

PROTON BEAM THERAPY (PBT)

This Model Policy* addresses coverage for Proton Beam Therapy.

DESCRIPTION

Proton Beam Therapy (PBT) is a technology for delivering conformal external beam radiation with positively charged atomic particles to a well-defined treatment volume. PBT is approved by the U.S. Food and Drug Administration.

Due to its unique dose deposition characteristics, PBT can, in certain situations, deliver the prescribed target dose while giving a lower dose to normal tissues as compared to photon-based forms of external beam radiotherapy.

Photon beams deposit their greatest amount of energy beneath the patient's surface with a gradual reduction in energy deposition along the beam path as photons pass through the target and then through an exit point out of the body. In contrast, the physical profile of a beam of proton particles allows for the majority of its energy to be deposited over a very narrow range of tissue at a depth largely determined by the energy of the proton beam. A proton beam deposits relatively less radiation energy upon entering the body compared to a photon beam. The energy deposition of the proton beam then rapidly increases over a narrow range of tissue at a desired depth to produce an intense dose distribution pattern called the Bragg peak. Beyond the Bragg peak, energy and dose deposition rapidly decrease, resulting in the absence of any significant exit dose deposited in normal tissue beyond the target.

TREATMENT

PBT Treatment Planning

PBT can allow for radiation treatment plans that are highly conformal to the target volume. PBT planning defines the necessary field sizes, gantry angles and beam energies needed to achieve the desired radiation dose distribution.

An assessment of patient suitability for PBT is an important step in the process of care. Changes in the density and composition of tissues in the path of the beam have much greater impact on the delivered dose for protons than photons. Tissue interfaces, especially those with large differences in electron density, can lead to larger or unacceptable dosimetric uncertainties in PBT for certain patients.

PBT treatment planning is a multi-step process and shares functions common to other forms of external beam radiotherapy planning:

1. **Simulation and Imaging:** Three-dimensional image acquisition of the target region by simulation employing CT, CT/ PET and/or MR scanning equipment is an essential prerequisite to PBT treatment planning. If respiratory or other normal organ motion is expected to produce significant movement of the target region during radiotherapy delivery, the radiation oncologist may additionally elect to order multi-phasic treatment planning image sets to account for motion when rendering target volumes. As in all forms of external beam

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radiation therapy, immobilization is critical. However, for PBT, the immobilization system can impact the dose distribution and therefore these devices must be carefully designed. Many photon-based patient immobilization devices are not appropriate for use in PBT.

2. **Contouring:** Defining the target and avoidance structures is a multi-step process:
 - a. The radiation oncologist reviews the three-dimensional images and outlines the treatment target on each slice of the image set. The summation of these contours defines the Gross Tumor Volume (GTV). For multiple image sets, the physician may outline separate GTVs on each image set to account for the effect of normal organ motion upon target location and shape. Some patients may not have GTVs if they have had previous treatment with surgery or chemotherapy, in which case treatment planning will be based on CTVs as described below.
 - b. The radiation oncologist draws a margin around the GTV to generate a Clinical Target Volume (CTV) which encompasses the areas at risk for microscopic disease (i.e., not visible on imaging studies). Other CTVs may be created based on the estimated volume of residual disease. For multiple image sets, the physician may draw this margin around an aggregate volume containing all image set GTVs to generate an organ-motion CTV, or Internal Target Volume (ITV).
 - c. In X-ray therapy, to account for uncertainties in the planning and delivery processes, a final margin is then added to create a Planning Target Volume (PTV). Analogous to the approach used in X-ray therapy, a lateral target expansion guards against under-dosing the target in the presence of daily setup variation and/or organ and patient motion. With PBT, however, the target expansion in the beam direction must also ensure coverage for uncertainties in the range of the proton beam which may not perfectly match the radiologic depth of the target. The expansion in the beam direction may be different from the lateral expansion. Because the lateral and range expansions may differ for each beam, there is no longer a single PTV that is sufficient for a multi-field proton plan. Rather than prescribing a uniform dose to a PTV, in PBT the plan should be designed to cover the CTV in the presence of expected uncertainties.
 - d. Nearby normal structures that could potentially be harmed by radiation (i.e., "organs at risk", or OARs) are also contoured.
3. **Radiation Dose Prescribing:** The radiation oncologist assigns specific dose coverage requirements for the CTV which will be met even in the presence of expected positional and range uncertainties. A typical prescription may define a dose that will be delivered to at least 99% of the CTV. This coverage requirement is often accompanied by a minimum acceptable point dose delivered within the CTV in the presence of expected uncertainties and a constraint describing an acceptable range of dose homogeneity. Additionally, PBT prescription requirements routinely include dose constraints for the OARs (e.g., upper limit of mean dose, maximum allowable point dose, and/or a critical volume of the OAR that must not receive a dose above a specified limit). Doses to normal structures must also be evaluated in the presence of delivery and range uncertainties. A treatment plan that satisfies these requirements and constraints should maximize the potential for disease control and minimize the risk of radiation injury to normal tissue.
4. **Dosimetric Planning and Calculations:** The qualified medical physicist or a supervised dosimetrist calculates a treatment plan to deliver the prescribed radiation dose to the CTV and simultaneously satisfy the normal tissue dose constraints by delivering significantly lower doses to nearby organs. Delivery mechanisms vary, but through the use of scanning magnets or scattering devices PBT plans spread protons laterally over the extent of a target volume. In some cases, the lateral spread of the protons is controlled through the use of an aperture. Additionally, multiple proton energies are combined, through the use of mechanical absorbers or accelerator energy changes, to deliver the planned dose distribution over the longitudinal extent of the target. Range compensation devices are sometimes used to match the range of the proton beam to the distal edge of the



target. Regardless of the delivery technique, all delivery parameters and/or field specific hardware are developed by a medical physicist or supervised dosimetrist and an expected dose distribution is calculated for the treatment plan. While PBT plans may be more conformal than X-ray therapy plans, they may also be more susceptible to uncertainties in patient positioning or proton range in the patient. Nominal treatment plans should be evaluated in the presence of both positional and range uncertainties to ensure that the planned CTV coverage and normal tissue sparing are likely to be preserved under the range of expected uncertainties.

5. **Patient Specific Dose Verification:** An independent dose calculation and/or measurement should confirm that the intended dose distribution for the patient is physically verifiable and feasible.

Documentation of all aspects of the treatment planning process is essential.

PBT Treatment Delivery

Proton delivery methods can be described in one of two forms: scattering or scanning.

In scattered deliveries, the beam is broadened by scattering devices, beam energies are combined by mechanical absorbers and the beam is shaped by placing material such as collimators and compensators into the proton path.

