Choroidal Melanoma

The Collaborative Ocular Melanoma Study

What you need to know! -- By Paul T. Finger, MD

The COMS offers the best evidence based medicine available about the diagnosis and treatment of choroidal melanoma.

Choroidal Melanoma

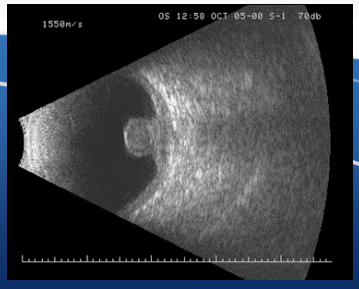
Choroidal melanoma is the most common primary intraocular tumor in adults. Initially appearing as a small freckle beneath the retina, choroidal melanoma can grow in height and diameter, and may eventually spread to other organs of the body, causing death. Because choroidal melanoma is intraocular (occurring inside the eye) and not usually visible to patients, patients with this disease may not recognize its presence until the tumor grows to a size that impairs vision by obstruction, retinal detachment, hemorrhage, or other complication. Periodic dilated retinal examination is the best means of early detection.

The Collaborative Ocular Melanoma Study (COMS) was a multicenter investigation designed to evaluate therapeutic interventions for patients who have choroidal melanoma. Evaluations conducted in the COMS were aimed at determining which alternative therapies better prolong the remaining lifetime of individuals diagnosed as having choroidal melanoma and, if treatment alternatives provide similar expectations of survival, to determine which offers the patient the longer cancer-free life and the better prognosis for vision overall.

Continued on Pages 3 and 4

Treatment Arms

Small Choroidal Melanoma	These tumors were initially treated with observation.
Medium Choroidal Melanoma	These tumors were randomized to plaque irradiation or enucleation (removal of the eye). The purpose of this study was to determine if there was a difference in survival.
Large Choroidal Melanoma	Treated by enucleation, half were pretreated with 20 Gy of external beam radiation therapy to see if it would prevent metastasis.



The COMS was funded by the National Institute of Health and The National Eye Institute. It started in 1985 and lasted 18 years.

Small Choroidal Melanoma Study

Entry Criteria:

- 1.0-3.0 mm in height, 5.0 – 16.0 largest basal diameter

Management:

- Chosen by ophthalmologist and patient (non-randomized)
- Followed with annual COMS visits annually for 2 years

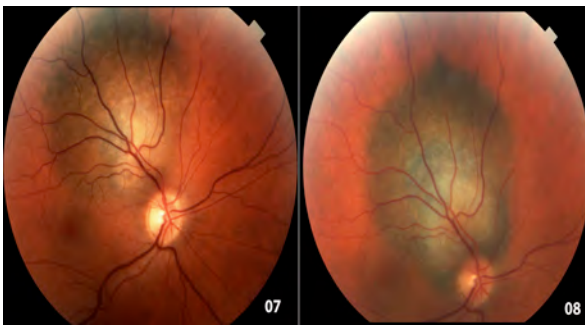
  With additional phone interviews

Results:

- Kaplan Meier: **Growth 21% at 2 years and 31% at 5 years**
- Most grew within the first 36 months of observation
- **Risk Factors for growth**: Size, orange pigment, absence of overlying drusen/RPE changes
- 3% died of metastatic choroidal melanoma

There exists a controversy surrounding treatment. Unlike dermatologists, eye cancer specialists are likely to offer "Observation As Treatment" for suspected small choroidal melanomas. Observation offers the patient time (without the risk of treatment-related vision loss) at the risk (small increase in the probability) of death from metastatic choroidal melanoma. This is despite the results of COMS evidence that **patient age** and **largest tumor diameter** are the best predictors for metastasis.

Current practice dictates that eye cancer specialists perform clinical assessments, classify such small choroidal tumors and discuss the potential risks and benefits of observation, biopsy and treatment with each patient.



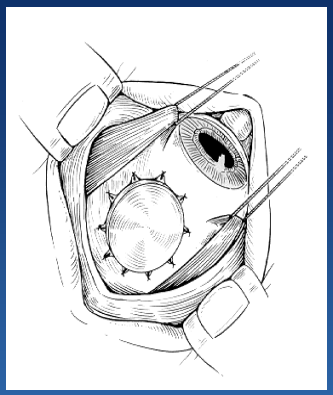
Small Choroidal Melanoma Growth

Further, we determine the patient's ability to understand what has been presented and recommend the approach that is likely to do the "least" harm.

Until there are better methods of diagnosis are available, "Observation as treatment" will continue to be the standard of care for benign and suspicious choroidal nevi, as well as most small indeterminate choroidal tumors.

