Age-related macular degeneration (ARMD) is the leading cause of legal blindness in persons over the age of 65, with most patients demonstrating the non-exudative or dry form (NATIONAL ADVISORY EYE COUNCIL 1998; KLEIN et al. 1992). However, approximately 90% of severe visual loss occurs secondarily to the exudative or wet type. It has been estimated that 5%-10% of all patients with age-related macular degeneration have the wet type.

The Macular Photocoagulation Study (MPS) demonstrated the benefit of laser photocoagulation over observation for the treatment of the classic extrafoveal or juxtafoveal choroidal neovascularization and for a subset of patients with subfoveal choroidal neovascularization (MPS GROUP 1982, 1991a, b, 1994a, b). However, severe visual loss often results with or without laser treatments (MPS Group 1982, 1991a, b, 1993, 1994a, b).

It is well known that the majority of patients with choroidal neovascularization do not meet the MPS guidelines for laser therapy and therefore this disease process complicating ARMD often remains an untreatable blinding disorder.

As a consequence of these findings, alternative therapies for choroidal neovascularization are needed, and the list of experimental treatments is extensive. These treatments have included steroids, antioxidants, vitamins, and antibiotics, as well as other antiangiogenic therapies aimed at inhibiting choroidal neovascularization (D’AMATO et al and ADAMIS 1995).

Radiation therapy has known antiangiogenic properties and been proposed as a modality for treatment of patients with severe visual loss in the exudative type of ARMD. The concept for this treatment modality originated in the observation and results of treatment of hemangiomas of the orbit and choroid with low-dose fractionated radiation therapy and the benefit that accrued as a consequence of that treatment program. However, even though the outlook for the use of radiation therapy in exudative ARMD is promising, most studies have been uncontrolled or non-randomized in character, with relatively short periods of follow-up.

The radiation therapy techniques used in treating the wet type macular degeneration involved delivery of low dose fractionated radiation therapy with external beam radiation therapy technologies (BRADY et al. 1997, FREIRE et al. 1996; SAGERMAN et al. in this volume), or brachytherapy techniques (FINGER et al. 1996 and in this volume). The evolution of treatment with external beam radiation techniques has been directed toward precise localization of the treatment volume to include the macula and its immediate surrounding tissues while sparing other structures within the orbit. This can be determined by the utilization of three-dimensional reconstructed computed tomography and, with appropriate three-dimensional reconstructed treatment planning, the area can be treated with a high level of precision while sparing the lens, the opposite eye, and other vital structures in and around the orbit (FREIRE et al. 1996). Most of the reported patient series have used low-dose fractionated radiation therapy techniques (HART et al. 1995, HORINO et al. 1997, HOLLICK et al. 1996, MATUSHASKI et al. 1996, PÖSTGENS et al. 1997, SCHLEICHER et al. 1997, SPAIDE et al. 1998, STALMANS et al. 1997, VALSEVIC et al. 1996). The major effort has been directed toward identifying the appropriate total radiation dose to be delivered through the area of the macula to maximize the potential benefit that might accrue from the treatment regimen. Over the years of investigation, the most frequently employed dose has been 20 Gy in ten fractions of 2 Gy each delivered in a 2-week period.
The brachytherapy technology proposed by Fingert et al. (1996) has used sealed radioactive sources, primarily palladium-103 in the form of a plaque that can be placed over the area for treatment delivering radiation to a small field while sparing the normal surrounding ocular and nonocular tissues. The advantages are related to the limitation of normal tissue radiation dosage and the specific localization characteristics of the plaque in directing the treatment to the macula. Disadvantages of the brachytherapy include the need for surgical invasion in order to suture the plaque in the appropriate position for the appropriate time.

Other radiation therapy techniques have been developed using the cyclotron generating beams of protons, or charged nuclei that can be directed toward the area delivering the energy at the maximum point utilizing the Bragg peak (Yonemoto et al. 1996). This method allows for the delivery of relatively high doses of radiation at the depth of the treatment area while sparing overlying normal tissue. Other technologies relative to radiation therapy involve stereotactic radiosurgery or stereotactic radiotherapy, where radiation can be delivered to a small volume by a stereotactically localized target of the macula (Arndt 1993). This can be done by x-rays or by gamma rays from the gamma knife. The most commonly used approach in the treatment of ARMD of the wet type is external beam radiation therapy employing photons.

All patients accepted in the treatment program for macular degeneration should have a thorough ophthalmologic examination to confirm the diagnosis and to develop baseline values against which future studies can be compared. The patients accepted for radiation therapy are those who have the wet type of ARMD.

With the development of highly specific, precisely defined radiation therapy technologies, the treatment program can be carried out without the risk of major toxicities to the structures in and around the orbit. Three-dimensional reconstructed treatment techniques should be utilized for identification of the area to be treated in the patient, who is immobilized by a prefabricated head restraint or custom-molded face mask in order to insure accuracy and reproducibility of positioning. Simulation is carried out with the patient in this immobilized position, allowing for reproducibility of positioning and treatment on a day-to-day basis (Freire et al. 1996).

The rationale for radiation therapy is based on the limited number of patients who meet the criteria for the application of laser photocoagulation, even though this remains the only proven therapy for choroidal neovascularization complicating ARMD. The MPS did demonstrate that laser treatment was beneficial in decreasing the risk of severe visual acuity loss in patients with classic, well-defined extrafoveal and juxtafoveal choroidal neovascularization (MPS Group 1982, 1994, 1991). Despite this benefit, however, at least one half of the treated eyes suffered severe visual loss usually associated with recurrence or persistence of the disease process. Therefore, there is a major and significant need for adjunctive therapies to decrease the rate of recurrence and perhaps to treat the disease effectively without major loss of vision or complications relative to the treatment program. Radiation therapy has been proposed as one of these alternative treatment regimens for exudative ARMD because of the known radiosensitivity of vascular endothelial cells. The capillary endothelium has long been recognized as radiosensitive, and therefore the basic biologic consideration for its use is appropriate and proper. The radiation dosage being utilized in the treatment of choroidal vascular neovascularization is lower than that which would cause toxicities to the cornea, conjunctiva, lacrimal system, retina, or optic nerve, and, because the lens is scrupulously excluded from the treatment field, even the potential for radiation cataract exists.

The radiation dosage chosen employs standard fractionation of external beam therapy in daily fractions of 2 Gy each for a total dose of 20 Gy over a 2-week period. When fraction sizes greater than 2.5 Gy are used, there is a predisposition to toxicity, especially if the total dose exceeds 35 Gy–45 Gy by conventional fractionation or less when alternate fractionation schemes are used.

The data that have been presented indicate the absence of significant side effects related to treatment and the potential for benefit that accrues as a consequence of the treatment program. A summary of the data would indicate those reports that indicate favorable responses (Becker et al. 1999; Bergink et al. 1994, 1995; Berson et al. 1996; Chakravarthy et al. 1993; Fingert et al. 1996; Freire et al. 1996; Gibbs et al. 1999; Gruschow et al. 1999; Imgart et al. 1999; Proceedings of the meeting on age-related macular degeneration 1999; Roeppe et al. 1999; Sagerman et al. in this volume; Staar et al. 1999; Varmagia et al. 1995), those with no change (Breyer et al 1999; Geliskan et al. 1999; Protttenhofer et al. 1998), and those with no significant effect noted (Augsburger et al.; Chakravarthy et al.; Vareilles et al. 1999; Weinberger et al. 1999).