

Yale CANCER
CENTER

answers

WNPR Connecticut Public Radio



Hosts

Edward Chu MD

Chief of Medical Oncology

Francine Foss MD

Professor of Medical Oncology

Diagnosing and Treating Eye
Cancers

Guest Expert:

Miguel Materin, MD

Assistant Professor of Ophthalmology

Yale Cancer Center Answers

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Welcome to Yale Cancer Center Answers with Dr. Ed Chu and Dr. Francine Foss. I am Bruce Barber. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and Dr. Foss is a Professor of Medical Oncology and Dermatology specializing in the treatment of lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is canceranswers@yale.edu and the phone number is 1888-234-4YCC. This evening Ed and Francine welcome Dr. Miguel Materin, an Assistant Professor of Ophthalmology at Yale School of Medicine. Here is Ed Chu.

- Chu Let's start off with two questions, one is how common is a diagnosis of eye cancer, and what different types of eye cancers are there?
- Materin I am happy that you are asking that question because eye cancer is a rare disease. I want to emphasize for the listeners of this program that eye cancer is not common. Having said that, it is important to know that eye cancer can affect any person at any age.
- Foss What are the different types of eye cancer?
- Materin We can divide eye cancer into primary tumors, which means that the cancer is from the eye, and secondary tumors, which means a cancer somewhere in the body metastasized to the eye.
- Chu Are the types of eye cancer the same for say younger kids as opposed to adults? Do we see the same spectra of eye cancers?
- Materin No, the most common intraocular cancer primary in kids is retinoblastoma. The most common intraocular primary cancer in adults is melanoma.
- Chu For this evening we are going to be focusing primarily on ocular melanoma, but perhaps Miguel, you could tell us a little about what retinoblastoma is, who gets it, and what age group?
- Materin Retinoblastoma basically has 2 types of presentation, it can affect one eye or it can affect both eyes in kids. The average age is about 1 year for kids with bilateral disease, which means that both eyes are affected, and about 2 years for unilateral disease, meaning affecting only one eye.
- Foss Miguel, how would a parent know that their child may have this kind of cancer?
- Materin Thank you for asking that question. The most common presentation is the white reflex in the center of the eye, either with a flash or like from regular photography, or sometimes a person notices that the pupil looks different or funny compared to the other eye. I would say that white reflex in the pupil, which is the black circle in the center of the eye, is the most common presentation, and the second most common presentation is strabismus.

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- Foss Is this picked up by the pediatrician in most instances?
- Materin A paper that was recently published said that the first person that most frequently notes this is the mother, second the pediatrician, third a grandparent, and fourth a father.
- Chu Typically then, the pediatrician gets the signals from the family members and they would then refer the patient to an ophthalmologist?
- Materin Yes, in general they will refer the patient to a pediatric ophthalmologist because white reflex in the eye does not mean absolutely it is a cancer, but it is very important to rule out cancer because there are other conditions that can present with a white pupil like cataracts, retinal detachment, and infections in the eye or congenital anomaly, but the most important thing is to rule out retinoblastoma because the patient's life is at risk. I want to emphasize that in the United States 95% to 98% of these kids survive this cancer.
- Foss Can you talk to us a little about how you treat it?
- Materin There are different modalities of treatment for retinoblastoma. I am going to mention them not in order of how often we use them, as all of them are important. Removing the eye is always an option. Systemic chemotherapy is another option. Sometimes we need to combine the chemotherapy with laser or cryotherapy. There are new methods of treatment and one of them is to provide chemotherapy through the ophthalmic artery so that the child will receive less chemotherapy.
- Chu Miguel, you had mentioned there are other benign conditions that can lead to this white reflex. I am just curious, are there any benign eye conditions that could potentially lead to retinoblastoma or other eye cancers?
- Materin No, the retinoblastoma develops because there is a mutation in the cells and this is extremely important and why kids with unilateral disease, 90% of them only had the mutation in the cells in the retina. When the retinoblastoma affects both eyes, that means the mutation is present in every single cell of the body of the patient and that puts the patient at higher risk to develop other problems in the future.
- Foss Is this a genetically inherited condition, bilateral retinoblastoma?
- Materin Yes, and it is dominant and the penetrance is about 80% to 90%.

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Foss So, that means that other children in the same family need to be screened carefully?

