

PROTON THERAPY LITERATURE

In the treatment of cancer, high doses of radiation are used to destroy cancer cells by damaging their DNA. When the DNA of a cancer cell is destroyed beyond repair, the cell dies and is then eliminated by the body through natural processes.

Proton therapy is an advanced form of radiation treatment that has been used to treat more than 160,000 people worldwide. By 2030, it is estimated that between 300,000 and 600,000 patients will have received proton therapy treatment.

The following are research studies published between 2016 and 2018 that underscore the benefits of proton therapy for certain cancer patients. The majority of the studies employ pencil beam scanning, the most precise form of proton therapy.

PROTON THERAPY

Giantsoudi D, Adams J, MacDonald S, Paganetti H. Can differences in linear energy transfer and thus relative biological effectiveness compromise the dosimetric advantage of intensity-modulated proton therapy as compared to passively scattered proton therapy? Acta Oncol. 2018 May 4:1-6.

Gao M, Mohiuddin MM, Hartsell WF, et. al. Spatially fractionated (GRID) radiation therapy using proton pencil beam scanning (PBS): Feasibility study and clinical implementation. Med Phys. 2018 Apr;45(4):1645-1653.

Carter R, Nickson C, et. al. Complex DNA Damage Induced by High Linear Energy Transfer Alpha-Particles and Protons Triggers a Specific Cellular DNA Damage Response. Int J Radiat Oncol Biol Phys. 2018 Mar 1; 100(3):776-784.

BREAST

Speleers B, Belosi FM, et. al. Comparison of supine or prone crawl photon or proton breast and regional lymph node radiation therapy including the internal mammary chain. Sci Rep. 2019 Mar 18;9(1):4755.

Leo L, Cuaron et al. Early outcomes of breast cancer patients treated with post-mastectomy uniform scanning proton therapy. Radiotherapy and Oncology. 2018.

Smith N, Jethwa KR, et. al. Early Toxicity and Patient Reported Outcomes of Post-Mastectomy Pencil-Beam Scanning Proton Therapy in Women with Immediate Tissue Expander Breast Reconstruction. Int J Radiat Oncol Biol Phys. 2018 Nov. 102(suppl 3): e573–e574.

Stick L, Yu J, et. al. Joint Estimation of Cardiac Toxicity and Recurrence Risks After Comprehensive Nodal Photon Versus Proton Therapy for Breast Cancer. Int J Radiat Oncol Biol Phys. 2017 Mar 15;97(4):754-761.

Bradley JA, Dagan R, et. al. Initial Report of a Prospective Dosimetric and Clinical Feasibility Trial Demonstrates the Potential of Protons to Increase the Therapeutic Ratio in Breast Cancer Compared With Photons. *Int J Radiat Oncol Biol Phys.* 2016 May 1;95(1):411-21.

GYNECOLOGIC CANCER

de Boer P, van de Schoot AJAJ, Westerveld H, et. al. Target tailoring and proton beam therapy to reduce small bowel dose in cervical cancer radiotherapy: A comparison of benefits. *Strahlenther Onkol.* 2018 Mar;194(3):255-263.

Lin LL, Kirk M, Scholey J, et. al. Initial Report of Pencil Beam Scanning Proton Therapy for Posthysterectomy Patients With Gynecologic Cancer. *Int J Radiat Oncol Biol Phys.* 2016 May 1;95(1):181-9.

HEAD, NECK, AND SKULL-BASE

Baumann BC, Lustig RA, et. al. A prospective clinical trial of proton therapy for chordoma and chondrosarcoma: Feasibility assessment. *J Surg Oncol.* 2019 May 20

Scholz SL, Hérault J, et. al. Proton radiotherapy in advanced malignant melanoma of the conjunctiva. *Graefes Arch Clin Exp Ophthalmol.* 2019 Mar 27.

Pearlstein KA, Wang K, Amdur RJ. Quality of Life for Patients With Favorable-Risk HPV-Associated Oropharyngeal Cancer After De-intensified Chemoradiotherapy. *Int J Radiat Oncol Biol Phys.* 2019 Mar 1;103(3):646-653.

Sakthivel V, Ganesh KM, et. al. Second malignant neoplasm risk after craniospinal irradiation in X-ray-based techniques compared to proton therapy. *Australas Phys Eng Sci Med.* 2019 Feb 6.

