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Reply LTE, Single Time Point Tumor Dosimetry Assuming Normal Distribution of tumor kinetics

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Dear Editor,

We thank the authors for their careful reading of our paper and for illustrating the value of single-timepoint imaging in the practical implementation of patient-specific dosimetry for radiopharmaceutical therapy (1). We chose to focus on fundamental knowns and unknowns, particularly tumor dose-response relationships, rather than addressing the admittedly challenging logistics of patient-specific dosimetry. As noted in the letter to the editor, single-time point formulations exist that may be applied to normal organ and tumor absorbed doses. Although due to the potentially larger variability in tumor kinetics there is a larger error in tumor activity quantification, depending on tumor size and this likely dominates the uncertainty in the dose calculations. The uncertainty associated with these methods is unlikely to be clinically impactful. Clinical experience suggests that a several fold-difference in in tumor absorbed dose is needed to overcome the impact of differences in tumor radiosensitivity, dose distribution within the tumor, dose-rate differences and other biological effects that impact tumor response to therapy in patients.

Recognizing the imperative of achieving the right balance, we would promote an approach that enables the treating physician to consider the multi-faceted tradeoffs among absorbed dose accuracy, health economics, the challenges of a busy clinic, and clinical aspects of the disease into establishing treatment doses. By defining a level of certainty or uncertainty to all calculated absorbed dose values, including those obtained by reduced or single-time point methods, the treating physician is provided the information needed to make what is ultimately a clinical decision for a specific patient. If, based on the disease extent and endpoints to be achieved, the physician may seek greater precision in the normal organ and tumor absorbed dose estimates, an extended multiple time point imaging protocol may be devised in conjunction with the medical physicist.

It is encouraging, that in addition to the work described by the letter authors, the loss of accuracy associated with using a single imaging time point compared with using multi-time points has been recently investigated. Amongst the ever-growing list of papers in this area, we note the early work on Peptide Receptor Radionuclide Therapy by Madsen (2) and Hänscheid (3) and the more recent extension of this approach to other RPTs by Hou (4) and Jackson (5).

We thank the letter authors and the editor for giving us the opportunity to address this important topic.

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