

# Proton therapy for craniospinal radiochemotherapy reduces myelotoxicity and improves chemotherapy completion in adult medulloblastoma

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## Introduction

- Combined radiochemotherapy for adult medulloblastoma (aMB) improves survival compared to radiation alone<sup>1</sup>
- Current chemoradiation regimens are associated with high rates of myelotoxicity and toxicity-related treatment termination
- Photon craniospinal irradiation (CSI) carries an inherent risk of myelotoxicity due to the exit dose to vertebral body marrow while proton CSI can be delivered via a marrow-sparing approach
- We therefore hypothesized that proton chemo-CSI could reduce rates of myelotoxicity and toxicity-related treatment termination relative to photon-based treatment
- Published results from the NOA-07 trial were used for comparison<sup>2</sup>

## Methods

- Patient population
  - Age ≥15
  - Received vertebral-body-sparing proton chemo-CSI for newly-diagnosed aMB
  - Planned to receive ≥4 cycles of chemotherapy
- Treatment: CSI dose of 23.4 or 36 CGE with boost to 55.8 CGE
- Myelotoxicity was evaluated using the NCI's CTCAE v3.0 to match grading scheme in NOA-07
- Correlations with toxicity were assessed using chi-square analysis; survival by Kaplan Meier

## Results

- Patients
  - 13 male, 11 female
  - Median age: 28 years (range 18–58)
  - 54% were average-risk
  - 50% received a CSI dose of 23.4 CGE
- Of 21 patients with available hematologic data: 95% received cisplatin, 76% vincristine, 67% CCNU, and 62% cyclophosphamide
- Median follow-up time: 2.4 years
- Survival: 2-year PFS: 88% | 2-year OS: 100%
- Adjuvant-phase cyclophosphamide was significantly associated with grade ≥3 leukopenia (p<0.01) and neutropenia (p=0.01).

Figure 1. Example Plan

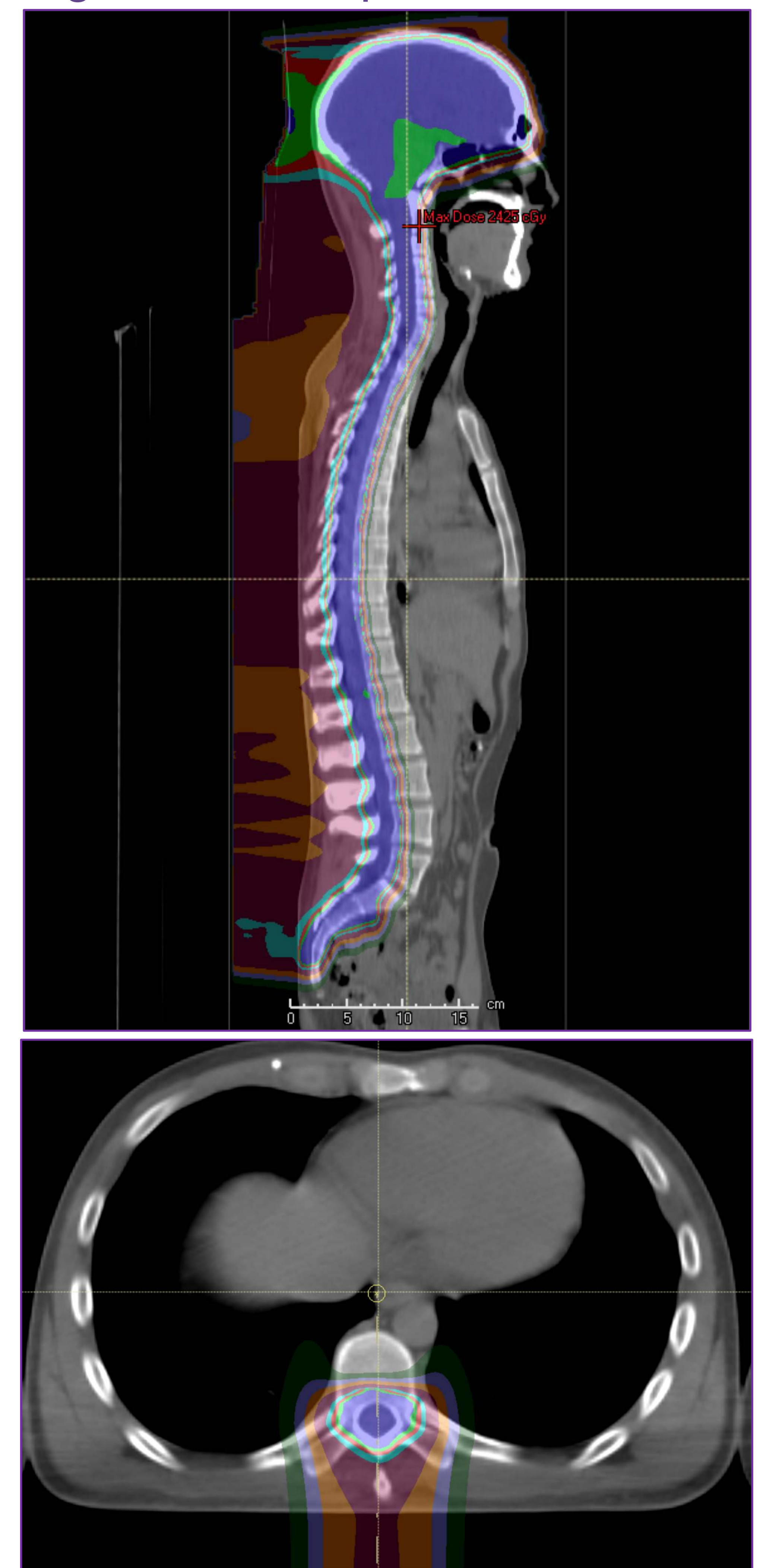


Table 1. Adjuvant Chemotherapy Completion

# Cycles	NOA-07	Proton chemo-CSI
4	70.0%	87.5%
5	70.0%	83.3%
6	63.3%	78.3%
7	43.3%	53.3%
8	33.3%	46.7%

Table 2. Myelotoxicity Results

Grade 3/4 Toxicity	Concomitant Phase		Adjuvant Phase		
	NOA-07	Proton chemo-CSI	NOA-07	Proton chemo-CSI	Proton chemo-CSI w/o cyclophosphamide
Leukopenia	36.7%	16.7%	66.7%	66.7%	25.0%
Thrombocytopenia	3.3%	8.3%	36.7%	42.9%	25.0%
Anemia	13.3%	12.5%	20.0%	42.9%	12.5%

## Conclusions

- Proton chemo-CSI for aMB increases rates of adjuvant chemotherapy completion and reduces rates of concomitant-phase leukopenia.
- In patients not receiving cyclophosphamide (an agent not included in the NOA-07 regimen) proton chemo-CSI lowers rates of adjuvant-phase myelotoxicity compared to contemporaneous photon-CSI control.

## References

1. Kocakaya S, Beier CP, Beier D. *Neuro-Oncology*. March 2016;18(3):408-416.
2. Beier D, Proescholdt M, Reinert C, et al. *Neuro-Oncology*. August 2018;20(3):400-410.

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