Patel S, Edgington S. et. al. Novel use of proton beam therapy for neoadjuvant treatment of radiation-associated squamous cell carcinoma of the esophagus. *J Gastrointest Cancer.* 2019 Feb;10(1):155-160.

Correia D, Terribilini D, et. al. Whole-ventricular irradiation for intracranial germ cell tumors: Dosimetric comparison of pencil beam scanned protons, intensity-modulated radiotherapy and volumetric-modulated arc therapy. *Clin Transl Radiat Oncol.* 2019 Jan 9;15:53-61.

Mercado CE, Holtzman AL, Rotondo R, Rutenberg MS, Mendenhall WM. Proton therapy for skull base tumors: A review of clinical outcomes for chordomas and chondrosarcomas. *Head Neck.* 2019 Feb;41(2):536-541.

Moreno A, Frank S, et. al. Intensity modulated proton therapy (IMPT) – The future of IMRT for head and neck cancer. *Oral Oncology.* 2018 Jan 88:66-74

Sharma S, Zhou O, Thompson R, et. al. Quality of Life of Postoperative Photon versus Proton Radiation Therapy for Oropharynx Cancer. *International Journal of Particle Therapy.* 2018. In-Press.

Adeberg S, Harrabi SB, et. al. Dosimetric Comparison of Proton Radiation Therapy, Volumetric Modulated Arc Therapy, and Three-Dimensional Conformal Radiotherapy Based on Intracranial Tumor Location. *Cancers (Basel)*. 2018 Oct 26;10(11).

Giantsoudi D, Adams J, MacDonald S, Paganetti H. Can differences in linear energy transfer and thus relative biological effectiveness compromise the dosimetric advantage of intensity-modulated proton therapy as compared to passively scattered proton therapy? *Acta Oncol*. 2018 Sep;57(9):1259-1264

Ardenfors O, Dsu A, Lillhök J, et. al. Out-of-field doses from secondary radiation produced in proton therapy and the associated risk of radiation-induced cancer from a brain tumor treatment. *Physica Medica: European Journal of Medical Physics*. 2018 Sep; 53: 129-136.

Leeman JE, Lee NY, Zhou Y, et. al. Endoscopic Resection Followed by Proton Therapy With Pencil Beam Scanning for Skull Base Tumors. *Laryngoscope*. 2018 Sep 12.

Gu W, O'Connor D, Nguyen D, et. al. Integrated beam orientation and scanning-spot optimization in intensity-modulated proton therapy for brain and unilateral head and neck tumors. *Med Phys*. 2018 Apr;45(4):1338-1350.

Murray FR, Snider JW, Bolsi A, et. al. Long-Term Clinical Outcomes of Pencil Beam Scanning Proton Therapy for Benign and Non-benign Intracranial Meningiomas. *Int J Radiat Oncol Biol Phys*. 2017 Aug 12.

Langendijk JA, Steenbakkers RJ. Optimizing Radiotherapy in HPV-Associated Oropharyngeal Cancer Patients. *Recent Results Cancer Res*. 2017;206:161-171. Review.

Apinorasethkul O, Kirk M, et al. Pencil beam scanning proton therapy vs rotational arc radiation therapy: A treatment planning comparison for postoperative oropharyngeal cancer *Medical Dosimetry*. 2017; 42 (1): 7-11.

Weber DC, Malyapa R, Albertini F, et. al. Long term outcomes of patients with skull-base low-grade chondrosarcoma and chordoma patients treated with pencil beam scanning proton therapy. *Radiother Oncol*. 2016 Jul;120(1):169-74.

Zhang W, Zhang X, Yang P, et. al. Intensity-modulated proton therapy and osteoradionecrosis in oropharyngeal cancer. *Radiother Oncol*. 2017 Jun;123(3):401-405.

Holm AIS, Petersen JBB, Muren LP, et. al. Functional image-guided dose escalation in gliomas using of state-of-the-art photon vs. proton therapy. *Acta Oncol*. 2017 Jun;56(6):826-831.

Geng C, Moteabbed M, Seco J, et. al. Dose assessment for the fetus considering scattered and secondary radiation from photon and proton therapy when treating a brain tumor of the mother. *Phys Med Biol*. 2016 Jan 21;61(2):683-95.

van Dijk LV, Steenbakkers RJ, ten Haken B, et. al. Robust Intensity Modulated Proton Therapy (IMPT) Increases Estimated Clinical Benefit in Head and Neck Cancer Patients. *PLoS One*. 2016 Mar 31;11(3):e0152477.

