The Relationship of Nuclear Magnetic Resonance to Nuclear Medicine: Friend or Foe?

As readers of this year's volume will note, reports of nuclear magnetic resonance (NMR) have been appearing in the *Journal of Nuclear Medicine*, both as a technique related to or correlated with nuclear medicine (*1*) and as a report of basic science investigations (*2*). Perhaps now the question should be considered as to whether these topics are appropriate to the *Journal* and are, in fact, of interest to those in the field of nuclear medicine. Does a relationship actually exist between nuclear medicine and nuclear magnetic resonance that suggests they have more in common than merely the first word of each discipline?

Concerning the interest of the nuclear medicine community in nuclear magnetic resonance, at this time there can be no doubt. One of the first symposia on the application of nuclear magnetic resonance to medicine was presented at The Society of Nuclear Medicine 29th Annual Meeting in June, 1982. (The organizer of this symposium, one of the early and present day leaders of nuclear magnetic resonance imaging (NMRI), was Dr. Leon Kaufman, a former SNM chapter president). This same meeting included a section of proffered papers on this topic and presented the first report on the use of EKG gating for cardiac nuclear magnetic resonance imaging (*3*). The present day interest may be appreciated by looking at the results of a preliminary survey conducted by Dr. James W. Fletcher for the Academic Council concerning the participation of nuclear medicine personnel in nuclear magnetic resonance (Fletcher JW, personal communication, 1985).

In this study, the directors of nuclear medicine training programs were contacted to see if their institutions either had NMRI systems or anticipated such systems and, if so, what was the participation or expected participation of the nuclear medicine personnel. It was found that ~45% of those responding already had NMRI systems in their institutions and of those, 74% of the nuclear medicine personnel were participating in some capacity with 24% reporting considerable participation. For those institutions in which NMRI systems were to be installed 58%, of the nuclear medicine groups expected to have considerable participation. This participation is even more surprising when it is realized that very few of the installations are headed or controlled by the nuclear medicine department or section, and thus, the nuclear medicine personnel were invited to participate. Of course, nuclear magnetic resonance has long been of interest to the training centers since questions on this topic have been included in the examinations by the American Board of Nuclear Medicine and the NMTCB for the last several years.

The reason for this interest, and the reason that so many of the contributors in clinical nuclear magnetic resonance have come from a background in nuclear medicine, is by now rather obvious. Of all the imaging procedures, NMRI comes closest to being a functional imaging technique similar to nuclear medicine imaging. Since the intensity levels of the NMRI signals are largely dependent on the relaxation times, T_1 and T_2, the images are quite similar to the parametric images that are so familiar to us in nuclear medicine. It is not surprising that one of the first investigators in clinical NMRI reported results directly in terms of parametric scans of T_1 values (*4*). These results were obtained by Prof. John R. Mallard of the University of Aberdeen, Scotland and the director of nuclear medicine at that institution. (Since one of Prof. Mallard's early contributions was a color-coded display for a rectilinear scanner, it is apparent that nuclear medicine techniques have long been part of his thought processes).

A number of other similarities exist between the characteristics of NMRI and nuclear medicine techniques. It has been discovered that the intensity and decay line shape of the NMR signal from flowing blood varies with the velocity (*5,6*). Flow studies can now be anticipated that will derive results similar to radionuclide dynamic studies. It took very little time for the NMR investigators to rediscover the potential of the chelating agents and to realize that if technetium can be tagged to diethylenetriamine pentaacetic acid (DTPA), it should be just as easy to tag the paramagnetic ion of gadolinium to this same agent.

In a similar sense, it has also been realized that monoclonal antibodies can carry paramagnetic ions as easily as they carry radioactive ions. (Well, probably not *quite* as easily since the number of ions needed are considerably greater, but the principle is the same). More and more, the radiochemist working in the nuclear medicine laboratory is finding his time monopolized by the NMR section.

Having considered the similarity of interest in the two nuclear techniques, it is now time to face the more difficult question of how these two methodologies relate. It is always tempting to call any two different modalities complementary. This statement is usually true but is not a realistic or helpful answer to the question. In the early days of transmission computed tomography (CT) it was shown that the combined accuracy of both a radionuclide brain scan and a CT brain scan was greater than either procedure alone (*7*). In spite of this demonstration of superiority, combined studies were seldom pursued. The supplantation of the radionuclide brain scan by the CT scan in many institutions was rapid and conclusive.

