Dose Tolerance for Stereotactic Body Radiation Therapy

Normal tissue complication probability (NTCP) results were detailed in the July 2001 issue of Seminars in Radiation Oncology\(^1\) for conventionally fractionated radiation therapy. After 7 years, an extensive collection of stereotactic ablative body radiotherapy (SABR) or stereotactic body radiation therapy (SBRT) dose-tolerance limits was presented in the October 2008 issue of Seminars in Radiation Oncology,\(^2\) but estimates of risk were not yet available. We now have sufficient data to combine the 2: NTCP for SBRT.

Physicians need a single parameter to make a clinical decision for each critical structure in the treatment plan. Ideally, this parameter would be directly associated with the expected outcome like NTCP. If every patient’s tumor control probability (TCP) was 99% or higher, and if every patient’s NTCP was 1% or lower, we would not need surrogate metrics like the conformity index, tumor coverage, and dose-tolerance limits. Note that in 3 consecutive sentences, we went from “need” to “ideally” to “if,” and in reality TCP and NTCP are often still uncertain, and are rarely as good as 99% and 1%, so we usually are highly dependent on the surrogate metrics of plan quality. In this issue of Seminars, we focus on both clinical practice and rigorous statistics, spending as little time in the middle as possible. Maximum likelihood parameter fitting and other statistical methods are required to obtain reliable estimates of risk, but the focus of this work is on the clinical utility.

Dose-tolerance limits are the stable bridge between clinical practice and rigorous estimation theory. Even as estimates of NTCP are continually updated with every new publication containing toxicity estimates, the same dose-tolerance limits can usually still be maintained, as long as the new estimate of NTCP is not dramatically different than the current expectations. This strategy of a constant dose limit is more stable than attempting to maintain a fixed NTCP limit, as estimates of NTCP continue to evolve in each new study.

The selection criteria for data in this issue of Seminars are the complete opposite of the criteria for the American Association of Physicists in Medicine (AAPM) SBRT Working Group (WGSBRT). The WGSBRT manuscripts are named High Dose per Fraction, Hypofractionated Treatment Effects in the Clinic (HyTEC). Many members of WGSBRT were authors of Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC),\(^3\) and they used the same primary ground rule: all data must already exist in the peer-reviewed literature. In that endeavor for SBRT, however, many anatomical critical structures were found to have too few published dose-response models to evaluate. The selection criteria for this issue of Seminars, therefore, are the complete opposite: each of these articles after the introduction presents new data and dose-response modeling from another institution, for a critical structure that previously did not have many published dose-response models for SBRT, or where an additional new model could supplement the information that had been sparse. We hope that both projects provide enduring value to the field.

SBRT and other high dose per fraction techniques have now been in clinical use for more than 20 years\(^4,5\) but initially the number of patients was small and it has taken most institutions quite some time to publish long-term statistical outcomes data for normal tissue tolerance. In 2002, the first Radiation Therapy Oncology Group (RTOG) trial for SBRT, RTOG 0236,\(^6\) was instituted. This was followed by several other RTOG trials 0618,\(^7\) 0631,\(^8\) 0813,\(^9\) 0915,\(^10\) and 1021,\(^11\) as well as the European co-operative trials such as CHART\(^12\) and ROSEL.\(^13\) The statistical outcomes data from these trials and several institutional studies are now emerging.

To help navigate this transition from expert opinion to statistical knowledge, the Dose-Volume Histogram (DVH) Risk Map\(^14,15\) includes a variety of information to show the state of the literature for each critical structure. For a given dose descriptor, the DVH Risk Map includes a plot of all published dose-tolerance limits in 1–5 fractions. From among those, for each fractionation, the highest commonly used limit is selected as the “high-risk” limit. From the remaining limits below a margin of safety, another limit is selected as the “low-risk” limit. Estimates of the risk level of the dose-tolerance limits are interpolated from statistical analysis of clinical data.

For relatively acceptable toxicity like grade 1–3 rib fractures and chest wall pain,\(^16\) the high-risk limits have 50% risk and the low-risk limits have 5% risk. The Emami et al\(^18\) work used...
50% and 5% risk levels for all critical structures whereas this effort used clinically acceptable ranges for each. In structures like aorta or spinal cord, where complications must be avoided, the high risk limits are closer to 3% and the low risk limits have about 1% risk in this issue of Seminars. These statistically based guidelines can help clinicians gauge the level of safety for each patient.

This issue of Seminars in Radiation Oncology is different from all previous issues, in that each institution's article contains a new clinical dataset that has never before been published, each of which has NTCP for SBRT, and almost all have a DVH Risk Map. Aside from those additional features, the articles still have the high-quality insightful and visionary reviews that you can expect from Seminars throughout the past quarter of a century.

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References