PROTOM INTERNATIONAL
CLINICAL EFFICACY SITE

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 280,000 people worldwide as of 2021. 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 2023 and 2025 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 (GENERAL)

Raheem AM, Abd NN, et al. Proton therapy for solid tumors: A comparative study between old and modern technologies, *Journal of Advanced Medical Technologies*, Volume 6, Issue 1, January-February 2025, Pages 517-521, ISSN (online): 2582-7138.

Hartsell W, Simone C, et al. Temporal Evolution and Diagnostic Diversification of Patients Receiving Proton Therapy in the United States: A Ten-Year Trend Analysis (2012-21) from the National Association for Proton Therapy. *International Journal of Radiation Oncology*Biology*Physics*. 2023; ISSN 0360-3016, https://doi.org/10.1016/j.ijrobp.2023.12.041.

CARDIAC

Shah KD, Chang CW, et al. A Comparative Dosimetric Study of Proton and Photon Therapy in Stereotactic Arrhythmia Radioablation for Ventricular Tachycardia, *arXiv*, 2025, https://doi.org/10.48550/arXiv.2501.18433.

BREAST

Loap, P., Vu-Bezin, J., De Marzi, L. *et al.* Proton therapy reduces the effective dose to immune cells in breast cancer patients. *Strahlenther Onkol* **200**, 1074–1079 (2024). https://doi.org/10.1007/s00066-024-02263-1

Qiao K, Wei Y, Tao C, et al. Proton therapy for breast cancer: Reducing toxicity. *Thorac Cancer*. 2024; 15(30): 2156–2165. https://doi.org/10.1111/1759-7714.15451

Chakraborty MA. Lozano A, et al. Reconstructive Outcomes and Complications after Mastectomy and Proton Therapy for Breast Cancer. *International Journal of Radiation Oncology, Biology, Physics*, Volume 120, Issue 2, e302. 2024; DOI: 10.1016/j.ijrobp.2024.07.670

G.W.Y. Chua, B.S. Ho, et al. Intensity-Modulated Proton Therapy (IMPT) Offered Advantageous Dosimetry Compared to Volumetric Arc Therapy (VMAT) or Helical Tomotherapy (HT) in Patients with Synchronous Bilateral Breast Cancer, *International Journal of Radiation Oncology*Biology*Physics, Volume 117, Issue 2, Supplement, 2023, Pages e169-e170, ISSN 0360-3016,* https://doi.org/10.1016/j.ijrobp.2023.06.1010.

Hisashi Yamaguchi, Nobuyoshi Fukumitsu, Haruko Numajiri et al. The Japanese nationwide cohort data of proton beam therapy for liver oligometastasis in breast cancer patients, 25 April 2023, *PREPRINT (Version 1) available at Research Square* [https://doi.org/10.21203/rs.3.rs-2768801/v1]

Brooks E, Vega R and et, al. Proton Therapy for Bilateral Breast Cancer Maximizes Normal-Tissue Sparing. *Int J Part Ther* 2023; doi: https://doi.org/10.14338/IJPT-22-00041.1

Lalani N, Alqarni S, Jimenez RB, et. al. The Potential of Proton Therapy for Locally Advanced Breast Cancer: Clinical and Technical Considerations. *Current Oncology*. 2023 Feb 28; 30(3):2869-2878. https://doi.org/10.3390/curroncol30030219

GYNECOLOGIC

Pollock, A. E., Risher, H., et. al. Clinical Outcomes of Intensity Modulated Proton Therapy (IMPT) Re-Irradiation for Gynecologic Malignancies. *Advances in Radiation Oncology*. 2023 Feb 25; 101191. ISSN 2452-1094. https://doi.org/10.1016/j.adro.2023.101191.

HEAD AND NECK

Bała, K., Samovich, Y. & Dorobisz, K. Proton Therapy in The Treatment of Head And Neck Cancers- Review. *Curr Oncol Rep* **26**, 1380–1387 (2024). https://doi.org/10.1007/s11912-024-01592-9

Das A, Sylvia J, At al. Impact of intensity-modulated proton therapy in reducing radiation-induced lymphopenia in glioma patients, Neuro-Oncology Advances, Volume 6, Issue 1, January-December 2024, vdae088, https://doi.org/10.1093/noajnl/vdae088

Iannalfi, A., Riva, G., Lillo, S. et al. Proton therapy for intracranial meningioma: a single-institution retrospective analysis of efficacy, survival and toxicity outcomes. J Neurooncol 169, 683–692 (2024). https://doi.org/10.1007/s11060-024-04751-x

