

MAJOR REVIEW

Radiation Therapy for Orbital Tumors: Concepts, Current Use, and Ophthalmic Radiation Side Effects

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Abstract. Radiation therapy is widely used for the treatment of orbital tumors and inflammatory disease. Both external beam teletherapy and implant brachytherapy radiation techniques are employed. External beam radiation therapy is the most common. It involves directing an external radiation source towards the eye, sinuses, and orbit. Whereas most patients are treated with linear accelerator-derived external beam radiation therapy, proton, neutron stereotactic radiosurgery, gamma knife, and intensity-modulated radiation therapy have become more available in developed countries. Radiation can be used alone or together with surgery or chemotherapy. Implant radiation therapy (brachytherapy) is also used to treat orbital tumors. Brachytherapy involves surgical placement of radiation sources within the tumor or targeted volume. Characteristically conformal, brachytherapy increases the dose within the target while maximally decreasing exposure of normal tissues. Orbital brachytherapy can be used to boost the dose to the target volume prior to orbital external beam radiation therapy. Herein, I explore the unique challenges associated with irradiation of the orbit, basic radiobiology, doses, indications, and results of treatment. The tolerances of normal ocular and orbital tissues are reported. This review of the literature offers a unique perspective, synthesizing the world's experience on the use of orbital radiation therapy. (*Surv Ophthalmol* 54:545–568, 2009. © 2009 Elsevier Inc. All rights reserved.)

Key words. carcinogenesis • eye • inflammation • melanoma • orbit • radiation • retinoblastoma • side effect • thyroid • tumor

I. Introduction

Orbital anatomy and ocular radiosensitivity provide unique challenges for radiation therapy. By definition, orbital tumors occur within the space between the eyeball and bony orbital walls. This includes tumors that extend from the eye into the orbit, as well as those from the adjacent adnexae, sinuses, bone, and brain.

Each radiation delivery system (teletherapy or brachytherapy) has unique characteristics that allow for distinctive dose distributions within the orbit. In order to better understand the differences between radiation modalities, I review their intrinsic characteristics and the reasons why each is employed.

Side effects have been reported after radiation therapy. There exists a spectrum of radiation tolerance among normal ocular tissues. For example, whereas orbital bones, muscle, and fat can tolerate relatively high doses; the lens, eyelashes, retina, and lacrimal system are more radiosensitive.²¹⁷ Side effects such as dry eye, eyelash loss, cataract, neovascular glaucoma, radiation retinopathy, and optic neuropathy are all potential local complications of orbital irradiation.^{8,58,162,210,222} Therefore, although tumor control is the primary goal, treatment plans (dose volumes) are shaped to avoid the retina, lacrimal system, and natural lens

(to decrease side effects). Lastly, there are oncogenic risks associated with ionizing radiation.^{94,95}

Radiation plays an indispensable role in the treatment of benign and malignant orbital disease. This is because the clinical benefits of improving survival and preserving vision clearly outweigh the risks. This study reviews how radiotherapy plays an integral role in the treatment of benign and malignant orbital tumors.

II. Methods of Radiation Delivery

A. EXTERNAL BEAM RADIATION THERAPY

External beam radiation therapy (EBRT) is currently delivered utilizing photons (gamma rays or X ray) or particles (protons or neutrons), with linear accelerators (LINACs) doing the bulk of the work.^{27,32,104,119,152,168,169,184,196} The LINAC creates energetic photons by using high-frequency electromagnetic waves to accelerate electrons through a microwave accelerator structure. This relatively low-energy electron beam offers limited penetration that can be used to treat superficial tumors (e.g., skin).^{9,32,53} More commonly, the electron beam is used to strike a high-Z target (within the LINAC) to produce high-energy, more penetrating bremsstrahlung X-rays to treat deep-seated tumors.^{191,192}

The LINAC's beam fields are usually shaped by a collimator into a square or rectangle as it passes through tissue (Fig. 1). Multiple, overlapping fields can be used to increase the dose to the targeted zone. Over the last 2 decades, several more complex forms of EBRT have evolved.

