

In summary, SNM CE in 2009 will be expanding to provide members and the larger medical community a bridge to the knowledge required for the future practice of our specialty and to recertification. The greatest challenge will be to convert this knowledge into docu-

mented improvements in our delivery of care through MOC Part IV.

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## From the Medical Internal Radiation Dose Committee

The Medical Internal Radiation Dose (MIRD) Committee was formed in 1965 “to provide medical and scientific communities with the most accurate estimate of the dose that a patient receives from radiopharmaceuticals administered for diagnostic studies” (1). The committee’s charter was to “collect, collate, and evaluate metabolic, chemical and nuclear data on various radiopharmaceuticals and merge this information into a realistic estimate of the patient dose using the most appropriate dose calculation techniques.” At its founding, Monte Blau, PhD, and Ed Smith, DSc, served as cochairs, and the initial membership also included John McAfee, MD, Richard Peterson, MD, James Robertson, MD, PhD, and Henry Wagner, Jr., MD. Mones Berman, PhD, Robert Loevinger, PhD, and Gordon L. Brownell, PhD, served as consultants to the committee. The group agreed that the mission of the committee would be the technical evaluation of dose and not the evaluation of hazards, efficacy, and other such topics as “critical” organ dose.

Early committee discussions focused on moving away from assumptions of uniform distributions of activity throughout the whole body and also on establishing a unified approach to performing dosimetry. The results of these efforts, published as MIRD Pamphlet No. 1 (Loevinger and Berman, 1968), revolutionized dosimetry by abandoning the use of the roentgen as a unit and devising a formulation that no longer used the specific  $\gamma$ -ray constant,  $\Gamma$ , and the geometric factor,  $\bar{g}$ , in absorbed dose calculations. In subsequent pamphlets, the MIRD Committee introduced the concepts of absorbed fraction and S value that now form the basis for almost all radionuclide dosimetry and that are embedded in such popular dosimetry software as OLINDA (2). Even more recently, the MIRD formalism has been extended to cellular and subcellular source and target regions, with the publication of a volume tabulating cellular S values (3).

Forty years after the publication of MIRD Pamphlet No. 1, the MIRD Committee is engaged in an expansion of its mission. To address the requirements of therapeutic nuclear medicine and the emerging use of  $\alpha$ -particle-emitting radionuclides, the committee is moving beyond “the technical evaluation of dose” for diagnostic studies and is cautiously espousing radiobiological modeling to help translate absorbed dose to biological effects for therapeutic studies. The committee has taken the first step in this direction with the recently published Pamphlet 20 (4). Pamphlet 20 uses the

multiregion kidney model of Pamphlet 19 to examine the biological implications of different spatial absorbed dose distributions delivered at different dose-rates. As shown in the Pamphlet 20, this analysis utilized the linear-quadratic model to characterize dose-dependent clonogenic cell survival and a model to describe repair of radiation-induced damage in order to arrive at a radiobiological model that accounts for the impact of dose-rate and spatial nonuniformity on cellular and organ survival.



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Radiobiological modeling requires expansion of the well-established MIRD schema described in Pamphlets 1–12 and in the MIRD primer (5). As a first step toward this objective, the MIRD Committee has extended the schema (Pamphlet 21, in press) to encompass calculations related to radiation protection as originally defined by the International Commission on Radiological Protection (ICRP). Accordingly, Pamphlet 21 is coauthored by 2 members of Committee 2 of the ICRP, who have endorsed the MIRD dose calculation formalism. To the relief of medical physics and radiation protection students, this should eliminate the confusion arising from having 2 different sets of symbols and equations representing the same physical quantities and calculations.

In recognition of the increasing prominence of  $\alpha$ -particle-emitter therapy in therapeutic nuclear medicine and the challenges that use of such high linear energy transfer emissions will present to absorbed dose estimation, the committee recently submitted a detailed review of  $\alpha$ -particle emitters considered or used in targeted radionuclide therapy as well as their dosimetry and radiobiology (Pamphlet 22).

