Clinical Appropriateness Guidelines: Radiation Oncology

Proton Beam Therapy Guidelines

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Proprietary

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AIM SpecialtyHealth®
8600 W Bryn Mawr Avenue
South Tower - Suite 800
Chicago, IL 60631
P. 773.864.4600
www.aimspecialtyhealth.com

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Description and Application of the Guidelines

AIM's Clinical Appropriateness Guidelines (hereinafter "AIM's Clinical Appropriateness Guidelines" or the "Guidelines") are designed to assist providers in making the most appropriate treatment decision for a specific clinical condition for an individual. As used by AIM, the Guidelines establish objective and evidence-based, where possible, criteria for medical necessity determinations. In the process, multiple functions are accomplished:

- To establish criteria for when services are medically necessary
- To assist the practitioner as an educational tool
- To encourage standardization of medical practice patterns
- To curtail the performance of inappropriate and/or duplicate services
- To advocate for patient safety concerns
- To enhance the quality of healthcare
- To promote the most efficient and cost-effective use of services

AIM's guideline development process complies with applicable accreditation standards, including the requirement that the Guidelines be developed with involvement from appropriate providers with current clinical expertise relevant to the Guidelines under review and be based on the most up to date clinical principles and best practices. Relevant citations are included in the "References" section attached to each Guideline. AIM reviews all of its Guidelines at least annually.

AIM makes its Guidelines publicly available on its website twenty-four hours a day, seven days a week. Copies of AIM's Clinical Appropriateness Guidelines are also available upon oral or written request. Although the Guidelines are publicly-available, AIM considers the Guidelines to be important, proprietary information of AIM, which cannot be sold, assigned, leased, licensed, reproduced or distributed without the written consent of AIM.

AIM applies objective and evidence-based criteria and takes individual circumstances and the local delivery system into account when determining the medical appropriateness of health care services. The AIM Guidelines are just guidelines for the provision of specialty health services. These criteria are designed to guide both providers and reviewers to the most appropriate services based on a patient's unique circumstances. In all cases, clinical judgment consistent with the standards of good medical practice should be used when applying the Guidelines. Guideline determinations are made based on the information provided at the time of the request. It is expected that medical necessity decisions may change as new information is provided or based on unique aspects of the patient's condition. The treating clinician has final authority and responsibility for treatment decisions regarding the care of the patient and for justifying and demonstrating the existence of medical necessity for the requested service. The Guidelines are not a substitute for the experience and judgment of a physician or other health care professionals. Any clinician seeking to apply or consult the Guidelines is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment.

The Guidelines do not address coverage, benefit or other plan specific issues. If requested by a health plan, AIM will review requests based on health plan medical policy/guidelines in lieu of AIM's Guidelines.

The Guidelines may also be used by the health plan or by AIM for purposes of provider education, or to review the medical necessity of services by any provider who has been notified of the need for medical necessity review, due to billing practices or claims that are not consistent with other providers in terms of frequency or some other manner.

Proton Beam Therapy Considerations

Proton beam radiation therapy, also known as proton beam therapy (PBT), is a type of external radiation treatment. Using a stereotactic planning and delivery system, positively charged subatomic particles (protons) are targeted to a specific tissue mass. Protons behave differently than x-rays or photons in that they have a low energy deposition rate as they enter the body, followed by a steep increased energy deposition when they reach their target. Although there is essentially no energy deposited beyond the target, there is lateral scatter and some uncertainty about their physical range in tissue. Compared to x-ray treatment, surrounding healthy tissue generally receives less radiation. Despite the proliferation of proton centers in recent years, there is a lack of high-quality evidence demonstrating improved outcomes vs other forms of precision radiation therapy. PBT remains an area of active clinical investigation, and recommendations for its use continue to evolve.

PBT may be appropriate in circumstances where intensity modulated radiation therapy (IMRT) or stereotactic would potentially damage critical structures, particularly in patients with a history of prior irradiation. PBT is also appropriate for pediatric patients because even low doses of scattered radiation in this population can affect growth and development and increase the risk of secondary malignancies later in life. This technique of radiation delivery is being actively studied in other clinical scenarios, and its role in these situations in many cases remains unclear. In situations where there is a lack of high-quality evidence comparing proton outcomes with photon-based therapies, proton therapy will be considered not medically necessary. In situations where proton therapy is appropriate, PBT should be administered as monotherapy.

