Medical Policy Manual

Intraocular Radiation Therapy for Age-Related Macular Degeneration

Effective: August 1, 2017

Next Review: April 2018
Last Review: June 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Epiretinal radiation describes the intraocular administration of radiation to the choroidal vascular bed of the retina to treat age-related macular degeneration (AMD).

MEDICAL POLICY CRITERIA

Epiretinal radiation therapy for the treatment of subfoveal choroidal neovascularization in patients with neovascular age-related macular degeneration is considered investigational.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

CROSS REFERENCES

1. Charged-Particle (Proton or Helium Ion) Radiation Therapy, Medicine, Policy No. 49
2. Stereotactic Radiosurgery and Stereotactic Body Radiation Therapy, Surgery Policy No. 16

BACKGROUND

Age-related macular degeneration (AMD) is characterized in its earliest stages by minimal
visual impairment and the presence of large drusen and other pigmentary abnormalities on ophthalmoscopic examination. Two distinctively different forms of degeneration may be observed. The first, called the atrophic or areolar or dry form, evolves slowly. Atrophic AMD is the most common form of degeneration and may be a precursor of the more visually impairing exudative neovascular form, also referred to as disciform or wet AMD. The wet form is distinguished from the atrophic form by the development of choroidal neovascularization (CNV) and serous or hemorrhagic detachment of the retinal pigment epithelium. Risk of developing severe irreversible loss of vision is greatly increased by the presence of CNV.

REGULATORY STATUS

There are no devices specifically approved by the U.S. Food and Drug Administration (FDA) for this procedure. An investigational device exemption has been granted by FDA for a phase III multicenter trial to provide data for application to the FDA of the NeoVista Epi-Rad90™ Ophthalmic System. This system has been developed to treat CNV by focal delivery of radiation to a subfoveal choroidal neovascular lesion. Using a standard vitrectomy procedure, the cannula tip of a handheld (pipette-like) surgical device is inserted into the vitreous cavity and positioned under visual guidance over the target lesion. The radiation source (strontium-90) is advanced down the cannula until it reaches the tip, which is then held in place over the lesion for a “prescribed” time to deliver focused radiation. The system is designed to deliver a one-time peak dose of beta particle energy (24 Gy) for a target area 3 mm in depth and up to 5.4 mm in diameter. This is believed to be below the dose that is toxic to the retina and optic nerve, and radiation exposure outside of the target area is expected to be minimal.

NOTE: Proton beam therapy and stereotactic radiation therapy for choroidal neovascularization (CNV) are considered in separate medical policies. See cross-reference section above.

EVIDENCE SUMMARY

Evidence from randomized controlled trials (RCTs) comparing patients treated with epiretinal radiation therapy, a form of brachytherapy, with those receiving standard treatment (such as treatment with anti–vascular endothelial growth factors) is necessary in order to establish the safety and efficacy of epiretinal radiation in the treatment of wet age-related macular degeneration (AMD).

EPI-RAD90™ BRACHYTHERAPY

Randomized Controlled Trials (RCTs)

In 2016 Jackson et al. reported the initial results from a phase 3 Macular Epiretinal Brachytherapy versus Ranibizumab (Lucentis) Only Treatment (MERLOT) trial, which was designed to investigate the safety and efficacy of epimacular brachytherapy (EMBT) as a second-line treatment for chronic, active neovascular AMD.[1] The primary objective was to assess if EMBT reduced the ongoing need for anti-VEGF therapy in those who had already commenced intravitreal injections. This study was a multi-center randomized controlled trial that enrolled 363 participants with AMD who were receiving ranibizumab therapy at the time of screening, with 224 patients being randomized to the ranibizumab plus EBMT arm, and the remaining 119 patients remaining in the ranibizumab alone group. At twelve months follow-up, the investigators reported that the proportion of participants losing fewer than 15 letters was 84% in the EMBT arm and 92% in the ranibizumab arm (p = 0.007). All of measurable
outcomes were not significant between the treatment groups. The investigators concluded that although still needing longer term follow-up to determine safety, that the initial results did not support the use of EMBT for chronic, active, neovascular AMD.

In a multicenter, randomized, active-controlled, phase III clinical trial, authors evaluated the safety and efficacy of epimacular brachytherapy (EMBT) for the treatment of neovascular AMD\cite{2} using results from the CABERNET study, which included 494 patients with treatment-naive neovascular AMD. Authors concluded the 2-year efficacy study did not support the routine use of EMBT for treatment-naive wet AMD, despite an acceptable safety profile. Authors suggested that further safety review is required. Using the same patient data set from the CABERNET study, authors reported the fluorescein angiography (FA) and optical coherence tomography (OCT) results of a clinical trial of EMBT used for the treatment of neovascular AMD.\cite{3} Authors concluded that both FA and OCT suggested that EMBT with pro re nata (PRN) ranibizumab results in an inferior structural outcome than quarterly plus PRN ranibizumab. Authors suggested that a non-vision-threatening radiation retinopathy occurs in 2.9% of eyes over 24 months, but longer follow-up is needed.

