

Proton Therapy







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ABOUT THE AMERICAN BRAIN TUMOR ASSOCIATION

Founded in 1973, the American Brain Tumor Association (ABTA) was the first national nonprofit organization dedicated solely to brain tumor research. The ABTA has since expanded our mission and now provides comprehensive resources to support the complex needs of brain tumor patients and caregivers, across all ages and tumor types, as well as the critical funding of research in the pursuit of breakthroughs in brain tumor diagnoses, treatments and care.

To learn more, visit abta.org.

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Proton Therapy

INTRODUCTION

This brochure is about proton therapy, an advanced method for delivering radiation treatments to patients with different types of cancers, including brain tumors.

About 70% of brain tumors are not cancerous, but they are still a serious medical condition and often require treatment. The remaining 30% of brain tumors are cancerous (malignant). Cancerous brain tumors generally grow faster and behave more aggressively than so-called benign tumors. They commonly invade other areas of the brain and spinal cord and can be deadly. Brain tumor treatments include surgery, radiation, and chemotherapy.

Radiation therapy may be used alone, or in combination with other treatments, to: 3,4,5

- Help prevent the tumor from returning after surgery or chemotherapy
- Relieve symptoms caused by a tumor
- Treat tumors that cannot be removed with surgery

The goal of radiation therapy is to destroy tumor cells and slow or stop the tumor from growing, while

limiting the amount of radiation to nearby healthy brain tissue. This is especially important for young children, as their developing brains and bodies are very sensitive to the potential long-term effects of radiation.

A doctor who specializes in giving radiation therapy is called a *radiation oncologist*. The radiation oncologist works with a team of doctors, medical physicists, technical experts, radiation therapists, and nurses.

Radiation therapy uses very focused, high-energy particles and waves (protons, electrons or photons) to kill the tumor cells and a margin – or border – of normal brain tissue surrounding the tumor.⁶ Treating the area near the tumor may help kill cancer that has spread into surrounding tissue. Often, the margin contains some healthy tissue and possibly vital structures, such as the brain stem and spinal cord, which, if damaged, may result in long-term side effects.

The most common type of radiation used to treat brain tumors is known as *external beam radiation therapy*, or EBRT.^{4,7} There are different EBRT methods, but all of them involve using a machine to deliver the radiation through the skin directly to the tumor. One type of EBRT is proton therapy.



The gantry rotates and directs the protons to the patient's tumor. Photo courtesy of MD Anderson Proton Therapy Center

WHAT IS PROTON THERAPY?

Proton therapy uses positively charged particles, known as protons, to send a high level of energy directly to the tumor site using a machine called a *synchrotron* or *cyclotron*. The energy fuels the protons to travel to the desired depth in the body. But unlike photon beams, the proton beams do not travel through the entire body. Once they reach the tumor, the proton beams deliver the targeted radiation dose to the tumor and then they stop moving through the tissue. 8.9

This unique feature helps to reduce the harm caused to surrounding healthy tissues and organs beyond the tumor. That, in turn, may result in fewer side effects, such as cognitive changes (a decline in mental sharpness, thought processes, and memory).

Proton therapy is typically recommended for the treatment of tumors that are smaller with well-defined margins and those that are located near vital organs and heathy brain tissue.^{3,5} It is usually not recommended for tumors that have spread to other areas of the body.

Brain tumors that may be suitable for proton therapy include:

- Arteriovenous malformations^{10,11}
- Atypical teratoid/rhabdoid tumor¹²
- Certain low- and high-grade gliomas 13,14,15
- Chondrosarcomas^{5,16,17}
- Chordomas^{5,17}
- Ependymomas^{14,18}
- Germ cell tumors^{19,20}
- Juvenile pilocytic astrocytomas^{21,22}
- Meningiomas^{5,23}
- Medulloblastomas14,24
- Pituitary adenomas^{25,26}
- Some brain tumors previously treated with radiation therapy^{27,28}
- Vestibular schwannomas/Acoustic neuromas^{29,30}

PENCIL BEAM PROTON THERAPY

A more advanced type of proton therapy, known as *pencil beam proton therapy*, delivers a single, narrower proton beam that is only a few millimeters wide. Using proton beam therapy on a tumor has been described as painting on a canvas, only using the tip of the brush instead of broad strokes. This treatment approach reduces the risk for side effects even more so than proton beam therapy. Pencil beam proton therapy has been shown to effectively treat brain tumors in both adults and children.^{31,32,33}

WHAT TO EXPECT

The healthcare team spends a great deal of time and effort to plan treatment with proton beam therapy. Keeping patients still, determining exactly where the proton beams must enter the body to reach the tumor, and choosing the best possible dose of radiation and schedule are all critical steps in the process.

