

Neutron Beam and Proton Beam Radiation Therapy

POLICY NUMBER UM XRT_2010	SUBJECT Neutron Beam and Proton Beam Radiation Therapy	DEPT/PROGRAM UM Dept	PAGE 1 OF 8
DATES COMMITTEE REVIEWED 04/14/21, 11/10/21, 11/09/22	APPROVAL DATE November 9, 2022	EFFECTIVE DATE November 28, 2022	COMMITTEE APPROVAL DATES 04/14/21, 11/10/21, 11/09/22
PRIMARY BUSINESS OWNER: UM		COMMITTEE/BOARD APPROVAL Utilization Management Committee	
URAC STANDARDS HUM v8: UM 1-2; UM 2-1	NCQA STANDARDS UM 2	ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS	APPLICABLE LINES OF BUSINESS Commercial, Exchange, Medicaid	

I. PURPOSE

The purpose of this policy is to provide general information applicable to the review and appropriateness of Radiation Therapy services. Although a service, supply or procedure may be medically necessary, it may be subject to limitations and/or exclusions under a member's benefit plan. If a service, supply, or procedure is not covered and the member proceeds to obtain the service, supply or procedure, the member may be responsible for the cost. Decisions regarding treatment and treatment plans are the responsibility of the physician. This policy is not intended to direct the course of clinical care a physician provides to a member, and it does not replace a physician's independent professional clinical judgment or duty to exercise special knowledge and skill in the treatment of members. NCH is not responsible for, does not provide, and does not hold itself out as a provider of medical care. The physician remains responsible for the quality and type of health care services provided to a member.

II. BACKGROUND

Neutron Beam Radiation Therapy (NBRT) differs from other forms of radiation particle treatment such as protons or electrons as they have no electrical charge. The treatment effects are the results of the neutron mass producing dense radiation energy distributions. This effect is high energy linear transfer (LET) and may offset the negative effects of low oxygen tension in tumors leading to increased rate of control in hypoxic tumors. Proton Beam Radiation Therapy (PBRT) is a type of external radiation treatment. Using a stereotactic planning and delivery system, positively charged subatomic particles (protons) are targeted to a specific cancer. Protons behave differently than x-rays or photons in that

they have a low energy deposition rate as they enter the body, followed by a steep increased energy deposition when they reach their target (the Bragg peak).

Radiation Therapy Treatment Process:

- A. Consultation
- B. Simulation
- C. Treatment Planning
- D. Treatment Delivery

III. TABLE OF CONTENTS

III. NEUTRON BEAM RADIATION THERAPY (NBRT)	2
IV. PROTON BEAM RADIATION THERAPY (PBRT)	2
V. APPROVAL AUTHORITY	3
VI. ATTACHMENTS	3
VII. REFERENCES	3

III. NEUTRON BEAM RADIATION THERAPY (NBRT)

Indications for Use/Inclusion Criteria¹⁻¹⁰

All requests for NBRT require Clinical Review by an NCH Physician.

A. Neutron Beam Radiation Therapy is medically necessary only in the treatment of:

1. Salivary gland cancers – when recurrent **OR** in the case of a second primary cancer **OR** following resection with gross residual disease or positive margins **OR** for re-treatment of a previously irradiated area.

Exclusion Criteria

- A. All other cancers are not considered medically necessary for Neutron Beam Radiation Therapy.

IV. PROTON BEAM RADIATION THERAPY (PBRT)

Indications for Use/Inclusion Criteria¹¹⁻⁸⁸

All requests for PBRT require Clinical Review by an NCH Physician.

A. Proton Beam Radiation Therapy is medically necessary only in the treatment of:

1. Chordomas and Chondrosarcomas of the base of the skull or spine when disease is localized (non-metastatic).
2. Primary or metastatic CNS malignancies when adjacent to critical structures such as the optic nerve, optic chiasm, brain stem, or spinal cord (an IMRT vs PBRT comparison study is required).
3. Hepatocellular cancer or intrahepatic cholangiocarcinoma – when unresectable and non-metastatic
4. Melanoma of the uveal tract – with no evidence of metastasis or extra scleral extension.