Central Nervous System Lesions

Radiation therapy is commonly used to treat central nervous system (CNS) tumors and other intracranial lesions such as arteriovenous malformations (AVM). Results of proton therapy have been reported for a variety of CNS lesions. In the treatment of gliomas, dose escalation to 68.2 centigray equivalent (CGE) did not improve outcomes in a phase I/II trial of protons in grade 2-3 astrocytoma. In another study, dose escalation to 90 CGE slightly increased median survival, but all patients had marginal failure just beyond the high-dose area and necrosis was seen in one third of patients. A more recent Japanese phase I/II study boosted glioblastomas to 96.6 CGE and reported a handful of long-term survivors, all of whom have developed necrosis. Benign tumors including meningiomas, acoustic neuromas and pituitary adenomas have also been treated with protons. Results of treatment are similar to those seen with non-proton techniques such as IMRT and stereotactic radiosurgery (SRS). A recent review of PBT to treat CNS lesions by Combs concluded that “no clinical data have shown superiority over advanced photon therapy.”

Use of PBT for CNS lesions is only medically necessary for specific cases where adjacent critical structures cannot be adequately spared with IMRT or SRS.

Chordoma and Chondrosarcoma

Chordomas and chondrosarcomas are rare bone and soft tissue tumors which occur along the spinal axis. The mainstay of treatment is surgery, but in many cases only biopsy or piecemeal resection is possible. Postoperative radiotherapy has been shown to improve outcomes. In the past, tumors occurring in the base of skull area were unable to be treated to high doses with conventional therapy due to the risk of damaging normal tissues. Protons were used to safely treat chordomas in this location with good results. In the most comprehensive review published to date, seven studies of proton therapy were compared to ten studies of conventional radiotherapy and reported improved local control and survival with protons compared to x-rays. The average five-year local control with protons was 69% vs only 36% with photons. The five-year survival rate was 80% with PBT vs 54% with x-rays. Chordomas and chrondrosarcoma of the spine are similarly difficult to treat given that doses above 70 Gy are given to areas in close proximity to the spinal cord and viscera. A recent prospective phase II trial of protons in this setting showed an impressive 94% five-year local control for primary tumors with acceptable late morbidity.

Results with modern radiotherapy techniques like IMRT and radiosurgery are improved compared to conventional radiotherapy, but given the excellent long-term results seen with protons, they are considered medically necessary for the treatment of base of skull and sacral chordomas and chondrosarcomas.

Uveal Melanoma

Curative treatment for ocular melanoma with preservation of vision can be achieved with either plaque brachytherapy or with PBT. A systematic review and meta-analysis of charged particle radiation therapy for uveal melanoma demonstrated that charged particle therapy (most commonly PBT) resulted in a lower local recurrence rate than plaque brachytherapy. PBT also showed better outcomes in terms of retinopathy and cataract formation. Enucleation and survival were similar with PBT and brachytherapy.

Proton therapy is considered medically necessary for the treatment of uveal melanoma.

Prostate Cancer

Historically, PBT was used as a boost technique for prostate cancer due to the ability to deliver a higher dose than could be safely delivered with 2D and 3D techniques. Single institution reports of PBT dose escalation showed favorable disease-free survival and acceptable toxicity in this era. Over the past two decades, there have been significant improvements in technology allowing similar dose escalation to be achieved with IMRT.

The only randomized trial of PBT compared low dose proton boost (19.8 CGE) with high dose proton boost (28.8 CGE) after a dose of 50.4 Gy to the pelvis with x-rays. In that study, the higher dose proton boost improved biochemical recurrence-free survival but also increased the frequency of acute gastrointestinal (GI) and genitourinary (GU) toxicity. There were no significant differences in late toxicity. The study did not evaluate whether proton therapy is more efficacious or less toxic than other forms of conformal radiation.

Although there are no reports from randomized trials comparing proton therapy with IMRT and 3D conformal radiation, there have been retrospective comparative studies. In a large-scale review of outcomes based on Medicare claims data, 684 patients treated with PBT were compared with 9,437 men treated with IMRT. Follow up was 46 to 50 months and the results were propensity score matched to account for baseline characteristics. Rates of urinary incontinence, other urinary morbidity and sexual dysfunction were similar for PBT and IMRT. Compared to IMRT, patients treated with PBT had a higher rate of GI morbidity (17.8 vs 12.2 per 100 person-years). In terms of disease control, IMRT was shown to be better than conformal therapy. Proton therapy did not provide additional benefit over IMRT.