In scanning deliveries, the beam is swept laterally over the target with magnets instead of with scattering devices. Collimators and range compensators are still sometimes used for lateral and distal beam shaping, but field specific hardware is not always required because the scanning magnets allow the lateral extent of the beam to be varied with each energy level, a technique sometimes called intensity-modulated proton therapy (IMPT).

The basic requirement for all forms of PBT treatment delivery is that the technology must accurately produce the calculated dose distribution described by the PBT plan. PBT dose distributions are sensitive to changes in target depth and shape and thus, changes in patient anatomy during treatment may require repeat planning. Such a change must be documented.

Precise delivery is vital for proper treatment. Therefore, imaging techniques such as stereoscopic X-ray or CT scan (collectively referred to as Image Guided Radiation Therapy or IGRT) should be utilized to verify accurate and consistent patient and target setup for every treatment fraction.

Documentation Requirements

Documentation in the patient medical record must:

1. Support one or more medical necessity requirement(s) as provided under the "Indications and Limitations of Coverage and/or Medical Necessity" section of this policy, if not enrolled on a clinical protocol or registry.
2. Include a treatment prescription that defines the goals of the treatment plan – including specific dose-volume parameters for the target and nearby critical structures – as well as pertinent details of beam delivery, such as method of beam modulation, field arrangement, and expected positional and range uncertainties.
3. Include a treatment plan, signed by a physician, which meets the prescribed dose-volume parameters for the clinical target volume (CTV) and surrounding organs at risk (OARs) in the presence of expected uncertainties.
4. Describe the target setup verification methodology, including patient positioning, immobilization and use of image guidance.
5. Include verification of planned dose distribution via independent dose calculation or physical measurement.



INDICATIONS AND LIMITATIONS OF COVERAGE AND/OR MEDICAL NECESSITY

Indications For Coverage

PBT is considered reasonable in instances where sparing the surrounding normal tissue cannot be adequately achieved with photon-based radiotherapy and is of added clinical benefit to the patient. Examples of such an advantage might be:

1. The target volume is in close proximity to one or more critical structures and a steep dose gradient outside the target must be achieved to avoid exceeding the tolerance dose to the critical structure(s).
2. A decrease in the amount of dose inhomogeneity in a large treatment volume is required to avoid an excessive dose "hotspot" within the treated volume to lessen the risk of excessive early or late normal tissue toxicity.
3. A photon-based technique would increase the probability of clinically meaningful normal tissue toxicity by exceeding an integral dose-based metric associated with toxicity.
4. The same or an immediately adjacent area has been previously irradiated, and the dose distribution within the patient must be sculpted to avoid exceeding the cumulative tolerance dose of nearby normal tissue.

PBT may offer dosimetric advantages as well as added complexity over conventional radiotherapy, 3D Conformal Radiation Therapy (3-D CRT) or Intensity Modulated Radiation Therapy (IMRT). Before applying PBT techniques, a comprehensive understanding of the benefits and consequences is required. In addition to satisfying at least one of the four selection criteria noted above, the radiation oncologist's decision to employ PBT requires an informed assessment of the benefits and risks including:

- Determination of patient suitability for PBT allowing for reproducible treatment delivery.
- Adequate definition of the target volumes and OARs.
- Equipment capability, including ability to account for organ motion when relevant.
- Physician, physicist and staff training.
- Adequate quality assurance procedures.

It is important to note that normal tissue dose volume histograms (DVHs) must be demonstrably improved with a PBT plan to validate coverage. Therefore, coverage decisions must extend beyond ICD-9 and ICD-10 codes to incorporate additional considerations of clinical scenario and medical necessity with appropriate documentation. The final determination of the appropriateness and medical necessity for PBT resides with the treating radiation oncologist who should document the justification for PBT for each patient.

Group 1

On the basis of the above medical necessity requirements and published clinical data, disease sites that frequently support the use of PBT include the following:

- Ocular tumors, including intraocular melanomas
- Tumors that approach or are located at the base of skull, including but not limited to:
 - Chordoma
 - Chondrosarcomas
- Primary or metastatic tumors of the spine where the spinal cord tolerance may be exceeded with conventional treatment or where the spinal cord has previously been irradiated
- Primary hepatocellular cancer treated in a hypofractionated regimen
- Primary or benign solid tumors in children treated with curative intent and occasional palliative treatment of childhood tumors when at least one of the four criteria noted above apply

- Patients with genetic syndromes making total volume of radiation minimization crucial such as but not limited to NF-1 patients and retinoblastoma patients

PBT is one of the acceptable forms of external beam radiation therapy that may be used to administer Stereotactic Body Radiation Therapy (SBRT) or Stereotactic Radiosurgery (SRS). Separate ASTRO Model Policies for SBRT⁶ and SRS⁷ include technology descriptions and a list of indications for which SBRT or SRS should be covered. When PBT is used to administer SBRT or SRS, the delivery and management codes relevant for SBRT or SRS apply, and the same clinical indications apply as for those treatment strategies.

Group 2

While PBT is not a new technology, there is a need for continued clinical evidence development and comparative effectiveness analyses for the appropriate use of PBT for various disease sites. All other indications not listed in Group 1 are suitable for Coverage with Evidence Development (CED). Radiation therapy for patients treated under the CED paradigm should be covered by the insurance carrier as long as the patient is enrolled in either an IRB-approved clinical trial or in a multi-institutional patient registry adhering to Medicare requirements for CED². At this time, no indications are deemed inappropriate for CED and therefore Group 2 includes various systems such as, but not limited to, the following:

- Head and neck malignancies
- Thoracic malignancies
- Abdominal malignancies
- Pelvic malignancies, including genitourinary, gynecologic and gastrointestinal carcinomas

In the treatment of prostate cancer, the use of PBT is evolving as the comparative efficacy evidence is still being developed. In order for an informed consensus on the role of PBT for prostate cancer to be reached, it is essential to collect further data, especially to understand how the effectiveness of proton therapy compares to other radiation therapy modalities such as IMRT and brachytherapy. There is a need for more well-designed registries and studies with sizable comparator cohorts to help accelerate data collection. Proton beam therapy for primary treatment of prostate cancer should only be performed within the context of a prospective clinical trial or registry⁵.

Coverage under CED requirements will help expedite more permanent coverage decisions for all indications. Due to the numerous studies under way, proton coverage policies need to be reviewed on a frequent basis. As additional clinical data is published, this policy will be revised to reflect appropriate coverage.

ICD-9-CM and ICD-10-CM Codes that May be Associated with Medical Necessity

Note: Diagnosis codes are based on the current ICD-9-CM and ICD-10-CM codes that are effective at the time of the Model Policy publication. Any updates to ICD-9-CM or ICD-10-CM codes will be reviewed by ASTRO, and coverage should not be presumed until the results of such review have been published/posted. These ICD diagnosis codes support medical necessity under this Model Policy.

