Radiation therapy following surgical excision of keloids

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Policy contains: Brachytherapy, electron beam radiation therapy, keloids, radiation therapy, radiotherapy, superficial X-ray therapy.

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Coverage policy

Radiation as adjunctive therapy following surgical excision of keloids is clinically proven and, therefore, medically necessary, provided ALL of the following criteria are met:

- The keloid caused functional impairment to the member.
- Surgery was performed only on members refractory to less invasive approaches.
- Therapy is either brachytherapy (iridium-192), electron beam radiation therapy, or superficial X-ray therapy.
- Radiation is administered within 48 hours of surgery (Puckett, 2009).
- Members receive a minimum of 12 months of follow-up after the treatment (Ellis, 2020; Mankowski, 2017; Siotos, 2019; van Leeuwen, 2015).

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

No alternative covered services were identified during the writing of this policy.

Background

Keloids are abnormal scars with an unknown cause, although experts have proposed an imbalance between an increased synthesis of collagen and extracellular matrix and decreased degradation of these products. They can occur on multiple body parts. Treatments include occlusive dressings, compressive therapy, topical imiquimod, intralesional steroids, topical mytomycin C, intralesional and topical 5-fluourouracil, interferons, bleomycin, cryotherapy, pulsed-dye laser, ablative laser, laser-assisted drug delivery, platelet-rich plasma, radiation therapy, and surgery (Betarbet, 2020).

Surgical excision of keloids often is followed by recurrence, the rate of which ranges from 45% to 100%. Experts speculate that recurrence may occur due to the inability to accurately estimate margins during surgery (Berman, 2017). Radiation therapy is used more frequently as an adjunct following surgery to reduce recurrence rates, and not as first-line therapy, for keloids (Betarbet, 2020).

Ongoing improvements in radiation technology have further increased the safety and efficacy of this combination protocol (Ogawa, 2019). After keloid surgery, several types of radiation can be used to deliver dose to a superficial target, including electrons (less than or equal to 6 MeV), X-rays (70 to 150 kV), and iridium-192 brachytherapy (Zainib, 2021).

Superficial X-ray therapy uses photon beams to deliver energy to a maximum depth of 5 mm. Similar to electron beam radiation, superficial X-ray therapy can treat superficial lesions without damaging the underlying structure. This method is also less costly and easier to use, but can result in uneven delivery of dosage since radiation drops off at the periphery (Zainib, 2021).

Superficial brachytherapy is also another post-surgical modality in keloid treatment. It has been successful, but not as widely used because all radiation centers do not have the needed radioactive iridium-192 (Zainib, 2021). Of the various radiotherapies that treat keloids after surgery, electron beam (β-ray) irradiation has been the most commonly used since the 1990s (Xu, 2017).

In 2013, the Food and Drug Administration approved the SRT-100™ superficial radiotherapy system (Sensus Healthcare) for the specific treatment of keloid scars. The SRT-100 can be used for first-line therapy of keloids as well as recurrent keloids after surgery (Jones, 2017).

Findings

No professional medical society guidelines addressing use of radiation therapy after surgery for keloid removal exist as of late 2020 (Betarbet, 2020). However, the use of various radiation treatments for this purpose has become accepted standard practice, and considered safe and efficacious, based on studies published in the peer-reviewed literature (van Leeuwen, 2015). The American Academy of Dermatology has no official guideline, but supports radiation treatments after surgical removal of keloids as one means of preventing recurrence (American Academy of Dermatology, 2021).

The American Academy of Family Physicians contends that surgery followed by radiation therapy is “a much more controversial option” than other treatments, due to risk of local growth inhibition in children and possibly subsequent cancer. The Academy cites studies that show reduced recurrence when radiation is administered immediately, or within 48 hours, after surgery. The Academy advises this approach be considered a last resort

for keloids refractory to all other approaches (Juckett, 2009).

A consensus guideline declared that superficial radiation therapy after surgery for keloids in basal cell and squamous cell cancer is a safe and effective treatment and should be considered as the first-line form of radiation treatment, due to its ability to lower recurrence rates (Nestor, 2019).

