Guest Editor’s Introduction to Radionuclide Therapy: The Role and Options for Dosimetry in Clinical Practice

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The five publications that are included in this special section of Cancer Biotherapy & Radiopharmaceuticals under the theme entitled, Radionuclide Therapy: The Role and Options for Dosimetry in Clinical Practice, represent the outcome of two Continuing Education Sessions at the 2001 Annual Meeting of the Society of Nuclear Medicine (SNM). These sessions were organized by the SNM’s Medical Internal Radiation Dose (MIRD) Committee and reflect the changing focus of the Committee toward addressing the needs of the physicians and scientists involved in the application of radiotherapeutic agents. This is indeed timely as an ever-increasing number of radioactive therapeutic agents are being introduced for the treatment of a variety of diseases.

The basic goal of these radionuclide therapies, as in all forms of radiation therapy, is to ensure that the appropriate activity is administered to the patient to deliver a radiation absorbed dose to diseased tissues that will produce an effective treatment outcome without causing undesired effects in healthy tissues. In the field of radiation oncology, dose-response relationships for local control of homogeneous tumor groups have been determined empirically. The higher the radiation dose delivered, the more likely is tumor control. The dose of radiation that can be delivered to a tumor is, however, limited by the probability of serious normal tissue complications. Therefore, patient-specific treatment planning is performed in order to ensure delivery of the tumor dose prescribed to optimize the probability of tumor control relative to normal tissue complications. Patient-individualized dose calculations are not as yet routinely applied in the treatment paradigm for radionuclide therapy.

The absorbed radiation dose from internally deposited radionuclides is a major factor in assessing risk and efficacy when evaluating new radiopharmaceuticals for use in the treatment of disease; thus, there is general agreement that radiation dosimetry should be an integral part of new radioactive drug development. Agreement is not universal with regard to the application of radiation dosimetry for guiding the activity to be administered to an individual patient. Unlike external beam radiation therapy, which is usually prescribed in terms of absorbed dose, there is no standard approach for the treatment prescription of radionuclide therapy. Treatment may be prescribed in terms of administered activity, administered activity adjusted for patient specific parameters (e.g., body weight or surface area), or absorbed radiation dose.

The absorbed dose calculations used for radionuclide therapy are far more complex, but have generally been less patient-specific, than they are for external beam therapy and brachytherapy. In addition, the radiation dose rate received from internal emitters is highly variable and is often delivered over a protracted time frame; consequently, the relation between absorbed dose and radiobiologic effect may not be inferred directly from the external beam experience. Many investigators are refining their dosimetry models to be more patient-specific. These model refinements have included measurement of biokinetic parameters, adjustments for anatomical parameters (e.g., actual organ mass), measurement of suborgan and/or voxel parameters, and adjustments for clinical parameters.
(e.g., bone marrow reserve). As absorbed dose measurements become more patient-specific, it is anticipated that improved correlations between calculated absorbed doses and the clinically observed effects for both tumors and normal tissues will be obtained. In the end, a balance must be struck between clinical feasibility and scientific accuracy in the attempt to bring therapy with internal emitters to a similar status as is routine in external beam therapy.

It therefore follows that improvements in the success of radiotherapy with internal emitters depend on the optimization of radiation doses to tumor and healthy tissues in individual patients, which in turn requires patient-specific measurements and application of models for estimating radiation dose. This latter viewpoint is somewhat controversial in that many believe that as long as simpler empirical methods provide a safe and effective treatment, there is no need to implement time-consuming (and hence more expensive) patient-specific dosimetry methods. It is the responsibility of the radionuclide therapy community to collect the necessary data and perform the appropriate analyses to shed further light on the optimal treatment approach in order to ensure that the best level of medical care is provided to patients.

The five publications included in this special section describe treatment strategies for radioactive agents, in both nonmyeloablative settings, where bone marrow toxicity is usually dose-limiting, and myeloablative settings, where other normal tissue toxicities may be dose-limiting. They also evaluate the role of radiation dosimetry in guiding the administration of these agents and in developing dose-response and dose-toxicity relationships. The first article by Stephen Thomas entitled, “Options for Radionuclide Therapy: From Fixed Activity to Patient-Specific Treatment Planning,” provides an historical overview of the early use of selected radionuclides in therapy and reviews the options for delivering radionuclide therapy. The second article by Ruby Meredith entitled, “Clinical Trial Design and Scoring of Radionuclide Therapy Endpoints: Normal Organ Toxicity and Tumor Response,” reviews the toxicity and efficacy scoring systems used in clinical trials and summarizes the available information on normal tissue toxicity and response from radionuclide therapy. The third paper in this series by James Sisson entitled, “Practical Dosimetry of $^{131}$I in Patients with Thyroid Carcinoma,” describes radioiodine treatments of patients with well-differentiated thyroid carcinoma and concludes that radiation dosimetry is a practical method for improving $^{131}$I therapy in these patients. The fourth article by Gerald DeNardo et al. entitled, “Radiation Dosimetry for Radionuclide Therapy in a Nonmyeloablative Strategy,” reviews the role of radiation dosimetry in radionuclide therapy studies in which bone marrow toxicity is dose-limiting. The final publication in the series by Hazel Breitz entitled, “Dosimetry in a Myeloablative Setting,” reviews high dose radionuclide therapy studies, and examines the role of radiation dosimetry in these studies.