Paul T. Finger, MD 2011

Metastasis to the Eye and Orbit

Diagnosis and Treatment

The most common sources of ocular metastasis are breast in women and lung in men. Dr. Finger says, "Early treatment offers the best chance for preservation of vision

Page 3

Early detection, diagnosis and prompt treatment offers the best chance to preserve vision

Choroidal metastases occur in up to 10% of patients with systemic metastatic disease (more than one organ). However, few of these patients come for eye examination. This is because most ocular metastases are occult, asymptomatic and do not cause loss of vision.

However, intraocular metastasis can affect the macula, optic nerve or anterior segment of the eye. The former causes vision loss and the latter can induce painful glaucoma. Similarly, orbital metastases can compress the optic nerve or push the eye forward (proptosis) leading to corneal exposure damage. Thus, ocular metastases can be emergencies that require prompt treatment.

The most common sources of ocular metastasis are breast cancer (primarily in women) followed by lung cancer (more commonly in men). However, other less common sources include gastrointestinal, prostate, lymphoid, leukemia, thyroid, kidney and skin (primarily melanoma).

Though prompt treatment with external beam radiation therapy typically offers the best chance for retention of vision and the eye, one must first

Continued on Page 2

Primary

Breast	A yellow poorly circumscribed tumor with no large vessels.
Lung	Gray tumor with formed vessels. Patient may note discomfort.
Kidney	
Melanoma	A relatively flat, darkly pigmented tumor. Often multifocal or vitreal. History of diffusely metastatic melanoma.
Leukemia	Yellow subretinal tumor with hemorrhage.

Ultrasonography will typically demonstrate a relatively flat tumor, with an irregular surface and variable internal reflectivity. Secondary retinal detachments are common.

Chemotherapy Versus Radiotherapy

determine the primary source.

It is important to note that 90% of patients who have a breast cancer primary have either a history of cancer or known multi-organ metastases. Though the rest are likely diagnosed by a breast examination or mammogram, most of these patients will undergo a systemic staging examination. At The New York Eye Cancer Center, we perform whole-body (scalp to toes) FDG-18, PET/CT for most patients with ocular metastasis and an unknown primary.

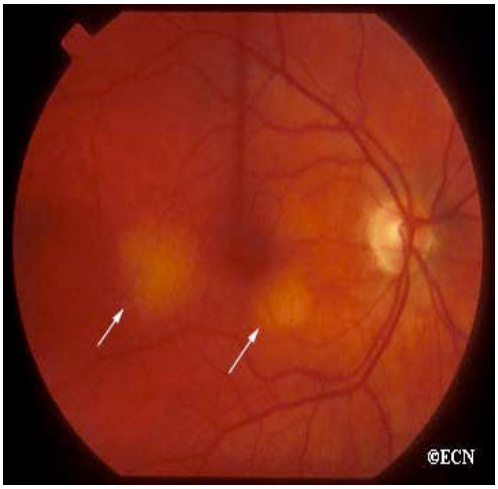
Lung cancer patients are most often found to have no detectable primary. In such cases, the eye tumor may provide a tissue diagnosis to guide subsequent focused diagnosis and systemic treatment.

Leukemia and lymphoma also affect the eye and orbit. Typically radiation sensitive, these tumors require relatively little radiation to effect local ocular control.

Systemic chemotherapy can also be used to treat metastatic tumors to the eye and orbit. However, the eye is typically a sanctuary due to the blood-brain barrier (limiting its effectiveness). Intraocular "intravitreal" methotrexate has been used to treat lymphoma, but this treatment is typically reserved for refractory cases.

Wilson MW, Czechonska G, Finger PT, Rausen A, Hooper ME, Haik BG. **Chemotherapy for Eye Cancer.** Survey of Ophthalmology 2001;45:416-444.

Rosenberg C, Finger PT, Furlan L, Iacob CE. **Bilateral epibulbar granulocytic sarcomas: a case of an 8-year-old girl with acute myeloid leukaemia.** Graefes Arch Clin Exp Ophthalmol. 2006;245(1):170-2.

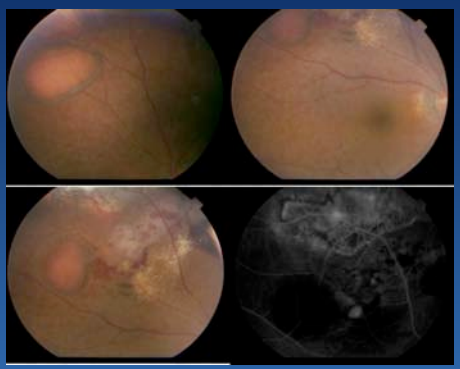


Multifocal Metastasis

Unlike most other choroidal tumors, metastases can be both multifocal and bilateral.

This fact underscores the need for careful inspection of all of the uvea and orbits of both eyes prior to treatment.

Finger PT. **Radiation Therapy for Orbital Tumors: Concepts, current use and ophthalmic radiation side effects.** Survey of Ophthalmology 2009;54(5):545-568.



