Radiotherapy of Graves’ ophthalmopathy was introduced more than 50 years ago.*

Initially, Rx directed to the pituitary & hypothalamus on the theory eye changes were due to hypersecretion of thyrotropin or a pituitary exophthalmogenic factor related to hypothalamic dysfunction.

* “Radiotherapy of Graves’ Ophthalmopathy,”
Pinchera A, et al, 1984

Orbital radiation was advocated in Graves’ disease because of the acute radiosensitivity of lymphocytes and the largely lymphocytic inflammatory infiltrate (lymphocytes, plasma cells, mast cells and macrophages) in orbits of affected patients.*

*“Radiotherapy of Graves’ Ophthalmopathy,”
Pinchera A, et al, 1984

Standard treatment protocols in the early 1980s (as now) generally combined orbital radiation with systemic steroids.

“Success” more often achieved with “new onset” Graves’ rather than longstanding orbitopathy.

*“Radiotherapy of Graves’ Ophthalmopathy,”
Pinchera A, et al, 1984
Radiation modalities and results from 1980s

Linear accelerator – 35-80*% positive results [less scatter – “safer” - than Cobalt]

Betatron - ~30% positive results [single study]

Cobalt – 20-80% positive results

*Kriss, JP, 1983

Among complications of orthovoltage radiotherapy for Graves’ disease were transient skin erythema, conjunctivitis, periorbital edema and chemosis. Longer-term complications included conj scarring, lacrimal gland damage with K. Sicca, keratitis, cataracts, retinopathy, multiple endocrine abnormalities.

[An increased incidence of thyroid and salivary gland tumors noted in adults subjects treated with head and neck radiation as children.]

*“Radiotherapy of Graves’ Ophthalmopathy,”
Pinchera A, et al, 1984

2008 Report by AAO

Technology Assessment of Orbital Radiation for Graves’ Orbitopathy

Medical literature databases were searched to identify all published reports relating to radiation for Graves’.

AAO Technology Assessment of Orbital Radiation for Graves’ Orbitopathy

*14 Studies were included: 5 observational, 9 randomized clinical trials.

* 3 of 5 observational trials reported favorable outcomes in 40-99% of patients w risk of radiation retinopathy 1-2%.

* 3 of 9 randomized trials were sham-controlled, & 2 of the 3 demonstrated improved vertical motility.
AAO Technology Assessment of Orbital Radiation for Graves’

Inclusion criterion:
Original data on Radiation for Graves’ disease
Case series or uncontrolled trial of ≥ 100 P’s,
OR randomized trial of any size
Follow-up for ≥ 3 months
*Abstracted data included study characteristics, patient characteristics, treatment response and safety information.

“The efficacy of orbital radiotherapy as single therapy remains unclear, whereas the combination of radiotherapy with corticosteroids has better efficacy than either radiotherapy or oral corticosteroids alone.”*
*I.V. steroids are better tolerated and have fewer side effects than oral steroids.
J Clin Endocrinol Metab. 2009 Aug;94(8):2708-16.

AAO Technology Assessment of Orbital Radiation for Graves’

Caveat: conclusions limited by the lack of standardization and the variable quality of published reports.
Overall: EOM impairment (vertical) may improve with radiation, but the evidence is mixed. Proptosis, eyelid retraction, and soft tissue changes do NOT improve.
* No certain information on efficacy of radiation on compressive optic neuropathy.

2008 Report by AAO
Technology Assessment of Orbital Radiation for Graves’
Summary: “Based on the highest quality random clinical trial evidence, orbital radiation has a limited role in treating non-sight-threatening Graves Ophthalmopathy.”
*No good data on success of radiation in cases of compressive optic neuropathy.
*Risk of 1-2% of definite retinopathy, & ≤ 21% possible retinopathy in first 10 yrs p Rads.
The efficacy of orbital radiotherapy as single therapy remains unclear, whereas the combination of radiotherapy with corticosteroids has better efficacy than either radiotherapy or oral corticosteroids alone.

Radiation Therapy in Graves’ Disease

Gary L. Aguilar, MD
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UCSF

2008 Report by AAO
Technology Assessment of Orbital Radiation for Graves’

Overall: EOM impairment may improve with radiation, but the evidence is mixed (mostly, vertical EOM is helped).
Proptosis, eyelid retraction, and soft tissue changes do NOT improve.
No certain information on efficacy of radiation on compressive optic neuropathy.
Retinopathy is rare, but occurs even in patients without diabetes who are appropriately treated.