Patient-reported outcomes for 3D conformal radiotherapy, IMRT and PBT have also been reported. Using validated quality of life (QOL) instruments, a 2013 study looked at scores in the immediate post-treatment period and at 12- and 24-month follow-up visits. In the immediate post-treatment interval, bowel QOL decreased for both 3D and IMRT treated patients but not the PBT group. At 12 and 24 months, all three groups showed decreased bowel/rectal QOL. With regard to urinary toxicity, IMRT treated patients showed decreased GU QOL in the immediate period but this had disappeared by 12 months. At 12 months, the PBT cohort demonstrated decreased urinary QOL while 3D and IMRT patients had returned to baseline. No meaningful urinary QOL changes were seen in any group at 24 months. Although timing of toxicity varied between cohorts, patients reported similar long-term QOL decrements irrespective of modality.

There is significant consensus among radiation oncologists that there is a lack of comparative effectiveness research on PBT for prostate cancer. Multiple evidence-based reviews of this topic have concluded that no clear evidence supports a benefit of proton therapy over IMRT in terms of efficacy or long-term toxicity. These include reports from AHRQ, Hayes, the American Urologic Association, the American College of Radiology and the ASTRO Subcommittee on Emerging Technology. In their 2017 update of the model policy on PBT, ASTRO maintains:

“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 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 registry.”

The body of evidence on PBT for prostate cancer largely consists of retrospective studies performed at tertiary centers. The evidence quality is low and there are insufficient data to determine how PBT compares to standard of care photon-based therapies, which are able to achieve excellent outcomes with low toxicity.

PBT is considered not medically necessary for the treatment of prostate cancer.

Lung Cancer

Radiotherapy is used as a primary treatment for early stage non-small cell lung cancer, particularly when surgical resection is not an option. In the treatment of stage I medically inoperable NSCLC, a meta-analysis of studies of PBT and stereotactic body radiotherapy (SBRT) has been reported. Two-year survival rates for stage I NSCLC treated with SBRT were 70% vs 61% for PBT. The five-year survival rates were similar. Both SBRT and proton therapy were significantly better than conventional radiotherapy for stage I disease. PBT is considered not medically necessary for small cell lung cancer and stage I NSCLC.

Radiation therapy, usually delivered with concurrent chemotherapy, is the standard of care for the treatment of unresectable stage III non-small cell lung cancer (NSCLC). In specific cases, IMRT is needed to achieve adequate sparing of organs at risk such as the normal lung. Significant lung and esophageal toxicity are common and these toxicities have hampered attempts at dose escalation.

PBT has been used for NSCLC in an attempt to allow dose escalation while minimizing lung and esophageal toxicity. Several institutions have reported on their experience. A systematic review by Widesott examined 17 studies. There were no prospective reports. Nine single institution studies reported on a total of 214 patients, most with stage I or II disease. Several studies focused on dose distributions and technical issues associated with PBT. They concluded that it was impossible to draw definitive conclusions about the superiority of PBT for non-small cell lung cancer. A subsequent phase II trial by Chang reported encouraging results in unresectable stage III disease. Recently, a prospective randomized trial comparing PBT with photon therapy was completed. That study was conducted at MD Anderson Cancer Center and preliminary results were reported at the 2016 ASCO meeting. A total of 255 patients were enrolled and 149 of these were randomized. Proton therapy did not improve local control nor did it improve survival compared to IMRT. The rate of pneumonitis was higher in the proton therapy arm (11%) vs the IMRT arm (7%). This study reinforces the importance of level 1 evidence in the study of proton therapy. NRG/RTOG protocol 1308 is a randomized trial of PBT versus IMRT both with concurrent platinum based chemotherapy in stage II-IIIB non-small cell lung cancer which should provide additional data on how proton therapy compares to standard treatment.

PBT is considered not medically necessary in the treatment of lung cancer.