5. Pediatric cancers – in all cases of pediatric cancers (in patients 18 yrs. old or younger) except in cases of bone metastases (see exclusion criteria below).
6. Cancer of the nasal cavity and paranasal sinuses – when tumor involves the base of skull and proton therapy is needed to spare the orbit, optic nerve, optic chiasm, or brainstem (an IMRT vs PBRT comparison study is required)
7. Re-irradiation – for re-treatment of a previously irradiated area

Exclusion Criteria

- A. All other cancers are not considered medically necessary for Proton Beam Radiation Therapy.
- B. Pediatric cancers in cases where the treatment is for previously untreated bone metastases.

V. APPROVAL AUTHORITY

- A. Review – Utilization Management Department
- B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

- A. None

VII. REFERENCES

1. NCQA UM 2022 Standards and Elements.
2. National Comprehensive Cancer Network (NCCN) Guidelines Version 2.2021 Head and Neck Cancers, Salivary Gland Tumors
3. National Comprehensive Cancer Network (NCCN) Radiation Compendium 2.2021, Head and Neck Cancers, Salivary Gland Tumors
4. Aihara T, Morita N, Kamitani N, et al. Boron neutron capture therapy for advanced salivary gland carcinoma in head and neck. In J Clin Oncol. 2014 Jun; 19(3):437-444.
5. Burmeister J, Spink R, Liang L, et al. Commissioning of intensity modulated neutron therapy (IMNRT). Med Phys 2013 Feb; 40(2):021718.
6. Douglas JG, Laramore GE, Austin-Seymour M, et al. Treatment of locally advanced adenoid cystic carcinoma of the head and neck with neutron radiotherapy. Int J of Radiat Oncol Biol Phys. 2000 Feb 1; 46(3):551-557.
7. Huber PE, Debus J, Latz D, et al. Radiotherapy for advanced adenoid cystic carcinoma: neutrons, photons or mixed beam? Radiotherapy and Oncology. 2001 May 1; 59(2):161-167.
8. Prott FJ, Micke O, Haverkamp U et al. Results of fast neutron therapy of adenoid cystic carcinoma of the salivary glands. Anticancer Research 2000 Sep-Oct; 20(5C):3743-9.
9. Stannard C, Vernimmen E, Carrara H, et al. Malignant salivary gland tumors: can fast neutron therapy results point the way to carbon ion therapy? Radiother Oncol. 2013 Nov; 109(2):262-268.
10. Davis C, Sikes J, Namaranian P, et al. Neutron beam radiation therapy: an overview of treatment and oral complications when treating salivary gland malignancies. J Oral Maxillofac Surg. 2016 Apr; 74(4):830-835.
11. Rockhill JK, Laramore GE. Chapter 20: Neutron Beam Radiotherapy. In: Gunderson L, Tepper J. editors. Clinical Radiation Oncology, 4th eds. Philadelphia, PA: Churchill Livingstone; 2016; (20):373-375.
12. Marshall, TI, Chaudhary, P, Michaelidesova, A, et al. Investigating the implications of a variable RBE on proton dose fractionation across a clinical pencil beam scanned spread-out Bragg peak. Int J Radiat Oncol Biol Phys. 2016;95(1):70-7.