Group 1:

Medically Necessary

Site		ICD-9 Codes	ICD-10 Codes
Ocular	Eye		
	-Malignant	190.0 – 190.9	C69.00 – C69.92
	-Benign	224.0 – 224.9	D31.00 – D31.92
	Carcinoma in situ of Eye	234.0	D09.20 – D09.22



Site		ICD-9 Codes	ICD-10 Codes
Spine	Spinal Cord		
	-Malignant	192.2	C72.0, C72.1
	-Benign	225.3	D33.4
	-Uncertain behavior	237.5	D43.4
	Spinal Meninges		
	-Malignant	192.3	C70.1
	-Benign	225.4	D32.1
	-Uncertain behavior	237.6	D42.1
Base of the Skull	Chondrosarcoma	170.9	C41.9
	Chordoma	170.0	C41.0
	Other rare histologies arising in this site	Various	Various
Liver	Hepatocellular Cancer	155.0	C22.0 – C22.8
Pediatric Patients	Solid and CNS Tumors for Pediatric Patients	Various	Various
Reirradiation	Various Regions	990*	T66.XXXA*

*ICD-9-CM 990 or ICD-10-CM T66.XXXA (Effects of Radiation, Unspecified) may only be used where prior radiation therapy to the site is the governing factor necessitating PBT in lieu of other radiotherapy. An ICD diagnosis code for the anatomic diagnosis must also be used with appropriate documentation.

Group 2:

The remaining ICD-9-CM (140-239) and ICD-10-CM (C00-D49) Neoplasm codes should be considered suitable for CED.

Limitations of Coverage

PBT is not considered reasonable and medically necessary unless at least one of the criteria listed in the “Indications of Coverage” section of this policy is present.

Use of PBT is not typically supported by the following clinical scenarios:

1. Where PBT does not offer an advantage over photon-based therapies that otherwise deliver good clinical outcomes and low toxicity.
2. Spinal cord compression, superior vena cava syndrome, malignant airway obstruction, poorly controlled malignant bleeding and other scenarios of clinical urgency.
3. Inability to accommodate for organ motion.
4. Palliative treatment in a clinical situation where normal tissue tolerance would not be exceeded in previously irradiated areas.



PHYSICIANS’ CURRENT PROCEDURAL TERMINOLOGY (CPT®)/HCPCS

Note: CPT is a trademark of the American Medical Association (AMA)

Preparing for Treatment

Due to the complexity of this treatment technology and the cases commonly appropriate for it, all PBT cases satisfy the criteria for complex clinical treatment planning. The clinical treatment plan is the initial process in preparing the patient for treatment.

CPT® Code for Clinical Treatment Planning

77263	Therapeutic Radiology Treatment Planning; complex <i>This code is typically reported only once per course of PBT.</i>
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Following clinical treatment planning and a decision to proceed with PBT, treatment simulation is performed. By definition, the simulation process is complex for protons since it involves particle therapy. CT guidance is now packaged into 77290 and is no longer separately billable.

CPT Code for Simulation

77290	Therapeutic radiology simulation-aided field setting; complex <i>This code is typically reported only once per course of PBT.</i>
+77293	Respiratory motion management simulation (List separately in addition to code for primary procedure) <i>This is an add-on code and cannot be billed on its own. It should be billed with either CPT code 77295 or 77301.</i>

The add-on code +77293 would be used in situations where respiratory motion may cause significant changes in target definition and localization for proton treatment delivery, most commonly in patients with lung or upper gastrointestinal malignancies.

Medical Radiation Physics, Dosimetry and Treatment Devices

In addition, when planning for any special beam such as particles (i.e. protons), a special teletherapy port plan may be necessary. The special teletherapy port plan must be reviewed, signed and dated by the radiation oncologist and physicist. The radiation oncologist must document involvement in the planning and selection of special beam parameters used for treatment.

CPT® Code for Special Teletherapy Port Plan

77321	Special teletherapy port plan, particles, hemibody, total body <i>Use for particle beam isodose planning. Use for electrons, protons and neutron therapy; half body or total body therapy.</i>
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Isodose planning typically involves 3-dimensional dosimetry. For cases in which there is a need to optimize the dose distribution by modulating the beam energy and/or fluence across the field, an intensity modulated treatment plan may be indicated and should be reported using CPT 77301.

CPT Codes for Isodose Planning

77295	Therapeutic radiology simulation-aided field setting; 3-dimensional <i>Use for particle beam isodose planning. Use for electrons, protons and neutron therapy; half body or total body therapy. This code has been moved to the medical physics and dosimetry section, since it represents the work of physics and dosimetry planning rather than the work performed in simulation.</i>
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77301	Intensity modulated radiotherapy plan, including dose-volume histograms for target and critical structure partial tolerance specifications <i>This code will typically be used for plans developed with pencil-beam scanning techniques. This code is typically reported only once per course of PBT.</i>
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After completion of isodose planning, an independent verification of the radiation dose should be performed by a medical dosimetrist, physicist or physician. A calculation is performed for each treatment field.

CPT Code for Dosimetry

77300	Basic radiation dosimetry calculation central axis depth dose calculation, TDF, NSD, gap calculation, off axis factor, tissue inhomogeneity factors, calculation of non-ionizing radiation surface and depth dose, as required during course of treatment, only when prescribed by the treating physician <i>This code can generally be billed once for each beam or arc up to a limit of ten. This code is used to report dosimetry calculations that arrive at the relationship between monitor units (or time) and dose, and the physician's verification, review and approval. The documentation should contain the independent check of each field, separate from the computer-generated PBT plan.</i>
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Immobilization devices are often required for reproducible and consistent patient setup. Even though these devices are utilized every day during treatment, they are only billed once at the time of design and fabrication.

CPT Codes for PBT Treatment Devices

77332	Treatment devices, design and construction; simple <i>Simple treatment devices include simple multi-use shaped blocks, bolus and passive, multiuse devices.</i>
77333	Treatment devices, design and construction; intermediate <i>Intermediate treatment devices include pre-cast or pre-made standard-shaped blocks, stents, and special bolus and bite blocks. For example, custom fabrication of a bolus to compensate for tissue defects; this would typically be done at the time of simulation.</i>
77334	Treatment devices, design and construction; complex <i>Complex treatment devices include custom-fabricated cast blocks, immobilization devices, wedges, compensators and eye shields. This may include custom fabrication of immobilization devices during simulation (such as a vacuum-lock device or thermoplastic mask), a custom compensator designed to adjust the depth of penetration of the protons throughout the treatment volume and utilized for daily treatment, or an aperture (custom fabricated blocking device to design the shape of the proton beam), which would also be utilized for daily treatment, There may be an aperture and compensator designed and constructed for each treated field.</i>

Apertures or compensators (77334 – complex treatment devices) may be used in some circumstances with pencil-beam scanning. An example of this would be a compensator used to decrease the proton range for tumors in more superficial locations, such as in the brain. If the compensator used is a standard compensator which can be used for multiple patients, this would qualify as a simple treatment device (77332).