People usually receive proton therapy in an outpatient setting, not a hospital. During a pre-treatment session known as a **simulation**, patients are guided into the position they will need to stay in for the sessions. ^{4,6} Next, patients will have a **computed tomography** (*CT*) **or magnetic resonance imaging** (MRI) scan. ^{5,34} The imaging scan will help clinicians tailor the radiation dose and number and shape of radiation beams as well as map out the exact area to be treated.

Patients having proton therapy for a brain tumor will need to be fitted with a **custom-made mask**. ^{5,34} This mask will keep patients still and help to precisely direct the proton beam during the actual procedure. The location where the proton beam will enter the skin is marked.



Patient receiving targeted radiation therapy while wearing a customized mask for head stabilization during treatment.

Before every treatment, the medical team will do either a CT or MRI scan, which helps ensure that patients are in the same exact position each time. That way, the proton beams will hit the tumor and not nearby tissue.

During the proton therapy session, patients are placed on a treatment table in a special treatment room. 5,6,16 Some treatment rooms have a gantry, which is a donut-shaped, rotating steel machine that is about 35 feet in diameter, three stories tall, and weighs up to 200 tons. Most of this massive machinery is built behind walls and is not visible to the patient in the treatment room. Once the patient is in the proper position, the medical team leaves the room to start the procedure. The gantry rotates around the table, directing the protons to the patient's tumor through a nozzle on the cyclotron/synchrotron. The proton beam travels through the gantry, guided by magnets, toward the tumor.

Typically, proton therapy treatments last 15 to 30 minutes, from beginning to end.⁵ The procedure itself takes only a few minutes and is painless.^{8,16}

The number of treatment sessions needed depends on the type and grade of the tumor.⁵ To minimize side effects, treatments are typically given five days a week for five to



The gantry with a patient during the procedure. Photo courtesy of MD Anderson Proton Therapy Center

seven weeks.^{3,7} This allows enough radiation into the body to kill the cancer while giving healthy cells time to heal.

Following proton therapy, patients should be able to return to their normal activities. Patients will likely see their doctor every three to six months for a follow-up exam.³

BENEFITS OF PROTON THERAPY

The greatest benefit proton therapy offers is that it reduces the amount of radiation to healthy tissues as well as vital organs and structures near the brain tumor. ^{5,9,35} As much as 60% less radiation is delivered to healthy tissues around the tumor using proton therapy compared with other forms of EBRT. ^{5,36} Sparing healthy tissues and organs may reduce the side effects that patients experience.

As the proton beams race toward the tumor site, they release a much smaller amount of energy on surrounding healthy tissues and organs than conventional forms of radiation. Other kinds of radiation therapy, such as photon beams, spread radiation as they exit the body whereas once the proton beams stop, there

is virtually no radiation released on the tissue beyond the targeted tumor.^{5,35}

Other benefits of proton therapy include:

- Resulting in fewer secondary cancers compared with other forms of EBRT^{37,38,39}
- Delivering a higher radiation dose to the tumor than is possible with conventional forms of radiation therapy^{5,16}
- Reaching tumors located near critical organs and brain tissue^{3,5,16}

Clinical trials are under way to compare proton beam therapy with conventional forms of radiation therapy for treating cancers, including brain tumors. Many of these studies are funded by the National Cancer Institute and the Patient-Centered Outcomes Research Institute.

Proton Therapy for Children. Children, especially younger ones, have the most to gain from proton therapy because their growth and development can be negatively affected by radiation exposure. ^{35,36} Treatment with proton therapy for brain tumors in children is associated with favorable cognitive outcomes, including those related to intelligence, processing speed, and functioning (ability to perform normal daily activities). ^{41,42}

Some studies have shown proton therapy results in better cognitive outcomes than conventional forms of radiation for children treated for brain and other central nervous system tumors.^{43,44} Researchers suggest that this could lead to a better quality of life and functioning in adult survivors of pediatric brain tumors.⁴¹ Children often tolerate proton therapy well, but younger children may need to be sedated if they cannot remain still during the procedure.

Disadvantage of Proton Therapy. A major drawback to proton therapy is that it requires highly specialized and expensive equipment⁵ costing upwards of \$200,000,000. Proton therapy is available in only a few medical centers in the United States. However, the number of proton therapy

treatment centers is growing. In 2006, there were five such centers in the U.S. By 2020, that number had risen to 35.45 Proton therapy costs more than conventional radiation therapy and insurance providers vary on which cancers they cover and how much the patient must pay.⁵ Smaller, single room facilities, which are less expensive and require less space, are becoming more common and should make proton therapy available in more areas and more affordable in the future.