13. McDonald, MW, Liu, Y, Moore, MG, et al. Acute toxicity in comprehensive head and neck radiation for nasopharynx and paranasal sinus cancers: cohort comparison of 3D conformal proton therapy and intensity modulated radiation therapy. *Radiat Oncol*. 2016;11(32):[10 p.].
14. McDonald, MW, Zolali-Meybodi, O, Lehnert, SJ, et al. Reirradiation of recurrent and second primary head and neck cancer with proton therapy. *Int J Radiat Oncol Biol Phys*. 2016;96(4):808-19.
15. Mishra, MV, Aggarwal, S, Bentzen, SM, et al. Establishing evidence-based indications for proton therapy: an overview of current clinical trials. *Int J Radiat Oncol Biol Phys*. 2017;97(2):228-35.
16. Yang, P, Xu, T, Gomez, DR, et al. Patterns of local-regional failure after intensity modulated radiation therapy or passive scattering proton therapy with concurrent chemotherapy for non-small cell lung cancer. *Int J Radiat Oncol Biol Phys*. 2019;103(1):123-31.
17. Yu, JB, Soulos, PR, Herrin, J, et al. Proton versus intensity-modulated radiotherapy for prostate cancer: patterns of care and early toxicity. *J Natl Cancer Inst*. 2013;105(1):25-32.
18. Zelefsky, MJ, Pei, X, Teslova, T, et al. Secondary cancers after intensity-modulated radiotherapy, brachytherapy and radical prostatectomy for the treatment of prostate cancer: incidence and cause-specific survival outcomes according to the initial treatment intervention. *BJU Int*. 2012;110(11):1696-701.
19. Zhou, J, Yang, B, Wang, X, et al. Comparison of the effectiveness of radiotherapy with photons and particles for chordoma after surgery: a meta-analysis. *World Neurosurg*. 2018;117:46-53.
20. Combs, SE. Does proton therapy have a future in CNS tumors? *Curr Treat Options Neurol*. 2017;19(3):article 12.
21. Cuaron, JJ, Chang, C, Lovelock, M, et al. Exponential increase in relative biological effectiveness along distal edge of a proton Bragg peak as measured by deoxyribonucleic acid double-strand breaks. *Int J Radiat Oncol Biol Phys*. 2016;95(1):62-9.
22. Dagan, R, Bryant, C, Li, Z, et al. Outcomes of sinonasal cancer treated with proton therapy. *Int J Radiat Oncol Biol Phys*. 2016;95(1):377-85.
23. DeLaney, TF, Liebsch, NJ, Pedlow, FX, et al. Long-term results of phase II study of high dose photon/proton radiotherapy in the management of spine chordomas, chondrosarcomas, and other sarcomas. *J Surg Oncol*. 2014;110(2):115-22.
24. ECRI Institute–Penn Medicine Evidence-based Practice Center. Therapies for clinically localized prostate cancer: update of a 2008 systematic review. Comparative effectiveness review. Number 146. (2014) Agency for Healthcare Research and Quality (AHRQ). Available from: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/prostate-cancer-therapies_update_research.pdf.
25. Efsthathiou, JA, Trofimov, AV, Zietman, AL. Life, liberty, and the pursuit of protons: an evidence-based review of the role of particle therapy in the treatment of prostate cancer. *Cancer J*. 2009;15(4):312-8.
26. Fitzek, MM, Thornton, AF, Harsh, Gt, et al. Dose-escalation with proton/photon irradiation for Daumas-Duport lower-grade glioma: results of an institutional phase I/II trial. *Int J Radiat Oncol Biol Phys*. 2001;51(1):131-7.
27. Fitzek, MM, Thornton, AF, Rabinov, JD, et al. Accelerated fractionated proton/photon irradiation to 90 cobalt gray equivalent for glioblastoma multiforme: results of a phase II prospective trial. *J Neurosurg*. 1999;91(2):251-60.
28. Frank, SJ, Blanchard, P, Lee, JJ, et al. Comparing intensity-modulated proton therapy with intensity-modulated photon therapy for oropharyngeal cancer: the journey from clinical trial concept to activation. *Semin Radiat Oncol*. 2018;28(2):108-13.