On the other hand, based on an international internet-based survey, the majority of eye cancer specialists will not recommend observation for small malignant choroidal melanomas that are documented to grow.

http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijovs/vol5n1/survey.xml



This is an image of a gold eye plaque surgically attached to the eye wall as to cover the malignant melanoma of choroid and a 2-3 mm margin.

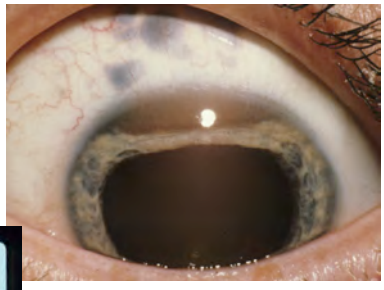
Eye Plaque Irradiation

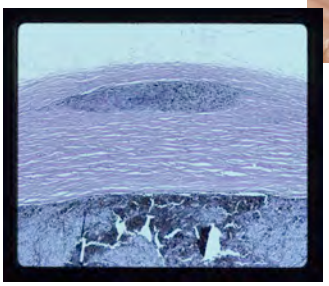
This photograph demonstrates how an eye plaque can be placed onto the sclera as to treat a portion of the choroid. Based on pre-operative ultrasound imaging, we calculate how deep the radiation needs to penetrate in order to destroy the underlying malignancy.

When COMS started in 1985, available radiation sources included cobalt-60 and iodine-125 plaques as well as proton and helium-ion charged particle therapy. Palladium-103 did not become available until 1991.

The COMS radiation oncologists chose to use iodine-125 seeds in gold plaques for the medium-sized tumor trial.

Medium-Sized Choroidal Melanoma Trial





This trial was conceived to determine if eye and vision-sparing radiation therapy was more, less or equally effective (compared to enucleation) for patient

Patient enrollment in the COMS' Randomized Trial of ***I-125 Brachytherapy for Medium Choroidal Melanoma*** began in February 1987 and was completed in July 1998. To be eligible for this trial, a patient had to have choroidal melanoma from **2.5 to 10.0 mm in apical height and no more than 16.0 mm in longest basal diameter**. Eligible patients were at least 21 years old, had no other primary tumor, and had no other disease that threatened their lives within the next five years. Previous treatment related to the eye cancer (including FNAB) rendered a patient ineligible. Eligible patients enrolled and received treatment at 43 clinical centers located in major population areas of the United States and Canada.

The study enrolled **1317 patients** with medium-sized choroidal melanoma. About 98 percent were non-Hispanic whites. The group was evenly divided by gender, and the **mean age was approximately 60 years**. Patients were assigned to one of two treatment groups by randomization. One group--660 patients--was assigned to have the affected eye removed. The other group--657 patients--was assigned to radiation treatment.
The radiation treatment was delivered via an iodine-125 episcleral plaque. Prior to the treatment, the dimensions of the tumor were measured. A gold plaque with a plastic seed carrier containing the proper dosage and configuration of radioactive iodine seeds was sutured to the outside of the eye over the base of the tumor. This procedure delivered a high dose of radiation to the tumor.

NEI Press Release - 2001

Scientists Find Similar Survival Rates for Eye Cancer Therapies

Research Also Increases Nationwide Availability of Treatments

"COMS certified eye cancer specialists were noted to achieve a diagnostic accuracy of 99.5% among enucleated cases."

"50% of tumors exhibited scleral invasion"

"Researchers have found that the survival rates for two alternative treatments for primary eye cancer--radiation therapy and removal of the eye--are about the same." Prior to this finding, there was a question in the medical community as to whether either treatment might result in lower mortality. Also, as a consequence of this research, the capability of doctors nationwide to provide more accurate diagnoses and state-of-the-art treatments for eye cancer has been greatly expanded. Mortality data are compared in the July 2001 issue of *Archives of Ophthalmology*.

SUGGESTED READING:

The COMS randomized trial of iodine 125 brachytherapy for choroidal melanoma. III. Initial mortality findings. COMS Report No. 18. Arch Ophthalmol 119: 969-982, 2001.

The COMS randomized trial of iodine 125 brachytherapy for choroidal melanoma: V. Twelve-year mortality rates and prognostic factors: COMS report No. 28. Arch Ophthalmol. 2006 Dec;124(12):1684-93.

Baseline echographic characteristics of tumors in eyes of patients enrolled in the Collaborative Ocular Melanoma Study: COMS report No. 29. Ophthalmology 2008;115(8):1390-1397.

Accuracy of diagnosis of choroidal melanomas in the Collaborative Ocular Melanoma Study: COMS report No. 1. Arch Ophthalmol 1990;108(9):1268-73.

Factors predictive of growth and treatment of small choroidal melanoma: COMS report No. 5. Arch Ophthalmol 1997:115(12) :1537-44.