A literature review declared that it was preferable for patients to receive radiation therapy after keloid excision, including superficial and orthovoltage radiotherapy, electron beam radiotherapy, and brachytherapy. Authors cited low complication and recurrence risk as the basis for its recommendation. However, the study did not endorse any particular radiation therapy (Cheraghi, 2017). A literature review of radiation therapy after keloid surgery found many articles do not describe treatment outcomes or use different definitions of keloid recurrence (Gold, 2020).

Adjunct to the lack of guidelines indicating need for use of radiation therapy is the lack of agreement on dose fractionation. One study included 238 patients treated with high-dose brachytherapy after surgery; a comparison of intervals/doses of 2 × 9 Gy, 3 × 6 Gy, and 2 × 6 Gy showed a recurrence rate of 8.3% after 12 months, but no observed significant differences between fractionation schemes. Authors recommended a biological equivalent dose of approximately 20 Gy based on low recurrence and complications (Biljard, 2018).

A systematic review/meta-analysis of 72 studies (n = 9,048) of surgical removal of keloids showed radiotherapy after surgery had a significantly lower recurrence rate versus radiotherapy alone (22% and 37%, *P* = .005). Post-operative brachytherapy had the lowest recurrence rate (15%) compared with X-ray and electron beam (both 23%, *P* = .04) (Mankowski, 2017).

A systematic review/meta-analysis of 12 studies (n = 400) determined the recurrence rate after radiation adjuvant to surgery for chest keloid removal was 22%. Only one of the studies was randomized, and authors note further studies comparing various treatments are warranted (Miles, 2021).

A systematic review/meta-analysis of 16 studies (n = 1,908) analyzed incidence of recurrent post-surgical keloids after adjuvant treatment with electron beam therapy. Recurrence was significantly lower in patients irradiated > 24 hours after surgery (3.80% versus 37.16%, *P* < .0001) (Hsieh, 2021).

A systematic review of 14 studies (n = 996) found that, compared to patients treated for keloids with no excision, those treated with surgery and follow-up radiation had a significantly lower recurrence rate (odds ratio = 0.39). The surgery/radiation group also had a significantly lower recurrence rate than those with surgery plus an adjuvant drug (Siotos, 2019).

A systematic review of 33 studies (n = 3,130) of people undergoing radiation therapy after keloid excision observed lower recurrence rates after high-dose-rate (versus low-dose-rate) brachytherapy and external radiation. Lower recurrence rates also were found after shorter (<7 hours versus > 24 hours) intervals between excision and irradiation. Because studies were classified as evidence level II (n = 6) or level III (n = 27), and only two were randomized, authors caution that quality of evidence needs improvement (van Leeuwen, 2015).

A systematic review/meta-analysis of 60 studies including 5,547 keloids showed that while the recurrence rate in patients with surgery and radiation was 18.7%, adding a third therapy reduced the rate to 7.7%, significant at *P* = .002 (Ellis, 2020).

A literature review concluded that, while electron beam radiation therapy is most commonly used in radiation therapy after keloid surgery, brachytherapy had superior recurrence rates (Goutos, 2017). Studies have reported

a recurrence rate from 8% to 29% after using electron beam (β-ray) irradiation following surgery to remove keloids (Ogawa, 2019).

A systematic review of 30 studies on patient-reported outcomes among patients treated for keloids noted that surgical excision “was a treatment modality that had relatively highly rates treatment outcomes when combined with adjuvant therapies, the most common of which were intralesional injections, pressure therapy, radiotherapy, and brachytherapy” (Tan, 2019).

A single-institution follow-up (median 15.4 months) of 284 patients undergoing keloid excision showed no difference in recurrence with versus without adjunctive radiation therapy (37.9% and 37.2%). Lower recurrence occurred in patients with higher radiation doses (Akinbiyi, 2021).

References

On November 5, 2020, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were brachytherapy, electron beam radiation therapy, keloids, radiation therapy, radiotherapy, and superficial x-ray therapy. We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

1/2021: initial review date and clinical policy effective date: 2/2021.

1/2022: Policy references updated.