Complementary tests are seldom used if reasonable sensitivity and specificity can be obtained by either one alone. The immediate acceptance of the CT brain scan was due not to a marked improvement in accuracy, but rather to many other factors including ease of interpretation, wealth of anatomic data, and the immediate availability of the CT images rather than waiting for a 2- to 4-hr delayed radionuclide scan. Economic considerations are also a factor and it was decided in most institutions that the cost of obtaining two examinations on each patient was excessive and that the cost of the CT scan could be in a similar range as the radionuclide scan.

Thus, the fact that NMRI and nuclear medicine tests are complementary does not answer the question of whether they are also competitive. Or to put it bluntly, are there present nuclear medicine procedures that will be taken away by NMRI?

It is difficult to answer this question because in spite of the tremendous excitement generated by this new modality, it must be realized that NMRI is a very complex technique whose potential may not be known until a considerable amount of clinical investigation has been accomplished. An illustration of a potentially important competitive procedure would be the possible supplantation of the thallium-201 (^{201}Tl) single photon emission computed tomography (SPECT) measurement for myocardial ischemia and infarction by an NMR technique. Early NMR studies reported in the *Journal of Nuclear Medicine* in 1980 had indicated a difference in T_1 relaxation times between normal and infarcted tissue (*8*). Later studies have shown these differences to be minor and have suggested that to differentiate ischemia a paramagnetic contrast material is desirable. With gadolinium-DTPA, differences of 50% in T_1 relaxation times and 22% in T_2 relaxation times were determined in acute studies in dogs (*9*).

To decide if the NMRI studies would be superior to ^{201}Tl studies, however, many other questions would have to be answered. Since the experimental studies were done with animals, with ischemia and infarction produced experimentally, a method of producing stress in patients undergoing the NMR procedure must be devised. Secondly, if a contrast material is used, dissociation of the gadolinium in vivo and its toxic effect must be controlled. Thirdly, would the contrast material be as accurate an index of myocardial perfusion as ^{201}Tl? In general, technetium-99m DTPA is not thought of as a particularly useful myocardial imaging agent. Would gadolinium-DTPA be much better? Many years have been spent in trying to find a technetium tagged substitute for ^{201}Tl. Lastly, if a suitable paramagnetic contrast material is found and techniques of stress and equilibrium recording with NMR are perfected, will the improved spatial resolution of NMRI give greater clinical information than ^{201}Tl SPECT or is the resolution primarily dependent on the perfusion-diffusion pattern and thus similar information would be obtained with both techniques? If better spatial information is found, it must still be demonstrated that the sensitivity of NMRI would equal ^{201}Tl SPECT and that the ease of diagnosis of myocardial ischemia by means of the readily available isotropic, three dimensional reconstructions of SPECT can be equalled by NMR.

The above example illustrates the more complex considerations of determination of functional aspects of an organ. When only anatomical features are desired the competition from an NMRI test is easier to judge. We who have seen almost a virtual replacement of radionuclide brain scans by CT are particularly sensitive to such circumstances. For anatomical resolution, however, the primary competition will probable be between NMRI and CT. Studies looking for liver metastases merely have one more modality to add to the radionuclide, CT, and ultrasound studies now going on. As the trend to reduce the number of procedures performed on the same patient increases, greater attention must be paid to the individual advantages of a specific test for a specific disease entity and all modalities would be expected to be available from which an individual choice can be made.

The last area to be considered is nuclear magnetic resonance spectroscopy (NMRS). This technique is probably even closer to the rationale of nuclear medicine investigators than is NMRI, since the observed spectra must be interpreted not as an image but with respect to the relative intensities or quantification of the various peaks. Clinical applications of NMRS are still in the future but it is apparent even now that interpretation will be more sophisticated than mere pattern recognition and must involve an appreciation of the metabolic changes themselves. The biochemical and physiologic directions to which present day nuclear medicine is turning will make NMRS interpretation quite compatible with other activities of nuclear medicine personnel. Again, there is the question whether NMRS will provide metabolic information not already available from positron emission tomography.

In summary, it might be said that the relationship of nuclear magnetic resonance to nuclear medicine represents a compatibility of aptitudes, training, and methodology. It must be remembered, however, that nuclear magnetic resonance measurements are clinically quite immature, and it is in the interests of nuclear medicine personnel to guide the maturation process by use of the same experience that has helped nuclear medicine in its 50 years of clinical growth.

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