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Green Technical Vision - Expert Opinion

**GTV Expert Opinion: The Past Is Part of the Prescription: Spatially Aware Cumulative Dose Assessment for Complex Reirradiation**

The technical requirements in this complex case (a third high-dose course to the skull base) center around the rigorous estimation of the cumulative 3D equieffective dose and the associated uncertainty in that estimate [1]. In this scenario, the spatially-aware cumulative dose assessment is a prerequisite for determining whether a third course of re-irradiation is technically feasible, and for defining the permissible aggressiveness of the focal treatment strategy that can be pursued.

The first prerequisite is that the DICOM dose and structure set files must be available for all prior treatments, preferably with treatment records confirming the number of fractions delivered. These datasets must then be imported into the treatment planning system.

Here, an image registration-based approach using deformable image registration (DIR) was used for dose accumulation. The cervical spine and the skull base are prone to complex anatomic deformations. DIR can be a useful technique for mitigating the impacts of these deformations. When using this technique, the uncertainties in the total dose should integrate both the voxel-level uncertainties in the registration, along with the associated dose gradients. This uncertainty-aware approach is especially important when treatment decisions rely on sparing portions of previously irradiated neurovascular structures while escalating the dose to focal meningeal disease.

We note that DIR is not available at all institutions, and is not necessarily a prerequisite for accurate cumulative dose assessment in reRT, even in this case. Oftentimes in the head and neck region, when a global rigid registration is inadequate, OAR-specific registrations can be used to calculate cumulative dose in a specific region of interest (essentially a 'manual' DIR). Alternatively, when the uncertainty in image registration-based strategies is too high, near-maxima point dose summation can sometimes still yield acceptable results, but this is highly patient-specific.

Treatment planning based solely on point-dose cumulative estimations is overly conservative in cases with partial dose overlap. This limits the dose to an entire organ when only part of it was treated previously, perhaps even precluding retreatment entirely. Spatially-aware dose accumulation, performed either manually by sub-segmenting overlap regions or via commercial/in-house software, becomes a technical prerequisite in the majority of cases like this. In this patient, the heterogeneous prior dose exposure, including subtherapeutic cumulative dose to the focal meningeal extension, led to the physician's decision to employ a highly conformal SIB strategy rather than forgoing locoregional therapy or defaulting to uniform dose de-escalation.

Finally, an estimation of radiobiological risk requires a conversion to equieffective dose, most commonly via the linear-quadratic model (EQD2). Where relevant, time-dependent recovery over long inter-

course intervals could be considered when interpreting cumulative EQD2. In cases where point dose summation is used, individual doses can be converted manually to EQD2 and then summed. This manual method can also be applied to individually sub-segmented regions. However, ideally, the entire 3D dose grid of each delivered plan would be converted into EQD2 prior to summation to determine cumulative equieffective dose metrics. This calculation is not natively supported by all treatment planning systems and is sometimes performed via in-house scripting.

CRedit authorship contribution statement

Manju Sharma: Writing – original draft, Writing – review & editing.
Kelly C Paradis: Writing – original draft, Writing – review & editing.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Kelly Paradis reports a relationship with Radformation Inc that includes: consulting or advisory. Manju Sharma, declares no competing financial interests or personal relationships that influence the work reported in this paper.

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