**Nonrandomized Studies**

In 2016, Ranjbar reported results from an retrospective study of 32 patients (32 eyes) with neovascular AMD who met criteria for the INTREPID trial for best responders and were treated with SRT (16-Gy) along with aflibercept or ranibizumab.\cite{4} For the study’s primary outcome, the number of anti-VEGF treatments in the 12 months post-SRT, significantly fewer intravitreal injections were given compared with the year preceding SRT (3.47 vs 6.81, P<0.00001). No ocular or systemic adverse events occurred.

Results at 12- and 24-month results from the multicenter MERITAGE study (NCT00809419) were reported in 2012 and 2013.\cite{5-7} MERITAGE was a Phase I/II study of the EPI-RAD90™ for the treatment of subfoveal CNV associated with wet AMD in patients requiring continued anti-VEGF therapy to maintain an adequate response. Following a single 24-Gy dose, the 53 patients in the study received retreatment with ranibizumab administered monthly (as needed). At 12-month follow-up, 81% of patients maintained stable vision (loss of fewer than 15 letters) with a mean of 3.49 anti-VEGF injections (0.29 per month). This was compared with 0.45 injections per participant per month in the 12 months before the study. Over 24 months, 68% of patients maintained stable vision with a mean of 8.7 anti-VEGF injections (0.72 per month), which was not less than the number of injections required in the 12 months before treatment.

A total of three publications from two studies have been reported by Avila et al. on epiretinal radiation using the EPI-RAD90™ system.\cite{8-10} One report described 12-month safety and visual acuity results of a feasibility study in 34 treatment-naive patients recruited between February 2005 and February 2006.\cite{10} The second report described 12-month safety and visual acuity results from 24-Gy epiretinal radiation combined with bevacizumab in 34 treatment-naïve patients enrolled between June 2006 and April 2007.\cite{8} Adverse events related to the device or procedure included subretinal hemorrhage (n=1), retinal tear (n=1), subretinal fibrosis (n=2), epiretinal membrane (n=1), and cataract (6 of 24; 24 patients were phakic at baseline). All occurrences of cataracts were deemed to be related to the vitrectomy procedure. Two- and 3-year results from this trial were published in 2012.\cite{8} All 34 subjects were followed up for 24 months; one site that enrolled 19 patients agreed to reconsenting and following patients for three years. On average, the cohort of subjects followed for 36 months received 3.0 bevacizumab injections.
A total of 12 of the 24 phakic patients (50%) developed cataracts, and 4 had phacoemulsification with intraocular lens implantation. The mean change in visual acuity at 36 months was +3.9 letters. Seven of 13 phakic patients (54%) developed cataracts, and 4 had phacoemulsification with intraocular lens implantation. One case of nonproliferative radiation retinopathy was observed at 36 months of follow-up.

Section Summary

While these studies contribute to the body of knowledge on epiretinal radiation by providing direction for future research, the evidence from these studies do not permit conclusions due to methodological limitations, including non-random allocation of treatment and a lack of adequate comparison group. Lack of adequate control groups limits the ability to control for many types of bias that may influence treatment outcomes.

PRACTICE GUIDELINE SUMMARY

AMERICAN ACADEMY OF OPHTHALMOLOGY (AAO)

In 2015, the AAO updated their Preferred Practice Parameter regarding AMD.[11] For extrafoveal CNV lesions, guideline authors stated that the evidence is insufficient to recommend radiation therapy. There was no discussion or recommendation for the use of radiation treatment for subfoveal CNV.

SUMMARY

There is not enough research to show that epiretinal radiation therapy improves health outcomes for people with wet age-related macular degeneration (AMD). No clinical guidelines based on research recommend epiretinal radiation therapy for people with wet AMD. Therefore, epiretinal radiation is considered investigational for all indications, including but not limited to wet AMD.

REFERENCES


### CODES

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<tr>
<th>Code</th>
<th>Number</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT</td>
<td>0190T</td>
<td>Placement of intraocular radiation source applicator (List separately in addition to primary procedure)</td>
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Note: 0190T differs from code 67218 (destruction of localized lesion of the retina (e.g., macular edema, tumors), one or more sessions; radiation by implantation of source) because the radiation source is not implanted.

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<thead>
<tr>
<th>Code</th>
<th>Number</th>
<th>Description</th>
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<tr>
<td></td>
<td>67036</td>
<td>Vitrectomy, mechanical, pars plana approach</td>
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Note: 0190T is to be used in conjunction with 67036

*Date of Origin: August 2008*