Materin When we see a patient with retinoblastoma, we have to evaluate the entire family, both parents and siblings.

Chu Presumably you could also do a blood test to see whether or not there is an alteration of the retinoblastoma gene.

Materin Yes, the gene that we usually evaluate is chromosome 13 and it is through a blood test. If we can have some tissue, which means the patient's eye has been removed, then we send that for analysis too.

Foss Are there other kinds of cancer associated with this retinoblastoma gene?

Materin Yes, and that is why I mentioned the germline mutation, which means that all the cells are affected by these mutations and these patients have a higher risk to develop second cancers or even third cancers down the line.

Foss How common is this familial retinoblastoma?

Materin It is not common fortunately. It is about 1 in 15,000 or 20,000 live births.

Foss We talked a little bit about the treatment for retinoblastoma. How many kids are actually cured?

Materin In the United States, or in developed countries, about 95% to 98% of them can be cured.

Chu Terrific, why don't we shift gears a little from retinoblastoma in the pediatric population and discuss ocular melanoma. I guess we always think about melanoma as being a very aggressive form of skin cancer, but can you describe for us what ocular melanoma is?

Materin Well, the first point that we need to make is that melanoma of the eye and melanoma of the skin act as different diseases. At this point it has not been proven that melanoma of the eye is related to sun exposure. However, melanoma in the eye is more frequently present in the white population, with blue eyes, and they are at high risk. That does not mean that every person with blue eyes will have a melanoma in the eye. Again, this is a rare condition. The incidence is about 6 persons in 6 million that will have this cancer.

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- Chu Again, is the incidence of ocular melanoma highest in highly exposed sun areas, regions of the United States and high sun exposure areas around the world?
- Materin Eye melanoma can affect different structures of the eye. The most common one is in the choroid, which is in the back of the eye, and that area does not have a lot of exposure to the sun. If we consider the eye melanoma also in the eyelid, or in the conjunctiva, well the eyelids are part of the skin and that could be related. The conjunctiva is less common and we have seen melanomas present even in African Americans and Hispanics, even in Asians.
- Foss Miguel we are now starting to see skin melanomas in younger and younger people. Can you talk about the age distribution for ocular melanoma?
- Materin That's an important question. Ocular oncologists all around the world are working and trying to improve the patient's survival for these cancers. It is a very difficult goal to be made because we don't know how the melanoma will react. What we have learned is that the eye melanoma is a systemic disease. We think of the eyes as a different part of the body, but the eyes belong to the body. I am saying this because we don't know exactly when the metastasis, mainly to the liver, will happen. We don't know at which point of the disease this is happening. We are focusing, when I say we, all the ocular oncologists, in trying to learn who is at higher risk to develop metastasis. That is why it is becoming standard of care to perform a biopsy from that little tiny tumor in the back of the eye. With that biopsy, we send tissue for analysis, but this analysis is not to study the cells, it is to study the DNA or the RNA of that tumor, which will tell us how aggressive the tumor is. Regarding the age population, it's more frequent in the early 50s, late 60s, but again, whoever is in this field has seen much older people and much younger people, we actually treated a 30-year-old lady last week.
- Foss How does an ophthalmologist notice this? What does the ophthalmologist see during an exam that would make him or her suspicious?
- Materin When we say ophthalmologist, we are talking about a general ophthalmologist, and this is with the full eye exam. Some patients have symptoms which are common symptoms like blurry vision, floaters, and decreased visual acuity. Sometimes patients don't have any symptoms and this is found in a routine eye examination. So with a fundus exam, the ophthalmologist can make or suspect a diagnosis and refer to a specialist.
- Foss In general terms, a patient would expect if they have a routine ophthalmologic evaluation by a general ophthalmologist that this should be picked up if it is present?

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Materin If it is present, it is most likely going to be picked up.

Foss Great. We would like to talk more about ocular melanoma when we come back from our break. You are listening to Yale Cancer Center Answers, I am Dr. Francine Foss and my co-host Dr. Ed Chu is with me and we are joined by Dr. Miguel Materin, Professor of Ophthalmology at Yale School of Medicine.