Head and Neck Cancer

Although there are several trials currently underway, there are currently no published randomized studies comparing proton therapy to IMRT in the treatment of head and neck cancers. In 2010, the Agency for Healthcare Research and Quality conducted a systematic review of different radiation modalities used in the treatment of head and neck malignancies including 2D radiation, 3D conformal radiation, IMRT and PBT. They concluded that there was insufficient evidence comparing PBT to other modalities. This report was updated in 2014 with the same conclusion. A 2012 ASTRO evidence based review of proton therapy stated that “current data do not provide sufficient evidence to recommend PBT in …head and neck cancers.”

A 2016 single institution report retrospectively compared intensity-modulated proton therapy (IMPT) to IMRT in the treatment of oropharyngeal cancer. There was no difference in progression-free survival between the modalities. IMRT treated patients were more likely to have a gastrostomy tube (G-tube) placed than proton treated patients but this was not statistically significant. Outcomes meeting statistical significance were patient reported xerostomia at three months and weight loss greater than 20% or G-tube presence one year after treatment. The authors concluded that prospective multicenter randomized trials are needed to validate these findings.

A systematic review and meta-analysis of charged particle therapy vs x-ray based therapy for treatment of paranasal sinus and nasal cancers was published by Patel et al. There were no head-to-head comparison trials so their analysis consisted of 41 observational studies. Of these, there were 13 reports for charged particle therapy and 30 cohorts treated with photons. In the meta-analysis of these reports, treatment with charged particle therapy was associated with higher survival at five years. Neurologic toxicity was significantly higher in the charged particle group as well. The studies reviewed included a very heterogeneous group. For photon therapy, treatment techniques included 2D, 3D, IMRT and brachytherapy. The charged particle cohorts included both protons and carbon ions with most patients being treated with passively scattered protons. A similar proportion of patients in both groups had advanced disease but the photon treated patients were more likely to have a high-risk histology. The heterogeneity of both the patient populations and treatment techniques as well as the inclusion of inadequate treatment techniques such as 2D and 3D conformal radiotherapy in the photon group make it impossible to draw meaningful conclusions.

PBT is considered not medically necessary for the treatment of head and neck cancer.

Breast Cancer

There are no randomized trials of PBT for breast cancer. A recent systematic review discussed nine original investigations of PBT for both whole breast treatment and accelerated partial breast irradiation (APBI). Skin toxicity and esophagitis were comparable to photon therapy. None of the outcomes reported were improved with PBT. There is a randomized trial comparing PBT to photon therapy underway.

PBT is considered not medically necessary for the treatment of breast cancer.

Hepatocellular Cancer

Hepatocellular carcinomas (HCC) are aggressive primary malignancies of the liver. All patients should be evaluated for potentially curative therapies including resection, transplantation and ablative treatment. Ablative therapies include radiofrequency ablation, microwave therapy and alcohol injection. Radiation therapy is considered for patients who are not candidates for resection. There is growing evidence for the use of SBRT. Charged particle therapy such as proton therapy has also been used in the treatment of hepatocellular carcinoma. There are no randomized trials comparing PBT to other forms of external radiation. A systematic review and meta-analysis comparing charged particle therapy to conventional radiation and SBRT has been reported. Overall survival, progression-free survival, and local control were equivalent for particle therapy and SBRT. Both charged particle therapy and SBRT were superior to conventional radiation.

Proton therapy has been compared to transarterial chemoembolization (TACE) for HCC in a randomized trial. A total of 69 subjects were reported. The primary endpoint was progression-free survival. There was a trend toward improved progression-free survival (48% vs. 31%, p=0.06) favoring protons but no significant difference in overall survival with a median overall survival of 30 months. Total days of hospitalization within 30 days of treatment was 166 days for the 36 TACE patients and 24 days for the proton patients ($p<0.001$).

PBT is considered not medically necessary for the treatment of HCC.

Other Gastrointestinal Cancers

There have been few reports of PBT to treat esophageal and gastroesophageal junction tumors. There are no prospective randomized trials. Wang et al. published a retrospective report of complications after trimodality therapy looking at IMRT and PBT compared to 3D conformal radiation. A total of 444 patients were reported. Both IMRT and PBT were associated with reduced risk of complications compared to 3D conformal radiation. No direct comparison of IMRT vs PBT was performed. Several phase II trials are underway but there is insufficient evidence to draw conclusions on how PBT compares to photon based therapy for esophageal cancer.