CPT Codes for Physics and Dosimetry Procedures

77331	Special dosimetry (eg, TLD, microdosimetry) (specify), only when prescribed by the treating physician <i>Explanation of medical necessity may be required.</i>
77336	Continuing medical physics consultation, including assessment of treatment parameters, quality assurance of dose delivery, and review of patient treatment documentation in support of the radiation oncologist, reported per week of therapy <i>Reported per 5 fractions of therapy.</i>
77370	Special medical radiation physics consultation <i>Radiation Oncologist makes a direct request to the qualified medical physicist for a special consultative report or for specific physics services for an individual patient</i>

Treatment Delivery

PBT delivery codes should be billed using one of the four following codes.

CPT® Codes for PBT Treatment Delivery

77520	Proton treatment delivery; simple, without compensation <i>Treatment to a single treatment area utilizing a single non-tangential/oblique port, custom block, without compensation.</i>
77522	Proton treatment delivery; simple, with compensation <i>Treatment to a single treatment area utilizing a single non-tangential/oblique port, custom block, with compensation.</i>
77523	Proton treatment delivery; intermediate <i>Treatment delivery to one or more treatment areas utilizing two or more ports or one or more tangential/oblique ports, with custom blocks and compensations.</i>
77525	Proton treatment delivery; complex <i>Treatment delivery to one or more treatment areas utilizing two or more ports per treatment area with matching or patching fields and/or multiple isocenters, with custom blocks and compensators.</i>

Compensation of the beams may be performed with specific physical compensating devices (custom fabricated lucite or wax compensators) or with compensation using electromagnetic alterations of the beam (pencil-beam scanning or spot scanning).



Image-Guided Radiation Therapy

Image Guided Radiation Therapy (IGRT) allows for modification of treatment delivery to increase precision. The following codes may be billed with PBT.

CPT® Codes for IGRT

76950	Ultrasonic guidance for placement of radiation therapy fields <i>Used with ultrasound-based 2 and 3D systems.</i>
77014	Computed tomography guidance for placement of radiation fields <i>Used with CT-based systems (i.e., integrated cone beam CT, CT/linear accelerator on rails, tomotherapy).</i>
77421	Stereoscopic X-ray guidance for localization of target volume for the delivery of radiation therapy <i>Used with stereoscopic X-ray-based systems (i.e., kV X-rays or MV X-rays: EPID (electronic portal imaging device) with fiducial markers).</i>
0197T	Intra-fraction localization and tracking of target or patient motion during delivery of radiation therapy (eg., 3D positional tracking, gating, and 3D surface tracking), each fraction of treatment <i>Used with implanted radiofrequency transponders and for 3D Surface tracking.</i>

ADDITIONAL INFORMATION

Coding Guidelines

As a reminder, for Medicare claims, the HCPC/CPT® code(s) may be subject to Correct Coding Initiatives (CCI) edits. This policy does not take precedence over CCI edits. Please refer to the CCI for correct coding guidelines and specific applicable code combinations prior to billing Medicare.



REFERENCES

The following is only a sample of the available literature that meets certain criteria and should not be utilized as an exhaustive list. Included articles were published within the last 10 years and report patient outcome data. For disease sites recommended for CED, dosimetry and technical feasibility publications were accepted.

General

1. Chung CS, Tock TI, Nelson K, et al. Incidence of second malignancies among patients treated with proton versus photo radiation. *Int J Radiat Oncol Biol Phys.* 2013; 87(1): 46-52.
2. Coverage with Evidence Development Requirements Position Statement. American Society for Radiation Oncology Web site. <https://www.astro.org/Practice-Management/Reimbursement/Coverage-Position-Statement.aspx>. Published November 15, 2013. Accessed December 13, 2013.
3. Foote RL, Stafford SL, Petersen IA, et al. The clinical case for proton beam therapy. *Radiat Oncol.* 2012; 7:174. doi: 10.1186/1748-717X-7-174.
4. ICRU. *Prescribing, Recording, and Reporting Proton Beam Therapy.* Bethesda, MD: International Commission on Radiation Units and Measurements; 2007. ICRU Report 78.
5. Proton Beam Therapy for Prostate Cancer Position Statement. American Society for Radiation Oncology Web site. <https://www.astro.org/Practice-Management/Reimbursement/Proton-Beam-Therapy.aspx>. Published November 15, 2013. Accessed April 9, 2014.
6. Stereotactic Body Radiation Therapy (SBRT) Model Policy. American Society for Radiation Oncology Web site. https://www.astro.org/uploadedFiles/Main_Site/Practice_Management/Reimbursement/2013HPcoding%20guidelines_SBRT_Final.pdf. Published April 17, 2013. Accessed April 9, 2014.
7. Stereotactic Radiosurgery (SRS) Model Coverage Policy. American Society for Radiation Oncology Web site. https://www.astro.org/uploadedFiles/Main_Site/Practice_Management/Reimbursement/SRSMPJuly2011.pdf. Published July 25, 2011. Accessed April 9, 2014.
8. T.F. Delaney and H.M. Kooy (eds). *Proton and Charged Particle Radiotherapy.* Lippincott Williams and Wilkins, 2007.

Anus/Rectum

9. Radu C, Norrlid O, Braendengen M, et al. Integrated peripheral boost in preoperative radiotherapy for the locally most advanced non-resectable rectal cancer patients. *Acta Oncol.* 2013; 52(3): 528-37.
10. Wolff HA, Wagner DM, Conradi L, et al. Irradiation with protons for the individualized treatment of patients with locally advanced rectal cancer: A planning study with clinical implications. *Radiother Oncol.* 2012; 102(1): 30-7.

Breast

11. Bush DA, Slater JD, Garberoglio C, et al. A technique of partial breast irradiation utilizing proton beam radiotherapy: comparison with conformal X-ray therapy. *Cancer J.* 2007; 13(2): 114-8.
12. Bush DA, Slater JD, Garberoglio C, et al. Partial breast irradiation delivered with proton beam: results of a phase II trial. *Clin Breast Cancer.* 2011; 11(4):241-245.
13. Chang JH, Lee NK, Kim JY, et al. Phase II trial of proton beam accelerated partial breast irradiation in breast cancer. *Radiother Oncol.* 2013; 108(2):209-214.
14. Kozak KR, Smith BL, Adams J, et al. Accelerated partial-breast irradiation using proton beams: Initial clinical experience. *Int J Radiat Oncol Biol Phys.* 2006; 66(3): 691-8.