29. Gray, PJ, Paly, JJ, Yeap, BY, et al. Patient-reported outcomes after 3-dimensional conformal, intensity-modulated, or proton beam radiotherapy for localized prostate cancer. *Cancer*. 2013;119(9):1729-35.
30. Grutters, JP, Kessels, AG, Pijls-Johannesma, M, et al. Comparison of the effectiveness of radiotherapy with photons, protons and carbon-ions for non-small cell lung cancer: a meta-analysis. *Radiother Oncol*. 2010;95(1):32-40.
31. Gunn, GB, Blanchard, P, Garden, AS, et al. Clinical outcomes and patterns of disease recurrence after intensity modulated proton therapy for oropharyngeal squamous carcinoma. *Int J Radiat Oncol Biol Phys*. 2016;95(1):360-7.
32. Hattangadi-Gluth, JA, Chapman, PH, Kim, D, et al. Single-fraction proton beam stereotactic radiosurgery for cerebral arteriovenous malformations. *Int J Radiat Oncol Biol Phys*. 2014;89(2):338-46.
33. Hoppe, BS, Hill-Kayser, CE, Tseng, YD, et al. Consolidative proton therapy after chemotherapy for patients with Hodgkin lymphoma. *Ann Oncol*. 2017;28(9):2179-84.
34. Mizumoto, M, Tsuboi, K, Igaki, H, et al. Phase I/II trial of hyperfractionated concomitant boost proton radiotherapy for supratentorial glioblastoma multiforme. *Int J Radiat Oncol Biol Phys*. 2010;77(1):98-105.
35. Mizumoto, M, Yamamoto, T, Takano, S, et al. Long-term survival after treatment of glioblastoma multiforme with hyperfractionated concomitant boost proton beam therapy. *Pract Radiat Oncol*. 2015;5(1):e9-16.
36. Moreno, AC, Frank, SJ, Garden, AS, et al. Intensity modulated proton therapy (IMPT) - the future of IMRT for head and neck cancer. *Oral Oncol*. 2019;88:66-74.
37. Nakajima, K, Iwata, H, Ogino, H, et al. Clinical outcomes of image-guided proton therapy for histologically confirmed stage I nonsmall cell lung cancer. *Radiat Oncol*. 2018;13(1):[9 p.].
38. National Cancer Institute (NCI). NCI dictionary of cancer terms [Internet] [cited 2018 Oct 24]. Available from: <https://www.cancer.gov/publications/dictionaries/cancer-terms>.
39. National Institutes of Health (NIH). U.S. National Library of Medicine (NLM). Course: finding and using health statistics: glossary [Internet] [cited 2020 Feb 24]. Available from: <https://www.nlm.nih.gov/nichsr/usestats/glossary.html>.
40. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer (Version 4.2020). Available at <http://www.nccn.org>. ©National Comprehensive Cancer Network, 2020.
41. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Non-Small Cell Lung Cancer (Version 4.2020). Available at <http://www.nccn.org>. ©National Comprehensive Cancer Network, 2020.
42. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Prostate Cancer (Version 1.2020). Available at <http://www.nccn.org>. ©National Comprehensive Cancer Network, 2020.
43. Olsen, DR, Bruland, OS, Frykholm, G, et al. Proton therapy - a systematic review of clinical effectiveness. *Radiother Oncol*. 2007;83(2):123-32.
44. Pan, HY, Jiang, J, Hoffman, KE, et al. Comparative toxicities and cost of intensity-modulated radiotherapy, proton radiation, and stereotactic body radiotherapy among younger men with prostate cancer. *J Clin Oncol*. 2018;36(18):1823-30.
45. 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(9):1027-38.