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 Jul 15;95(4):1107-14.

Blanchard P, Garden AS, Gunn GB, et. al. Intensity-modulated proton beam therapy (IMPT) versus intensity-modulated photon therapy (IMRT) for patients with oropharynx cancer - A case matched analysis. Radiother Oncol. 2016 Jul;120(1):48-55.

McKeever MR, Sio TT, Gunn GB, et. al. Reduced acute toxicity and improved efficacy from intensity-modulated proton therapy (IMPT) for the management of head and neck cancer. Chin Clin Oncol. 2016 Aug;5(4):54.

Holliday EB, Kocak-Uzel E, Feng L, et. al. Dosimetric advantages of intensity-modulated proton therapy for oropharyngeal cancer compared with intensity-modulated radiation: A case-matched control analysis. Med Dosim. 2016 Autumn;41(3):189-94.

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 Sep 1;96(1):30-41.

Adeberg S, Harrabi SB, Bougatf N, et. al. Intensity-modulated proton therapy, volumetric-modulated arc therapy, and 3D conformal radiotherapy in anaplastic astrocytoma and glioblastoma : A dosimetric comparison. Strahlenther Onkol. 2016 Nov;192(11):770-779.

LIVER

Mondlane G, Gubanski M, Lind PA, et. al. Comparative study of the calculated risk of radiation-induced cancer after photon- and proton-beam based radiosurgery of liver metastases. Phys Med. 2017 Mar 30.

LUNG

Rice SR, Saboury B, et. al. Quantification of global lung inflammation using volumetric 18F-FDG PET/CT parameters in locally advanced non-small-cell lung cancer patients treated with concurrent chemoradiotherapy: a comparison of photon and proton radiation therapy. Nucl Med Commun. 2019 Jun;40(6):618-625.

Chen J, Lu JL, et. al. Early stage non-small cell lung cancer treated with pencil beam scanning particle therapy: retrospective analysis of early results on safety and efficacy. Radiat Oncol. 2019 Jan 25;14:16.

Kim H, Pyo H, Noh JM, et. al. Preliminary result of definitive radiotherapy in patients with non-small cell lung cancer who have underlying idiopathic pulmonary fibrosis: comparison between X-ray and proton therapy. Radiat Oncol. 2019 Jan 28;14(1):19.

Liu C, Sio TT, et. al. Small-spot intensity-modulated proton therapy and volumetric-modulated arc therapies for patients with locally advanced non-small-cell lung cancer: A dosimetric comparative study. J Appl Clin Med Phys. 2018 Oct 17.

Huang Q, Jabbour SK, Xiao Z, et. al. Dosimetric feasibility of 4DCT-ventilation imaging guided proton therapy for locally advanced non-small-cell lung cancer. Radiat Oncol. 2018 Apr 25;13(1):78.

Lee E, Zeng J, Miyaoka RS, et. al. Functional lung avoidance and response-adaptive escalation (FLARE) RT: Multimodality plan dosimetry of a precision radiation oncology strategy. Med Phys. 2017 Jul;44(7):3418-3429.

Ho JC, Nguyen QN, Li H, et. al. Reirradiation of thoracic cancers with intensity modulated proton therapy. Pract Radiat Oncol. 2017 Jul 8. pii: S1879-8500(17)30196-0.

Diwanji TP, Mohindra P, Vyfhuis M, et. al. Advances in radiotherapy techniques and delivery for non-small cell lung cancer: benefits of intensity-modulated radiation therapy, proton therapy, and stereotactic body radiation therapy. Transl Lung Cancer Res. 2017 Apr;6(2):131-147.

LYMPHOMA

Ntentas G, Dedeckova K, et. al. Clinical intensity-modulated proton therapy for Hodgkin lymphoma: which patients benefit the most? Pract Radiat Oncol. 2019 Jan 29. pii: S1879-8500(19)30007-4.

Zeng C, Plastaras J, et. al. Proton pencil beam scanning for mediastinal lymphoma: treatment planning and robustness assessment Acta Oncologica 2016; 55 (9-10).