15. MacDonald SM, Patel SA, Hickey S, et al. Proton therapy for breast cancer after mastectomy: early outcomes of a prospective clinical trial. *Int J Radiat Oncol Biol Phys.* 2013; 86(3):484-90.

Central Nervous System

16. Brown AP, Barney CL, Grosshans DR, et al. Proton Beam Craniospinal Irradiation Reduces Acute Toxicity for Adults With Medulloblastoma. *Int J Radiat Oncol Biol Phys.* 2013; 86(2): 277-84.
17. Hattangadi JA, Chapman PH, Bussiere MR, et al. Planned Two-Fraction Proton Beam Stereotactic Radiosurgery for High-Risk Inoperable Cerebral Arteriovenous Malformations. *Int J Radiat Oncol Biol Phys.* 2012; 83(2): 533-41.
18. Hauswald H, Rieken S, Ecker S, et al. First experiences in treatment of low-grade glioma grade I and II with proton therapy. *Radiat Oncol.* 2012; 7:189.
19. Mizumoto M, Tsubio 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.
20. Nishimura H, Ogino T, Kawashima M, et al. Proton-beam therapy for olfactory neuroblastoma. *Int J Radiat Oncol Biol Phys.* 2007; 68(3): 758-62.
21. Silander H, Pellettieri L, Enblad P, et al. Fractionated, stereotactic proton beam treatment of cerebral arteriovenous malformations. *Acta Neurol Scand.* 2004; 109(2):85-90.
22. Weber, DC, Chan AW, Bussiere MR, et al. Proton Beam Radiosurgery for Vestibular Schwannoma: Tumor control and cranial nerve toxicity. *Neurosurgery.* 2003; 53(3): 577-88.
23. Weber DC, Schneider R, Goitein G, et al. Spot scanning-based proton therapy for intracranial meningioma: long-term results from the Paul Scherrer Institute. *Int J Radiat Oncol Biol Phys.* 2012;83(3):865-871.
24. Vernimmen FJ, Mohamed Z, Slabbert JP, et al. Long term results of stereotactic proton beam radiotherapy for acoustic neuromas. *Radiother Oncol.* 2009; 90(2): 208-12.

Chordoma

25. Ares C, Hug EB, Lomax AJ, et al. Effectiveness and safety of spot scanning proton radiation therapy for chordomas and chondrosarcomas of the skull base: first long-term report. *Int J Radiat Oncol Biol Phys.* 2009;75(4): 1111-1118.
26. 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.
27. Deraniyagala RL, Yeung D, Mendenhall WM, et al. Proton therapy for skull base chordoma: an outcomes study from the University of Florida Proton Therapy Institute. *J Neurol Burg B Skull Base.* 2014; 75(1): 53-7.
28. Igaki H, Tokuyue K, Okumura T, et al. Clinical Results of Proton Beam Therapy for Skull Base Chordoma. *Int J Radiat Oncol Biol Phys.* 2004; 60(4): 1120-6.
29. McDonald MW, Linton OR, Shah MV. Proton Therapy for Reirradiation of Progressive or Recurrent Chordoma. *Int J Radiat Oncol Biol Phys.* 2013; 87(5): 1107-14.



30. Mima M, Demizu Y, Jin D, et al. Particle Therapy Using Carbon Ions or Protons as a Definitive Therapy for Patients with Primary Sacral Chordoma. *Br J Radiol*. 2013 Nov 28 [Epub Ahead of Print].

31. Sciubba DM, Chi JH, Rhines LD, et al. Chordoma of the spinal column. *Neurosurg Clin N Am*. 2008; 19(1): 5-15.

32. Staab A, Rutz HP, Ares C, et al. Spot-scanning-based proton therapy for extracranial chordoma. *Int J Radiat Oncol Biol Phys*. 2011; 81(4):e489-96.

Esophagus

33. Echeverria A, McCurdy M, Castillo R, et al. Proton therapy radiation pneumonitis local dose–response in esophagus cancer patients. *Radiother Oncol*. 2013; 106: 124-9.

34. Lin SH, Komaki R, Liao Z, et al. Proton Beam Therapy and Concurrent Chemotherapy for Esophageal Cancer. *Int J Radiat Oncol Biol Phys*. 2012; 83(3): e345-51.

35. Mizumoto M, Sugahara S, Nakayama H, et al. Clinical Results of Proton-Beam Therapy for Locoregionally Advanced Esophageal Cancer. *Strahlenther Onkol*. 2010; 186(9): doi: 10.1007/s00066-010-2079-4.

36. Mizumoto M, Sugahara S, Okumura T, et al. Hyperfractionated concomitant boost proton beam therapy for esophageal carcinoma. *Int J Radiat Oncol Biol Phys*. 2011; 81(4): e601-6.

37. Sugahara S, Tokuyue K, Okumura T, et al. Clinical Results of Proton Beam Therapy for Cancer of the Esophagus. *Int J Radiat Oncol Biol Phys*. 2005; 61(1): 76-84.

Gynecologic

38. Clivio A, Kluge A, Cozzi L, et al. Intensity Modulated Proton Beam Radiation for Brachytherapy in Patients with Cervical Carcinoma. *Int J Radiat Oncol Biol Phys*. 2013; 87(5): 897-903.

Head and Neck

39. Fukumitsu N, Okumura T, Mizumoto M, et al. Outcome of T4 (International Union Against Cancer Staging System, 7th edition) or recurrent nasal cavity and paranasal sinus carcinoma treated with proton beam. *Int J Radiat Oncol Biol Phys*. 2012; 83(2):704-11.

40. Hojo H, Zenda S, Akimoto T, et al. Impact of early radiological response evaluation on radiotherapeutic outcomes in the patients with nasal cavity and paranasal sinus malignancies. *J Radiat Res*. 2012; 53(5):704-9.

41. Ramaekers BL, Grutters JP, Pijls-Johannesma M, et al. Protons in Head-and-Neck Cancer: Bridging the Gap of Evidence. *Int J Radiat Oncol Biol Phys*. 2013; 85(5): 1282-8.

42. Truong MT, Kamat UR, Liebsch NJ, et al. Proton radiation therapy for primary sphenoid sinus malignancies: treatment outcomes and prognostic factors. *Head Neck*. 2009; 31(10): 1297-308.