SIDE EFFECTS

As with all radiation therapy, there is the potential for patients undergoing proton therapy to experience side effects from the treatment. Different people experience different side effects. If side effects do occur, they tend to start after a few treatments and usually stop shortly after the final treatment.4

Common side effects from proton therapy include fatigue (extreme tiredness even after sleeping), mild skin reactions (redness, irritation, swelling, dryness, or blistering), hair loss near the treated area, upset stomach (nausea, vomiting, diarrhea, and loss of appetite), and headache.5,16

Some long-term side effects may occur months or years after treatment is finished. These may include secondary cancers, infertility (inability to become pregnant or father a child),4 and radiation necrosis (death of healthy tissue due to the treatment) at or near the treatment site.34

Follow-up studies have shown that both adults and children treated with proton therapy for brain tumors did not have a significant decline in cognitive skills and functioning, even years after treatment.^{15,46,47,48}

Side effects depend on:3-5

- Tumor type, size, and location
- Part of the body being treated
- Types of healthy tissue near the tumor
- Treatment dose
- · Patient's overall health

Relieving symptoms of side effects, whether they are caused by the tumor itself or treatments, is an important part of the care plan for all patients with brain tumors.

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

Educational brochures are available on our website or can be requested in hard copy format for free by calling the ABTA. Most brochures are available in Spanish, with exceptions marked with an asterisk.

GENERAL INFORMATION

About Brain Tumors: A Primer for Patients and Caregivers Brain Tumor Dictionary* Brain Tumors Handbook for the Newly Diagnosed* Caregiver Handbook*

TUMOR TYPES

Ependymoma Glioblastoma and Anaplastic Astrocytoma Medulloblastoma Meningioma Metastatic Brain Tumors Oligodendroglioma and Oligoastrocytoma Pituitary Tumors

TREATMENT

Chemotherapy
Clinical Trials
Conventional Radiation Therapy
Proton Therapy
Stereotactic Radiosurgery*
Steroids
Surgery

AMERICAN BRAIN TUMOR ASSOCIATION INFORMATION, RESOURCES AND SUPPORT

INFORMATION

ABTA WEBSITE | ABTA.ORG

Offers more than 200 pages of information, programs, support services and resources, including: brain tumor treatment center and support group locators, caregiver resources, research updates and tumor type and treatment information across all ages and tumor types.

EDUCATION & SUPPORT

- ABTA Educational Meetings & Webinars
 In-person and virtual educational meetings led by nationally-recognized medical professionals.
- ABTA Peer-to-Peer Mentor Program
 Connect with a trained patient or caregiver mentor to help navigate a brain tumor diagnosis.
- ABTA Connections Community
 An online support and discussion community of more than 25,000 members.
- ABTA CareLine

For personalized information and resources, call 800-886-ABTA (2282) or email info@abta.org to connect with a CareLine staff member.

GET INVOLVED

- Join an ABTA fundraising event.
- Donate by visiting abta.org/donate.

CONTACT THE ABTA

CareLine: 800-886-ABTA (2282)

