MIRDOSE 3.1 Gives Erroneous Results Under Windows NT

TO THE EDITOR: In a 1996 article, Michael G. Stabin (*1*) describes his widely used program MIRDOSE 3.1 for internal dosimetry estimation. It was written for the Microsoft Windows 3.1 computing environment.

In our institution, Microsoft Windows NT is rapidly becoming the standard desktop computing environment. Readers should be cautioned that MIRDOSE 3.1 can be installed and will load and appear to run under Windows NT 3.51 and Windows NT 4.0, but in fact gives erroneous results. We have confirmed this on Pentium and Pentium Pro central processing units. If the table of S-values is examined and many appear to be identically zero, that is indicative of this problem. It can be confirmed by inputting a simple example with a known answer, such as Example 6 in Part 2 of the *MIRD Primer* (*2*). Markedly different results indicate erroneous program functioning.

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REPLY: I appreciate Drs. Wendt and McCullough taking this opportunity to make the user community aware of the fact that MIRDOSE 3.1 does not run on the NT platform. The problem noted appears to be a case of the program not accessing the files for photon-specific absorbed fractions. I would not agree that this represents an error in the program, but rather use of the program on an unsupported platform. We have been aware of this issue for some time, and we have notified many users privately that MIRDOSE is not supported on NT machines (as it similarly is not supported on Macintosh, UNIX and other platforms).

MIRDOSE 3 and 3.1 were compiled in 1994 and 1995 in VisualBasic 3.0, in the Windows for Workgroups 3.11 environment. We were pleased to see that migration to Windows 95 did not require a new release of the software, but we became aware from several reports from users that the software as compiled does not work properly in the NT environment. We have discussed this problem with Microsoft Corporation, and it is possible that compiling the software in a more recent version of VisualBasic, under Windows 95, may produce a version that will work on NT machines. Or, we may need to compile a version directly on an NT machine. Our center does not have an NT machine, but we believe that we can use one within our company for testing and/or compilation. Thus, we may be able to release a new version that will be supported either in the Windows 95 or NT environment. We will keep the user community informed about this. Progress can be monitored through our web page at http://www.ora-u.gov/ehsd/ridic.htm, and we will also send announcements through the Dose-Net mailing list and by other means should a new version become available.

Additionally, Microsoft still does not have VisualBasic for the Macintosh; we do not envision a release of Version 3 for the Macintosh. There are, however, plans to rewrite the software in a form compatible to both Windows and Macintosh environments, and it is possible that Version 4, which will incorporate several other new features, may work on the Macintosh.

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Iodine-123-Iomazenil SPECT in Alzheimer's Disease

TO THE EDITOR: A 1997 article by Fukuchi et al. (*1*) made the interesting suggestion that ^{123}I-omazenil (IMZ) SPECT scans are more sensitive in the detection of Alzheimer's disease than ^{99m}Tc-HMPAO scans. Improved sensitivity of SPECT scans for this purpose is certainly needed, but the article raises several questions.

The main conceptual problem is the putative quality of these tracers. Although the early ^{123}I-IMZ images may be influenced by perfusion, the delayed images, which were reported to be most sensitive, probably reflect receptor density, and, therefore, neuronal density. Thus, in contrast to the authors' description of these scans as visualizing "neuronal activity" (p. 469), they may be better described as visualizing tissue atrophy, since lower counts probably reflect loss of receptor-bearing neurons. This, in turn, suggests that the extensive deficits seen by the authors in Alzheimer's disease patients are contributed to a large extent, if not completely, by focal atrophy in frontal and parietal cortex. Yet, such atrophy has not been reported by MRI, and the authors do not present a quantitative analysis of their own structural imaging. In fact, they state (p. 467) that the CT/MRI scans were largely negative except for "mild generalized atrophy," a common finding in the aged. Thus, it is unclear whether the delayed ^{123}I-IMZ images reflect metabolism (through perfusion), neuronal loss, or both, to an unknown degree.

The lack of theoretical face validity may not be fatal if the scans are empirically demonstrated to offer superior sensitivity. Such demonstration is hampered by methodological concerns in this case. First, the order of scans (HMPAO versus IMZ) is not specified, although the authors state there was an average interval of 1.36 mo between them. Second, the raters were apparently not blind to tracer type, but only to clinical history, thus introducing the possibility of bias. Third, no quantitative data are presented for the extent and location of deficits with either tracer. These factors, combined, make it difficult to interpret the results, especially in the presence of the conceptual ambiguity noted above and contradictory PET data (*2*).

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Quantification of Left Ventricular Function with Thallium-201 Myocardial Gated SPECT

TO THE EDITOR: I read with great interest the article by Germano et al. (*1*) titled "Quantitative LVEF and Qualitative Regional Function from Gated Thallium-201 Perfusion SPECT." Their article further validates the concept that gated SPECT can be effectively performed with ^{201}Tl to assess left ventricular function.