This patient presents with multifocal yellow choroidal metastases with hemorrhage (and a history of systemic leukemia).

Radiation destroys cells in several ways:

- It slices the tumor cell DNA, so when it tries to divide (multiply) the DNA crumbles and the cell dies.
- Second, radiation creates free-radicals (primarily hydroxyl – OH^-) that combine with and destroy cell components.
- Radiation also works against cancer by destroying blood vessels within and around the tumor.
- Unfortunately, radiation can also affect the normal tissues in its path.

Modern radiation is performed either by inserting radioactive elements (e.g. seeds) into or next to the tumor. This is called brachytherapy and is the most common treatment for choroidal melanoma.

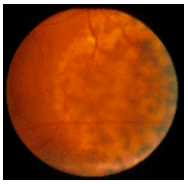
A second method is called external beam radiation therapy or EBRT. This type of treatment is delivered from the outside of the patient and travels through normal tissue to the tumor. Some examples of EBRT are LINAC, gamma knife, electron beam and proton therapy.

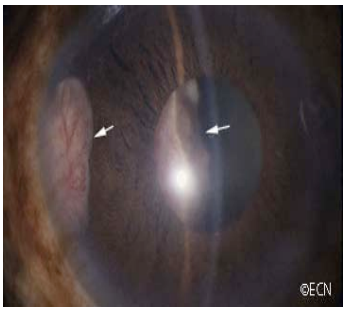
Imaging of Ocular Metastases

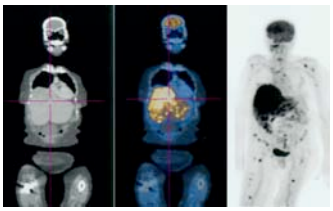
Imaging plays a central role for the diagnosis and treatment of metastatic tumors.

Slit lamp photography should be used to document anterior segment tumors. Fundus photography with angiography (including pictures of all quadrants) may detect small, otherwise hidden multifocal tumors.

Orbital tumors are evaluated with CT and/or MRI. Total body PET/CT imaging can be used for systemic staging or to detect occult primary cancers.







"Imaging is crucial to document tumor size, assess tumor growth and determine systemic disease."

Photography is an important tool for management of tumors within and around the eye. Since these tumors can grow quickly, documentation of tumor size and location can help your physician tell how fast it is growing and how quickly treatment should be started. Photography can be performed with a slit-lamp camera (anterior tumors) or with a fundus camera. Intraocular angiograms can be used to determine the tumors circulation pattern. Specialized **Fundus Auto fluorescent (FAF) Imaging** can be used to highlight the progressive destruction of the retinal pigment epithelium over growing choroidal metastases.

Ultrasonography (USG) is commonly used to evaluate intraocular and select orbital tumors. Intraocular metastases (breast and lung) have a characteristic variable internal reflectivity that helps distinguish it from melanoma and hemangioma.

Computed tomography (CT) is more commonly used for tumors adjacent to and behind the eye (in the orbit). CT is best for determining bone invasion.

Magnetic resonance Imaging (MRI) is more commonly used for tumors that do not invade bone, or to determine inflammation or compression of the optic nerve. MRA (angiography) is particularly helpful for vascular tumors and abnormalities that affect the orbit.

Positron emission tomography (PET) is used to evaluate the metabolic activity of tissues. For example, malignant tumors tend to be active or bright on PET. Over the last 10 years, PET has been coupled with CT in the same scanner. This union placed form (CT) and function (PET) on the same diagnostic page. **PET/CT** is commonly used for the detection and staging of lymphomas, melanomas and other cancers.
At The New York Eye Cancer Center, we have found PET/CT to be helpful for initial tumor staging, evaluation of metastases with no known primary and for rare ocular metastases.

Special Imaging Techniques Reported by Researchers at The New York Eye Cancer Center

Natesh S, Chin K, Finger PT. **Fundus Autofluorescence of Diffuse Uveal Melanocytic Proliferation.** Ophthalmic Surgery, Lasers and Imaging 2010;5:1-7.

Semenova EA, Chin KJ, Natesh S, Finger PT. **Fundus Autofluorescence of Diffuse Uveal Melanocytic Proliferation.** Ophthalmic Surgery, Lasers and Imaging 2010;9:1-3.

Shulman JP, Latkany P, Chin KJ, Finger PT. **Whole-body 18FDG PET-CT Imaging of Systemic Sarcoidosis: Ophthalmic Oncology and Uveitis.** Ocular Immunology and Inflammation 2009;17(2):95-100.

Garcia JP Jr, Finger PT, Kurli M, Holliday RA. **3D-ultrasound coronal C-scan imaging for optic nerve sheath meningioma.** British Journal of Ophthalmology 2005 Feb;89(2):244-5.

Radiation Tolerance of the Eye

Because both breast and lung cancers are radiation sensitive, most patients with uveal metastasis can be treated with relatively low-dose external beam radiation therapy. Occasionally, higher dose ophthalmic plaque irradiation or enucleation is required for radiation-resistant tumors (e.g. renal metastasis).