43. Weber DC, Chan AW, Lessell S, et al. Visual outcome of accelerated fractionated radiation for advance sinonasal malignancie employing photons/protons. *Radiother Oncol*. 2006; 81(3): 243-9.

44. Zenda S, Kawashima M, Nishio T, et al. Proton Beam Therapy as a nonsurgical approach to mucosal melanoma of the head and neck: a pilot study. *Int J Radiat Oncol Biol Phys*. 2011; 81(1): 135-9.

45. Zenda S, Kohno R, Kawashima M, et al. Proton beam therapy for unresectable malignancies of the nasal cavity and paranasal sinuses. *Int J Radiat Oncol Biol Phys*. 2011; 81(5): 1473-8.

Liver

46. Fukumitsu N, Hashimoto T, Okumura T, et al. Investigation of the geometric accuracy of proton beam irradiation in the liver. *Int J Radiat Oncol Biol Phys*. 2012; 82(2): 826-33.

47. Fukumitsu N, Sugahara S, Nakayama H, et al. A prospective study of hypofractionated proton beam therapy for patients with hepatocellular carcinoma. *Int J Radiat Oncol Phys*. 2009; 74(3): 831-6.

48. Hashimoto T, Tokuyue K, Fukumitsu N, et al. Repeated proton beam therapy for hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys*. 2006; 65(1): 196-202.

49. Hata M, Tokuyue K, Sugahara S, et al. Proton beam therapy for aged patients with hepatocellular carcinoma. *Int J Radiat Oncol Biol Phys*. 2007; 69(3): 805-12.

50. Hata M, Tokuyue K, Sugahara S, et al. Proton beam therapy for hepatocellular carcinoma with limited treatment options. *Cancer*. 2006; 107: 591-8.

51. Kawashima M, Furuse J, Nishio T, et al. Phase II study of radiotherapy employing proton beam for hepatocellular carcinoma. *J Clin Oncol*. 2005; 23: 1839-46.

52. Mizumoto M, Okumura T, Hashimoto T, et al. Proton beam therapy for hepatocellular carcinoma: a comparison of three treatment protocols. *Int J Radiat Oncol Biol Phys*. 2011; 81(4): 1039-45.

53. Mizumoto M, Tokuyue K, Sugahara S, et al. Proton beam therapy for hepatocellular carcinoma adjacent to the porta hepatis. *Int J Radiat Oncol Biol Phys*. 2008; 71(2): 462-67.

54. Nakayama H, Sugahara S, Fukuda K, et al. Proton beam therapy for hepatocellular carcinoma located adjacent to the alimentary tract. *Int J Radiat Oncol Biol Phys*. 2011; 80(4): 992-5.

55. Nakayama H, Sugahara S, Tokita M, et al. Proton beam therapy for hepatocellular carcinoma: the University of Tsukuba experience. *Cancer*. 2009; 115(23): 5499-506.

56. Sugahara S, Oshiro Y, Nakayama H, et al. Proton Beam Therapy for Large Hepatocellular Carcinoma. *Int J Radiat Oncol Biol Phys*. 2010; 76(2): 460-6.

57. Takayuki Hashimoto T, Tokuyue K, Fukumitsu N, et al. Repeated Proton Beam Therapy for Hepatocellular Carcinoma. *Int J Radiat Oncol Biol Phys*. 2006; 65(1): 196-202.

Lung

58. Bush DA, Cheek G, Zaheer S, et al. High-Dose Hypofractionated Proton Beam Radiation Therapy Is Safe and Effective for Central and Peripheral Early-Stage Non-Small Cell Lung Cancer: Results of a 12-Year Experience at Loma Linda University Medical Center. *Int J Radiat Oncol Biol Phys*. 2013; 86(5): 964-98.

59. Bush DA, Slater JD, Shin BB, et al. Hypofractionated Proton Beam Radiotherapy for Stage I Lung Cancer. *Chest*. 2004; 126: 1198-203.

60. Chang JY, Komaki R, Lu C, et al. Phase 2 Study of High-Dose Proton Therapy With Concurrent Chemotherapy for Unresectable Stage III Nonsmall Cell Lung Cancer. *Cancer*. 2011; 117(20): 4707-13.

61. Chang JY, Komaki R, Wen HY, et al. Toxicity and Patterns of Failure of Adaptive/Ablative Proton Therapy For Early-stage, Medically Inoperable Non-small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys*. 2011; 80(5): 1350-1357.

62. Gomez DR, Gillin M, Liao Z, et al. Phase 1 Study of Dose Escalation in Hypofractionated Proton Beam Therapy for Non-Small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys.* 2013; 86(4): 665-70.

63. Hata M, Tokuyue K, Kagei K, et al. Hypofractionated High Dose Proton Beam Therapy for Stage 1 Non Small Cell Lung Cancer: Preliminary Results of a Phase I/II Clinical Study. *Int J Radiat Oncol Biol Phys.* 2007; 68(3): 786-93.

64. Hoopes BS, Flampouri S, Henderson RH, et al. Proton Therapy With Concurrent Chemotherapy for Non-Small-Cell Lung Cancer: Technique and Early Results. *Clin Lung Cancer.* 2012; 13(5): 352-8.

65. Iwata H, Murakami M, Demizu Y, et al. High-dose proton therapy and carbon-ion therapy for stage I nonsmall cell lung cancer. *Cancer.* 2010; 116(10): 2476-85.

66. Iwata H, Demizu Y, Fujii O, et al. Long-term outcome of proton therapy and carbon-therapy for large (T2a-T2bN0M0) non-small-cell lung cancer. *J Thorac Oncol.* 2013; 8(6): 726-35.

67. Koay EJ, Lege D, Mohan R, et al. Adaptive/Nonadaptive Proton Radiation Planning and Outcomes in a Phase II Trial for Locally Advanced Non-small Cell Lung Cancer. *Int J Radiat Oncol Biol Phys.* 2012; 84(5): 1093-100.

68. Kraysenbuehl J, Hartmann M, Lomax AJ, et al. Proton therapy for malignant pleural mesothelioma after extrapleural pleuropneumectomy. *Int J Radiat Oncol Biol Phys.* 2010; 78(2): 628-34.

69. Nakayama H, Satoh H, Sugahara S, et al. Proton Beam Therapy Of Stage II and III Non-Small-Cell Lung Cancer. *Int J Radiat Oncol Biol Phys.* 2011; 81(4): 979-84.

70. Oshiro Y, Mizumoto M, Okumura T, et al. Results of Proton Beam Therapy without Concurrent Chemotherapy for Patients with Unresectable Stage III Non-small Cell Lung Cancer. *J Thorac Oncol.* 2012; 7(2): 370-5.