46. Paulino, AC, Mahajan, A, Ye, R, et al. Ototoxicity and cochlear sparing in children with medulloblastoma: proton vs. photon radiotherapy. *Radiother Oncol.* 2018;128(1):128-32.
47. Phan, J, Sio, TT, Nguyen, TP, et al. Reirradiation of head and neck cancers with proton therapy: outcomes and analyses. *Int J Radiat Oncol Biol Phys.* 2016;96(1):30-41.
48. Pompos, A, Durante, M, Choy, H. Heavy ions in cancer therapy. *JAMA Oncol.* 2016;2(12):1539-40.
49. Qi, WX, Fu, S, Zhang, Q, et al. Charged particle therapy versus photon therapy for patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Radiother Oncol.* 2015;114(3):289-95.
50. Romesser, PB, Cahlon, O, Scher, E, et al. Proton beam radiation therapy results in significantly reduced toxicity compared with intensity-modulated radiation therapy for head and neck tumors that require ipsilateral radiation. *Radiother Oncol.* 2016;118(2):286-92.
51. Romesser, PB, Cahlon, O, Scher, ED, et al. Proton beam reirradiation for recurrent head and neck cancer: multi-institutional report on feasibility and early outcomes. *Int J Radiat Oncol Biol Phys.* 2016;95(1):386-95.
52. Allen, AM, Pawlicki, T, Dong, L, et al. An evidence based review of proton beam therapy: the report of ASTRO's emerging technology committee. *Radiother Oncol.* 2012;103(1):8-11.
53. American Society for Radiation Oncology (ASTRO). ASTRO model policies: proton beam therapy (PBT) (Approved June 2017) [20 p.]. Available from: <https://www.astro.org/Daily-Practice/Reimbursement/Model-Policies>.
54. Badiyan, SN, Rutenberg, MS, Hoppe, BS, et al. Clinical outcomes of patients with recurrent lung cancer reirradiated with proton therapy on the Proton Collaborative Group and University of Florida Proton Therapy Institute Prospective Registry studies. *Pract Radiat Oncol.* 2019;9(4):280-8.
55. Blue Cross and Blue Shield Association, Evidence-based Practice Center. Radiotherapy treatments for head and neck cancer update. Comparative effectiveness review. Number 144. (2014) Effective Health Care Program, Agency for Healthcare Research and Quality (AHRQ). Available from: https://effectivehealthcare.ahrq.gov/sites/default/files/pdf/head-neck-cancerupdate_research.pdf.
56. Boker, A, Pilger, D, Cordini, D, et al. Neoadjuvant proton beam irradiation vs. adjuvant ruthenium brachytherapy in transscleral resection of uveal melanoma. *Graefes Arch Clin Exp Ophthalmol.* 2018;256(9):1767-75.
57. Brada, M, Pijls-Johannesma, M, De Ruyscher, D. Current clinical evidence for proton therapy. *Cancer J.* 2009;15(4):319-24.
58. Bush, DA, Smith, JC, Slater, JD, et al. Randomized clinical trial comparing proton beam radiation therapy with transarterial chemoembolization for hepatocellular carcinoma: results of an interim analysis. *Int J Radiat Oncol Biol Phys.* 2016;95(1):477-82.
59. Ronson, BB, Schulte, RW, Han, KP, et al. Fractionated proton beam irradiation of pituitary adenomas. *Int J Radiat Oncol Biol Phys.* 2006;64(2):425-34.
60. Sachsman, S, Flampouri, S, Li, Z, et al. Proton therapy in the management of non-Hodgkin lymphoma. *Leuk Lymphoma.* 2015;56(9):2608-12.
61. Saltzman, AF, Cost, NG. Current treatment of pediatric bladder and prostate rhabdomyosarcoma. *Curr Urol Rep.* 2018;19(1):[9 p.].
62. Sanda, MG, Chen, RC, Crispino, T, et al. Clinically localized prostate cancer: AUA/ASTRO/SUO guideline. (2017) [56 p.]. Available from: <https://www.auanet.org/guidelines/prostate-cancer-clinically-localized-guideline>.