Large Choroidal Melanoma Study

Patient enrollment in the COMS' Randomized Trial of ***Pre-Enucleation Radiation for Large Choroidal Melanoma*** began in November 1986 and was completed in December 1994. A total of **1003 patients** enrolled on the trial and were assigned to one of two treatment groups, and of this number, 994 were treated as assigned. Eligible patients were at least 21 years old, had no other primary tumor, and had no other disease that threatened their lives within five years. Previous treatment for choroidal cancer or secondary treatment related to the eye cancer rendered a patient ineligible. Nearly two-thirds of all patients enrolled had at least one blood relative with cancer.

Patients were divided into two groups by randomization. The mean age of patients in both groups was approximately **60 years**. One group -- 506 patients -- were assigned to have the affected eye removed without the radiation treatment. The other group -- 497 patients -- were assigned radiation treatment to the eye before it was removed. **The dosage of external beam radiation given to patients was 2000 rads (cGy) in five fractions** (A total dose of 2000 rads is as large a dose as radiation oncologists believe reasonable to treat preoperatively for this tumor). The eye was removed as soon as possible after the last radiation treatment, on the same day whenever possible but no more than 80 hours later.

By July 1997, researchers knew the five-year survival status of 80 percent (801) of all 1003 patients enrolled. **About 38 percent (181) of the patients assigned to the radiation treatment died within five years after treatment, compared with 43 percent (202) of those patients who did not have radiation treatment.** Scientists found that the radiation treatment had no effect on patients' survival rates for up to eight years after treatment. There is no evidence to date of radiation damage to the other eye.

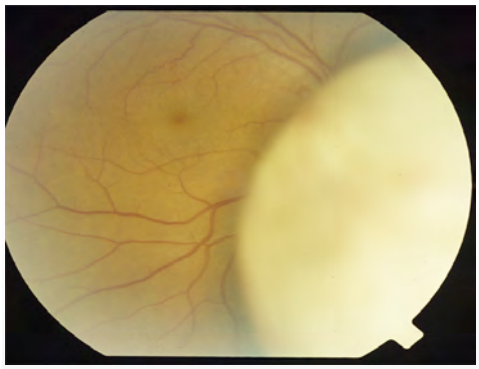
NEI Press Release

NATIONAL INSTITUTES OF HEALTH
National Eye Institute

Radiation Treatment for Eye Cancer Does Not Change Patients' Five-Year Survival

Researchers found that patients with large eye melanomas had similar five-year survival rates regardless of whether they were treated with radiation prior to removal of the eye or had their eye removed without prior radiation therapy. These findings appear in a scientific paper published in the June 1998 issue of the *American Journal of Ophthalmology.*

"**This clinical trial found neither benefit nor harm from treating ocular melanoma patients with radiation before removal of the eye**," said Dr. Carl Kupfer, director of the NEI. "Radiation therapy is costly and has the potential for side effects. Unless a survival benefit is shown with further follow-up, **it is unlikely doctors will advise it** for their patients with large melanoma eye tumors."



Treatment of Large Choroidal Melanoma

In 1985, when the COMS started, it was widely accepted that tumors greater than 16 mm in largest basal diameter or more than 10 mm in height should be treated by enucleation.

Encouraged by the results of the medium-sized COMS trial (showing no survival advantage to enucleation) larger and larger plaques were manufactured to treat larger and larger tumors.

At The New York Eye Cancer Center, we have up to 24 mm wide plaques and will treat tumors as large as 16 mm in height.

Dr. Finger has been pleased to find that most of these patients retain their eye and some useful vision. Those who don't are typically grateful for having had a chance to keep their eye.

SUGGESTED READING:

Collaborative Ocular Melanoma Study Group: **The Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation of large choroidal melanoma. IV. Ten-year Mortality findings and prognostic factors.** COMS Report No. 24. Am J Ophthalmol 138:936-951, 2004.

Study Centers for the COMS Clinical Trial

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About Paul T. Finger, MD

Dr. Finger was a principal investigator for the Collaborative Ocular Melanoma Study and has created world-renowned web sites (e.g. http://eyecancer.com and http://eyecancerbig.com).

Dr. Finger was certified by "COMS" as a visual acuity examiner, ultrasonographer, ophthalmic oncologist and surgeon. He is a Fellow of both the American College of Surgeons and the American Academy of Ophthalmology and cares for patients from all over the world.

Dr. Finger has developed new methods for the diagnosis and treatment of many ocular tumors, holds several patents and has written hundreds of scientific publications. Dr. Finger lectures frequently at local, national and international meetings.

Dr. Finger has a particular interest in choroidal melanoma, ciliary body melanoma and iris melanomas.

Dr. Finger is a Clinical Professor of Ophthalmology at New York University School of Medicine and Director of Ocular Tumor Services at The New York Eye Cancer Center, The New York Eye and Ear Infirmary, Manhattan Eye, Ear and Throat Hospital and NYU-Affiliated Hospitals

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