10 Principles and Technique of Radiotherapy of Age-Related Macular Degeneration

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10.1 Introduction
This chapter gives the reader not familiar with radiotherapy an introduction to the principles and techniques of irradiation of the eye.

Since the discovery of X-rays, radiation therapy has been employed in the management of benign conditions. Roentgen therapy was used for retinal diseases with newly formed vessels as early as 1948, and long-term treatment results of age-related macular degeneration (AMD) were reported in 1975 (GUYTON and REESE 1948; SAUTTER and UTERMANN 1975). Experimental studies and recent favorable clinical results have renewed interest in the potential benefit of radiotherapy for AMD-related subfoveal choroidal neovascularization (CNV) (CHAKRAVARTHY et al. 1993). To date, a variety of treatment techniques and dose fractionation regimens have been developed.

10.2 Rationale of Radiotherapy for Age-Related Macular Degeneration
The radiosensitivity of capillary endothelium has long been recognized. Radiotherapy is effective in choroidal hemangiomas (ALBERTI 1986; SCOTT et al. 1991). Doses of 20 Gy induced the resorption of subretinal exudation (SCHILLING et al. 1996).

The interaction of radiation with tissue is complex. On a molecular level, the main target is DNA. Ionizing radiation can cause double-strand breaks that result in immediate or reproductive cell death and ultimately in cell depletion. Less extensive lesions, so-called sublethal damage, can be repaired so that the cell recovers from the radiation injury (RAICU et al. 1993; WITHERS and McBRIDE 1997). Further observed mechanisms of radiation include a decrease in cell replication and reduction of prostacyclin production (Hosm et al. 1993; RUBIN et al. 1996). Radiation also increases cell permeability and cell adhesion molecule expression and induces apoptosis of microvascular cells in vitro (GAUGLER et al. 1997; HECKMANN et al. 1998; LANGLEY et al. 1997; WATERS et al. 1996).

The rationale for radiotherapy of AMD-associated CNV is the observation that the radiosensitivity of vascular endothelium is high due to the high proliferation rate of capillary endothelial cells (CHAKRAVARTHY et al. 1989a; De GOWIN et al. 1976; JOHNSON et al. 1982). The goal of irradiation is to inhibit further pathologic endothelial cell proliferation. Furthermore, radiotherapy possibly suppresses the inflammatory and exudative component of AMD (ARCHAMBEAU et al. 1998; CHAKRAVARTHY et al. 1989a). All of these features were demonstrated in experimental choroidal neovascularization in rabbit eyes (MIYA-
Moto et al. 1999). The degenerative process itself and the persistence of the stimuli that upregulate
the growth factors and angiogenesis are probably not
altered by radiotherapy (Spaide et al. 1998).

10.3
Techniques of Radiotherapy

Ideally, the target volume, i.e., the macula region, is
irradiated while sparing the adjacent normal tissue.
The most radiosensitive structures are the lens,
retina, and optic nerve of the treated and the fellow
eye. Frequently, the tolerance dose of these organs
at risk is similar to or even lower than the effective
treatment dose, thus limiting it. Therefore, the goal of
treatment technique is twofold: homogeneous, suf-

ciently high dose distribution within the target and
a steep dose gradient to the surrounding structures.
In modern radiotherapy, a wide array of ionizing
beams with given physical properties is available.
Each method has specific characteristics that offer
specific advantages. In the planning procedure, beam
quality, field arrangement, and beam modifiers are
chosen for optimal dose delivery.

10.3.1
External Beam Radiotherapy

The term external beam therapy or teletherapy deno-
tes radiation delivered at the large distance of 80-120
cm from the patient. Most commonly, photon beams
of 4–8 MeV energy generated by a linear accelerator
are employed.

10.3.1.1
Planning and Treatment Procedures

In the following the procedures of treatment prepa-
ration and delivery frequently used in radiotherapy
are outlined. Treatment planning refers to the design
of treatment portals that hit the target volume and
spare the volume at risk and is achieved with a simu-
lator. This is a machine with a diagnostic X-ray tube
attached to a gantry that is positioned exactly like the
treatment machine around the patient. It provides a
high-quality image of the treatment portal in rela-
tion to the patient's anatomy so that the optimal
treatment portal can be identified and marked on
the patient or on a positioning device. Due to the
small volume of the target and the proximity of
critical structures prohibiting large safety margins,
more sophisticated treatment techniques are some-
times used, especially if higher doses are aimed
for. Such treatments are designed with computer-
asstisted planning on a computed tomogram of the
patient’s head fixed in treatment position. Cross-
sectional anatomy and modern three-dimensional
planning facilities allow optimization including the
choice of multiple portals, gantry rotation, and beam
modifiers.

For the planning procedures and therapy, the
patient is placed comfortably in supine position on
the table. The head is immobilized with an individual
face mask of thermoplastic material to ensure setup
accuracy (Fig. 10.1). Thus, day-to-day setup devia-
tions during a 2- to 4-week treatment course may be
limited to a range of 2–5 mm (Sweeney et al. 1998;
Vakaet et al. 1998). A cutout in the region of the
eye allows the patient's gaze angle to be monitored
during simulation and treatment.

Fig. 10.1. Treatment setup in the accelerator room. The treat-
ment portal is marked on the head mask

10.3.1.2
Dosimetry

Radiotherapy is best described by isodose distribu-
tions superimposed on cross-sectional anatomy on
computed tomograms.

Frequently a half-beam technique is used. The ante-
rior beam edge is placed a few millimeters poste-
riorly to the lens and the gantry is angled 5–10° poste-
rionally to avoid irradiating the lenses. An absorber in
the shape of a D corresponding to the form of the eye
globe may be added to protect surrounding structures