

Yale CANCER  
CENTER

*answers*

WNPR Connecticut Public Radio



*Hosts*

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Melanoma of the Eye

**Guest Expert:  
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**Yale Cancer Center Answers**

is a weekly broadcast on

**WNPR** Connecticut Public Radio

Sunday Evenings at 6:00 PM

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*Welcome to Yale Cancer Center Answers with doctors Francine Foss and Lynn Wilson. I am Bruce Barber. Dr. Foss is a Professor of Medical Oncology and Dermatology, specializing in the treatment of lymphomas. Dr. Wilson is a Professor of Therapeutic Radiology and an expert in the use of radiation to treat lung cancers and cutaneous lymphomas. If you would like to join the conversation, you can contact the doctors directly. The address is [canceranswers@yale.edu](mailto:canceranswers@yale.edu), and the phone number is 1-888-234-4YCC. This week, Francine is joined by Dr. Miguel Materin for a conversation about ocular cancer. Dr. Materin is Assistant Professor of ophthalmology and Director of Ocular Oncology at Yale School of medicine. Here is Francine Foss.*

- Foss I am very excited to hear about ocular cancer. It is certainly not one of the things that we discuss frequently. Could you define ocular cancer for our audience?
- Materin We call the field ophthalmic oncology and it involves every single area in and around the eye. We basically treat patients with benign and malignant tumors that can affect the eye.
- Foss Is ocular oncology a new area, a new specialty?
- Materin I do not think so, what we know is that doctors are full time dedicated to this field, and it was several centuries ago that eye cancers were described.
- Foss How many people in the United States are now specializing in eye cancer?
- Materin I do not know the exact number, but it is my understanding that between 10 and 15 centers have a full time physician dedicated to the field.
- Foss Can you tell us how long you have been here? You have recently come to Yale Cancer Center.
- Materin Yes, I moved to Connecticut in January 2009, so it has been two years since we started working with Connecticut patients and the surrounding areas for this specialty.
- Foss Can you tell us how you first got interested in this whole area of ocular tumors?
- Materin We need to go back almost 20 years, but what I remember is that I was a retinal specialist in Buenos Aires when I received the first referral for a patient with a uveal melanoma, which is a malignant tumor in the back of the eye, and this is how I become interested. Also, there was a lack of full time specialists in the field, and I found it interesting, so here I am.
- Foss Can you tell us, Miguel, how common these types of cancers are, and what age group do they usually occur in? What are the different types?
- Materin I am glad that you are asking me that question because eye cancer is a very very rare disease. We see patients because we received referrals and I do not want anybody who might be listening to this conversation to rush to the doctor and ask if he or she, or a relative, has an eye cancer. I am

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saying this because sometimes patients do not have symptoms and these tumors are found in a routine eye examination, and sometimes they do have symptoms. Regarding who can have an eye cancer, unfortunately, depending on what type of tumor it is, it can happen at anytime in life from young babies to older people and there is no difference for gender.

Foss Can you tell us what the specific types of eye cancer are?

Materin That will take a long time, but I can share with you and with the audience what the most common tumors are that can affect the eye. In children, the most common intraocular malignant tumor is called retinoblastoma. In adults, the most common intraocular primary cancer is called melanoma, but we also see and treat patients who have other cancers, any type of cancers that can give a metastasis or spread to the eye. Finally, the other types of patients that we see are patients that have a systemic cancer, or other type of cancers, and because of the treatment, they have ocular side effects. Basically that is the field of ophthalmologic oncology.

Foss So you treat children as well with retinoblastoma?

Materin Yes.

Foss Can you tell us a little about that disease?

Materin It is an uncommon cancer, however, is the most common intraocular malignancy in children. Usually it affects babies between 1 and 2 years of age, however, we have seen these in teenagers and most of the time it is a relative, the parents, that bring the baby in because they notice white reflex on one eye or both eyes.

Foss What is that again?

Materin White reflex in the pupil. It may be that they are taking several photos and they see instead of being red reflex, there is a white reflex and that is the most common sign on babies with retinoblastoma. The second most common sign is strabismus. Now again, there are many many people who can have a white reflex and that is because of the flash and it is not because they have a retinoblastoma. When it happens, when it is noticed in different photos at different times, that is when we start to be concerned.

Foss It is there anything apparent we would notice say just looking at a baby, are there are any external manifestations that would make a parent worry?

Materin White reflex is number one. Sometimes, when it is an advanced disease, the babies can have pain and they would not tell the parents because again, these are babies and might not think I have pain in my eyes, so they are very irritable or they do not sleep at night and touch their eyes a lot. And

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there is a different color between the eyes and most of the time, parents, when they see their baby is not having a good time for whatever reason, they take their baby to the doctor.