We presented this concept at the Society of Nuclear Medicine Annual Meeting in June 1996 (*2*) and published an article titled "Quantification of Left Ventricular Function with Thallium-201 and Technetium-99m-Sestamibi Myocardial Gated SPECT" (*3*). We are pleased that Germano et al.'s (*1*) article confirms our observations that were submitted earlier but delayed in publication.

Again, we are happy to learn that another research group has confirmed these results. We believe that gated SPECT with ^{201}Tl is both effective and reliable. Therefore, clinical sites that prefer ^{201}Tl for myocardial perfusion imaging can perform gated SPECT and obtain useful functional information that was once thought to be possible only with ^{99m}Tc-sestamibi.

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Is Technetium-99m-MIBI a Relevant Tracer to Tumor Response to Chemotherapy of Bone Lesions?

TO THE EDITOR: We do not agree with Taki et al.'s (*1*) conclusion that ^{99m}Tc-MIBI detects bone and soft-tissue lesions and assesses tumor response to chemotherapy comparable to ^{201}Tl. Technetium-99m-MIBI accumulation in tumors is modulated by blood flow, cell viability and the level of permeability glycoprotein (Pgp) expression (*2*). Technetium-99m-MIBI is a well-documented transport substrate for Pgp, which is induced by overexpression of the multidrug resistance (MDR) gene, which in turn is a major cause of chemotherapy resistance and failure (*3–5*). In MDR gene cells, a high concentration of Pgp on the cellular membrane induces a rapid excretion of ^{99m}Tc-MIBI; ^{99m}Tc-MIBI accumulation by MDR tumor cells remains low. This low ^{99m}Tc-MIBI uptake can help assess MDR gene overexpression (*6*).

Table 2 in Taki et al.'s (*1*) article clearly indicates such a possibility. Patients 10 and 12 had decreased ^{99m}Tc-MIBI tumor uptake postchemotherapy (−5% and −19% compared to prechemotherapy), which is consistent with MDR development. Uptake ratio of ^{201}Tl did not decrease (+21% and +1%), and the tumors did not respond to chemotherapy. Patients 23 and 25 seem more complex: ^{99m}Tc-MIBI uptake ratios increased after chemotherapy, although the tumors were nonresponsive (Table 2) (*1*). Thallium-201 uptake, however, decreased only moderately after chemotherapy (−18% and −3%, respectively), indicating residual tumor viability.

We conclude that the observation of ^{99m}Tc-MIBI uptake decrease after chemotherapy is consistent with either weakening of tumor viability or induction of MDR.

Technetium-99m-MIBI provides more information than ^{201}Tl in assessing tumor response to chemotherapy.

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Time for a Change?

TO THE EDITOR: Perhaps those of us in nuclear medicine should consider following the example of the American College of Physicians (ACP) and the American Society of Internal Medicine (ASIM). The ASIM was founded by some internists who did not believe that ACP adequately addressed the socioeconomic issues of medical practice, in view of ACP's great interest in education.

The American College of Nuclear Physicians (ACNP) was formed because it was believed by some nuclear medicine physicians that the Society of Nuclear Medicine (SNM) did not adequately address the practice concerns of physicians, being interested primarily in research and education. There remain some areas of duplication of efforts, although many important activities have been coordinated or combined.

ACP now appears to be close to joining forces with the ASIM. The members and leadership have concluded that there is really no longer a reason to have two different organizations. They want internal medicine to speak with one voice. In a survey of the 100,000 members of ACP and the 20,000 members of the ASIM, informing them of the possibility of a merger, reaction ran about 5 to 1 in favor of the merger. It might be interesting to poll members of both groups on their opinion about the desirability of a possible merger of SNM and ACNP, a merger, not a takeover of ACNP by SNM.

Not the least of the advantages of a merger of SNM and ACNP is the beautiful and luxurious building SNM now owns in Reston, VA.

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Gene Radiotherapy; Gene Targeted Versus Targeted by Gene Product

TO THE EDITOR: The editorial by Larson et al. (*1*) describes a very interesting and promising approach for in vivo detection of the expression of a gene delivered into tumor cells. In referring to a personal communication from one of the coauthors, the writers suggest the use of this approach also to deliver higher doses of therapeutic radiation to cells expressing a "marker gene." This method, which the authors call "gene-targeted radiotherapy," if demonstrated to actually work, is potentially extremely powerful. We, however, have concerns about the terminology they used to describe their approach.

The application of the methods of molecular biology have recently become more evident in nuclear medicine. This symbiosis can be extremely productive and result in significant progress in both tumor imaging and radiotherapy. As often happens in a new field, the terminology has not been standardized and different approaches are sometimes called by the same name. For example, we also have described a type of "gene-targeted radiotherapy" in an interview and article written by Kotz (*2*).

For the last 4 years, we have been developing our approach for targeting Auger-electron emitters (AEs) to specific genes using triplex-forming oligonucleotides (TFOs) as delivery molecules. This method combines the