There are no moderate or high-quality studies comparing PBT to 3D conformal radiotherapy or IMRT for gastric or pancreatic cancer.

PBT is considered investigational for the treatment of esophageal, gastric or pancreatic cancer.

Lymphoma

Data on PBT for treatment for lymphoma are limited. A recent review examined the use of consolidative PBT after chemotherapy for patients with Hodgkin lymphoma. A total of 138 patients enrolled on tracking protocols or registry studies were reviewed. Forty-two percent of the patients were pediatric and received a median dose of 21 Gy equivalent. Adult patients received a median dose of 30.6 Gy equivalent. With a median follow-up of 32 months, three-year relapse-free survival was 92%. The authors concluded that early survival rates were similar to photon based therapy and the continued follow-up to assess for late effects is needed.

Data on proton therapy for non-Hodgkin lymphoma (NHL) are limited. A small retrospective cohort has been reported. Eleven patients were treated between 2008 and 2014. Follow up was 38 months. Two-year local control was 91%. Toxicities were grade 2 or less. The study concluded that longer-term follow-up and more patients were needed to confirm their findings.

PBT is considered not medically necessary for the treatment of Hodgkin lymphoma and non-Hodgkin lymphoma.

Risk Reduction

There have been multiple publications theorizing a reduced risk of second malignancies with the use of proton therapy. These generally compare dosimetric data from proton plans compared to IMRT plans and use mathematical modeling to predict the cancer risk. These models are largely untested and there is a dearth of actual data reporting on the risk posed by scattered radiation, especially in adults.

Several studies have looked the actual risk of second malignancy following radiotherapy and have compared this to patient who have not been irradiated. Zelefsky reported on the 10-year risk of second cancer among men with prostate cancer treated with radical prostatectomy (RP), brachytherapy (BT) and external beam radiotherapy (EBRT). The risk of developing bladder or colorectal cancer was 3% for RP, 2% for BT and 4% for EBRT at 10 years (p=0.29). For all second cancers, there was a slightly higher risk in the irradiated patients but on multivariate analysis this difference was found to be attributable to age and smoking history rather than treatment received. Another report examined the risk of second cancers after radiotherapy in three randomized trials and compared this to patients randomized to no radiotherapy. A total of 2,554 patients were analyzed who had participated in the TME trial for rectal cancer, the PORTEC-1 and PORTEC-2 trials in endometrial cancer. Although all patients in these trials were at somewhat higher risk of second malignancy than the general population, the patients who received radiotherapy had no higher probability of developing second cancers than those treated with surgery alone.

Chung et al. have reported on the incidence of second malignancy in 558 patients treated with proton therapy at the Harvard Cyclotron facility and compared this to matched controls in the Surveillance, Epidemiology and End Results (SEER) database. The incidence of second cancers in the proton group was approximately 7 per 1000 person-years vs. approximately 10 per 1000 person-years in the matched photon group (p=0.085). Limitations include different methods of data collection, lack of radiation field size and dose and the fact that 26% of the proton treated patients were lost to follow up and second malignancy information was not available for this group. The authors conclude that the results are hypothesis generating and warrant further study.

Uncertainties of Proton Beam Therapy

The longest experience with protons has been using passively scattered beams. This technique is a robust method of proton delivery which is less sensitive to treatment and patient variables. Passive scattered protons produce neutrons and these affect surrounding tissues negatively. Newer proton beam centers use pencil beam scanning technology. This allows for more conformal treatment delivery and has been also termed intensity modulated proton therapy. Long-term follow-up with this technology is lacking. Additionally, there are significant uncertainties about the physics and biology of protons in this setting. These include the complex interaction of scanning beams with moving tissues of different densities, less predictable dose distributions during treatment of radiosensitive HPV-positive tumors and questions about the variable radiobiologic effectiveness of protons in situ. Proton plans generally assume a uniform relative biological effectiveness (RBE) of 1.1 compared to photons. The actual RBE is dependent on the fractionation and depth. At the distal edge of the Bragg peak, RBE has been measured at more than 5 times the assumed value. The existence of this uncertainty highlights the need for further prospective study of proton therapy, especially as treatment techniques such as pencil beam scanning continue to evolve.

