Anthem

Medical Policy

Subject: Neutron Beam Radiotherapy
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Description/Scope

This document addresses neutron beam radiation therapy. Radiobiologic principles suggest that neutron beam radiotherapy (NBT) is associated with a higher linear energy transfer (LET) compared with conventional photon or electrons resulting in a high radiation biological effect (RBE). Certain tumors seem to be more susceptible to the cytotoxic effects of neutrons, including salivary gland tumors. NBT or neutron beam radiation therapy is not to be confused with boron neutron capture therapy (BNCT) for cancer, which is not addressed within this document.

Position Statement

Investigational and Not Medically Necessary:

Neutron beam radiotherapy is considered **investigational and not medically necessary** for all indications.

Rationale

Huber and colleagues (2001) compared radiotherapy with neutrons, photons, and a photon/neutron mixed beam in participants with advanced adenoid cystic carcinoma (n=75). Local control, survival, distant failure and complications were analyzed. Follow-up ranged from 1 to 160 months (median, 51 months), and the surviving individuals had a minimum follow-up of 3 years at the time of analysis. The actuarial 5-year local control was 75% for neutrons and 32% for both mixed beam and photons (p=0.015, log-rank). In spite of better local control in the neutron therapy group, there were no significant differences in survival across the groups. Acute toxicity was similar in all 3 radiotherapy groups, although severe late grade 3 and 4 toxicity was significantly more prevalent with neutrons (19%) than with mixed beam (10%) and photons (4%) (p>0.1). While neutron therapy did show improved local control, this did not translate into an improvement in overall survival. In addition, neutron therapy had significant associated toxicities as compared to other treatments.

There have been a few retrospective analyses done evaluating the safety and effectiveness of neutron therapy in salivary gland neoplasms. Local control and toxicity rates were consistent with previously reported outcomes. These studies lack comparison with other treatments (Douglas, 2003; Stannard, 2013).

Maucort-Boulch and colleagues (2010) reported a meta-analysis that included four randomized controlled trials (RCTs; total n=316) evaluating neutron therapy alone, neutron therapy with photon therapy, and photon therapy alone for treatment of glioblastoma. Follow-up at 12 months showed a 7% increase in mortality (range, 5% to 20% increase) and at 24 months, a 6% increase in mortality (range, 3% to 15% increase) in neutron therapy compared with photon therapy. This meta-analysis showed that neutron therapy did not improve survival rate.

Spratt and colleagues (2014) note that much of the data supporting superior local control (LC) in neutron therapy versus photon radiotherapy (RT) is more than 20 years old and there have been many advances in oncological treatment since that time. The researchers reviewed the records of 27 individuals with primary unresectable salivary gland cancer treated with photon RT between 2000 and 2009. These results were compared to results reported in a 1993 randomized controlled trial comparing neutron and photon therapy. The 2- and 5-year LC for photon therapy compared to historical neutron therapy outcomes were similar (65%, 55% versus 67%, 56%, respectively). While the current study data showed lower rates of toxicity in comparison to the historical neutron therapy data, there are limitations associated with comparing current and historical data and additional study is needed with concurrent comparison to alternative treatments to understand relevant clinical outcomes.

Timoshchuk and colleagues (2019) examined the 6- and 10-year locoregional control and survival rates of individuals with salivary gland malignancies who underwent high-energy neutron radiotherapy. A total of 545 individuals were included in the retrospective cohort study. After 6 years, the locoregional control rate was 84% and the survival rate was 72%. Following 10 years, the locoregional control rate was 79% and the survival rate was 62%. The authors suggest that this study provides evidence that, when compared to outcomes reported from previous studies regarding photon radiotherapy, neutron radiotherapy provides favorable outcomes. While this was a large study, the limitations associated with the study reduce the applicability of the results. Of the 559 individuals who met the inclusion criteria, only 473 individuals had data available for survival, recurrence, or metastases analysis. The geographical diversity of the participant base and length of time which had passed since treatment increases the risk of inadequate documentation or identification in the medical records reviewed. Finally, comparisons to photon radiotherapy were limited to statistics published in previous studies.

The Head and Neck Cancer guideline developed by the National Comprehensive Cancer Network® (NCCN®) Clinical Practice Guidelines in Oncology removed the recommendation for neutron beam radiotherapy as both a definitive radiation therapy option and a postoperative treatment option for salivary gland tumors in 2015. NCCN noted concern that any potential disease control advantages are offset by the toxicity of neutron therapy. Neutron therapy risks increase with time, with some estimates as high as 20% at 9 years post-treatment. As concerns about toxicity increased, the number of centers offering this treatment in the United States (U.S.) has decreased. At this time, there is only one center in the U.S. which offers neutron therapy (NCCN, 2023).

Background/Overview

Neutron beam therapy is a form of external beam radiation therapy. It has been proposed as a treatment of inoperable tumors or tumors that are resistant to conventional radiation therapy. Neutrons have a greater biologic impact on cells than other types of radiation.