*Medical
Minute*

The American Cancer Society estimates that in 2009 there will be over 62,000 new cases of melanoma in this country and about 2400 patients will be diagnosed here in Connecticut alone. Although melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths, but when detected early melanoma is easily treated and highly curable. Clinical trials are under way at federally designated comprehensive cancer centers such as Yale Cancer Center to test innovative new treatments for melanoma. Patients enrolled in these trials are given access to newly available medicines which have not yet been approved by the Food and Drug Administration. This has been a medical minute and you will find more information at yalecancercenter.org. You are listening to the WNPR health forum from Connecticut Public Radio.

Foss Welcome back to Yale Cancer Center Answers. This is Dr. Francine Foss and I am joined by my co-host Dr. Ed Chu and Dr. Miguel Materin, Assistant Professor of Ophthalmology at Yale School of Medicine. We have been talking about ocular melanoma and we talked a little bit about the diagnosis. You mentioned surgically biopsying these tumors. Can you talk a little bit about how that's actually done?

Materin Yes. We plan a treatment, once the diagnosis is made, most of the time clinically in the office. We take the patient to the operating room with the plan already set for this tumor. The different options of treatment again, if the tumor is too big or if there are no chances for future vision, we remove the eye, which means enucleation of the affected eye. Then we send the tissue for analysis. The most common treatment that is performed is the application of the radioactive plaque, and that is placed on the surface of the eye wall in the operating room. That plaque, which to give you an idea has a diameter of a penny, is placed using 2 sutures to hold that plaque and that will stay on the eye for about 4 or 5 days. Immediately before placing the plaque, we do the biopsy using a very thin, tiny needle. What we send for analysis may be 4 or 5 cells, and then the patient will stay in the hospital for 4 or 5 days until the plaque is removed.

Chu Miguel, can you clarify a little bit, does this plaque contain radioactivity that's being emitted to treat the ocular melanoma?

Materin Yes. The plaque is made of gold, and within the plaque the group from radiation oncology, they

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design the radiation dose and they place a couple of seeds with radioactivity that will kill the cancer.

Chu Okay.

Materin Having said this, all these patients need future follow-up examinations by general oncologists to have all the tests done to rule out any spreading of that tumor, mainly to the liver or lungs.

Chu 10 to 15 years ago, one of the treatment options was to give external beam radiation therapy. It sounds like that's no longer a favorite treatment option.

Materin Some centers in the United States use what is called a proton beam radiation. The response from the tumor is similar to the radioactive plaque. There are some advantages and some disadvantages of one over the other, and that depends on the doctor's choice.

Foss Are there frequent centers around the country that use proton beam as opposed to this plaque therapy? Is it more common to receive the plaque?

Materin In the United States and worldwide the plaque is the most common treatment, and there are, to my knowledge, 2 or 3 centers in the United States that still use a proton beam.

Chu And Miguel, is there a risk for loss of vision if one uses this eye plaque or proton beam radiation therapy?

Materin With any treatment that we perform to the eye that has a melanoma in it, there is always a risk for vision loss. But I want to make this important point, which is that in ocular oncology, we have different goals. The number 1 goal is to save the patient's life. Number 2 goal is to save the patient's eye, and vision comes 3rd. Yes, we want to keep as much vision as possible but our goal is to kill that cancer.

Foss If patients have metastasis elsewhere in the body and they receive chemotherapy, is that chemotherapy as likely to penetrate the eye and to help to treat the disease there as well, or does chemotherapy not get into the eye itself?

Materin Chemotherapy for melanoma is a different topic because the radiation will kill the cancer in the eye with or without combination of some lasers that we use. If the metastasis is already clinically observed by the general oncologist, that is a different story, and there are different trials in the United States and worldwide trying to extend the survival of these patients. It is a very difficult situation.