PANCREAS

Jethwa K, Tryggestad E, et. al. Initial experience with intensity modulated proton therapy for intact, clinically localized pancreas cancer: Clinical implementation, dosimetric analysis, acute treatment-related adverse events, and patient-reported outcomes. Advances in Radiation Oncology. 2018;3(3):314-321.

PEDIATRICS

Hashimoto T, Shimizu S, et. al. Clinical experience of craniospinal intensity-modulated spot-scanning proton therapy using large fields for central nervous system medulloblastomas and germ cell tumors in children, adolescents, and young adults. J Radiation Res. 2019 May 21; pii: rrz022.

Sakthivel V, Ganesh KM, et. al. Second malignant neoplasm risk after craniospinal irradiation in X-ray-based techniques compared to proton therapy. Australas Phys Eng Sci Med. 2019 Feb 6.

Hill-Kayser CE, Tochner Z, et. al. Outcomes after Proton Therapy for Treatment of Pediatric High-Risk Neuroblastoma . Int J Radiat Oncol Biol Phys. 2019 Feb 7. pii: S0360-3016(19)30190-7.

Journy N, Indelicato D, Withrow D, et. al. Patterns of proton therapy use in pediatric cancer management in 2016: An international survey. Radiotherapy and Oncology. 2018. In Press.

Huynh M, Marcu LG, Giles E, et. al. Current status of proton therapy outcome for paediatric cancers of the central nervous system - Analysis of the published literature. Cancer Treat Rev. 2018 Nov;70:272-288.

Arcott WT, Cope C. et. al. Proton Therapy for Management of Pediatric Hodgkin Lymphoma Involving the Mediastinum: Evaluation of Toxicity and Evolution of Therapy Over 7 Years of Experience. Int J Radiat Oncol Biol Phys. 2018 Nov. 102(suppl 3): S53-S54.

Ladra MM, MacDonald SM, Terezakis SA. Proton therapy for central nervous system tumors in children. *Pediatr Blood Cancer*. 2018 Jul;65(7):e27046.

Pulsifer MB, Duncanson H, Grieco J, et al. Cognitive and Adaptive Outcomes Following Proton Radiation for Pediatric Patients with Brain Tumors. *Int J Radiat Oncol Biol Phys*. 2018.

Haas-Kogan D, Indelicato D, Paganetti H, et. al. National Cancer Institute Workshop on Proton Therapy for Children: Considerations Regarding Brainstem Injury. *Int J Radiat Oncol Biol Phys*. 2018 May 1;101(1):152-168.

Bojaxhiu B, Ahlhelm F, Walser M, et. al. Radiation Necrosis and White Matter Lesions in Pediatric Patients With Brain Tumors Treated With Pencil Beam Scanning Proton Therapy. *Int J Radiat Oncol Biol Phys*. 2018 Mar 15;100(4):987-996.

Vogel J, Both S, Kirk M, et al. Proton therapy for pediatric head and neck malignancies. *Pediatr Blood Cancer*. 2017;00: e26858.

Vogel, J., Lin, H., Both, S., et. al. Pencil beam scanning proton therapy for treatment of the retroperitoneum after nephrectomy for Wilms tumor: A dosimetric comparison study. *Pediatr Blood Cancer*. 2017, 64: 39–45.

Farace P, Bizzocchi N, Righetto R, et. al. Supine craniospinal irradiation in pediatric patients by proton pencil beam scanning. *Radiother Oncol*. 2017 Apr;123(1):112-118.

Giantsoudi D, Seco J, Eaton BR, et. al. Evaluating Intensity Modulated Proton Therapy Relative to Passive Scattering Proton Therapy for Increased Vertebral Column Sparing in Craniospinal Irradiation in Growing Pediatric Patients. *Int J Radiat Oncol Biol Phys*. 2017 May 1;98(1):37-46.

Weber DC, Murray FR, Correia D, et. al. Pencil beam scanned protons for the treatment of patients with Ewing sarcoma. *Pediatr Blood Cancer*. 2017 Dec;64(12).

Leiser D, Calaminus G, Malyapa R, et. al. Tumour control and Quality of Life in children with rhabdomyosarcoma treated with pencil beam scanning proton therapy. *Radiother Oncol*. 2016 Jul;120(1):163-8.