Definitions

Fast neutron beam therapy: A type of external radiation treatment in which neutral charge subatomic particles (neutrons) are precisely

targeted to a specific tissue mass by using a sophisticated stereotactic planning and delivery system; an interventional radiologist performs this therapy at a treatment facility equipped with a superconducting accelerator (cyclotron); pretreatment planning usually involves computed tomography (CT) to locate and determine the tumor volume prior to radiation therapy.

Glioblastoma: A fast-growing type of central nervous system tumor that forms from glial (supportive) tissue of the brain and spinal cord. Glioblastoma usually occurs in adults and affects the brain more often than the spinal cord. Glioblastoma is also called grade IV astrocytoma, glioblastoma multiforme and GBM.

Unresectable: Unable to be removed with surgery.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

When Services are Investigational and Not Medically Necessary:

CPT

77423	High energy neutron radiation treatment delivery; 1 or more isocenter(s) with coplanar or non-coplanar geometry with blocking and/or wedge, and/or compensator(s)

ICD-10 Procedure

D0005ZZ-D0075ZZ	Beam radiation of central and peripheral nervous system using neutrons [includes codes D0005ZZ, D0015ZZ, D0065ZZ, D0075ZZ]
D7005ZZ-D7085ZZ	Beam radiation of lymphatic and hematologic system, using neutrons [includes codes D7005ZZ, D7015ZZ, D7025ZZ, D7035ZZ, D7045ZZ, D7055ZZ, D7065ZZ, D7075ZZ, D7085ZZ]
D8005ZZ	Beam radiation of eye using neutrons
D9005ZZ-D9055ZZ	Beam radiation of ear/nose/hypopharynx/mouth/tongue using neutrons [includes codes D9005ZZ, D9015ZZ, D9035ZZ, D9045ZZ, D9055ZZ]
D9065ZZ	Beam radiation of salivary glands using neutrons
D9075ZZ-D90F5ZZ	Beam radiation of sinuses/palate/larynx/pharynx using neutrons [includes codes D9075ZZ, D9085ZZ, D9095ZZ, D90B5ZZ, D90D5ZZ, D90F5ZZ]
DB005ZZ-DB085ZZ	Beam radiation of respiratory system using neutrons [includes codes DB005ZZ, DB015ZZ, DB025ZZ, DB055ZZ, DB065ZZ, DB075ZZ, DB085ZZ]
DD005ZZ-DD075ZZ	Beam radiation of gastrointestinal system using neutrons [includes codes DD005ZZ, DD015ZZ, DD025ZZ, DD035ZZ, DD045ZZ, DD055ZZ, DD075ZZ]
DF005ZZ-DF035ZZ	Beam radiation of hepatobiliary system and pancreas using neutrons [includes codes DF005ZZ, DF015ZZ, DF025ZZ, DF035ZZ]
DG005ZZ-DG055ZZ	Beam radiation of endocrine system using neutrons [includes codes DG005ZZ, DG015ZZ, DG025ZZ, DG045ZZ, DG055ZZ]
DH025ZZ-DH0B5ZZ	Beam radiation of skin using neutrons [by body area, includes codes DH025ZZ, DH035ZZ, DH045ZZ, DH065ZZ, DH075ZZ, DH085ZZ, DH095ZZ, DH0B5ZZ]
DM005ZZ-DM015ZZ	Beam radiation of breast using neutrons [includes codes DM005ZZ, DM015ZZ]
DP005ZZ-DP0C5ZZ	Beam radiation of musculoskeletal system using neutrons [includes codes DP005ZZ, DP025ZZ, DP035ZZ, DP045ZZ, DP055ZZ, DP065ZZ, DP075ZZ, DP085ZZ, DP095ZZ, DP0B5ZZ, DP0C5ZZ]
DT005ZZ-DT035ZZ	Beam radiation of urinary system using neutrons [includes codes DT005ZZ, DT015ZZ, DT025ZZ, DT035ZZ]
DU005ZZ-DU025ZZ	Beam radiation of ovary/cervix/uterus using neutrons [includes codes DU005ZZ, DU015ZZ, DU025ZZ]
DV005ZZ-DV015ZZ	Beam radiation of prostate/testis using neutrons [includes codes DV005ZZ, DV015ZZ]
DW015ZZ-DW065ZZ	Beam radiation of anatomic regions using neutrons [includes codes DW015ZZ, DW025ZZ, DW035ZZ, DW045ZZ, DW055ZZ, DW065ZZ]

ICD-10 Diagnosis

	All diagnoses

References

Peer Reviewed Publications:

