LET painting for adenoid cystic carcinoma patients: comparative analysis of Carbon Ion and Multi-ion Therapy

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BACKGROUND AND AIMS

Adenoid cystic carcinoma (ACC) is a rare but aggressive tumor, marked by intrinsic radioresistance and hypoxia. Carbon ion therapy (CIRT), employing high-LET particles, holds the potential of superior biological effectiveness [1]. It is however difficult to achieve uniform high dose-averaged LET (LET_d) within the target while maintaining plan robustness and minimizing LET_d exposure to organs at risk (OARs) [2]. This study investigates the potential of multi-ion radiotherapy (MIRT) to address these challenges and enhance ACC treatment outcomes.

METHODS

Eleven ACC patients, consecutively treated with CIRT at the National Centre for Oncological Hadrontherapy (CNAO), were included in the study. The prescribed RBE-weighted dose was 65.6 Gy(RBE) delivered in 16 fractions, with a sequential boost strategy. The RBE was calculated for all ion species using the modified MKM model [3]. For each patient, two CIRT plans were robustly optimized: a nominal plan (PlanD), with a purely-dosimetric objective function, and an LET_d-optimized plan (PlanL), including a near-to-minimum LET_d objective to the GTV (minLET_d) and secondary LET_d constraints for clinically relevant OARs, adjusted per patient to maintain comparable dosimetric robustness with PlanD. Furthermore, using the same dose and LET_d objective approach, a MIRT plan (PlanM) was optimized combining protons, helium, carbon, and oxygen ions, to deliver uniform high LET to the GTV (Figure1) while minimizing the high dose-LET_d combinations to OARs involved in frequent acute and late toxicity events, involving e.g. temporal lobe, eye, and mucosa of the pharynx and oral cavity. Dose and dose-LET_d-volume (DLVH) parameters were compared for significance with the Mann-Withney U test.

RESULTS

The introduction of LET_d functions increased the GTV L99% from 42±4 keV/μm (PlanD) to (56±3) and (68±2) (keV/μm), for PlanL and PlanM, on average, while clinical goals remained robustly comparable to PlanD. MIRT significantly reduced the volume percentage receiving high LET_d at all dose levels for the OARs analysed, in particular in the low-medium dose range (ipsilateral temporal lobe is shown in Figure2).

CONCLUSIONS

MIRT allowed the delivery of high-LET_d selectively to the tumor target while reducing dose-LET_d exposure to OARs and maintaining robust plan quality. This strategy might be a promising approach to overcome ACC's radioresistance in clinical practice.