Absorbed dose estimates for  $\alpha$ -particle emitters, as well as DNA-incorporated Auger-electron emitters, have highlighted a fundamental problem with the current dosimetry formalism in terms of the available dosimetric quantities and related units. In radiation protection or in the diagnostic use of radiopharmaceuticals (in the realm of stochastic effects), the product of absorbed dose in grays and the radiation weighting factor is defined as the equivalent dose. Equivalent dose values are designated by a special named unit, the sievert. Unlike the situation for stochastic effects, no well-defined formalism or associated special named quantities have

been widely adopted for deterministic effects observed in therapeutic nuclear medicine. As a first step in addressing this, the MIRD Committee has recently published a commentary on the issue (7). The commentary suggests that the barendson (to be abbreviated as Bd) be adopted as a specially named quantity for dose weighted to account for deterministic effects. A formalism for how to weight absorbed dose for deterministic effects is also proposed. As noted in the commentary, adoption of these proposals will require approval by the appropriate international organizations and acceptance by the scientific communities.

The MIRD Committee's move toward dosimetry for therapeutic nuclear medicine is further reflected by the upcoming publication of a dose estimate report for the first U.S. Food and Drug Administration–approved targeted radiotherapeutic combination,  $^{111}\text{In}$ - and  $^{90}\text{Y}$ -ibritumomab tiuxetan (Zevalin; Cell Therapeutics, Inc., Seattle, WA) (8). This report provides an independent and authoritative estimation of the dosimetry associated with this very promising and effective agent.

In 2008 the MIRD Committee also added to its published list of essential dosimetry resources. An updated version of the MIRD Radionuclide Data and Decay Schemes (9), originally published in 1989, is now available for purchase through SNM. The update includes 88 radionuclides that were not addressed in the earlier edition, bringing the total to 330 radionuclides. These reflect additional radionuclides that are either currently in use or offer promise for future use in imaging, other diagnostic applications, or therapy or as daughter products of these radionuclides. Accompanying this edition is a compact disk that provides access to the  $\beta$  spectra, tabulated decay data, decay schemes, and other data in largely unabridged electronic format.

The MIRD Committee's other 2008 activities included establishing an internship program, sponsoring a continuing medical education session on uncertainty in absorbed dose estimation at the 2008 SNM Annual Meeting, and organizing an upcoming symposium on radionuclide therapy and radiopharmaceutical dosimetry. The internship program is designed to give junior SNM members and those of the SNM Young Professionals Committee an opportunity to attend 1 or 2 MIRD Committee meetings per year and to work with internal dosimetry experts on 1 or more specific dosimetry-related projects. The internship duration is 2 y. The 2 recently selected interns will be highlighted in an upcoming Newsline article.

The MIRD Committee is also organizing the upcoming 3rd International Symposium on Radionuclide Therapy and Radiopharmaceutical Dosimetry (ISRTRD) to be held in conjunction with the 2009 SNM Annual Meeting in Toronto, Canada. These symposia are designed to bring together all disciplines concerned with radiopharmaceutical dosimetry and radionuclide therapy, with the objective of stimulating interdisciplinary scientific discussions. The 3rd Symposium will also include the 6th in a series of workshops on therapy with  $\alpha$ -emitters. This series originated with workshops held in Karlsruhe, Germany, in 1995,

organized by the Institute of Transuranium Elements (ITU), and in Toronto in 1996, organized by the U.S. Department of Energy. Subsequently, a series of international symposia on this topic was initiated by ITU, including meetings in Karlsruhe (1997, 2000); Heidelberg, Germany (2002); Düsseldorf, Germany (2004); and Aachen, Germany (2007). To put all of this together, the MIRD Committee is working with the Dosimetry Committee of the European Association of Nuclear Medicine and with organizers of the  $\alpha$ -particle–emitter therapy symposia.

Finally, as the committee continues to move toward the inclusion of dosimetric methods and radiobiological models for radionuclide therapy, I would like to repeat the appeal issued to the nuclear medicine community by the ICRP task group on the Protection of the Patient in Radionuclide Investigations in 1971 (10) and repeated in the 1988 publication of ICRP 53 (11) to secure “the maximum information possible from any investigation” of radiopharmaceutical agents. The objective of dosimetry is to predict response and to guide clinical investigation toward safe and effective implementation of diagnostic and therapeutic radiopharmaceuticals. These objectives can only be met if advances in computational and physics tools are coupled with advances in our understanding of the biokinetic behavior and radiobiology of radiopharmaceuticals. The latter requires that clinical and preclinical investigations of new radiolabeled agents be conducted with an eye toward collecting and publishing as much information as possible on the biodistribution and kinetics of the agent. The MIRD Committee stands ready to serve the SNM community toward this and other dosimetry-related objectives.

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