Ares C, Albertini F, Frei-Welte M, et. al. Pencil beam scanning proton therapy for pediatric intracranial ependymoma. *J Neurooncol*. 2016 May;128(1):137-45.

Geng C, Moteabbed M, Xie Y, et. al. Assessing the radiation-induced second cancer risk in proton therapy for pediatric brain tumors: the impact of employing a patient-specific aperture in pencil beam scanning. *Phys Med Biol*. 2016 Jan 7;61(1):12-22.

PROSTATE

Dutz A, Agolli L, et. al. Early and late side effects, dosimetric parameters and quality of life after proton beam therapy and IMRT for prostate cancer: a matched-pair analysis. *Acta Oncol*. 2019 Mar 18:1-10.

Wang CJ, Guarisco. Prospective Safety and Patient-Reported Quality-of-Life Outcome for Prostate Cancer Treated with Image-Guided Compact Pencil-Beam Proton Unit. *Int J Radiat Oncol Biol Phys*. 2018 Nov. 102(suppl 3): e148.

Ong A, Ang, KW, et. al. Intensity-modulated radiotherapy for whole pelvis irradiation in prostate cancer: A dosimetric and plan robustness study between photons and protons. *Technical Innovations & Patient Support in Radiation Oncology*. 2018;6:11-19.

Lee H, Macomber M, et. al. Early toxicity and patient reported quality-of-life in patients receiving proton therapy for localized prostate cancer: a single institutional review of prospectively recorded outcomes. *Radiation Oncology*. 2018;13(1):1-9.

Takagi M, Demizu Y, et. al. Long-term outcomes in patients treated with proton therapy for localized prostate cancer *Cancer Med*. 2017 Oct; 6(10): 2234–2243.

Bryant C, Smith T, et al. Five-Year Biochemical Results, Toxicity, and Patient-Reported Quality of Life After Delivery of Dose-Escalated Image Guided Proton Therapy for Prostate Cancer. *Int J Radiat Oncol Biol Phys*. 2016 May; 95(1): 422-434.

RECTAL

Blanco Kiely JP, White BM. Robust Proton Pencil Beam Scanning Treatment Planning for Rectal Cancer Radiation Therapy. *Int J Radiat Oncol Biol Phys*. 2016 May 1;95(1):208-15.

SPINAL CORD

Ho JC, Nguyen QN, Li H, et. al. Reirradiation of thoracic cancers with intensity modulated proton therapy. *Pract Radiat Oncol*. 2018 Jan - Feb;8(1):58-65.

Snider JW, Schneider RA, Poelma-Tap D, et. al. Long-Term Outcomes and Prognostic Factors After Pencil-Beam Scanning Proton Radiation Therapy for Spinal Chordomas: A Large, Single-Institution Cohort. *Int J Radiat Oncol Biol Phys*. 2018 May 1;101(1):226-233.

Stieb S, Snider JW 3rd, Placidi L, Kliebsch U, Lomax AJ, et. al. Long-Term Clinical Safety of High-Dose Proton Radiation Therapy Delivered With Pencil Beam Scanning Technique for Extracranial Chordomas and Chondrosarcomas in Adult Patients: Clinical Evidence of Spinal Cord Tolerance. *Int J Radiat Oncol Biol Phys*. 2017 Sep 4.

PROTON THERAPY AND IMMUNOTHERAPY

Wang Y, Deng W, Li N, et al. Combining Immunotherapy and Radiotherapy for Cancer Treatment: Current Challenges and Future Directions. *Front Pharmacol*. 2018;9:185.

Zhang H, Chen J. Current status and future directions of cancer immunotherapy. *J Cancer* 2018; 9(10):1773-1781.

Lee HJ, Zeng J, Rengan R. Proton beam therapy and immunotherapy: an emerging partnership for immune activation in non-small cell lung cancer. *Transl Lung Cancer Res*. 2018;7(2):180-188.

De Felice F, Polimeni A, et. al. Radiotherapy Controversies and Prospective in Head and Neck Cancer: A Literature-Based Critical Review. Neoplasia. 2018; 20(3): 227-232.

UPPER GASTROINTESTINAL

Liu C, Bhangoo RS, et. al. Dosimetric comparison of distal esophageal carcinoma plans for patients treated with small-spot intensity-modulated proton versus volumetric-modulated arc therapies. J Appl Clin Med Phys. 2019 May 21; 257(6):1309-1318.