

On Proselytism, Retroversion and Fiscal Nihilism in Nuclear Cardiology

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Having just completed my monthly perusal of the *Journal*, I remain impressed by the continuing evolution of the science of nuclear medicine chronicled monthly in these pages. I was drawn by a provocative title to read the Commentary, "Tough Choices: Who Is to Make the Call [34;5:860-861]."

Morton E. Kalus, Jr., a practicing cardiologist with a professional interest in nuclear cardiology, outlined his views regarding the potential impact of anticipated health care reform on physician choice as new radiopharmaceuticals are introduced to replace existing diagnostic or therapeutic agents. Dr. Kalus raised issues of genuine concern, opinions most likely shared by our colleagues in academic and private practice settings. We indeed face "tough choices," and must advocate to be included in the health care decision-making process. In this era of cost-containment, medical professionals must actively propose and investigate new ideas, validate novel operational approaches and reevaluate whether orthopraxy (business as usual) is acceptable.

The pharmaceutical industry has confronted these issues for years, albeit in a different context, in which scientific "hypothesis testing" is termed pre-clinical "research and development," and phase I-IV clinical research studies are dubbed "pre-marketing and post-marketing" trials. Traditional research funding and industry-sponsored investigation are increasingly interdependent, synergistically producing important medical advances such as the antibiotics and clot-selective thrombolytics about which the commentator is so troubled. The so-called "brain drain" from academic medicine to industry has not spared nuclear medicine. However, this phenomenon does not occur in a vacuum, and has contributed to many therapeutic and diagnostic advances, including development of ^{99m}Tc -based radiopharmaceuticals for cardiac imaging.

Although Dr. Kalus and others might disagree, I contend that science drives the pharmaceutical business and that drug companies which lose sight of this principle are destined to fail. Major pharmaceutical houses remain strong by keeping new drugs in the pipeline. Smaller firms, unable to develop a significant product that can weather FDA scrutiny and emerge into the marketplace, are short-term business casualties. The fact that four major radiopharmaceutical companies have made large investments in developing ^{99m}Tc -based myocardial perfusion imaging compounds strongly argues that the existing perfusion agent (i.e., ^{201}Tl) is not optimal with respect to imaging quality, availability, dosimetry or patient scheduling. Recognizing these suboptimal characteristics does not vitiate the proven track record of ^{201}Tl for coronary disease detection, prognostication or myocardial viability assessment.

The ongoing search for a better myocardial perfusion agent stems from the natural desire of scientists to respond to and improve on the recognized limitations of an existing compound, so that clinicians will be better equipped for patient care. Reasonable men and women may disagree as to whether any of the existing ^{99m}Tc perfusion agents represent a major advance over ^{201}Tl , just as one could argue about the business wisdom of developing such a product in the first place. However, if the initial results of drug development were always accepted as "good enough for government work," we would still be using perhexiline maleate as the calcium entry blocker of choice. There are no guarantees for companies undertaking the daunting and expensive proposition of new drug development and seeking eventual FDA approval. If a drug or diagnostic agent survives this process, neither physicians, patients nor government policy-makers should be surprised or offended at the company's desire to aggressively market and sell the compound.

As a Canadian-educated physician working in the United States, I am familiar with the medical system upon which a new U.S. health care system might be patterned. My Canadian colleagues are restricted, not in their choice of myocardial perfusion agent or the number of cardiac diagnostic studies a patient can undergo annually, but by government-limited hospital budgets and laboratory licensing. The Canadian Health Protection Branch approved use of ^{99m}Tc -sestamibi, and left the choice of radioisotope to

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the physician. Most large volume nuclear cardiology laboratories in Canada perform and are reimbursed for a significant number of sestamibi studies. In the government's view, sestamibi's capacity to derive useful perfusion and ventricular function data is considered cost-efficient. Many Canadian laboratories "squeeze" a few extra doses from the *Cardiolite*[®] vial. This approach, which may also be relatively common in this country, does not bother the consciences of Canadian physicians operating the laboratories.

The cost of drugs in Canada is generally lower than that in the United States for reasons too numerous and complex to consider in this forum. In both countries, 3–4 mCi of ²⁰¹Tl is marginally less expensive than sestamibi. Competition between drug companies and radiopharmacies for market share drove the cost of ²⁰¹Tl to record low levels in recent years. The Canadian company that produces sestamibi and its competitors who had no marketable ^{99m}Tc perfusion agent, participated in this pricing war with different business motives. As with other pharmaceuticals, the cost of sestamibi will no doubt decrease when research and development costs are recouped by the manufacturer or if a serious competitor triggers the law of supply and demand. In busy laboratories, the cost of sestamibi per dose is marginally higher than that of ²⁰¹Tl, representing a relatively small expense compared to the total technical and professional fees that doubtless will be targeted in the reformed U.S. health care plan.

To paraphrase Secretary Lloyd Bentsen: "I know physicians in private practice, I work with physicians in private practice . . . I am not in private practice." I can only imagine that what stimulates interest and modulates enthusiasm for a new drug or medical technique in an academic setting may be the very thing that frustrates my colleagues on the clinical firing line. While I and other investigators who have worked with ²⁰¹Tl-sestamibi, teboroxime and the newest generation of ^{99m}Tc-based perfusion agents to derive "MRB" (maximum research benefit), our clinical colleagues are likely to direct their attention to more practical issues. We have lectured, and may have "proselytized," to

audiences at national scientific meetings and continuing medical education courses around the country. But nobody puts words in our mouths with which to "detail" or convert our medical colleagues. The initial ballyhoo about RP-30 (now *Cardiolite*[®]) was justified, the FDA approval delays were disappointing, and the "vigorous media blitz" Dr. Kalus refers to is no different from that encountered when any new pharmaceutical is introduced. My own enthusiasm for ^{99m}Tc-sestamibi is based on published data and the studies we perform daily in our nuclear laboratories. We, too, recognize that no available perfusion agent is perfect.

These are the times to try the medical profession's collective soul. The nuclear medicine community will not be spared scrutiny or be permitted to stand pat. Do we convert or retrovert under pressure? Failure to accept change will not be rewarded and may not be tolerated. However, while change is necessary and inevitable, change for the sake of change is generally imprudent.

We, like Dr. Kalus, make daily decisions of conscience and cost-benefit. Just as a once-a-day ACE inhibitor may not represent a major improvement over captopril, higher energy ^{99m}Tc-sestamibi may not be a quantum level better than ²⁰¹Tl. As is the case in Canada, this is not for the government alone to decide.

As an individual who cut his teeth on ²⁰¹Tl myocardial perfusion imaging nearly ten years ago at Massachusetts General Hospital, I believe that ²⁰¹Tl continues to have an important role in nuclear cardiology practice. However, ²⁰¹Tl users are not the only "honest", fiscally or clinically responsible nuclear physicians. Furthermore, let's not kid ourselves into thinking that the health care reform mavins in Washington know or care deeply about the differences between ²⁰¹Tl and ^{99m}Tc perfusion agents. They have bigger fish to fry, and much tougher choices to make.

My advice to Dr. Kalus is, as always, to make his own call and do what he believes is in the best interest of his patients. In the long run, the rest of this argument may well be reduced to the domain of medical trivia.