Dosimetry in Radiopharmaceutical Therapy

TO THE EDITOR: Regarding "Dosimetry in Radiopharmaceutical Therapy" (*1*), in general this is a very good paper, and I am pleased to see attention being drawn to this important topic. Unfortunately, however, it ends on the familiar sour note that we should not do any dosimetry at this time, as it may not be perfect, and we should wait and wait until there is absolute proof of its usefulness.

First, as a minor point, the 1962 Benua "dose to blood" method (*2*) is completely outdated, being superseded by several detailed dosimetry models for the red marrow (*3*). Dose to blood itself is not relevant to internal dose calculations; this was a poor early surrogate for the truly important dose to active red marrow and ignores valiant efforts by many (Spiers, Eckerman, Bolch, and others) to develop good marrow dose models. The Eckerman model is implemented in the easy-to-use OLINDA/EXM software (*4*). The Benua method should not be cited as a recommended standard dosimetry method.

Second, the authors state that "Treating patients according to [prescribed tumor-absorbed dose] is a concept extended from [external-beam radiotherapy] practice. However, there are few dose–response data available for [radiopharmaceutical therapy] on which to base treatment prescription." They also state that "dosimetry is not performed because dose–response data are lacking, and dose–response data are lacking because dosimetry is not performed." The authors conclude that "If dosimetry is to become more than an academic exercise, we need to show that it makes a significant difference to clinical outcomes with [radiopharmaceutical therapy]. Ultimately, the only acceptable way of achieving this is through multicenter randomized controlled clinical trials comparing dosimetry-based prescriptions with one-size-fits-all activity-based prescriptions." The authors did not mention Garin et al., who said, "Compared with standard dosimetry, personalized dosimetry significantly improved the objective response rate in patients with locally advanced hepatocellular carcinoma." (*5*). As the authors note, we cannot mature in our understanding of dose–response relationships with no understanding whatsoever of what the potential radiation doses are. Our colleagues in external-beam radiotherapy knew years ago that dosimetry was essential to radiation therapy. Their methods were not perfect at the start but have improved over the years. If we continue to refuse to even start, we will never progress. Furthermore, for any future therapy applications of radiation in these patients, radiation doses from prior therapies are needed.

Thus, as noted some years ago (*6*), radiopharmaceutical therapy patients are clearly being treated at a lower standard of care than external-beam radiotherapy patients. I ask anyone advocating against calculation of patient-individualized dosimetry of cancer patients whether they would accept this if it were their spouse, child, or other loved one receiving therapy without optimization of their therapy, which requires patient-individualized dosimetry. We need to break this vicious cycle of endless, pointless discussions while inaction dominates and patients are given substandard medical care.

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Reply: Dosimetry in Radiopharmaceutical Therapy

REPLY: We are grateful for the commentary on our paper (*1*) by Dr. Stabin and agree with almost everything he says (*2*). We would, however, take issue with his characterization of our conclusions, especially the "sour note that we should not do any dosimetry at this time . . . ." This is certainly not the conclusion we intended to convey and is difficult to reconcile with the fact that the paper is devoted largely to how to do dosimetry.

We probably all agree that the main goal of performing dosimetry is to improve clinical outcomes. This means it must, in some way, affect the treatment prescription. A patient-individualized, dosimetry-driven treatment prescription will almost certainly be different from a standard "one-size-fits-all" treatment prescription. Most medical physicists and nuclear medicine physicians likely agree that an individualized approach would be better, but it remains to be determined how much better in terms of objective clinical endpoints such as progression-free survival and overall survival. Other stakeholders (e.g., medical oncologists, pharma sponsors, medical insurers, administrators, and perhaps even patients themselves) may resist the additional time and effort, expense, and logistic complexity unless there is a demonstrable and significant cost benefit. Compelling data from randomized, multicenter clinical trials comparing a dosimetry-based prescription with simpler alternatives are therefore

essential for broad acceptance of dosimetry-based radiopharmaceutical therapy. Although specialists in our field may not need convincing, the greater community very much does.

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