63. Sanford, NN, Pursley, J, Noe, B, et al. Protons versus photons for unresectable hepatocellular carcinoma: liver decompensation and overall survival. *Int J Radiat Oncol Biol Phys.* 2019;105(1):64-72.
64. Steinmeier, T, Schulze Schleithoff, S, Timmermann, B. Evolving radiotherapy techniques in paediatric oncology. *Clin Oncol.* 2019;31(3):142-50.
65. Verma, V, Rwigema, JM, Malyapa, RS, et al. Systematic assessment of clinical outcomes and toxicities of proton radiotherapy for reirradiation. *Radiother Oncol.* 2017;125(1):21-30.
66. Verma, V, Shah, C, Mehta, MP. Clinical outcomes and toxicity of proton radiotherapy for breast cancer. *Clin Breast Cancer.* 2016;16(3):145-54.
67. Verma, V, Simone, CB, 2nd, Mishra, MV. Quality of life and patient-reported outcomes following proton radiation therapy: a systematic review. *J Natl Cancer Inst.* 2018;110(4):341-53.
68. Wang, J, Wei, C, Tucker, SL, et al. Predictors of postoperative complications after trimodality therapy for esophageal cancer. *Int J Radiat Oncol Biol Phys.* 2013;86(5):885-91.
69. Wang, Z, Nabhan, M, Schild, SE, et al. Charged particle radiation therapy for uveal melanoma: a systematic review and metaanalysis. *Int J Radiat Oncol Biol Phys.* 2013;86(1):18-26.
70. Widesott, L, Amichetti, M, Schwarz, M. Proton therapy in lung cancer: clinical outcomes and technical issues. a systematic review. *Radiother Oncol.* 2008;86(2):154-64.
71. Wiltink, LM, Nout, RA, Fiocco, M, et al. No increased risk of second cancer after radiotherapy in patients treated for rectal or endometrial cancer in the randomized TME, PORTEC-1, and PORTEC-2 trials. *J Clin Oncol.* 2015;33(15):1640-6.
72. Indelicato, DJ, Bradley, JA, Rotondo, RL, et al. Outcomes following proton therapy for pediatric ependymoma. *Acta Oncol.* 2018;57(5):644-8.
73. Indelicato, DJ, Rotondo, RL, Uezono, H, et al. Outcomes following proton therapy for pediatric low-grade glioma. *Int J Radiat Oncol Biol Phys.* 2019;104(1):149-56.
74. Jett, JR, Schild, SE, Kesler, KA, et al. Treatment of small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* 2013;143(5 Suppl):e400S-e19S.
75. Kahalley, LS, Douglas Ris, M, Mahajan, A, et al. Prospective, longitudinal comparison of neurocognitive change in pediatric brain tumor patients treated with proton radiotherapy versus surgery only. *Neuro Oncol.* 2019;21(6):809-18.
76. Kong, FS. What happens when proton meets randomization: is there a future for proton therapy? *J Clin Oncol.* 2018;36(18):1777-9.
77. Leeman, JE, Romesser, PB, Zhou, Y, et al. Proton therapy for head and neck cancer: expanding the therapeutic window. *Lancet Oncol.* 2017;18(5):e254-e65.
78. Lewis, GD, Holliday, EB, Kocak-Uzel, E, et al. Intensity-modulated proton therapy for nasopharyngeal carcinoma: decreased radiation dose to normal structures and encouraging clinical outcomes. *Head Neck.* 2016;38 Suppl 1:E1886-95.
79. Liao, Z, Lee, JJ, Komaki, R, et al. Bayesian adaptive randomization trial of passive scattering proton therapy and intensity modulated photon radiotherapy for locally advanced non-small-cell lung cancer. *J Clin Oncol.* 2018;36(18):1813-22.
80. Macomber, MW, Bowen, SR, Gopan, O, et al. Heart dose and outcomes in radiation treatment for esophageal cancer. *Cureus.* 2018;10(3):e2378.
81. Zietman, AL, Bae, K, Slater, JD, et al. Randomized trial comparing conventional-dose with high-dose conformal radiation therapy in early-stage adenocarcinoma of the prostate: long-

- term results from proton radiation oncology group/american college of radiology 95-09. *J Clin Oncol*. 2010;28(7):1106-11.
82. Seifert, V, Stolke, D, Mehdorn, HM, et al. Clinical and radiological evaluation of long-term results of stereotactic proton beam radiosurgery in patients with cerebral arteriovenous malformations. *J Neurosurg*. 1994;81(5):683-9.
 83. Sheets, NC, Goldin, GH, Meyer, AM, et al. Intensity-modulated radiation therapy, proton therapy, or conformal radiation therapy and morbidity and disease control in localized prostate cancer. *Jama*. 2012;307(15):1611-20.
 84. Simone, CB, 2nd, Bogart, JA, Cabrera, AR, et al. Radiation therapy for small cell lung cancer: an ASTRO clinical practice guideline. *Pract Radiat Oncol*. 2020;10(3):158-73.
 85. Sio, TT, Lin, HK, Shi, Q, et al. Intensity modulated proton therapy versus intensity modulated photon radiation therapy for oropharyngeal cancer: first comparative results of patient-reported outcomes. *Int J Radiat Oncol Biol Phys*. 2016;95(4):1107-14.
 86. Chang, JY, Verma, V, Li, M, et al. Proton beam radiotherapy and concurrent chemotherapy for unresectable stage III non-small cell lung cancer: final results of a phase 2 study. *JAMA Oncol*. 2017;3(8):e172032.
 87. Chen, YL, Liebsch, N, Kobayashi, W, et al. Definitive high-dose photon/proton radiotherapy for unresected mobile spine and sacral chordomas. *Spine*. 2013;38(15):E930-6.
 88. Chung, CS, Yock, TI, Nelson, K, et al. Incidence of second malignancies among patients treated with proton versus photon radiation. *Int J Radiat Oncol Biol Phys*. 2013;87(1):46-52.