REFERENCES

[1] Durante 2017

[2] Fredriksson 2023

[3] Osburg 2024

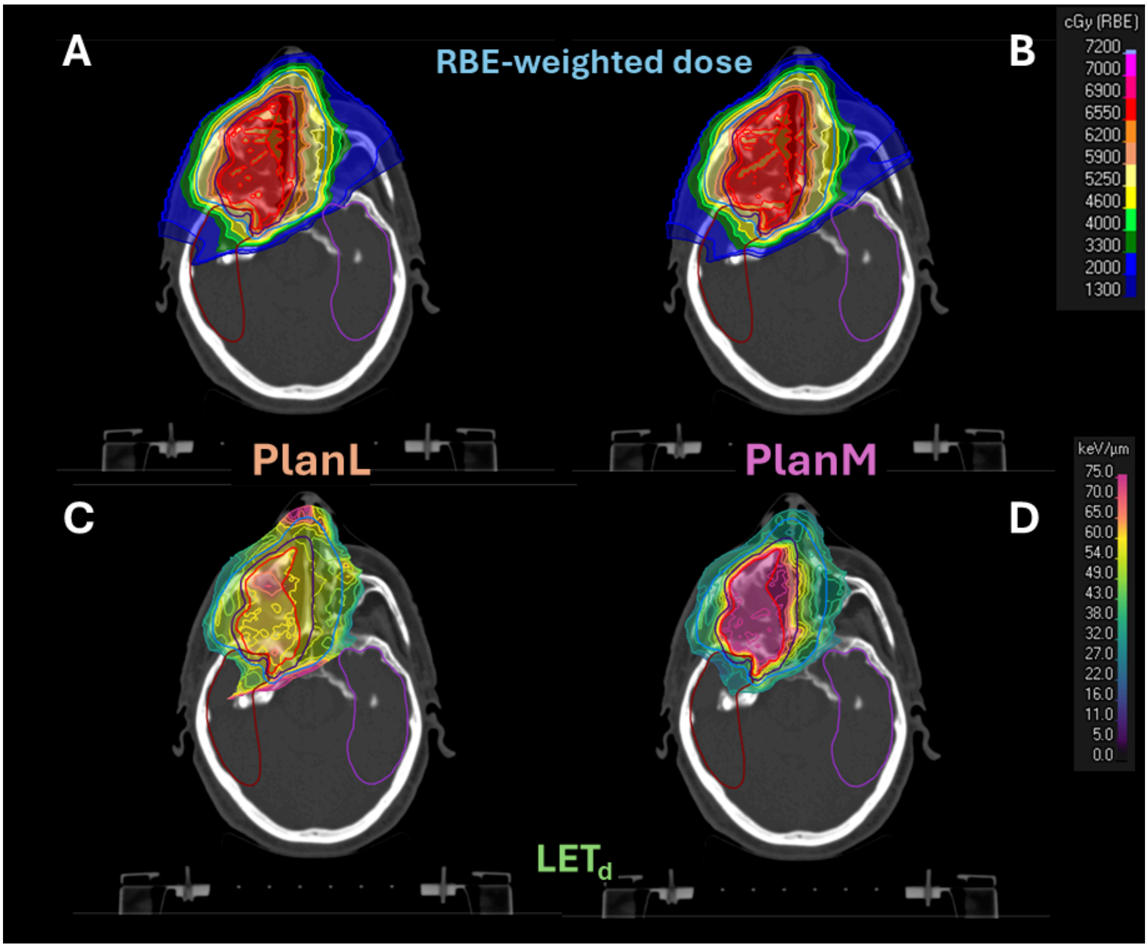

Figure 1: RBE-weighted dose (A-B) and LET_d (dose threshold set to 25 Gy(RBE)) distributions (C-D) of an exemplary LET_d-optimized CIRT plan (PlanL, A-C) and MIRT plan (PlanM, B-D). The low-risk (CTV-LR) and high-risk (CTV-HD) CVTs are shown in blue and light blue, respectively; the GTV is outlined in red; the left and right temporal lobes are contoured in purple and red, respectively.

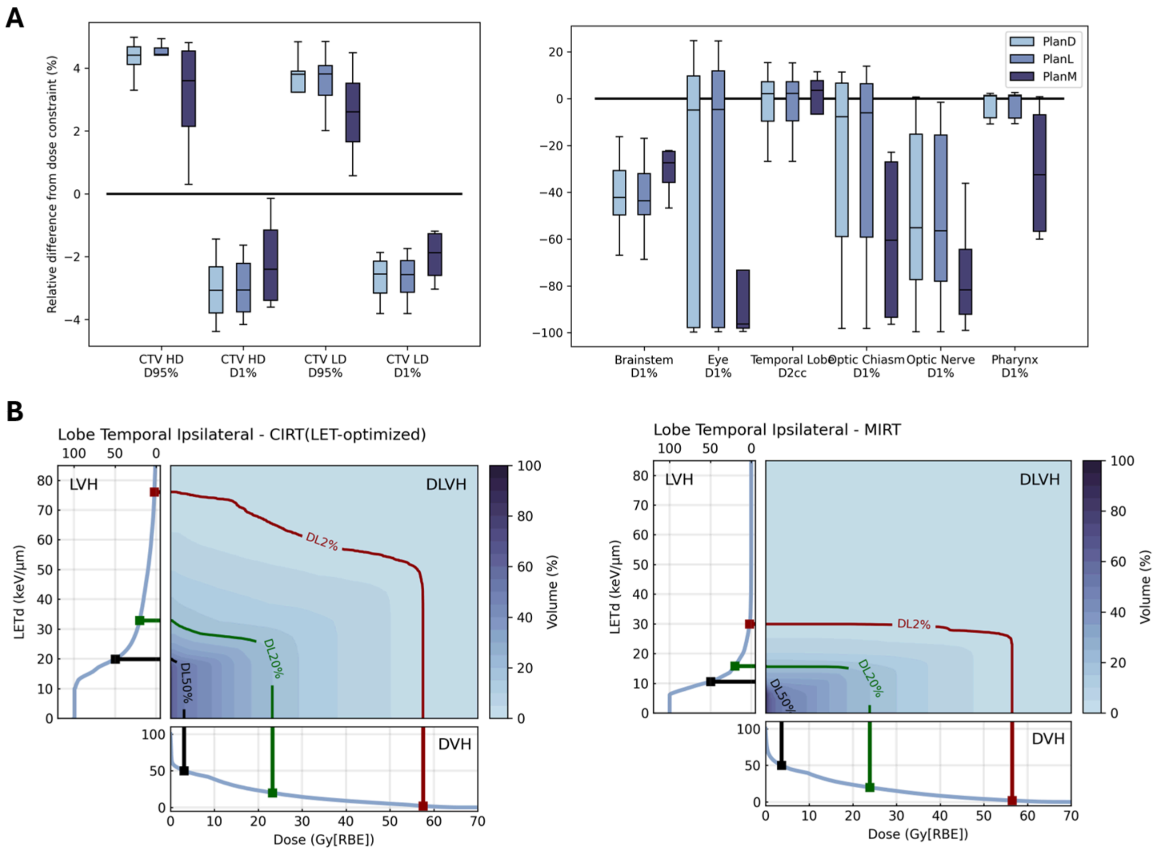

Figure 2: (A) Relative comparison of DVH metrics for low- and high-risk CTV coverage ($D_{95\%}$ and $D_{1\%}$) and key clinical objectives for relevant OARs between the nominal carbon plan (PlanD), LET_d-optimized carbon plan (PlanL), and MIRT plan (PlanM). Differences are expressed as $(D_{plan}-D_{constraint})/D_{constraint}$. (B) Median DVH across the patient cohort for the ipsilateral temporal lobe is presented as an illustrative case.