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Editorial

Updating historical normal tissue dose/volume constraints to current levels of treatment precision and accuracy

Radiotherapy practise is a balancing act between prescribing (and delivering) high doses to tumours while restricting the doses to critical normal tissues to be within established limits. Our collective knowledge about the radiation tolerance of various organs has for more than 30 years been formulated in so-called dose/volume histogram (DVH) constraints, ever since the hallmark paper of Emami et al, now cited more than 3800 times [1]. This has been updated, but even the most recent compilations of radiation tolerance data for conventionally fractionated treatments collected in the Quantec papers [2] still largely reflect practice of 3D conformal radiotherapy.

However, radiotherapy is a rapidly developing field which is integrated with other treatment modalities including immunotherapy [3,4] and emerging theranostics [5,6] procedures. Even in radiotherapy alone technology and techniques are changing quickly [7]. A lot of these changes are aimed at better physical targeting thereby reducing margins and improving conformity of the delivery. This rapid development can affect our ability to utilise clinical experience from the past for future practice. More recent compilations of normal tissue toxicity are available for hypofractionationation (HyTEC) [8] and pediatric radiotherapy (PENTEC) [9]. To make matters worse radiotherapy outcomes are often occurring late: be it confirmed long-term survival, recurrence or late toxicity. This is clearly visible in the PENTEC data where investigators struggle to extract high-quality dose/volume planning data from treatments often more than 30 years old [10,11]. Not only are the changes in technology fast but also the feedback loops that confirm that the change has been for the better are slow.

This is where the paper by Stroom et al [12] in the present issue of our journal is of interest. The authors propose to adjust DVH constraints to account for better accuracy in targeting. As the ability to confine dose to the target improves, the likelihood of spilling dose to surrounding critical structures diminishes. If the underlying radiobiology does not change, this should result in changed DVH constraints for treatment planning. The authors develop a mathematical framework to recalculate the constraints for organs at risk in terms of maximum dose and various dose/volume endpoints.

The concept is demonstrated on data of 348 patients treated for a variety of cancer types with different fractionations. This shows the potential of the method and illustrates how it can be applied to parallel and serial organs. However, it is not yet a recipe ready to apply for others who instead need to carefully analyse their own data and possibly commence with one tumour stream for which the technological improvements can be well quantified on a population basis. The large uncertainties affecting historical DVH data mentioned already in the context of the PENTEC work will make this more difficult [11] but possibly more successful when working with local data.

The use of geometric safety margins for targets [13] and organs at risk [14,15] has been the most established method to account for uncertainties in treatment planning and delivery. More recent strategies to account for uncertainties explicitly take the uncertainty distributions into account and are referred to as probabilistic planning methods [16,17]. These are currently the standard approach for proton and particle therapy, often also called robust planning. An interesting application of this concept incorporating anatomical variations in individual patients recently demonstrated a different way to take uncertainties into account [18]. In any case, robust planning needs to be used when comparing proton and photon plans to select patients who benefit the most from protons [19]. As this decision is typically dependent on organ at risk dose, the paper by Stroom et al [12] provides some useful insights on the photon part of the comparison as the competing photon treatment will generally also be at highest achievable geometric accuracy.

The approach suggested by Stroom et al. could have additional benefits in the context of clinical trials. There is often reluctance of conducting trials in radiotherapy that could be outdated in terms of technology by the time they are ready for evaluation [20]. As can be seen in the context of proton radiotherapy, this can lead to gaps in evidence which in many countries held back the introduction of the technique. The promise of approaches such as the one by Stroom et al [12] could be that dose/volume based outcomes can be translated to the new dose delivery paradigm provided all relevant parameters are accurately captured, a long standing request of co-operative clinical trials groups.

'We stand on the shoulders of giants' (attributed to Sir Isaac Newton) when we optimise treatment plans using DVH constraints and margins. Our 'giants' have conducted clinical trials and reported on findings which inform what we are doing today. Given the fact that toxicity from radiation can develop many years after treatment delivery we are often required to refer to clinical experience that is based on different technology and techniques [21]. This is often acknowledged but not much is done about it. The paper by Stroom et al [12] gives some pointers as to how to deal with this.

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Declaration of competing interest

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Tomas Kron
Peter MacCallum Cancer Centre, Melbourne, Australia
Sir Peter MacCallum Department of Oncology, University of Melbourne, Australia
Centre of Medical Radiation Physics, University of Wollongong, Australia

Marnix Witte
Netherlands Cancer Institute, Amsterdam, the Netherlands

Ludvig P. Muren
Danish Centre for Particle Therapy, Aarhus University Hospital, Aarhus, Denmark
Dept of Clinical Medicine, Aarhus University, Aarhus, Denmark