13 External Beam Radiation Therapy for Age Related Macular Degeneration: Two-Year Results

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13.1 Introduction

Age-related macular degeneration (ARMD) is the leading cause of blindness in people older than 65 and the second most common cause for patients aged 45–64 years (GANLEY and ROBERTS 1983; LEIBOWITZ et al. 1980a, 1980b; KLEIN et al. 1992). There are approximately 200,000 new cases of ARMD each year, with over 100,000 people considered legally blind. The prevalence ranges from 0.1% in persons aged 43–54 years to 7.1% in those older than 75 (KLEIN et al. 1992; MITCHELL et al. 1995; VINGERLING et al. 1995).

The accepted therapy for choroidal neovascularization (CNV) is laser photocoagulation based on randomized studies performed by the Macular Photocoagulation Study Group (MPS 1982). The MPS demonstrated a delay in the worsening of visual acuity. Eyes with extrafoveal CNV and visual acuity of 20/200 or better were treated with laser photocoagulation and compared with the control arm. The incidence of severe visual loss at 18 months was 25% for treated eyes vs. 60% for untreated eyes. Visual acuity decreased by 6 or more lines in 46% of treated eyes and 64% of untreated eyes. However, over 50% of the treated eyes developed recurrent neovascularization.

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Eyes with juxtafoveal and subfoveal CNV were also studied and demonstrated similar results, but the consequence of laser therapy for subfoveal lesions is an immediate and permanent decrease in visual acuity (MPS 1982b, 1991c, 1994a, 1994b). Unfortunately, the MPS criteria are strict and excluded many patients because they had occult CNV, large CNV, subretinal fibrosis, or severe loss of visual acuity.

Radiotherapy has long been known to affect the vascularity of an organ. Clinically, radiotherapy is very effective in controlling hemoptysis due to lung cancer and vaginal bleeding from cervical carcinomas. It has also been quite effective with benign tumors such as arteriovenous malformations (COLOMBO et al. 1989; STEINER et al. 1992) and choroidal hemangiomas (ALBERTI 1986; PLOWMAN et al. 1986, 1997; SCHILLING et al. 1997). Radiation has also been used to modify healing of ocular wounds (CHAKRAVARTHY et al. 1989). This led CHAKRAVARTHY et al. (1993) to propose its use as an alternative to laser photocoagulation or when laser photocoagulation could not be used or was not acceptable to the patient because of the immediate decrease in acuity.

There is extensive literature regarding the effects of irradiation on the structures of the eye, both when the eye is the site of the lesion (e.g., retinoblastoma (EGBERT et al. 1978; GAGNON et al. 1980), melanoma (PETROVICH et al. 1993), hemangioma (PLOWMAN and HARNETT 1986, 1997; SCHILLING et al. 1997) or when it is radiated incidentally (e.g., in sinus cancer) (PARSONS et al. 1988) and „safe doses“ have been defined for each structure (EGBERT et al. 1978; GAGNON et al. 1980; Parsons et al. 1983, 1988; PETROVICH et al. 1993).

13.2 Materials and Methods

After careful consideration of the number of patients and facilities required, the authors decided to undertake a prospective pilot study of low-dose irrad-
ation for subfoveal CNV which began in June of 1996. All patients were seen and evaluated by a group of retinal/vitreous surgeons. Clinical evaluation included family history as well as the patient's ophthalmological history. A complete physical examination, including blood pressure and pulse rate, was performed. All medications were listed. Ophthalmological examination included intraocular pressure, indirect ophthalmoscopy, inspection of the macula with a 78D lens and/or Hruby contact lens, and visual acuity. Fluorescein angiography and/or indocyanine green angiography was carried out and patients were classified as having classic, occult, or strongly suspected subfoveal choroidal neovascularization. When it was concluded that laser photocoagulation would cause an immediate and significant loss of visual acuity, all alternative managements were reviewed with the patient. No patient was excluded by virtue of age, sex, or other general health criteria. In cases of symptomatic unilateral involvement, a careful description of the contralateral eye was recorded.

One hundred forty-five consecutive patients who elected to proceed with low-dose irradiation signed an informed consent, were registered, and were followed up for 6 months to 2 years. Complete reevaluation was accomplished at 1.5, 3, 6, 12, and 24 months.

The visual acuity data of the pilot study patients was compared with that of an age-matched population who represented the untreated control patients of the National Subfoveal Photocoagulation Study published in 1991. We acknowledge with gratitude the change in lines of visual acuity from baseline in these untreated patients supplied by the MPS. Visual acuity measurements were recorded as letter scores and also as LogMar or Snellen acuity. Visual acuity was measured according to the early treatment diabetic retinopathy study (ETDRS).

The mean age of the patients was 75 years, with a range of 49 to 90 years. The majority (56%) were between 71 and 80 years of age (Table 13.1). The mean age for the MPS control group was also 75 years. Sixty-two percent of the study population and 59% of the controls were female. The size of the neovascularization in both groups was less than 3.5 disc areas. In contrast to the MPS controls, the study group had a greater percentage of patients with better visual acuity ($\leq 20/80$) (32.4% vs. 15.2%) and with worse vision ($<20/400$) (16.6% vs. 0.5%). Twenty-six percent of the patients in our study had previous laser photocoagulation, while such patients were excluded from the MPS Studies. Forty-two percent of our treated patients were legally blind in the other eye vs. 20% in the MPS study.

13.3 Technique

Radiation therapy began at varying times after ophthalmological evaluation, ranging from a few days to 1-2 months. This occurred for various patient-centered reasons and, although all patients were asked whether or not their vision had changed from the time of ophthalmological evaluation, visual acuity was not remeasured.

Radiation therapy was delivered with a Clinac 2100 C (Varian, Palo Alto, Ca, USA) employing 6-MV photons at 1-m target axis distance through a 10° left or right anterior oblique field after careful patient fixation. For the majority of patients, 1600 cGy was delivered in eight equal fractions of 200 cGy over a period of 9 days; time constraints (e.g., holidays) led to some patients receiving 1610 cGy in seven fractions of 230 cGy each over a period of 7-8 days. A half-field block technique was utilized, with the central axis being set just behind the limbus. Each treatment field was set visually after fixation of the head and with the patient focusing on a distant object.

13.4 Results

Through 12 months, irradiated patients had significantly better visual acuity than the MPS control patients. In both populations, the median visual acuity decreased over time but to a lesser degree in the irradiated patients (Fig. 13.1). At 3 months, the median loss in visual acuity was -0.6 lines in the study patients and -1.7 lines in the MPS control group. This difference persisted at 6 months (-1.2 vs. -2.8 lines), at 12 months (-2.3 vs. -4.8 lines), and at 24 months (-3.4 vs. -4.8 lines) ($p=0.034$).

In the MPS study, failure was measured as a loss of 6 lines on the ETDRS scale. When comparing our