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Stanley J. Goldsmith, MD, of the Mount Sinai Medical Center in New York City.

Sponsored by The Society of Nuclear Medicine (SNM) Education & Research (E&R) Foundation, the High Country Conference is dedicated to promoting professional interdisciplinary dialogue on the current status and future directions of diagnostic imaging. In addition to radionuclide

procedures and nuclear magnetic resonance (NMR), the program often includes presentations on other modalities.

Myocardial Perfusion with Ultrafast CT

Last year during the Seventh High Country Conference, for example, Stuart Rich, MD, of the University of Illinois College of Medicine in Chicago, spoke on the impact of

ultrafast x-ray computed tomography (CT) on cardiac imaging. In addition to anatomic studies, such as determinations of cardiac volume, myocardial perfusion studies are being conducted by assessing uptake and wash-out of contrast media with ultrafast CT, reported Dr. Rich. Ejection fraction and regional wall motion studies with ultrafast CT are also being evaluated.

The Eighth High Country Confer-

from them. Sometimes I say, "Look, if I could measure this for you, why would it be important? How could this measurement help you treat your patients better?" Nuclear medicine people, of course, have engaged in this type of interaction for years, but we need to be more aggressive about it—both from a scientific and clinical standpoint.

We also need to reevaluate the quest for a "gold standard," a nuclear medicine procedure that will provide a definitive diagnostic answer, which is detrimental for three reasons:

- It channels our investigators' efforts toward one ultimate answer to a diagnostic problem, and encourages the premature rejection of alternative solutions. PET researchers, for example, have often disparaged single-photon emission computed tomography (SPECT). The heated debate over the best bone densitometry method, as another example, has diverted attention from the actual clinical benefits of bone mineral measurements.

- The idea of depending on a gold standard is diametrically opposed to the type of diagnostic medicine that should be practiced as we introduce more and more sophisticated techniques of examining patients. To deliver the most complete and accurate health care possible, the results of a diagnostic test should serve as one piece of information that is integrated with several other results. The future diagnosis of mental illnesses, for example, could depend upon PET scan data, genetic information, family history, and the classical patient history and physical examination. In the future, perhaps, a physician may work with a check list of medical information to be gathered, and a certain combination of results would indicate an estimated probability that the patient has the suspected disease. Physicians today, of course, do correlate pieces of medical information to reach a conclusion, but this practice will require far more sophistication as nuclear medicine enables physicians to obtain more *in vivo* physiologic data.

- Our obsession with gold standards has encouraged third-party payers to deny reimbursement for procedures that do not serve as the single test that determines a diagnosis. I have heard people say, "If you can't prove that a patient has schizophrenia with a PET scan, then what good is it?" Similarly, part of the argument that third-party payers use to deny coverage to bone densitometry procedures centers around the doubt that bone mineral measurements alone can provide a negative or positive indication of osteoporosis or future bone fractures. Health care professionals, starting with the nuclear medicine community, need to educate third-party payers about the evolving approach to patient diagnosis that entails an assessment of several test results. We need to explain to third-party payers that a new test we have developed may be a little expensive now, but that it will get cheaper in the future and it plays a complementary role in identifying disease.

Admittedly, some diagnostic tests—such as the ventilation-perfusion lung scan to detect pulmonary embolism—do provide definitive answers about the absence of disease, and often about its presence. Our unrealistic expectations, however, for finding such gold standard tests for the intractable diseases that medical science is just beginning to understand are preventing patients from benefitting from some of the more recently developed nuclear medicine procedures.

Nuclear medicine has a bright future, and it will continue to provide valuable information for scientific as well as diagnostic advances. It will provide that information to far more physicians, however, if we actively work toward the integration of various medical specialties and of complementary patient data.

Dean F. Wong, MD,
The Johns Hopkins
Medical Institutions,
Baltimore, Maryland

ence, to be held March 13–18, 1988, will include a comparison of imaging modalities for the diagnosis of coronary artery disease. Other clinical topics include bone densitometry and various brain imaging techniques, such as metabolic, blood flow, and receptor-based studies.

Industry traditionally plays an integral role in the High Country program. This year, 13 of the 33 faculty members are from instrumentation or

radiopharmaceutical companies. One afternoon session, for example, will cover new radiopharmaceutical developments at Squibb, Du Pont, and Amersham. (Morning scientific sessions begin at 7:00 am; afternoon sessions are held late in the day, sometimes stretching into the early evening. Midday hours are reserved for cross country or downhill skiing.)

