KAISER PERMANENTE®

Clinical Review Criteria

Neutron Beam Radiotherapy

- Soft Tissue Sarcoma
- Salivary Gland Tumors
- Locally Advanced Prostate Cancer

Criteria

For Medicare Members

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	Stereotactic Radiation Therapy: Stereotactic Radiosurgery (SRS) and Stereotactic Body Radiation Therapy (SBRT) (L34151).
Local Coverage Article	None

For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or will provide better long term outcomes than current standard services/therapies. Requests will be reviewed on a case-by-case basis.

The following information was used in the development of this document and is provided as background only. It is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

Background

Neutron radiotherapy is an alternative to conventional photon radiotherapy. Photon radiation is a type of low linear-energy-transfer (LET) radiation. After LET radiation, there is a relatively high chance that damaged tumor cells can repair themselves and continue to grow. In contrast, with neutrons, which are high LET radiation, damaged tumor cells are much less likely to resume growth. Because of the higher biological effectiveness of neutron radiotherapy, the required tumor dose with neutrons is about one-third the dose needed with photons and a lower total number of treatments is needed.

Neutrons were first used to treat patient tumors in 1938 using an early cyclotron. Research was discontinued due to World War II and began again in the 1960s in England. In the late 1970s, the National Cancer Institute awarded contracts for four modern cyclotrons in the U.S. According to a recent review article (Laramore, 1997), of the four centers, only the one at the University of Washington (UW) is still in operation. There are currently two other operating neutron radiotherapy centers in the country; the others are located at Harper-Grace Hospital in Detroit and the Fermi National Laboratory in Illinois. The UW built a new control system for its cyclotron, completed in July 1999. The UW materials state that the UW has the only facility with a computer-controlled, multi-leaf collimator for field shaping.

Neutron radiotherapy is believed to be most beneficial for malignant salivary gland tumors. The modern neutron facilities can deliver neutron radiation doses of approximately 20 Gy to the head and neck which corresponds to a proton dose of about 60-70 Gy-equivalent for normal tissues and approximately 160 Gy-equivalent for the tumor. In his review article, Laramore (1997) states that other than for salivary gland tumors, neutron radiotherapy has been shown to be most promising for sarcomas of soft tissue, bone and cartilage and locally advanced prostate cancer.

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Evidence and Source Documents

Soft Tissue Sarcoma
Salivary Gland Tumors
Locally Advanced Prostate Cancer

Medical Technology Assessment Committee (MTAC)

Neutron Beam Radiotherapy for Soft Tissue Sarcoma

06/12/2002: MTAC REVIEW

Evidence Conclusion: There were only two case series that had sample sizes greater than n=10. The Schwartz study had n=73 (n=42 was treatment with curative intent) and was conducted at UW, where patients from Kaiser Permanente would be sent. The Schonekaes study, which was conducted in Germany, reports on two independent series of patients. Schwartz found a 68% local relapse-free 4-year survival rate and 66% overall 4-year survival rate in the 42 curative patients. Schonekaes found a 52% 5-year local recurrence-free survival rate and a 42.5% overall 5-year survival rate. In both studies, patients varied greatly in clinical characteristics, there was a lack of clear eligibility criteria, the intervention received was not consistent (e.g., dose of radiation). The Schwartz article did not have a control or comparison group. The efficacy of neutron radiotherapy for the treatment of soft-tissue sarcoma cannot be determined from these descriptive reports.

Articles: The search yielded 13 articles, many of which were review articles or opinion pieces. There were no randomized controlled trials or meta-analyses. There were four case series, two of which had sample sizes of ten or less. The two largest case series (n=73 and n=161) were critically appraised. Schwartz DL, Einck J, Bellon J, Laramore GE. Fast neutron radiotherapy for soft tissue and cartilaginous sarcomas at high risk for local recurrence. *Int J Radiation Oncology Biol Phys* 2001: 50: 449-456. See Evidence Table. Schonekaes K-G, Prott F-J, Micke O et al. Radiotherapy on adult patients with soft tissue sarcoma with fast neutrons or photons. *Anticancer Res* 1999; 19: 2355-2360. See Evidence Table.