Clinical Trials and Registries

There have been calls to cover the costs of PBT for patients enrolled in registry trials, but these studies lack the basic underpinning of clinical equipoise and there is inherent bias among both patients and investigators that favors proton therapy. PBT will not be covered when the PBT is the experimental arm of a clinical trial or when used as part of a clinical registry unless criteria above are otherwise met.

Indications for Proton Beam Therapy

This guideline outlines different applications of proton beam therapy in the treatment of malignant and benign tumors and arteriovenous malformations.

Central Nervous System

Arteriovenous Malformation (AVM)

Proton beam is appropriate for AVM when **ANY** of the following conditions are met.

- Intracranial AVM not amenable to surgical excision or other conventional forms of treatment **OR**
- Adjacent to critical structures such as the optic nerve, brain stem or spinal cord

Central Nervous System (CNS) Tumors

Proton beam is appropriate for CNS tumors when ALL the following conditions are met

- Including, but not limited to, primary or metastatic CNS malignancies, such as gliomas **(both must be met)**
  - When adjacent to critical structures such as the optic nerve, brain stem, or spinal cord **AND**
  - When other standard radiation techniques such as IMRT or standard stereotactic modalities would not sufficiently reduce the risk of radiation damage to the critical structure

Pediatric CNS Tumors

Proton beam is appropriate for pediatric CNS tumors when the following condition is met

- Age less than 21

Chordoma, Chondrosarcoma

Proton beam is appropriate for chordoma, chondrosarcoma when the following condition is met

- As postoperative therapy for individuals who have undergone biopsy or partial resection of a chordoma or low-grade (I or II) chondrosarcoma of the basisphenoid region (e.g. skull-base chordoma or chondrosarcoma), cervical spine, or sacral/lower spine and have residual, localized tumor without evidence of metastasis

Melanoma

Ocular Melanoma

Proton beam is appropriate for ocular melanoma when the following condition is met

- As primary therapy for melanoma of the uveal tract (including the iris, choroid, or ciliary body) involving tumors of up to 24 mm in largest diameter and 14 mm in height, and with no evidence of metastasis or extrascleral extension

Pediatric patients

All tumor types

Proton beam is appropriate for pediatric patients (age less than 21) when the following condition is met

- To treat all pediatric tumors

Re-irradiation

Proton beam therapy is appropriate for the repeat irradiation of previously treated fields where the dose tolerance of surrounding normal structures would be exceeded with 3D conformal radiation or IMRT

Proton Beam Therapy is not medically necessary for the treatment of all other conditions including:

- Breast cancer
- Esophageal cancer
- Gastric cancer
- Gynecologic cancer
- Head and neck cancer
- Hepatobiliary cancer
- Lung cancer
- Lymphoma (Hodgkin and non-Hodgkin)
- Pancreatic cancer
- Prostate cancer

Coding

CPT

77520..... Proton treatment delivery; simple, without compensation

77522..... Proton treatment delivery; simple, with compensation

77523..... Proton treatment delivery; intermediate

77525..... Proton treatment delivery; complex

Central Nervous System

Arteriovenous Malformation

ICD-10 Diagnoses

Q28.2	Arteriovenous malformation of cerebral vessels
Q28.3	Other malformations of cerebral vessels

Central Nervous System Tumors (excludes pituitary)

ICD-10 Diagnoses

C71.0 - C71.9	Malignant neoplasm of brain
C72.0 - C72.9	Malignant neoplasm of spinal cord, cranial nerves, and other parts of central nervous system
C79.31	Secondary malignant neoplasm of brain
C79.49	Secondary malignant neoplasm of other parts of nervous system
D09.8	Carcinoma in situ of other specified sites
D33.0 - D33.9	Benign neoplasm of brain and other parts of central nervous system
D42.0 - D42.9	Neoplasm of uncertain behavior of meninges
D43.0 - D43.9	Neoplasm of uncertain behavior of brain and central nervous system
D49.6	Neoplasm of unspecified behavior of brain

Chordoma, Chondrosarcoma

ICD-10 Diagnoses

C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified

Melanoma

Ocular Melanoma

ICD-10 Diagnoses

C69.30	Malignant neoplasm of unspecified choroid
C69.40	Malignant neoplasm of unspecified ciliary body
C69.90	Malignant neoplasm of unspecified site of unspecified eye

Pediatric Patients

Tumors - All types

ICD-10 Diagnoses

All ICD-10 diagnoses when age less than 21 years

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