In Reply to Oskan

We would kindly thank Mr. Oskan for his critical comments on our international multicenter work, “Planning benchmark study for SBRT of liver metastases,” which has been completed with the participation of 35 experienced liver stereotactic body radiation therapy (SBRT) centers and received an independently verified Radiotherapy Treatment Planning study Guidelines (RATING) score of 98% (201 out of 205 points). In his letter, he implies that we are advocating a change of general SBRT practice from the established planning target volume (PTV) surrounding isodose to “utopic” gross tumor volume (GTV) D50% prescription concepts. The careful reader will perceive that this is not the case. However, it is important to consider the striking physical and clinical evidence supporting the use of GTV D50% for plan evaluation as a predictor for efficacy and especially a means for harmonization of dose prescription and reporting in future clinical trials.

(1) The main problem of published studies on SBRT was often the nonstandardized dose reporting with statistical analyses of the prescription doses alone. With that, the minimal and maximal doses within the PTV stayed unknown, making dose-response evaluations almost impossible.

(2) One also has to keep in mind that the PTV is not defined by any anatomic concept like the GTV. In fact, the GTV is the most robustly defined volume in SBRT whereas the PTV is dependent on irradiation platforms, motion management techniques, and tissue heterogeneities. In essence, the PTV surrounding isodose could be described as “theoretical” as it does not reflect the actual delivered dose in vivo, whereas the GTV D50% is comparatively more robust against dose calculation and delivery inaccuracies as has been demonstrated for countless techniques.

(3) That said, we need to consider the available clinical evidence that supports the physical concepts of robustness. Arguably, the largest data come from our German Expert Group on liver SBRT, where we pooled 623 metastases for joined analysis. We only found a weak dose-response-relationship between PTV surrounding isodose and local control, and hence used isocenter maximum dose, which is a close surrogate to GTV D50%, as primary dose parameter for modeling. In a later work on 1500 lung SBRT cases we could demonstrate a similar dose-response-relationship between GTV D50% and local control.

Still, the question remains: how should we prescribe and report SBRT doses in general practice and especially in planned multicenter, multiphase prospective trials to be able to compare applied doses to the outcome? The answer is, it is important to look at several parameters: the PTV (near) surrounding isodose for predicting recurrences as a consequence of insufficient marginal dose and the GTV D50% and the (near) maximum to model in-field recurrences, as advocated in our planning and clinical studies. In clinical practice, of course, all parameters should be optimized and safely maximized with well-known dose constraints for each individual clinical case, and in fact the 3 presented cases have been successfully treated with GTV D50% optimized dose distributions. However, in controlled multicenter, multiphase clinical trials with varying technologies, other means for harmonization are needed, as a single dose prescription parameter is not sufficient to be able to define a reproducible dose distribution.

To conclude, we would like to state “Utopias are often just premature truths” (Alphonse de Lamartine) and encourage all pioneers in the field of radiation oncology to continue to strive for improved quality and optimal outcome by critically reassessing common practice.

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References