71. Sejal S, Komaki R, Tsao A, et al. Early Findings on Toxicity of Proton Beam Therapy With Concurrent Chemotherapy for Nonsmall Cell Lung Cancer. *Cancer.* 2011; 117(13): 3004-13.

Lymphoma

72. Andolino DL, Hoene T, Xiao L, et al. Dosimetric Comparison of Involved Field Three Dimensional Conformal Photon Radiotherapy and Breast Sparing Proton Therapy for Treatment of Hodgkin's Lymphoma in Female Pediatric Patients. *Int J Radiat Oncol Biol Phys.* 2011; 81(4): e667-71.

73. Hoppe BS, Flampouri S, Lynch J, et al. Improving the Therapeutic Ratio in Hodgkin Lymphoma Through the Use of Proton Therapy. *Oncology (Williston Park).* 2012; 26(5): 456-9, 462-5.

74. Hoppe BS, Flampouri S, Su Z, et al. Consolidated Involved-Node Proton Therapy for Stage IA-IIIb Mediastinal Hodgkin Lymphoma: Preliminary Dosimetric Outcomes From a Phase II Study. *Int J Radiat Oncol Biol Phys.* 2012; 83(1): 260-7.

75. Hoppe BS, Flampouri S, Su Z, et al. Effective Dose Reduction to Cardiac Structures Using Protons Compared With 3DCRT and IMRT in Mediastinal Hodgkin Lymphoma. *Int J Radiat Oncol Biol Phys.* 2012; 84(2): 449-55.

76. Li J, Dabaja B, Reed V, et al. Rationale for and preliminary results of proton beam therapy for mediastinal lymphoma. *Int J Radiat Oncol Biol Phys.* 2011; 81(1):167-74.

Ocular Melanoma

77. Caujolle J, Mammar H, Chamorey E, et al. Proton beam radiotherapy for uveal melanomas at Nice Teaching Hospital: 16 years' experience. *Int J Radiat Oncol Biol Phys.* 2010; 78(1): 98-103.

78. Caujolle J-P, Paoli V, Chamorey E, et al. Local recurrence after uveal melanoma proton beam therapy: recurrence types and prognostic consequences. *Int J Radiat Oncol Biol Phys.* 2013;85(5):1218-24.

79. Damato B, Kacperek A, Chopra M, et al. Proton beam radiotherapy of choroidal melanoma: the Liverpool-Clatterbridge experience. *Int J Radiat Oncol Biol Phys.* 2005; 62(5): 1405-11.

80. Damato B, Kacperek A, Chopra M, et al. Proton beam radiotherapy of iris melanoma. *Int J Radiat Oncol Biol Phys.* 2005; 63(1):109-115.

81. Dendale R, Lumbroso-Le Rouic L, Noel G, et al. Proton beam radiotherapy for uveal melanoma: results of Curie Institut-Orsay proton therapy center (ICPO). *Int J Radiat Oncol Biol Phys.* 2006; 65(3):780-787.

82. Desjardins L, Lumbroso-Le Rouic L, Levy-Gabriel C, et al. Combined proton beam radiotherapy and transpupillary thermotherapy for large uveal melanomas: a randomized study of 151 patients. *Ophthalmic Res.* 2006; 38(5):255-260.

83. Egger E, Zografos L, Schalenbourg A, et al. Eye retention after proton beam radiotherapy for uveal melanoma. *Int J Radiat Oncol Biol Phys.* 2003; 55(4): 867-80.

84. Lumbroso-Le Rouic L, Delacroix S, Dendale R, et al. Proton beam therapy for iris melanomas. *Eye (Lond).* 2006; 20(11): 1300-5.

85. Macdonald EC, Cauchi P, and Kemp EG. Proton beam therapy for the treatment of uveal melanoma in Scotland. *Br J Ophthalmol.* 2011; 95(12): 1691-5.

86. Marucci L, Ancukiewicz M, Lane AM, et al. Uveal Melanoma Recurrence after Fractionated Proton Beam Therapy: Comparison of Survival in Patients Treated With Reirradiation or with Enucleation. *Int J Radiat Oncol Biol Phys.* 2011; 79(3): 842-6.

87. Mosci C, Lanza FB, Barla A, et al. Comparison of clinical outcomes for patients with large choroidal melanoma after primary treatment with enucleation or proton beam radiotherapy. *Ophthalmologica.* 2012; 227(4): 190-6.

88. Sethi RV, Shih HA, Yeap BY, et al. Second Nonocular Tumors Among Survivors of Retinoblastoma Treated With Contemporary Photon and Proton Radiotherapy. *Cancer.* 2014; 120(1): 126-33.

Pancreas

89. Hong TS, Ryan DP, Blaszkowsky LS, et al. Phase I study of preoperative short-course chemoradiation with proton beam therapy and capecitabine for resectable pancreatic ductal adenocarcinoma of the head. *Int J Radiat Oncol Biol Phys.* 2011; 79(1): 151-7.

90. Nichols RC Jr, George TJ, Zaiden RA Jr, et al. Proton therapy with concomitant capecitabine for pancreatic and ampullary cancers is associated with a low incidence of gastrointestinal toxicity. *Acta Oncologica.* 2013; 52: 498-505.

91. Nichols RC Jr, Huh SN, Prado KL, et al. Protons Offer Reduced Normal Tissue Exposure for Patients Receiving Postoperative Radiotherapy for Resected Pancreatic Head Cancer. *Int J Radiat Oncol Biol Phys.* 2012; 83(1): 158-63.

92. Terashima K, Demizu Y, Hashimoto N, et al. A phase I/II study of gemcitabine-concurrent proton radiotherapy for locally advanced pancreatic cancer without distant metastasis. *Radiother Oncol.* 2012; 103(1): 25-31.

Pediatrics

93. Amsbaugh MJ, Grosshans DR, McAleer MF, et al. Proton therapy for spinal ependymomas: planning, acute toxicities, and preliminary outcomes. *Int J Radiat Oncol Biol Phys.* 2012;83(5):1419-24.

94. Childs SK, Kozak KR, Friedmann AM, et al. Proton radiotherapy for parameningeal rhabdomyosarcoma: clinical outcomes and late effects. *Int J Radiat Oncol Biol Phys.* 2012;82(2):635-642.

95. Cotter SE, Herrup DA, Friedmann A, et al. Proton Radiotherapy for Pediatric Bladder/ Prostate Rhabdomyosarcoma: clinical Outcomes and Dosimetry Compared to Intensity Modulated Radiation Therapy. *Int J Radiat Oncol Biol Phys.* 2011; 81(5): 1367-73.