Lillo S, Mirandola A, et al. Current Status and Future Directions of Proton Therapy for Head and Neck Carcinoma. *Cancers*. 2024; 16(11):2085. https://doi.org/10.3390/cancers16112085

Wu C, Wang J, et al. Intensity-modulated proton therapy versus volumetric-modulated ARC therapy in patients with nasopharyngeal carcinoma: A long-term, multicenter cohort study. *Radiotherapy and Oncology*, Volume 202, 2025, 110648, ISSN 0167-8140, https://doi.org/10.1016/j.radonc.2024.110648.

Sami M, Yousuf M, et al. Proton Radiation Therapy for Head and Neck Cancers. *Cureus. Vol. 16, Iss. 10*, (2024). DOI:10.7759/cureus.70752

Chang C-L, Lin K-C, et al. Comparing the oncologic outcomes of proton therapy and intensity-modulated radiation therapy for head and neck squamous cell carcinoma. *Radiotherapy and Oncology, Volume 190,* 2024, 109971, ISSN 0167-8140, doi:10.1016/j.radonc.2023.109971

Lütgendorf-Caucig C, Pelak M, et al. Prospective analysis of radiation-induced contrast enhancement (RICE) and health-related quality of life following proton therapy for CNS and skull base tumors. *International Journal of Radiation Oncology*Biology*Physics,* 2024, ISSN 0360-3016, doi.org:10.1016/j.ijrobp.2024.01.007.

Xu S, Frakulli R, Lin Y. Comparison of the Effectiveness of Radiotherapy with 3D-CRT, IMRT, VMAT and PT for Newly Diagnosed Glioblastoma: A Bayesian Network Meta-Analysis. *Cancers.* 2023; 15(23):5698. https://doi.org/10.3390/cancers15235698

Chang C, Lin K, et al. Comparative Effectiveness of Intensity-Modulated Proton Therapy Versus Intensity-Modulated Radiotherapy for Inoperable Esophageal Squamous Cell Carcinoma Patients Undergoing Curative-Intent Concurrent Chemoradiotherapy. *Journal of Thoracic Oncology.* 2023; ISSN 1556-0864, https://doi.org/10.1016/j.jtho.2023.12.021.

Zhou P, Du Y, Zhang Y, et al. Efficacy and Safety in Proton Therapy and Photon Therapy for Patients With Esophageal Cancer: A Meta-Analysis. *JAMA Netw Open*. 2023;6(8):e2328136. Published 2023 Aug 1. doi:10.1001/jamanetworkopen.2023.28136

Nangia S, Gaikwad U, Noufal MP, et al. Proton therapy and oral mucositis in oral & oropharyngeal cancers: outcomes, dosimetric and NTCP benefit. Radiat Oncol. 2023;18(1):121. Published 2023 Jul 19. doi:10.1186/s13014-023-02317-1

Chang C, Lin K, et al. Comparing the Oncologic Outcomes of Proton Therapy and Intensity-Modulated Radiation Therapy for Head and Neck Squamous Cell Carcinoma. *The Lancet.* June 2023; Available at SSRN: https://ssrn.com/abstract=4465968 or http://dx.doi.org/10.2139/ssrn.4465968

Krcek R, Leiser D, García-Marqueta M, et al. Long Term Outcome and Quality of Life of Intracranial Meningioma Patients Treated with Pencil Beam Scanning Proton Therapy. *Cancers (Basel)*. 2023;15(12):3099. Published 2023 Jun 7. doi:10.3390/cancers15123099

Hanna Ek, Ingrid Fagerström Kristensen, et al. Transitioning from conventional photon therapy to proton therapy for primary brain tumors. *Acta Oncologica*. 62:4, 391-399. Published 2023 May 18. DOI: 10.1080/0284186X.2023.2200150

Hiroshima Y, Ishikawa H, Sumiya T, et al. Clinical Impact of Proton Beam Therapy for Postoperative Lymph Node Oligorecurrence of Esophageal Cancer. *In Vivo*. 2023;37(3):1253-1259. doi:10.21873/invivo.13202

Mavrikios, A, Goudjil, F, Beddok, A, et al. Proton therapy and/or helical tomotherapy for locally advanced sinonasal skull base adenoid cystic carcinoma: Focus on experience of the Institut Curie and review of literature. *Head & Neck*. 2023; 1- 13. doi:10.1002/hed.27371

