Clinically Relevant Standards for Intensity-Modulated Radiation Therapy Dose Prescription

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Intensity-modulated radiation therapy (IMRT) offers definite advantages over traditional three-dimensional (3D) treatment methods but at the expense of increased complexity, to say nothing of increased labor. Clinicians involved with multicenter clinical trials have learned that both IMRT and 3D treatment plans can be difficult to compare among institutions because of varying physician preferences in defining the tumor bed and nodal volumes on which the radiation is targeted (1,2). However, with 3D treatment planning, we can expect, at least, that methods of radiation dose prescription, calculation, and reporting are reasonably unambiguous if investigators follow a common framework for target definition and prescription, such as Report 50 of the International Commission on Radiation Units (3), and for dose determination, such as the Task Group 51 report of the American Association of Physicists in Medicine (4). With IMRT planning, this expectation is much less certain and may fail completely.

The difficulties already encountered with 3D are compounded in IMRT by the presence of many more variables, such as the more numerous and more ambitious dosimetric goals of an IMRT plan (eg, assigning dose limits to multiple critical normal tissue structures), the wide latitude available when choosing dosimetric objectives and their relative priorities, and the spectrum of commercially available treatment planning systems (TPSs). Each such system attempts to meet the user’s stated objectives by means of a unique algorithm that has its own set of preferences that cannot be controlled by the user. Therefore, multiple factors conspire against a straightforward harmonization of IMRT planning standards among institutions.

In this issue of the Journal, Das et al. (5) raise important and timely issues concerning the variability in IMRT planning and reporting among institutions. Their principal finding is that different institutions, when employing different IMRT planning software, may produce treatment plans that differ dramatically with regard to indices such as the minimum dose delivered to the target. This information is valuable for radiation oncologists and medical physicists who take part in or who manage multicenter clinical IMRT trials. The study by Das et al. (5) also provides a large and relevant clinical dataset on the subject of target dosimetric accuracy according to various metrics and for multiple institutions, planning systems, and disease sites. The authors are to be commended for providing this dataset to the radiotherapy community and for their efforts in analyzing 803 clinical IMRT plans.

We are in complete agreement with Das et al. (5) that greater harmonization of methods for IMRT dose specification and reporting is needed. In our roles as the principal investigator (LK) and physics cochair (JW) of the Radiation Therapy Oncology Group (RTOG) 0529 trial examining IMRT for anal canal carcinoma, we have experienced firsthand the need for IMRT standardization. Because there are no prevailing standards for dosimetric acceptability of pelvic IMRT plans, an ad hoc set of standards had to be devised that was based largely on the clinical intuition and test planning of the investigators who were organizing the trial. Other trials, such as the RTOG 0415 trial for prostate cancer and the RTOG 0522 trial for head and neck carcinomas, have also had to develop their own sets of IMRT dosimetry guidelines without the support of prevailing standards.

The question, then, is how to go about setting universal IMRT planning and reporting standards. First, we suggest abandoning any reference to the dose delivered to the isocenter (the point of rotation of the treatment unit). We thoroughly agree with Das et al. (5) on this point. In our own experience, the isocenter rarely receives the prescribed dose regardless of the disease site and frequently is located outside any of the planning target volumes (PTVs). When the isocenter is located inside a PTV, it may lie within or at the boundary of an air cavity, where dose calculation may be less reliable than usual. Specifying the dose at the isocenter is especially problematic when treating head and neck cancer, as illustrated by Das et al. (5). In our own experience, it has often been necessary to ignore the isocenter and instead specify the dose at a selected point in the soft tissue within the primary gross tumor volume. When completing the plan, we typically rescale all doses upward or downward by a fixed ratio, just as in 3D radiation planning. This rescaling of dose brings the PTV dose into good overall agreement with prescription, and success is usually determined by the fraction of the PTV that receives the nominal radiation dose. However, much uncertainty exists in such a method regarding the “right”, or even an acceptably good, result, thus highlighting the value of IMRT planning and reporting standards.

Second, we suggest setting reasonable limits on how much radiation over the peak dose (relative to the intended dose per the physician’s prescription) is acceptable with IMRT. On this point, we are also in agreement with Das et al. (5). Because the actual clinical impact of the peak radiation dose is not yet well understood, we chose not to specify peak dose in the RTOG 0529 trial. However, in our own clinical IMRT practice, we generally limit
the percent overdose to approximately 10% but recognize that this choice is only conventional and is not dictated by clinical data or by widely accepted guidelines.

However, unlike Das et al. (5), we are not persuaded that the median radiation dose is very useful as an indicator of IMRT plan quality. Although the median radiation dose may be strongly associated with the prescription dose, as was demonstrated in figure 1 of Das et al. (5), its clinical utility is open to question. The median dose, like any single value that is used to represent the overall quality of a complex dose–volume histogram (DVH), can conceal as much as it reveals. Niemierko (6) has noted that DVHs that have identical median (and mean) doses can have very different amounts of inhomogeneity; thus, median and mean doses may not by themselves be highly relevant in the clinic. We have seen many examples of such behavior in our daily practice and assume that others have as well.