B. INTENSITY-MODULATED RADIATION THERAPY

Intensity-modulated radiation therapy (IMRT) utilizes controlled X-ray accelerators to create

a three-dimensional (3-D)-shaped conformal treatment zone. With IMRT, a computer program is used to selectively block portions of the beam, thereby modulating and controlling the intensity of the radiation beam. This allows the therapist to focus a higher radiation dose to the tumor (targeted zone) while minimizing radiation exposure to surrounding normal tissues (see Fig. 1). IMRT is carefully planned using 3-D computed tomography images and dose calculations to best conform to the tumor's shape. Conformal 3-D treatments require combinations of several intensity-modulated fields (coming from different beam directions).¹⁹⁴

IMRT allows for a higher and more effective radiation dose to be delivered to the tumor, with fewer normal-tissue side effects (compared with standard external beam radiotherapy techniques). For example, orbital IMRT has been used to reduce the exposure of normal orbital structures in the treatment of retinoblastoma.^{130,193}

A newer form of IMRT called image-guided radiation therapy involves coupling real-time imaging (e.g., computed tomography) to guide the IMRT source during treatment. Both IMRT and image-guided radiation therapy also offer real-time, computerized adjustments ("gating") that compensate for patient movements (e.g., breathing), keeping the beam on target.

C. VOLUMETRIC MODULATED ARC RADIATION THERAPY

Recently introduced by Varian, RapidArc (Varian Medical Systems, Palo Alto, CA) is a volumetric arc therapy that delivers a precisely sculpted 3-D dose distribution with a single 360° rotation of the LINAC gantry. It is made possible by a treatment-planning algorithm that simultaneously changes three parameters during treatment: rotation speed of the gantry,

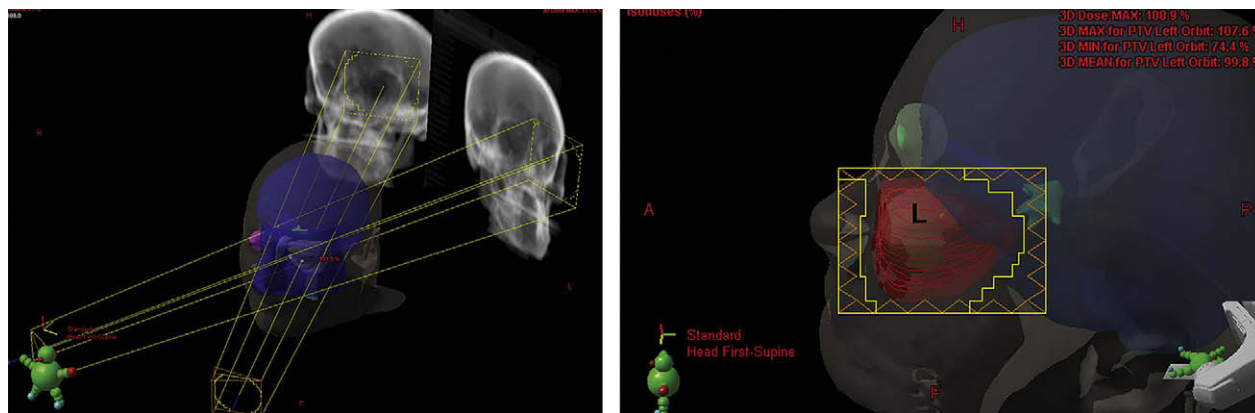


Fig. 1. Left: LINAC-based external beam radiation therapy beam fields are usually shaped like a square or rectangle as they pass through tissue. Right: intensity-modulated radiation therapy (IMRT) uses controlled X-ray accelerators to create a three-dimensional (3-D)-shaped, more conformal treatment zone. L = orbital lymphoma.

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