Yahya, N.; Manan, H.A. Quality of Life and Patient-Reported Outcomes Following Proton Therapy for Oropharyngeal Carcinoma: A Systematic Review. *Cancers* 2023, *15*, 2252. https://doi.org/10.3390/cancers15082252

Petruccelli A, Parent A and et, al. Estimating Potential Benefits to Neurocognition with Proton Therapy in Adults with Brain Tumors. *Int J Part Ther* 2023; doi: https://doi.org/10.14338/IJPT-22-00024.1

Press RH, Hu L, et al. Dosimetric Comparison of Intensity-Modulated Radiation Therapy (IMRT) and Intensity-Modulated Proton Therapy (IMPT) for a Novel Oral Tongue Avoidance Concept in Low-Risk Squamous Cell Carcinoma of the Oral Tongue. *Int J Part Ther*. 2023 Feb 16; DOI: https://doi.org/10.14338/IJPT-22-00032.

LIVER

Bush, DA, Volk, M., Smith, JC, et al. Proton beam radiotherapy versus transarterial chemoembolization for hepatocellular carcinoma: Results of a randomized clinical trial. *Cancer.* 2023; 1-10. doi:10.1002/cncr.34965

Chen MF, Chen PT, Hsieh CC, Wang CC. Effect of Proton Therapy on Tumor Cell Killing and Immune Microenvironment for Hepatocellular Carcinoma. *Cells*. 2023;12(2):332. Published 2023 Jan 15. doi:10.3390/cells12020332

LUNG AND THORACIC

Patel JS, McCall NS, et al. Immune System Dose With Proton Versus Photon Radiotherapy for Treatment of Locally Advanced NSCLC. *International Journal of Particle Therapy*, Volume 12, 2024, 100016, ISSN 2331-5180, https://doi.org/10.1016/j.ijpt.2024.100016.

Cortiula F, Hendriks L, et al. Proton and photon radiotherapy in stage III NSCLC: Effects on hematological toxicity and adjuvant immune therapy. *Radiotherapy and Oncology.* Volume 190, 2024; 110019, ISSN 0167-8140, https://doi.org/10.1016/j.radonc.2023.110019.

Nakamura M, Ishikawa H, Ohnishi K, et al. Effects of lymphopenia on survival in proton therapy with chemotherapy for non-small cell lung cancer, *Journal of Radiation Research*, 2023;, rrac084, https://doi.org/10.1093/jrr/rrac084

PANCREAS

Jacob Eckstein, Isabelle Choi , et al. Proton Therapy for Unresectable and Medically Inoperable Locally Advanced Pancreatic Cancer: Results from a Multi-Institutional Prospective Registry. *Advances in Radiation Oncology,* 2023, 101250, ISSN 2452-1094, https://doi.org/10.1016/j.adro.2023.101250.

PEDIATRICS

Brisson R, Indellicato D, et al. Long-term Outcomes Following Proton Therapy for Pediatric Low-grade Glioma of the Spine (LGGS), *International Journal of Radiation Oncology* Biology *Physics*, Volume 121, Issue 3, 1 March 2025, Page e5. https://doi.org/10.1016/j.ijrobp.2024.11.023.

Gill, GS, Allison AW, et al. Long Term Proton Therapy Outcomes in the Reirradiation Setting for Recurrent Pediatric Ependymoma. I*nternational Journal of Radiation Oncology, Biology, Physics,* Volume 120, Issue 2, e687. 2024; DOI: 10.1016/j.ijrobp.2024.07.1509

Vennarini S, Colombo F, et al. Proton therapy for pediatric malignancies: Indications and challenges focusing on the oncological landscape. *Tumori Journal*. 2024;110(6):416-421. doi:10.1177/03008916241287016

Blommaert J, De Saint-Hubert M, Depuydt T, et al. Challenges and opportunities for proton therapy during pregnancy. *Acta Obstet Gynecol Scand*. 2024; 103: 767-774. doi:10.1111/aogs.14645

C.E. Hill-Kayser, Y. Li, et al. Survival and Local Recurrence Risk in Patients with High-Risk Neuroblastoma Treated with Proton Therapy over a 10 Year Interval, *International Journal of Radiation Oncology*Biology*Physics, Volume 117, Issue 2, Supplement, 2023, Pages e516-e517, ISSN 0360-3016*, https://doi.org/10.1016/j.ijrobp.2023.06.1780.