96. De Amorim Bernstein K, Sethi R, Trofimov, et al. Early clinical outcomes using proton radiation for children with central nervous system atypical teratoid rhabdoid tumors. *Int J Radiat Oncol Biol Phys.* 2013; 86(1):114-20.

97. Habrand J-L, Schneider R, Alapetite C, et al. Proton therapy in pediatric skull base and cervical canal low-grade bone malignancies. *Int J Radiat Oncol Biol Phys.* 2008; 71(3):672-5.

98. Hattangadi JA, Rombi B, Yock TI, et al. Proton radiotherapy for high-risk pediatric neuroblastoma: early outcomes and dose comparison. *Int J Radiat Oncol Biol Phys.* 2012; 83(3):1015-22.

99. Hill-Kayser C, Tochner Z, Both S, et al. Proton versus photon radiation therapy for patients with high-risk neuroblastoma: the need for a customized approach. *Pediatr Blood Cancer.* 2013; 60(10):1606-11.

100. Hoch BL, Nielsen GP, Liebsch NJ, Rosenberg AE. Base of skull chordomas in children and adolescents. A clinicopathologic study of 73 cases. *Am J Surg Pathol.* 2006; 30(7):811-8.

101. Jimenez RB, Sethi R, Depauw N, et al. Proton radiation therapy for pediatric medulloblastoma and supratentorial primitive neuroectodermal tumors: outcomes for very young children treated with upfront chemotherapy. *Int J Radiat Oncol Biol Phys.* 2013; 87(1):120-06.

102. Kuhlthau KA, Pulsifer MB, Yeap BY, et al. Prospective study of health-related quality of life for children with brain tumors treated with proton radiotherapy. *J Clin Oncol.* 2012; 30(17): 2079-86.

103. MacDonald SM, Sethi R, Lavally B, et al. Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients. *Neuro Oncol.* 2013; 15(11): 1552-9.

104. Oshiro Y, Mizumoto M, Okumura T, et al. Clinical results of proton beam therapy for advanced neuroblastoma. *Radiat Oncol.* 2013;8(1):142.

105. Rombi B, Ares C, Hug EB, et al. Spot-scanning proton radiation therapy for pediatric chordoma and chondrosarcoma: clinical outcome of 26 patients treated at Paul Scherrer Institute. *Int J Radiat Oncol Biol Phys.* 2013; 86(3):578-84

106. Timmermann B, Schuck A, Niggli F, et al. Spot-scanning proton therapy for malignant soft tissue tumors in childhood: first experiences at the Paul Scherrer Institute. *Int J Radiat Oncol Biol Phys.* 2007; 67(2):497-504.

Prostate

107. Coen JJ, Bae K, Zietman AL, et al. Acute and late toxicity after dose escalation to 82 GyE using conformal proton radiation for localized prostate cancer: initial report of American College of Radiology phase II study 03-12. *Int J Radiat Oncol Biol Phys.* 2011; 81(4):1005-9.

108. Coen JJ, Paly JJ, Niemierko A, et al. Long-term quality of life outcome after proton beam monotherapy for localized prostate cancer. *Int J Radiat Oncol Biol Phys.* 2012; 82(2):e201-9.

109. Henderson RH, Hoppe BS, Marcus RB Jr, et al. Urinary functional outcomes and toxicity five years after proton therapy for low- and intermediate-risk prostate cancer: results of two prospective trials. *Acta Oncol.* 2013; 52(3):463-9.

110. Hoppe BS, Michalski JM, Mendenhall NP, et al. Comparative effectiveness study of patient-reported outcomes after proton therapy or intensity-modulated radiotherapy for prostate cancer. *Cancer.* 2013. [Epub ahead of print].

111. Hoppe BS, Nichols RC, Henderson RH, et al. Erectile function, incontinence, and other quality of life outcomes following proton therapy for prostate cancer in men 60 years old and younger. *Cancer.* 2012; 118(18):4619-26.

112. Johansson S, Astrom L, Sandin F, Isacson U, Montelius A, Turesson I. Hypofractionated proton boost combined with external beam radiotherapy for treatment of localized prostate cancer. *Prostate Cancer.* 2012; 654861.

113. Mendenhall NP, Hoppe BS, Nichols RC, et al. Five-year outcomes from 3 prospective trials of image-guided proton therapy for prostate cancer. *Int J Radiat Oncol Biol Phys.* 2014; 88(3): 596-602.

114. 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.

Sarcomas

115. Ciernik IF, Niemierko A, Harmon DC, et al. Proton based radiotherapy for unresectable or incompletely resected osteosarcoma. *Cancer.* 2011; 117(19): 4522-30.

116. Delaney TF, Liebsch NJ, Pedlow FX, et al. Phase II Study of High Dose photon/Proton Radiotherapy in the management of Spine Sarcomas. *Int J Radiat Oncol Biol Phys.* 2009; 74(3): 732-9.

117. Weber DC, Rutz HP, Bolsi A, et al. Spot scanning proton therapy in the curative treatment of adult patients with sarcoma: the Paul Scherrer Institute experience. *Int J Radiat Oncol Biol Phys.* 2007; 69(3):865-871.

Skull Base

118. Ares C, Hug EB, Lomax AJ, et al. Effectiveness and safety of spot scanning proton radiation therapy for chordomas and chondrosarcomas of the skull base: first long-term report. *Int J Radiat Oncol Biol Phys.* 2009; 75(4): 1111-8.

119. Combs SE, Kessel K, Habermehl, et al. Proton and carbon ion radiotherapy for primary brain tumors and tumors of the skull base. *Acta Oncol.* 2013; 52(7):1504-1509.

120. Noël G, Feuvret L, Calugaru V, et al. Chordomas of the base of the skull and upper cervical spine. One hundred patients irradiated by a 3D conformal technique combining photon and proton beams. *Acta Oncol.* 2005; 44(7):700-8.



121. Pehlivan B, Ares C, Lomax AJ, et al. Temporal lobe toxicity analysis after proton radiation therapy for skull base tumors. *Int J Radiat Oncol Biol Phys.* 2012;83(5):1432-1440.
122. Pommier P, Liebsch NJ, Deschler DG, et al. Proton Beam Radiation Therapy for Skull Base Adenoid Cystic Carcinoma. *Arch Otolaryngol Head Neck Surg.* 2006; 132(11): 1242-9.
123. Ronson BB, Schulte RW, Han KP, Loredon LN, Slater JM, Slater JD. Fractionated proton beam irradiation of pituitary adenomas. *Int J Radiat Oncol Biol Phys.* 2006; 64(2):425-434.
124. Slater JD, Loredon LN, Chung A, et al. Fractionated proton radiotherapy for benign cavernous sinus meningiomas. *Int J Radiat Oncol Biol Phys.* 2012;83(5):e633-e637.