Email: info@abta.org Website: abta.org

REFERENCES

- ¹ American Brain Tumor Association. Brain Tumor Education. 2019. https://www.abta.org/ about-brain-tumors/brain-tumor-education/ (Accessed 5-18-20)
- ² National Foundation for Cancer Research. 7 Facts You Need to Know About Brain Tumors. 2017. https://www.nfcr.org/blog/blog7-facts-need-know-brain-tumors/ (Accessed
- 3 U.S. National Library of Medicine: MedLine Plus. Radiation Therapy. 2018. https:// medlineplus.gov/ency/article/001918.htm (Accessed 4-28-20)
- 4 ASCO® answers: Radiation Therapy. 2016. https://www.cancer.net/sites/cancer.net/files/ asco_answers_radiation_therapy.pdf (Accessed 4-28-20)
- 5 Proton Therapy. Doctor-Approved Patient Information from ASCO®. 2018. https://www. cancer.net/navigating-cancer-care/how-cancer-treated/radiation-therapy/proton-therapy (Accessed 4-23-20)
- 6 National Comprehensive Cancer Network. NCCN guidelines for patients®. Brain Cancer: Gliomas. Version 1.2016. https://www.nccn.org/patients/guidelines/brain-gliomas/files/ assets/common/downloads/files/gliomas.pdf (Accessed 4-28-20)
- ⁷ American Society for Radiation Oncology (ASTRO). RT Answers. How does radiation therapy work? 2019 https://ww.rtansers.org/How-does-radiation-therapy-work/External-Beam-Radiation-Therapy. (Accessed 4-28-20)
- 8 National Cancer Institute. External beam radiation therapy for cancer. 2018. https://www. cancer.gov/about-cancer/treatment/types/radiation-therapy/external-beam (Accessed
- ⁹ Tian X, Liu K, Hou Y, et al. The evolution of proton beam therapy: Current and future status (review). Mol Clin Oncol. 2018;8(1):15-21.
- 10 Walcott BP, Hattangadi-Gluth JA, Stepleton CJ, et al. Proton beam stereotactic radiosurgery for pediatric cerebral arteriovenous malformations. Neurosurgery. 2014;74(4):367-74
- 11 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
- 12 McGovern SL, Okcu MF, Munsell MF, et al. Outcomes and acute toxicities of proton therapy for pediatric atypical teratoid/rhabdoid tumor of the CNS. Int J Radiat Oncol Biol Phys. 2014;90(5):1143-52.
- 13 Jhaveri J, Cheng E, Tian S, et al. Proton vs. photon radiation therapy for primary gliomas: An analysis of the National Cancer Data Base. Frontiers Oncol. 2018;8:440.
- 14 Stross WC, Malouff TD, Waddle MR, et al. Proton beam therapy utilization in adults with primary brain tumors in the United States. J Clin Neurosci. 2020;75:112-6.
- 15 Tabrizi S, Yeap BY, Sherman JC, et al. Long-term outcomes and late adverse effects of a prospective study on proton radiotherapy for patients with low-grade glioma. Radiother Oncol. 2019;137:95-101.
- U.S. National Library of Medicine: MedLine Plus. Proton Therapy. 2018. https:// medlineplus.gov/ency/article/007281.htm (Accessed 4-28-20)
- 17 Baumann BC, Lustig RA, Mazzoni S, et al. A prospective clinical trial of proton therapy for chordoma and chondrosarcoma: Feasibility assessment. J Surg Oncol. 2019;120(2):200-5.
- 18 Indelicato DJ, Bradley JA, Rotondo RL, et al. Outcomes following proton therapy for pediatric ependymoma. Acta Oncol. 2018;57(5):644-8.
- 19 Park J, Park Y, Lee SU, et al. Differential dosimetric benefit of proton beam therapy over intensity modulated radiotherapy or a variety of targets in patients with intracranial germ cell tumors. Radiat Oncol. 2015;10:135.
- ²⁰ Correia D, Terribilini D, Zepter S, et al. Whole-ventricular irradiation for intracranial germ cell tumors: Dosimetric comparison of pencil beam scanned protons, intensitymodulated radiotherapy and volumetric-modulated arc therapy. Clin Translat Radiat Oncol. 2019;15:53-61.
- ²¹ Mannina EM, Bartlett GK, McMullen KP. Extended volumetric follow-up of juvenile pilocytic astrocytomas treated with proton beam therapy. Int J Part Ther. 20-16;3(2):291-
- 22 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.
- ²³ Adeberg S, Harrabi SB, Verma V, et al. Treatment of meningioma and glioma with protons and carbon ions. Radiat Oncol. 2017:12:193
- ²⁴ Grewal AS, Li Y, Fisher MJ, et al. Tumor bed proton irradiation in young children with localized medulloblastoma. Pediatr Blood Cancer. 2019;66(12):e27972.
- 25 Kennedy WR, Dagan R, Rotondo RL, et al. Proton therapy for pituitary adenoma. Applied Radiat Oncol. 2015;4(1):22-7.
- ²⁶ Wattson DA, Tanguturi SK, Spiegel DY, et al. Outcomes of proton therapy for patients with functional pituitary adenomas. Int J Radiat Oncol Biol Phys. 2014;90(3):532-9.
- ²⁷ Imber BS, Neal B, Casey DL, et al. Clinical outcomes of recurrent intracranial
- meningiomas treated with proton beam reirradiation. Int J Part Ther. 2019;5(4):11-22. ²⁸ Eaton BR, Chowdhry V, Weaver K, et al. Use of proton therapy for re-irradiation in
- ²⁹ Weber DC, Chan AW, Bussiere MR, et al. Proton beam radiosurgery for vestibular schwannoma: tumor control and cranial nerve toxicity. Neurosurgery. 2003;53(3):577-86.

pediatric intracranial ependymoma. Radiother Oncol. 2015;116(2):301-8.