1. Douglas JG, Koh WJ, Austin-Seymour M, Laramore GE. Treatment of salivary gland neoplasms with fast neutron radiotherapy. Arch Otolaryngol Head Neck Surg. 2003; 129(9):944-948.
2. Huber PE, Debus J, Latz D, et al. Radiotherapy for advanced adenoid cystic carcinoma: neutrons, photons or mixed beam? Radiother Oncol. 2001; 59(2):161-167.
3. Maucort-Boulch D, Baron MH, Pommier P, et al. Rationale for carbon ion therapy in high-grade glioma based on a review and a meta-analysis of neutron beam trials. Cancer Radiother. 2010; 14(1):34-41.
4. Pfister DG, Spencer S, Brizel DM, et al. Head and Neck Cancers, Version 1.2015. J Natl Compr Canc Netw. 2015; 13(7):847-855.
5. Spratt DE, Salgado LR, Riaz N, et al. Results of photon radiotherapy for unresectable salivary gland tumors: is neutron radiotherapy's local control superior? Radiol Oncol. 2014; 48(1):56-61.
6. Stannard C, Vernimmen F, Carrara H, et al. Malignant salivary gland tumours: can fast neutron therapy results point the way to carbon ion therapy? Radiother Oncol. 2013; 109(2):262-268.
7. Timoshchuk MA, Dekker P, Hippe DS, et al. The efficacy of neutron radiation therapy in treating salivary gland malignancies. Oral Oncol. 2019; 88:51-57.

Government Agency, Medical Society, and Other Authoritative Publications:

1. National Cancer Institute (NCI). Salivary Gland Cancer Treatment (PDQ). Updated August 22, 2023. Available at: https://www.cancer.gov/types/head-and-neck/hp/adult/salivary-gland-treatment-pdq. Accessed on September 22, 2023.

2. NCCN Clinical Practice Guidelines in Oncology® (NCCN). © 2023 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on September 22, 2023.
    - Head and Neck Cancer (V2.2023). Revised May 15, 2023.

Websites for Additional Information

1. American Cancer Society (ACS). Radiation Therapy for Salivary Gland Cancer. Last Revised: March 18, 2022. Available at: https://www.cancer.org/cancer/types/salivary-gland-cancer/treating/radiation-therapy.html. Accessed on September 22, 2023.
2. American Society of Clinical Oncology (ASCO). Salivary Gland Cancer Treatment. May 2020. Available at: http://www.cancer.net/cancer-types/salivary-gland-cancer/treatment-options. Accessed on September 22, 2023.

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Document History

Status	Date	Action
Reviewed	11/09/2023	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Rationale, References and Websites for Additional Information sections.
Reviewed	11/10/2022	MPTAC review. Updated Rationale, References and Websites sections.
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Reviewed	11/05/2020	MPTAC review. Updated Rationale, References and Websites sections.
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Reviewed	01/24/2019	MPTAC review. References and Websites sections updated.
Reviewed	01/25/2018	MPTAC review.
Reviewed	01/17/2018	Hematology/Oncology Subcommittee review. References and Websites sections updated.
Reviewed	11/02/2017	MPTAC review.
Reviewed	11/01/2017	Hematology/Oncology Subcommittee review. The document header wording updated from “Current Effective Date” to “Publish Date.” Rationale, References and Websites sections updated. Updated Coding section with 01/01/2018 CPT changes to remove 77422 deleted 12/31/2017.
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Reviewed	11/02/2016	Hematology/Oncology Subcommittee review. Rationale, References and Websites sections updated.
Revised	11/05/2015	MPTAC review.
Revised	11/04/2015	Hematology/Oncology Subcommittee review. Changed the document number from RAD.00047 to THER-RAD.00008. Removed the medically necessary indications for the treatment of salivary gland tumors. Updated investigational and not medically necessary statement to include all indications. Rationale, Coding and References sections updated. Removed ICD-9 codes from Coding section.
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Reviewed	11/14/2013	MPTAC review.
Reviewed	11/13/2013	Hematology/Oncology Subcommittee review. Rationale and Reference sections updated.
Reviewed	11/08/2012	MPTAC review.
Reviewed	11/07/2012	Hematology/Oncology Subcommittee review. Rationale, Definition and Reference sections updated.
Reviewed	11/17/2011	MPTAC review.
Reviewed	11/16/2011	Hematology/Oncology Subcommittee review. Rationale and References updated.
Reviewed	11/18/2010	MPTAC review.
Reviewed	11/17/2010	Hematology/Oncology Subcommittee review. Rationale and References updated.
Reviewed	11/19/2009	MPTAC review.
Reviewed	11/18/2009	Hematology/Oncology Subcommittee review. References updated.
Reviewed	11/20/2008	MPTAC review.
Reviewed	11/19/2008	Hematology/Oncology Subcommittee review. References were updated.
Reviewed	11/29/2007	MPTAC review.
Reviewed	11/28/2007	Hematology/Oncology Subcommittee review. The phrase “investigational/not medically necessary” was clarified to read “investigational and not medically necessary.” References were updated.
Reviewed	12/07/2006	MPTAC review. References and coding were updated.
Reviewed	12/01/2005	MPTAC review. Description was reworded for clarity based on input from outside consultant.
Revised	09/22/2005	MPTAC review. Revision based on Pre-merger Anthem and Pre-merger WellPoint Harmonization.

Pre-Merger Organizations	Last Review Date	Document Number	Title
Anthem, Inc.			No prior document
WellPoint Health Networks, Inc.	12/02/2004	4.11.06	Neutron Beam Radiotherapy

Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The member's contract benefits in effect on the date that services are rendered must be used. Medical Policy, which addresses medical efficacy, should be considered before utilizing medical opinion in adjudication. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.