Likewise, we believe that the minimum radiation dose has serious limitations as an IMRT plan quality indicator. Others have cautioned, on theoretical grounds, against attaching importance to a minimum PTV dose without knowing the volume over which it occurs (7). Furthermore, the minimum dose to the PTV tends to occur either in the buildup region (which consists of skin and other superficial tissue and unavoidably receives a reduced dose because of the nature of the x-rays being used for treatment) or at the margins of the intended radiation field but most often adjacent to a normal organ at risk. Clinicians have well-founded reasons to accept such peripheral imperfections in target dose, especially when the goal is to protect normal organs at risk, as long as treatment of the clinical target volume (the area of suspected microscopic disease) is not compromised. The widespread (and perhaps almost universal) practice of accepting or rejecting dosimetric imperfections based on their exact location may explain why the concept of equivalent uniform dose (6), which assigns equal weight to all portions of the PTV, has a low level of acceptance in clinical practice, as noted by Das et al. (5). Correct weighting of different portions of the PTV would require knowledge of the spatial distribution of clonogens, which (to make things even worse) would be time dependent, especially for rapidly shrinking tumors. Acquiring even a good estimate of this distribution and following it over time would (even if possible) involve effort and costs that may be prohibitive.

The findings presented by Das et al. (5)—particularly the striking variation in the scatter in minimum PTV dose values among institutions—seem to support our doubts about the utility of the minimum dose. The authors specifically call attention to the fact that the institution using Pinnacle for IMRT planning and the one using Oncentra observed extremely different patterns of PTV minimum dose. We suggest that if the PTV minimum dose is actually relevant to clinical outcome, then there should be some observable difference in treatment efficacy between these two groups of patients. This is an interesting point that was not addressed by Das et al. (5) but should be in a future study. If real differences cannot be observed between cohorts with such different minimum dose distributions, then the minimum dose, by itself, may not have much to say about the actual clinical utility of an IMRT treatment plan. The power of such a study might be further enhanced by grouping the two systems with a low degree of observed scatter in the PTV minimum dose (Pinnacle and Eclipse) and the three systems with a much higher degree of scatter (Oncentra, BrainScan, and XiO).

For IMRT planning in our practice, we prefer to use traditional indicators of plan quality such as the percentage of PTV encompassed within the radiation prescription isodose surface ($V_{100}$). Clinicians intuitively want to know how much of the PTV is covered or missed by the prescription dose. As we have suggested, isocenter dose, median dose, and minimum dose may not be dependable as IMRT specification parameters. For example, a clinically suboptimal plan, such as one that underdoses a substantial volume of the PTV, may nonetheless comply with a criterion that is based on isocenter or median doses. However, a DVH that has an acceptable index of $V_{100}$ simply cannot have a large volume of PTV underdose, whatever its other shortcomings may be. The question of what constitutes “acceptable” remains to be settled by the radiotherapy community.

We do note one limitation in the study by Das et al. (5) that was not clearly acknowledged as such by the authors—namely, that a change of planning software (TPS) simultaneously implies a change of institution. That is, no TPS was used by more than one of the clinics in the study. Therefore, it is impossible to determine just how much variation in dosimetry data from one center to another was caused by the varying TPS and how much was caused by the varying methods and preferences of the radiation oncologists. For this reason, we are wary of any suggestion that this study indicates the superiority of one planning system over another. For example, on the basis of differing amounts of minimum-dose scatter between the Oncentra and Pinnacle cohorts of prostate (and only prostate) plans, Das et al. (5) suggest that Pinnacle may provide a superior IMRT plan and that the question may be fully answered by further evaluation of the planning systems. The confounding factor is that TPSs are used by people who bring to the work their own standards and styles. Although we are longtime Pinnacle users, we remain to be convinced that these data carry a strong message about the TPS themselves, independent of how they are used. We agree that some software is better than others, and this may yet prove to be true in this case. But to settle the question, it would be necessary to analyze dosimetric results from multiple TPS used by the same set of practitioners and based on the same (or similar) sets of patients. The study by Das et al. (5) has many strong points, but it was not structured along those lines.

In summary, we agree with Das et al. (5) that patients are likely to benefit when there is greater harmonization of prescription and reporting standards for IMRT plans. Widespread use of IMRT planning standards would not only facilitate multicenter clinical trials but would also provide clinicians with solid guidance in their everyday practice on the question of what constitutes a “good” IMRT plan. At the same time, any standardization should be done in a way that prioritizes clinical utility and preserves flexibility for the practitioner to encourage acceptance. The work of Das et al. (5) is commendable and should stimulate further study, but its particular set of quality indicators may not point toward the most practical set of guidelines. Although median dose is easy to visualize on a DVH, it may not be the surest guide to sound planning decisions. Any written standards that are to be distributed in the radiotherapy community should be formulated with an eye to intuitive appeal and probable or demonstrated clinical impact, or we should not be surprised if general acceptance remains elusive.
References