Foss If this occurs, say in an older child or a teenager, is the major symptom pain, or are there other symptoms as well?

Materin There could be pain, but there could also be no pain at all. They may notice decreased vision, but maybe they did not ever have good vision and they do not notice that, and that is when the white reflex comes in to play again. It is very uncommon to see these over the age of four, but I have seen it on 15 year olds and 17 year olds, but there is not a unique sign or symptom just for these.

Foss Can you tell us a little bit about what causes retinoblastoma?

Materin There is a mutation, or a gene alteration that can happen in two different types. One is called a somatic mutation and that means that these genes only have the problem in the retina. The other type of mutation is called germline mutation and that means that early in the development of that baby all the cells of their body have this type of mutation. This is very important, why, because when we treat a baby with somatic mutation, depending again on many factors, most of the time we can say that after the treatment the patient is cured. With the germline mutation, usually there is some family history of retinoblastoma or both eyes are effected, or there are multiple tumors in one eye, and the important thing is that we can cure these babies from the retinoblastoma, but since they have these germline mutations, they at higher risk compared to the rest of the population for second or third cancers in their life.

Foss Do you routinely do genetic testing on all of these patients who come in with retinoblastoma?

Materin We strongly recommend to parents that every baby with retinoblastoma should have genetic analysis, yes.

Foss And does that also extend to other family members such as other children in the family?

Materin When we see a baby with a retinoblastoma, we perform an exam on both parents and on the siblings because they may not even know that they have retinoblastoma for whatever reason, so we do examine the entire family.

Foss Can you tell us, when you look at the eye of one of these patients, say an asymptomatic family member that may have retinoblastoma, what do you see?

Materin We see a tumor. It is a white tumor that involves the retina.

Foss Do those patients have any problems with their vision?

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Materin It depends on several factors, the location of that tumor, the size of the tumor, and whether or not there is retinal attachment with these tumors. The larger the tumor the more symptoms or the worse vision these patients can have. They can also have a small tumor located in the central part of the retina called the fovea and that patient will have poor vision too.

Foss You mentioned that you can often times cure these patients, these younger patients with retinoblastoma, can you talk a little bit about that, what kind of treatment it requires and what are the outcomes for those patients?

Materin Yes, in first world countries the cure rate for retinoblastoma is about 95%, so patients survive the cancer. There are different treatments that can be applied. The most common one is chemotherapy, systemic chemotherapy, and that shrinks the size of the tumor and then, in general, we perform a laser or cryotherapy local radiation. Sometimes systemic chemotherapy does not control the disease, and many times we still need to remove the eye through surgeries called enucleation in order to cure the baby. There are new methods of treatment and one is the application of chemotherapy through the ophthalmic artery. It is a local way of doing chemotherapy and it has been done for few years now and it looks like it is having good results.

Foss It sounds to me like you have a combined modality approach to these tumors, can you talk a little bit about how you work with other members of the team to develop a treatment plan for these patients?

Materin For any patient with an ophthalmic cancer, this is not a one doctor treatment. We work with other specialties, pediatric oncology, radiation oncology, and pathology. We also strongly suggest family psychological support for the family and so it is a group of specialties that are involved in the care of these babies.

Foss I would like to pick up there when we come back from our short break for a medical minute. Please stay tuned to learn more information about ocular cancer with Dr. Miguel Materin.

*Medical  
Minute*

*The American Cancer Society estimates that last year there were over 65,000 new cases of melanoma in this country and over a thousand patients are diagnosed annually in Connecticut alone. While melanoma accounts for only about 4% of skin cancer cases, it causes the most skin cancer deaths. Early detection is the key. When detected early, melanoma is easily treated and highly curable and new treatment options and surgical techniques are giving melanoma survivors more hope than they have ever had before. Clinical trials are currently underway at Yale Cancer Center Connecticut's federally designated comprehensive cancer center to test innovative new treatments for melanoma. The specialized programs of research excellence in skin cancer grant at Yale, also known as the SPORE Grant, will help establish national guidelines on modifying behavior and on prevention as well as identification of new drug targets. This has been a medical minute brought to you as a public service by Yale Cancer Center. More information is available*