PROTON THERAPY

- ³⁰ Zhu S, Rotondo R, Mendenhall WM, et al. Long-term outcomes of fractionated stereotactic proton therapy for vestibular schwannoma: A case series. Int J Part Ther. 2018;4(4):37-46.
- ³¹ Ares C, Albertini F, Frei-Welte M, et al. Pencil beam scanning proton therapy for pediatric intracranial ependymoma. J Neurooncol. 2016;128(1):137-45.
- ³² Badiyan SN, Ulmer S, Ahlhelm FJ, et al. Clinical and radiologic outcomes in adults and children treated with pencil-beam scanning proton therapy for low-grade glioma. Int J Part Ther. 2017;3(4):450-60.
- ³³ Weber DC, Ares C, Malyapa R, et al. Tumor control and QoL outcomes of very young children with atypical teratoid/rhabdoid tumor treated with focal only chemo radiation therapy using pencil beam scanning proton therapy. J Neurooncol. 2015;121(2):389-97.
- ³⁴ Mitin T. (2019). Radiation therapy techniques in cancer treatment. In SR Vora (Ed.), UpToDate. Retrieved from https://www.uptodate.com/contents/radiation-therapy-techniquesin-cancer-treatment?search=proton%20therapy&source=search_result&rselectedTitle=1~150& usage_type=default&rdisplay_rank=1 (Accessed 4-23-20)
- 35 Lau C, Teo WY. (2019). Overview of the management of central nervous system tumors in children. In C Armsby (Ed.), UpToDate. Retrieved from https://www.uptodate.com/contents/overview-of-the-management-of-central-nervous-system-tumors-in-children?search=proton%20therapy&rsource=search_result&rselectedTitle=2~150&rusage_type=default&rdisplay_rank=2 (Accessed 4-23-20)
- ³⁶ Delaney TF. Proton therapy in the clinic. Front Radiat Ther Oncol. 2011;43:465-85.
- ³⁷ Miralbell R, Lomax A, Cella L, et al. Potential reduction of the incidence of radiation-induced second cancers by using proton beams in the treatment of pediatric tumors. Int J Radiat Oncol Biol Phys. 2002;54(3):824-9.
- Xiang MH, Chang DT, Pollom EL, et al. Risk of subsequent cancer diagnosis in patients treated with 3D conformal, intensity modulated, or proton beam radiation therapy. J Clin Oncol. 2019;37(15)suppl. 1503.
- ³⁹ 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.
- 40 Bekelman J, Denicoff A, Buchsbaum J. Randomized trials of proton therapy: Why they are at risk, proposed solutions, and implications for evaluating advanced technologies to diagnose and treat cancer. J Clin Oncol. 2018;36(24:2461-4.
- ⁴¹ Gross JP, Powell S, Zelko F, et al. Improved neuropsychological outcomes following proton therapy relative to x-ray therapy for pediatric brain tumor patients. Neuro-Oncol. 2019;21(7):934-43.
- ⁴² Antonini TN, Ris MD, Grosshans DR, et al. Attention, processing speed, and executive functioning in pediatric brain tumor survivors treated with proton beam radiation therapy. Radiother Oncol. 2017;124(10:89-97.
- ⁴³ Pulsifer MB, Sethi RV, Kuhlthau KA, et al. Early cognitive outcomes following proton radiation in pediatric patients with brain and CNS tumors. Int J Radiat Oncol Biol Phys. 2015;93(2):400-7.
- ⁴⁴ Kahalley LS, Peterson R, Ris MD, et al. Superior intellectual outcomes after proton radiotherapy comkpared with photon radiotherapy for pediatric medulloblastoma. J Clin Oncol 2019;38:454-61.
- ⁴⁵ National Association of Proton Therapy. 2020. https://www.proton-therapy.org/science/ (Accessed 4-23-20)
- ⁴⁶ Dutz A, Agolli L, Butof R, et al. Neurocognitive function and quality of life after proton beam therapy for brain tumour patients. Radiother Oncol. 2020;143:108-16.
- ⁴⁷Pulsifer MB, Duncanson H, Grieco J, et al. Cognitive and adaptive outcomes after proton radiation for pediatric patients with brain tumors. Int J Radiat Oncol Biol Phys. 2018;102(2):391-8.
- ⁴⁸ Greenberger BA, Pulsifer MB, Ebb DH. Clinical outcomes and late endocrine, neurocognitive, and visual profiles of proton radiation for pediatric low-grade gliomas. Int J Radiat Oncol Biol Phys. 2014;89(5):1060-8.

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