Due to current improvements in long-term survival among patients with ocular metastases, the incidence of secondary radiation retinopathy and local tumor recurrence has increased. This suggests a divergent need to lower the radiation dose (or dose-volume) to protect against radiation oculopathy while maintaining the dose to prevent late tumor recurrence. Depending on the initial dose and whether enough time elapses after that first radiation treatment, a second course can be applied.

The eye and orbit contain a variety of normal tissues with different radiation tolerances. From front to back, the eyelashes can be lost either temporarily with low doses, or irreversibly with high-dose radiation therapy. Similarly, the lacrimal (tear making) apparatus can only tolerate low-dose treatments. The cornea and scleral eye wall are particularly radiation resistant. In contrast, the lens is very radiation sensitive and will form a cataract with as little as 20 Gy. Thankfully, radiation cataracts can be removed and sight restored.

Radiation retinopathy and optic neuropathy will typically occur after high dose treatments used for more radiation resistant tumors. Researchers at The New York Eye Cancer Center have shown that anti-VEGF therapy can slow the progress of maculopathy and optic neuropathy as well as spare vision.

Useful Reading:

Finger PT. **Radiation Therapy for Orbital Tumors: Concepts, current use and ophthalmic radiation side effects.** Survey of Ophthalmology 2009;54(5):545-568.

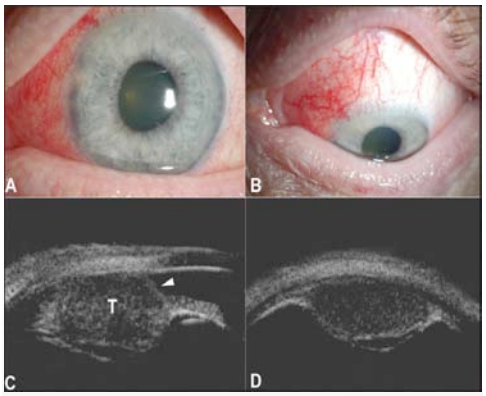
Finger PT. **Anti-VEGF Bevacizumab (Avastin ®) for Radiation Optic Neuropathy**. American Journal of Ophthalmology 2007 Feb;143(2):335-338.

Finger PT, Chin K. **Anti-Vascular Endothelial Growth Factor Bevacizumab (Avastin) for Radiation Retinopathy**. Archives of Ophthalmology June 2007;125(6):751-756.

Finger PT. **Radiation retinopathy is treatable with anti-vascular endothelial growth factor bevacizumab (Avastin).** International Journal of Radiation Oncology Biology Physics 2008;70(4):974-7.

Finger PT, Chin KJ. **Intravitreous Ranibizumab (Lucentis) for Radiation Maculopathy.** Archives of Ophthalmology 2010;128:249-252.

Finger PT, Chin KJ. **Anti Vascular Endothelial Growth Factor (anti-VEGF) for Radiation Optic Neuropathy: Secondary to Plaque Radiation Therapy.** International Journal of Radiation Oncology Biology Physics 2010, In Press.



High-Frequency Ultrasound Imaging

This monograph reveals aspects that emphasize the importance of expert diagnosis and treatment for patients with metastatic cancers. Another example is the use of **high-frequency ultrasound imaging (UBM).**

High frequency ultrasound can be the only way to see if a tumor is right behind the iris. Dr. Finger and colleagues have described high frequency ultrasound characteristics of intraocular metastases including endometrioid carcinoma, plasmacytoma, lymphoma and other tumors. However, this work underscores the need to evaluate each patient to find the entire extent of the tumor.

When metastatic tumors extends into the front of the eye, typical findings include: thickening of the anterior uvea, anterior rotation of the iris, narrow angles, an enlarged ciliary body and tumor extension into the iris.

At The New York Eye Cancer Center, when a patient found to have anterior metastases with high-frequency ultrasound imaging (UBM), the treatment plan is changed to make sure the entire tumor is removed or destroyed.

Akcaer M, Milman T, Finger PT. **Imaging of Endometrioid Adenocarcinoma of the Uterus Metastatic to the Ciliary Body.** Ophthalmic Surgery, Lasers and Imaging 2008;39:246-9.

About Paul T. Finger, MD

In his efforts to save life, conserve eyes and vision; Dr. Finger has been involved in ophthalmic radiation therapy research since 1980.

In order to better inform his patients, he has created the world-renowned web sites: http://eyecancer.com and http://paultfingermd.com He founded The Eye Cancer Foundation http://eyecancerfoundation.net to promote multicenter, international research.

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 is certified by "The American Board of Ophthalmology," a Fellow of the American College of Surgeons, a Senior Fellow of the American Academy of Ophthalmology and cares for patients from all over the world.

Dr. Finger has published research on imaging and/or treatment of metastatic cutaneous melanoma, sebaceous carcinoma, lymphoma, adenoid cystic carcinoma, and cancer-related retinopathy.

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

The New York Eye Cancer Center

115 East 61st Street – Suite 5B
New York, New York, USA 10065

Telephone 1212-832-8170 and http://paultfingermd.com

Address Line 1
Address Line 2
Address Line 3
Address Line 4