



# Proton Therapy for Skull Base Chondrosarcoma

Dennis M. Tang<sup>1</sup> Raffaello M. Cutri<sup>1</sup> Arthur W. Wu<sup>1</sup> Chirag Patil<sup>2</sup> Zachary S. Zumsteg<sup>3</sup>

<sup>1</sup>Department of Otolaryngology, Cedars-Sinai Medical Center, Los Angeles, California, United States

<sup>2</sup>Department of Neurosurgery, Cedars-Sinai Medical Center, Los Angeles, California, United States

<sup>3</sup>Department of Radiation Oncology, Cedars-Sinai Medical Center, Los Angeles, California, United States

**Address for correspondence** Dennis M. Tang, MD, Division of Otolaryngology, Cedars-Sinai Medical Center, 8631 W 3rd St, Suite 915E, Los Angeles, CA 90048, United States (e-mail: Dennis.tang2@cshs.org).

J Neurol Surg Rep 2023;84:e144–e145.

## Abstract

Chondrosarcoma is a type of an endochondral bone malignancy that is primarily treated surgically with radiation therapy used in the adjuvant setting or in cases of unresectable disease. Proton therapy has potential advantages compared with traditional photon therapy for the treatment of tumors in close proximity to critical structures due to the theoretic lower exit dose. Studies have shown improved survival in patients with skull base chondrosarcoma who undergo proton therapy. However, there is a lack of randomized data. Further studies are needed to define the role of proton therapy in the treatment of skull base chondrosarcoma.

## Keywords

- ▶ skull base
- ▶ chondrosarcoma
- ▶ radiation therapy
- ▶ proton therapy

A 69-year-old gentleman presented with sudden vision loss in his left eye. Imaging revealed a large sinonasal mass involving the left sinuses, pterygopalatine fossa, orbit, and middle cranial fossa. Biopsy was consistent with a grade II chondrosarcoma. The multidisciplinary tumor board recommended proton beam radiotherapy, but there were concerns that the tumor's proximity to the optic chiasm would limit the ability to deliver therapeutic doses. Therefore, the patient underwent an endoscopic endonasal debulking of the tumor to decompress the optic chiasm. He subsequently underwent proton radiotherapy to a total dose of 7000cGy over 8 weeks. Twelve months post-treatment, his imaging demonstrated no progression of his cancer.

Chondrosarcomas are a heterogeneous group of endochondral bone neoplasms comprising approximately 6% of skull base tumors.<sup>1</sup> Chondrosarcomas are classified based on histology, with conventional/classic being the most common (80%).<sup>2</sup> Other subtypes include clear cell, mesenchymal, and dedifferentiated. Chondrosarcomas are graded from I to III based on histopathologic differentiation.<sup>1,3,4</sup>

The recommended primary treatment modality is complete surgical resection when possible.<sup>5</sup> However, gross total resection cannot be achieved in approximately 60 to 80% of chondrosarcomas given frequent involvement of critical neurovascular structures.<sup>6,7</sup> Radiation therapy can be used as primary treatment for unresectable cases or adjuvantly for positive margins in high-grade tumors. Chondrosarcomas are historically considered radioresistant due to low mitotic activity and poor vascularity.<sup>8,9</sup> Given this, relatively high radiation doses are recommended. However, proximity to critical structures can limit the ability to deliver doses in this range for photon-based radiotherapy.

Proton radiotherapy (PT) was developed as an alternative to photon-based radiotherapy. Photon radiotherapy beams have significant exit doses due to the massless, chargeless nature of X-rays.<sup>10</sup> PT has markedly decreased exit dose due to its Bragg peak, a physical property of proton beams that results in the radiation dose being deposited at a specific depth, with rapid fall-off beyond the target. This lack of exit dose can help minimizing damage to adjacent critical

received  
September 27, 2023  
accepted  
October 6, 2023  
accepted manuscript online  
October 16, 2023

DOI <https://doi.org/10.1055/a-2192-5775>  
ISSN 2193-6358.

© 2023. The Author(s).

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

structures.<sup>10</sup> Doses can also be escalated while maintaining similar doses to normal organs at risk.<sup>11–13</sup>

There is little randomized data available for PT for chondrosarcoma. Local control rates at 5 years after PT are between 75 and 99%.<sup>14–17</sup> A recent analysis of the National Cancer Database demonstrated that patients receiving surgery with adjuvant PT had significantly better overall survival at 5 years (95.4 vs. 82.3%) and 10 years (85.1 vs. 72.8%) compared with surgery with adjuvant photon-based radiotherapy.<sup>18</sup> In a systematic review of proton versus photon radiotherapy for paranasal sinus cancers, PT was associated with superior 5 years disease-free survival and locoregional control.<sup>19</sup> Complications after PT are similar to traditional radiotherapy including fatigue, pituitary insufficiency, hearing impairment, and visual disorders; however, they potentially may occur less frequently or with less severity.<sup>16,17,20,21</sup> Although there is strong rationale for PT in the treatment of radioresistant skull base tumors like chondrosarcoma, optimal treatment regimen remains controversial. A systematic review of 33 studies demonstrated variations in radiotherapy-protocols did not yield differences between post-treatment symptom improvement or tumor volumes.<sup>5</sup> Moreover, widespread utilization is limited by the relative scarcity of centers offering PT.