The use of neutron beam radiotherapy in the treatment of soft tissue sarcoma does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Neutron Beam Radiotherapy for Salivary Gland Tumors

06/12/2002: MTAC REVIEW

Evidence Conclusion: There was one small RCT (n=32 randomized, n=25 analyzed) comparing neutron radiotherapy to photon radiotherapy. This study (Griffin, 1988; Laramore, 1993) had methodological limitations but dramatic findings. At ten years, there was a statistically significant 39% absolute risk reduction for local/regional control favoring the neutron group. For survival, there was an absolute risk reduction of 37% at two years and 10% at ten years. Differences in survival rates were not statistically significant and the study may have been under powered. A case series from the UW with 128 patients was also reviewed. Actuarial local/regional control at five years was 59% and the 5-year survival rate was 39%. The evidence suggests that neutron radiotherapy is superior to traditional photon radiotherapy, but case series and one small, compromised RCT do not provide conclusive evidence.

Articles: The search yielded 34 articles, most of which were review articles, opinion pieces, dealt with technical aspects of the procedures or addressed other, similar treatments. There was one randomized controlled trials, published in 1993 and five newer case series with more than 50 patients. Some of the case series were from the same institution and there was overlap in the patients included in the articles. The RCT and the largest, most recent case series from the UW were reviewed. Laramore GE, Krall JM, Griffin TQ et al. Neutron versus photon irradiation for unresectable salivary gland tumors: Final report of an RTOG-MRC randomized clinical trial. *Int J Radiat Oncol Biol Phys* 1993; 27: 235-240. See Evidence Table. Douglas JG, Lee S, Laramore GE et al. Neutron radiotherapy for the treatment of locally advanced major salivary gland tumors. *Head Neck* 1999; 21: 255-263. See Evidence Table.

The use of neutron beam radiotherapy in the treatment of salivary gland tumors does not meet the *Kaiser Permanente Medical Technology Assessment Criteria.*

Neutron Beam Radiotherapy for Locally Advanced Prostate Cancer

06/12/2002: MTAC REVIEW

Evidence Conclusion: There were two RCTs; Laramore compared photon radiation to mixed photon-neutron radiotherapy and Russell compared photon radiation to neutron radiotherapy alone. Laramore found higher local/regional control and higher 5-year and 10-year survival rates in the neutron radiotherapy group. Russell found greater local/regional control but no difference in 5-year survival rates. It is possible that there could be a

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difference in effectiveness between mixed-beam and neutron-only radiotherapy, but this has not been studied. Neither study presented baseline demographic or clinical information, so the possibility of selection bias cannot be ruled out. The Laramore study has been criticized in the literature for the low rates of local/regional control and survival in the photon-treated group. The final reports on each of these RCTs were published in the early 1990s. No more recent studies were identified.

Articles: The search yielded 15 articles, many of which were review articles, dealt with technical aspects of the procedures or addressed other, similar treatments. There were two randomized controlled trials and one small case series on mixed-beam (mixed photon-neutron) treatment. The two RCTs were reviewed. Laramore GE, Krall JM, Thomas FJ et al. Fast neutron radiotherapy for locally advanced prostate cancer: Final report of Radiation Therapy Oncology Group Randomized Clinical Trial. *Am J Clin Oncol* 1993; 16: 164-67. See Evidence Table. Russell KJ, Caplan RJ, Laramore GE et al. Photon versus fast neutron external beam radiotherapy in the treatment of locally advanced prostate cancer: Results of a randomized prospective trial. *Int J Radiat Oncol Biol Phys* 1993; 28: 47-54. See Evidence Table.

The use of neutron beam radiotherapy in the treatment of locally advanced prostate cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*

Date Created	Date Reviewed	Date Last Revised
6/12/2002	Initiated annual review because of Medicare criteria 04/05/2011 MDCRPC, 02/07/2012 MDCRPC, 12/04/2012 MDCRPC, 10/01/2013 MPC, 08/05/2014 MPC, 06/02/2015 MPC, 04/05/2016 MPC, 02/07/2017 MPC	07/25/2002

MDCRPC Medical Director Clinical Review and Policy Committee
MPC Medical Policy Committee

Revision History	Description
05/26/2015	Added CPT codes
09/08/2015	Revised LCD L34151

Codes

CPT: 77422, 77423

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