D. Leiser, T. Dantonello, R. Krcek, et al. Long Term Clinical Outcome and Quality of Life of Children, Adolescents and Young Adults Treated with Pencil Beam Scanning Proton Therapy for Rhabdomyosarcoma, *International Journal of Radiation Oncology*Biology*Physics, Volume 117, Issue 2, Supplement, 2023, Page S77, ISSN 0360-3016*, https://doi.org/10.1016/j.ijrobp.2023.06.391.

J. Sienna, L. Kahalley, et al. Dose Reductions to Critical Brain Organs-at-Risk and Better Cognition in Children with Medulloblastoma Receiving Proton Therapy, *International Journal of Radiation Oncology*Biology*Physics, Volume 117, Issue 2, Supplement, 2023, Page S134, ISSN 0360-3016,* https://doi.org/10.1016/j.ijrobp.2023.06.536.

Berlin E, Eisenberg R, Hill-Kayser C, et al. Delivery of Re-irradiation and Complex Palliative Radiotherapy Using Proton Therapy in Pediatric Cancer Patients. Authorea Preprints; 2023. DOI: 10.22541/au.168301665.52443287/v1.

Grippin AJ, McGovern SL. Proton therapy for pediatric diencephalic tumors. *Front Oncol*. 2023;13:1123082. Published 2023 May 5. doi:10.3389/fonc.2023.1123082

Myrsini Ioakeim-Ioannidou, Andrzej Niemierko, et al. Surgery and proton radiation therapy for pediatric base of skull chordomas: Long-term clinical outcomes for 204 patients, *Neuro-Oncology*, 2023;, noad068, https://doi.org/10.1093/neuonc/noad068

PROSTATE

K.R. Gergelis, M. Bai, et al. Long-Term Patient-Reported Bowel and Urinary Quality of Life in Patients Treated with Intensity-Modulated Radiotherapy and Intensity-Modulated Proton Therapy for Localized Prostate Cancer. *International Journal of Radiation Oncology*Biology*Physics, Volume 117, Issue 2, Supplement, 2023, Page e385, ISSN 0360-3016,* https://doi.org/10.1016/j.ijrobp.2023.06.2502.

Sosa AJ, Thames HD, Sanders JW, et al. Proton Therapy for the Management of Localized Prostate Cancer: Long-Term Clinical Outcomes at a Comprehensive Cancer Center . Published online ahead of print, 2023 Aug 17. *Radiother Oncol*. 2023;109854. doi:10.1016/j.radonc.2023.109854

Mariluz De Ornelas, Giuseppe Carlo Iorio, et al. Bone marrow sparing in prostate cancer patients treated with Post-operative pelvic nodal radiotherapy – A proton versus photon comparison. *Physica Medica, Volume 112*, 2023, 102644, ISSN 1120-1797. doi.org/10.1016/j.ejmp.2023.102644.

Goginen Ei, Cruickshank L, et al. In silico comparison of whole pelvis intensity-modulated photon versus proton therapy for the postoperative management of prostate cancer. *Acta Oncol*. 2023 Jun 22;1-6. doi: 10.1080/0284186X.2023.2224925

RECTAL

M.Fok, S. Toh, J.E. Maducolil, et al. 455 Proton Beam Therapy in Rectal Cancer: A Systematic Review and Meta-Analysis. *British Journal of Surgery*, Volume 108, Issue Supplement_2, May 2021, znab135.020, https://doi.org/10.1093/bjs/znab135.020

Koroulakis A, Molitoris J, Kaiser A, et, al. RE-IRRADIATION FOR RECTAL CANCER USING PENCIL-BEAM SCANNING PROTON THERAPY: A SINGLE INSTITUTIONAL EXPERIENCE, *Advances in Radiation Oncology.* 2020 Oct 14.

Vaios E, Wo J, et. al. Proton beam radiotherapy for anal and rectal cancers. *J Gastrointest Oncol*. 2020 Feb; 11(1): 176–186.

OCULAR

Chan AW, Lin H, Yacoub I, et al. Proton Therapy in Uveal Melanoma. *Cancers*. 2024; 16(20):3497. https://doi.org/10.3390/cancers16203497

SARCOMA

Nakajima K, Sudo S, et al. Image-Guided Proton Therapy for Unresectable Trunk Soft-Tissue Sarcoma. *International Journal of Radiation Oncology, Biology, Physics*, Volume 120, Issue 2, e474 - e475. 2024; DOI: 10.1016/j.ijrobp.2024.07.1055