#### Conflict of Interest

D.M.T. is a consultant for Acclarent, Inc. and 3-D Matrix.

A.W.W. is a consultant for 3-D Matrix.

#### References

- Noel G, Gondi V. Proton therapy for tumors of the base of the skull. *Chin Clin Oncol* 2016;5(04):51
- Amichetti M, Amelio D, Cianchetti M, Enrici RM, Minniti G. A systematic review of proton therapy in the treatment of chondrosarcoma of the skull base. *Neurosurg Rev* 2010;33(02):155–165
- Simon F, Feuvret L, Bresson D, et al. Surgery and proton therapy in Grade I and II skull base chondrosarcoma: a comparative retrospective study. *PLoS One* 2018;13(12):e0208786
- Hasegawa H, Vakharia K, Graffeo CS, et al. Long-term outcomes of grade I/II skull base chondrosarcoma: an insight into the role of surgery and upfront radiotherapy. *J Neurooncol* 2021;153(02):273–281
- Palmisciano P, Haider AS, Sabahi M, et al. Primary skull base chondrosarcomas: a systematic review. *Cancers (Basel)* 2021;13(23):5960
- Crockard HA, Cheeseman A, Steel T, et al. A multidisciplinary team approach to skull base chondrosarcomas. *J Neurosurg* 2001;95(02):184–189
- Bohman LE, Koch M, Bailey RL, Alonso-Basanta M, Lee JY. Skull base chordoma and chondrosarcoma: influence of clinical and demographic factors on prognosis: a SEER analysis. *World Neurosurg* 2014;82(05):806–814
- Chow WA. Update on chondrosarcomas. *Curr Opin Oncol* 2007;19(04):371–376
- Gelderblom H, Hogendoorn PC, Dijkstra SD, et al. The clinical approach towards chondrosarcoma. *Oncologist* 2008;13(03):320–329. Doi: 10.1634/theoncologist.2007-0237. Erratum in: *Oncologist*. 2008 May;13(5):618. PMID: 18378543
- Nguyen QN, Chang EL. Emerging role of proton beam radiation therapy for chordoma and chondrosarcoma of the skull base. *Curr Oncol Rep* 2008;10(04):338–343
- St Clair WH, Adams JA, Bues M, et al. Advantage of protons compared to conventional X-ray or IMRT in the treatment of a pediatric patient with medulloblastoma. *Int J Radiat Oncol Biol Phys* 2004;58(03):727–734
- Dabaja BS, Hoppe BS, Plastaras JP, et al. Proton therapy for adults with mediastinal lymphomas: the International Lymphoma Radiation Oncology Group guidelines. *Blood* 2018;132(16):1635–1646
- MacDonald SM, Trofimov A, Safai S, et al. Proton radiotherapy for pediatric central nervous system germ cell tumors: early clinical outcomes. *Int J Radiat Oncol Biol Phys* 2011;79(01):121–129
- Rosenberg AE, Nielsen GP, Keel SB, et al. Chondrosarcoma of the base of the skull: a clinicopathologic study of 200 cases with emphasis on its distinction from chordoma. *Am J Surg Pathol* 1999;23(11):1370–1378
- Hug EB, Loredon LN, Slater JD, et al. Proton radiation therapy for chordomas and chondrosarcomas of the skull base. *J Neurosurg* 1999;91(03):432–439
- Weber DC, Badiyan S, Malyapa R, et al. Long-term outcomes and prognostic factors of skull-base chondrosarcoma patients treated with pencil-beam scanning proton therapy at the Paul Scherrer Institute. *Neuro-oncol* 2016;18(02):236–243
- Feuvret L, Bracci S, Calugaru V, et al. Efficacy and safety of adjuvant proton therapy combined with surgery for chondrosarcoma of the skull base: a retrospective, population-based study. *Int J Radiat Oncol Biol Phys* 2016;95(01):312–321
- Rimmer RA, Mace JC, Andersen PE, et al. Determinants of survival in sinonasal and skull base chondrosarcoma: an analysis of the National Cancer Database. *Int Forum Allergy Rhinol* 2022;12(05):699–713
- Patel SH, Wang Z, Wong WW, et al. Charged particle therapy versus photon therapy for paranasal sinus and nasal cavity malignant diseases: a systematic review and meta-analysis. *Lancet Oncol* 2014;15(09):1027–1038
- Li PC, Liebsch NJ, Niemierko A, et al. Radiation tolerance of the optic pathway in patients treated with proton and photon radiotherapy. *Radiother Oncol* 2019;131:112–119
- De Leo AN, Holtzman AL, Ho MW, et al. Vision loss following high-dose proton-based radiotherapy for skull-base chordoma and chondrosarcoma. *Radiother Oncol* 2021;158:125–130