Since 1986, the last day of the High Country Conference has been devoted

to a panel discussion on regulatory affairs, moderated by James F. Lamb, PhD, of Imagents, Inc., in Houston, Texas. This spring, five representatives of the United States (US) Food and Drug Administration (FDA) will present information and answer questions. Thomas Hoffman, MD, of the FDA Office of Biologics Research and Review, will discuss "Monoclonal Antibody-Targeted Imaging: Safe-

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ty and Efficacy." Key issues of radiopharmaceutical approval will be discussed by members of the FDA Division of Oncology and Radiopharmaceuticals: John F. Palmer, MD, A. Eric Jones, MD, and Rebecca Wood, PhD. Lastly, Robert Phillips, PhD, of the FDA Office of Device Evaluation, will speak on the approval of radiology devices. Typically, comments during this session—as well as throughout the week—are made with candor, one of the main attractions of this conference.

"In the past, conference attendees would bring up various FDA problems, and we realized that we needed people here who could answer those questions," said Dr. O'Brien. In the future, representatives of third-party payers may possibly be included because reimbursement questions often arise during the conference.

Future Lies in Biochemistry

"Biochemistry is the future of nuclear medicine," said William C. Eckelman, PhD, of the Squibb Institute for Medical Research in New Brunswick, New Jersey, during the 1987 High Country Conference. The challenge of receptor-based radiopharmaceuticals lies in separating blood flow agents from true receptor-binding tracers, noted Dr. Eckelman. "Blood flow and receptor binding are not two distinct processes, but rather a kinetically determined process. For receptor-based radiopharmaceuticals, the biochemical process is the rate-determining step," he explained.

A radiotracer that has been validated as a receptor-binding ligand may still not be suitable for development as a clinical tracer. "There has been a fair amount of confusion because many people assume that if the radioactivity binds to the receptor, you have a sensitive method to measure

the change in receptor concentration as a function of disease," said Dr. Eckelman. That conclusion cannot be assumed, however, because there may be a very nonlinear relation between receptor concentration and the amount of radioactivity in the target organ, he explained. In addition, investigators need to determine whether a change in tracer uptake results from a pathologic change in receptor concentration or an altered affinity. Receptor-based radiopharmaceuticals could play a role in the future diagnosis of mental illnesses.

Characterization of biochemistry *in vivo* could also play a future role in ischemic heart disease. Markus Schwaiger, MD, then of the University of California in Los Angeles (UCLA), described the use of metabolic parameters for defining ischemia and determining tissue viability with positron emission tomography (PET). "A transient episode of ischemia causes profound alteration of regional function. This physiologic abnormality remains, despite reperfusion, for a fairly long time period, leading to the recently coined term 'stunned myocardium.'"

Areas of impaired fatty acid oxidation (indicated by abnormal carbon-11 palmitate kinetics) and increased glucose utilization (detected by increased uptake of fluorine-18 deoxyglucose) define ischemically injured myocardium, reported Dr. Schwaiger. "We need a larger patient group to determine whether these PET studies can serve as predictive indicators of tissue viability and recovery, but the results so far are promising."

In contrast to brain studies, metabolic heart studies are quite complicated because the heart switches substrates, resorting to glucose when its capacity to oxidize fatty acid is impaired. "Is it enough to use one tracer to answer the metabolic questions, or will we need a battery of tracers to

look at mitochondrial and cytosolic function at different steps of each metabolic pathway?" asked Dr. Schwaiger.

Socioeconomic Factors

Several of the conference discussions went beyond the scientific core of a new diagnostic procedure to encompass its socioeconomic and political ramifications. Gerd Muehllehner, PhD, of the University of Pennsylvania, described current advances in PET instrumentation. "In nuclear medicine, we can show images that have poor resolution and say that it's because we do physiologic imaging. In the end, though, the physician who has the better image will be the one to see smaller structures and defects, and will be better able to help the patient," said Dr. Muehllehner.

The basic PET camera could be manufactured for about \$600,000, but it would acquire, reconstruct, and analyze data sequentially rather than simultaneously. In order to reach an acceptable rate of patient "throughput," manufacturers must add more computers and processing electronics, which drives up the cost.

Donald O. Elliott, PhD, of General Electric (GE) Medical Systems in Milwaukee, Wisconsin, pointed out that a cooperative effort among several special groups is necessary to find out whether NMR spectroscopy will be medically useful. "We're involved in a collaboration of NMR spectroscopists and imagers, pathologists, chemists, and physicians. We need to find out what will make NMR spectroscopy clinically viable, or to prove that it has no significant clinical value and quit working on it."