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- Foss Even if a patient has metastasis, they are going to receive direct treatment to the eye in addition to whatever chemotherapy they would receive?
- Materin There are two points. Point number one is that at the time of the diagnosis of ocular melanoma, less than 2% of patients will have metastasis, clinical diagnosed metastasis. Point number two is what I mentioned before, these days we consider a uveal melanoma as systemic disease. So, together with medical oncology we are trying to find ways to keep these metastasis under control if we think, and if we agree, that they are subclinical, or already there. We do not know what happens that triggers those metastases to become clinically active and put the patient's life at risk.
- Chu In general, if a patient presents with ocular melanoma, would you recommend CT scanning evaluation to look at potential involvement at other sites throughout the body?
- Materin I prefer the medical oncologist to make that final decision because sometimes the patients are not from the town where we are working. They are coming from some other distance, but in general, what they need is a liver function test which is blood work. They need liver MRI and they need a chest x-ray two times or three times a year depending on the results of the biopsy as I mentioned before.
- Foss Are there any blood tests, molecular tests, which could be done in the blood that would help us to know whether a patient has metastasis?
- Materin There is a lot of research about that, and what I can tell you, and again this is changing almost every year, but the biopsy we take is the main predictor. Again, in January 2010 the main important predictor for metastatic disease is coming from the result of the biopsy we perform in the operating room. Recently it was the chromosome number 3, again within that tumor these days, there are other tests like RNA analysis classifying these tumors into class 1 and class 2; class 1 being the better prognosis, and class 2 having the worst prognosis.
- Chu Miguel, we have been talking about the eye melanoma spreading to other parts of the body and we mentioned that the liver seems to be one of the preferred target sites, but does the reverse happen? Does skin melanoma ever metastasize and spread to the eye?
- Materin The answer is yes. It is not the most common place for a metastasis of skin cancer, and there are other cancers like breast cancer or lung cancer that spread to the eye much more often than skin melanoma, but the answer is yes.
- Foss In some cases, a skin melanoma may have completely regressed and you find a patient who has

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metastasis. Could there potentially be a situation where an ocular melanoma could have arisen from the skin? Can you tell that with the molecular test you are doing on the tumor? You talked about chromosome 3, for instance. Are there specific tests to tell you that this came from the eye and not from the skin originally?

Materin Most of the time, I can say more than 90% of the time, when the patient has skin melanoma giving metastasis to the eye the patient already knows, or the doctor knows, that there is a metastasis somewhere else. So it is very unlikely that the skin melanoma will give metastasis to the eye only, or being the ophthalmologist, the first one to make the diagnosis of metastasis from skin melanoma; can that happen? Yes, but I think it is less than 5%, or 2% of the cases.

Chu If a patient presents with an eye melanoma, what is the risk of spread to the other eye?

Materin It is very unlikely. There are publications and there are a few, very, very uncommon syndromes that can put patients at higher risk for uveal melanoma in both eyes, but it is published and there are papers, I have seen them, but it is very, very unlikely. That is a very common question that we answer for patients and their family, and another important point to be clear about is that the melanoma is not a hereditary condition. It is very unlikely that somebody in the family will have melanoma in the eye.

Foss If a patient is successfully treated for a uveal, or an intraocular melanoma, are they at risk over the next couple of years? Are they at risk for recurrence or are they at risk for complications from the radiation treatment that they received?

Materin The incidence of recurrences, which means the tumor coming back after the treatment, is about 5% depending on the treatment that we are using. When we combine the radioactive plaque with laser, the chances are 3%. If only a plaque is used the chances are about 10% for the tumor to come back. This means that with the radiation, we can control a tumor within the eye. The problem is that we do not know when these metastases occur.

Foss Effectively, patients are always at risk for recurrence?

Materin When we see a patient with an eye melanoma, that is a patient with us forever, or with the local doctor, or with whomever they decide. Regarding your question about the side effects from the treatment, yes they have a 50% chance more or less, depending on location, size of the tumor, and amount of radiation received, to have decreased visual acuity in the affected eye between 1 to 3 years. We have seen decreased vision before that, after that, and we have seen patients who kept good vision forever.

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Chu And Miguel, if the decision is made for surgical removal of the eye melanoma, what is the role of eye implants after surgery has been performed?

Materin For resection of that melanoma we have 2 different ways. One is to resect only the tumor and the other one is to remove the eye. If we remove the eye, there is a profession called ocularist and they can make an artificial eye that looks exactly like the opposite eye.

Chu Miguel, it has been great having you on the show this evening to share your experience on eye cancers.

Materin Thank you. Thank you for the invitation.

Chu You have been listening to Yale Cancer Center Answers and we would like to thank our guest expert Dr. Miguel Materin for joining us this evening. Until next week, this is Ed Chu from Yale Cancer Center wishing you a safe and healthy week.

If you have any questions or would like to share your comments, go to yalecancercenter.org where you can also subscribe to our podcast and find written transcripts of past programs. I am Bruce Barber and you are listening to the WNPR health forum from Connecticut Public Radio.