Introduction to Kidney Dose–Response for Radionuclide Therapy

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EDITORIAL

The proceedings of a MIRD-sponsored continuing medical education session entitled, “Kidney Dose–Response for Radionuclide Therapy,” held at the 50th Annual Meeting of the Society of Nuclear Medicine, in New Orleans in 2003, have been collected in this special section of Cancer Biotherapy & Radiopharmaceuticals. A few years ago, hematologic toxicity was the focus of concern in radionuclide therapy. The shift to concerns over renal toxicity reflects a number of developments in radionuclide therapy. Although the developments encompass, for example, peptide-mediated receptor targeting,1 metabolic targeting using bone-seeking radionuclides,2 and engineered low-molecular-weight multivalent targeting,3 these can be generally described as a shift to constructs that have molecular weights substantially lower than the 150,000 daltons of intact antibodies. These smaller agents clear much more rapidly from the circulation than intact antibodies and, therefore, require substantially greater administered activities to deliver tumoricidal absorbed doses.

The higher administered activities, the rapid-clearance kinetics, and, most importantly, observations of delayed renal failure in a number of patients at kidney total absorbed doses not found to be toxic in external-beam radiotherapy experience2,4 have required a reexamination of:

(1) the manner in which external-beam experience is used to predict radionuclide therapy toxicity
(2) the use of total absorbed dose as a measure of potential toxicity without consideration of the rate at which the total absorbed dose was delivered
(3) the value of the mean absorbed dose over a normal organ volume as a predictive measure of toxicity, particularly when the organ is as anatomically and radiobiologically complex as the kidney.

The papers included in this special section provide a starting point for addressing these questions. The first paper presents an overview of the clinical aspects of radiation nephropathy. The second paper examines how the linear quadratic equation, developed to model cell-survival measurements following external-beam radiation, may be extended to account for the impact of a time-varying dose rate as such that occurs in radionuclide therapy. The third paper examines the effect of construct molecular weight and radionuclide choice upon the spatial distribution of the absorbed dose rate in the kidney. The fourth paper provides a detailed review of the external-beam radiotherapy experience as it relates to renal toxicity. The CME session proceedings are summarized and put into perspective by one of the Guest Editors in the last paper.
REFERENCES