Cost effectiveness has become a key issue in health care, particularly in high-technology medicine. Elias Botvinick, MD, of the University of California at Davis, pointed out that

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a new procedure needs to either replace an existing test or add a unique capability to the medical armamentarium to be considered truly cost-effective. "On the other hand, a minimal clinical advance—or just pretty pictures—available only at great expense is not acceptable clinically or commercially," noted Dr. Botvinick.

Dr. Goldsmith, of Mount Sinai, said that he would urge the nuclear medicine community to stress efficacy and cost when comparing diagnostic tests, and to refrain from pointing out that a competing procedure exposes the patient to less ionizing radiation. "Although I think it's correct to discuss dosimetry, the amount of radiation exposure to a patient from *any* diagnostic procedure is exceedingly small. When we overemphasize the potential benefit of giving a patient a *very* minute instead of a minute dose of radiation, we do ourselves and our patients a disservice by unreasonably exaggerating the risk associated with one procedure."

Although practical concerns will, to some extent, control a procedure's acceptance in medicine, Dr. Goldsmith warned that too much speculation could be detrimental. "Our final determination of whether or how these techniques will be used in clinical practice depends on a mixture of scientific and economic factors. Too often in recent years, though, we've seen investigators get distracted by socioeconomic and political aspects. If we compromise the scientific evaluation because we're concerned about cost, then we never really know the true value of an idea," he explained.

This narrow-minded thinking also leads to a defeatist attitude toward the development of diagnostic tests for diseases that are, as yet, untreatable. "Improved diagnosis will lead to improved therapy, as medicine has demonstrated over and over in the past,"

said Dr. Goldsmith. Investigators who advocate the clinical use of experimental procedures often find that their arguments are dismissed as the subjective views held by persons with vested interests. Dr. Goldsmith pointed out, however, that the investigators who prefer that a procedure remain a tool for basic research may have somewhat hidden vested interests themselves. "If one's work is funded by research grants that would not be forthcoming if the technique under study were clinically acceptable, then one has a vested interest in making sure that the technique remains in the domain of research," he suggested.

Historians, Not Pioneers

"As Niels Lassen of Copenhagen often says, 'Let's not be pioneers, let's be historians,'" said Thomas C. Hill, MD, of New England Deaconess Hospital in Boston. Historically, it's important for clinical investigators to know why certain physiologic measurements have been sought by the medical community. Articles published in the medical literature almost three decades ago, for example, show that global oxygen consumption and glucose utilization are related to cerebral blood flow. By remembering the development of diagnostic tests that are routine today, investigators can find parallels with current trends in radiopharmaceutical development. To predict where neuronuclear medicine will be in 10 years, Dr. Hill recommends looking back at nuclear cardiology in the early 1970s. "At that time, nobody thought there was any clinical relevance to radionuclide heart studies. When speakers got up to lecture on nuclear cardiology, half the audience left the room to take a coffee break," he recalled.

Most nuclear physicians thought that these heart studies were irrelevant because the radiopharmaceuticals weren't available, the images were

photon-deficient, "and nobody believed that these techniques would ever assess myocardial perfusion or wall motion abnormalities on a routine, clinical basis," said Dr. Hill, noting that today cardiac studies account for about 40% of all nuclear procedures. "Neurologic radionuclide studies will dominate our clinical practice within the next five to 10 years," he added.

In order to foster open and informal discussions, total enrollment for the Eighth High Country Nuclear Medicine Conference will be limited to 125 registrants. "It's important that everyone plans to participate for the entire week. Much of the discussions build upon information previously presented, and it defeats the purpose of the conference for registrants and speakers to fly into Vail for just a day or two," said Dr. O'Brien.

The High Country Conference evolved from a 1980 meeting sponsored by the SNM Rocky Mountain Chapter. "Tom Verdon, Tom Raven, and I wanted to hold a local meeting that featured speakers from all over the country who were working on the cutting edge of nuclear medicine science. Our chapter was small, and we looked around for an added incentive to draw high-caliber speakers. The answer was obvious—the Rocky Mountains, an opportunity for recreational activities," said Dr. O'Brien.

The chapter decided in 1981 not to sponsor the High Country Conference, and the SNM Education & Research (E&R) Foundation took over that role. Since that time, the conference has donated about \$8,000 to the E&R Foundation—investing in the future of nuclear medicine in addition to talking about it.

[For more information, contact: Hal O'Brien, PhD, 107 La Senda Rd., Los Alamos, NM 87544 (505) 665-0250.]

Linda E. Ketchum