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- Foss This is Dr. Francine Foss and I am joined today by my guest Dr. Miguel Materin, and we are here today discussing ocular cancers. Miguel, at the beginning of the show we talked a lot about retinoblastoma and ocular cancers in children, and you mentioned also that the most common ocular cancer in adults was melanoma. Can you talk a little bit about that?
- Materin Melanoma, as we said, is the most common intraocular cancer in adults. Usually it happens during the fifth or sixth decade of life. However, we have seen these in younger patients. Recently, we received a patient who at the time of diagnosis was 14 years old. Melanoma is very common. There are about 2500 new cases per year in the United States and mostly affect the white population with fair skin and light eyes.
- Foss Can you tell us a little bit about risks factors, whether it is sun as it is with systemic melanomas or whether there are other risks factors for ocular melanoma?
- Materin It has not been proven that there is a sun exposure relationship with ocular melanoma. It is more common in white people but there is no relationship with either sun exposure or anything that the patient could have done in the light. Just to give an example, it is believed that about 6% of the white population has a mole in the back of the eye, only six per million will develop a melanoma, so it is infrequent.
- Foss How would a patient know if they have a mole in the back of their eyes, is that something that you see routinely when you do an eye exam?
- Materin It can be seen in a routine eye exam, absolutely. The patient may not have any symptoms, or the patient may have different types of symptoms from blurry vision to floaters or flashes, but that does not mean that every patient with floaters or flashes will have a melanoma. Those are very very common symptoms in general, but any type of symptoms or even asymptomatic patients can have a mole or melanoma in the back of the eye.
- Foss If you see that on a routine exam in a patient who is asymptomatic, what you do to follow that patient?
- Materin Clinically, 98% of the time we can say whether it is a benign or malignant tumor. When it is benign, we call it a nevus and we follow that nevus once or twice a year. Particularly at Yale, I prefer to alternate the exam with the referring doctors. We take photographs from the back of the eye and that's how we follow the patient. We can do ultrasounds, which routinely we do. Regarding melanoma, we don't watch them, we treat them. There are different ways of treatment.

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- Foss Before we get into that we should ask the question, how are these diagnosed, given that they are obviously in the back of the eye.
- Materin We use an ophthalmoscope. It is used in any ophthalmic office or a slit lamp when it is more anterior. We dilate the pupil and then we check the back of the eye. We would perform the ultrasound and then we can perform what is called fluorescein angiography. That means that we inject a dye in one of the veins and we take photos from the vasculature of the back of the eye. Basically, those are the most common tests that we do for these patients.
- Foss Are those tests, including that injection, done right in your office or do you have to have a special facility for that?
- Materin No, that is done in the office and most ophthalmic offices will have this equipment.
- Foss Generally speaking, in cancer we always tell patients, you do not have cancer until I have a piece of tissue that I am looking at under the microscope that says you have cancer. You obviously must biopsy these lesions?
- Materin The accuracy of the clinical diagnosis is 98%. Few times we do need to do the biopsy to make a diagnosis. Most of the time, we do not need to do a biopsy. Once we decide to treat the patients, at least at Yale, we perform three different biopsies, one biopsy is to study the cells, called cytology, the second biopsy is to study the genes within the tumor, and that is called gene expression profile, and the third biopsy is trying to culture melanoma in the lab and then we perform the treatment at the same time.
- Foss Can you talk a little bit about the treatment once you have made the diagnosis? What happens next?
- Materin It depends on many factors, it depends on the age of the patient, it depends on the status of the opposite eye, but in general I can tell you that when the tumor, when the melanoma is small, or medium size, up to 10 mm in thickness, an application of the radiation device can be performed and that is our favorite treatment here at Yale. When the tumor is larger, or when there is no hope for any vision, then most of the time we need to remove the eye.
- Foss If you do something short of removing the eye, such as radiation, how often does the patient maintain their vision?
- Materin With radiation, we expect some vision loss between one and three years after the treatment, however that depends again on location and size of the tumor, and this is because the larger the tumor the more radiation will be needed, and radiation does not distinguish between normal tissue and that tissue. So, the good tissue can be affected. The goal is to keep the eye for this patient.

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Foss Is there a role for chemotherapy in this situation?

Materin The answer today is no, and I feel very confident in saying no instead of I do not know because there is a lot of research going on these days, not only for uveal melanoma but also for skin melanoma, trying to extend the survival of patients with this serious disease.

Foss Do these melanomas in the eye metastasize to other areas of the body or to the other eye?

Materin It is extremely unlikely that it will go to the other eye. The main organ that melanoma of the eye, uveal melanoma, gives metastasis to is the liver.

Foss And how often does that happen?

Materin That is an excellent question. On average, it's 50% of the time and when I mention the fine needle aspiration biopsies, when we do the gene expression profile or when we send the tissue for gene expression profile, there are two types of melanomas, class I or class II. The class I tumors, they have less risk for metastatic disease and class II has a higher risk for metastatic disease.

Foss If you know that a patient say has a class II tumor, do you do anything differently?

Materin There are clinical trails starting in different places in the United States and possibly around the world, and I can compare at this time to what's happening with cutaneous melanoma where different mutations were found and there are specific treatments for those mutations, this is only just starting with melanoma of the eye.

Foss At this point, are you using some of these new drugs that we have heard about, some of these biological targeted agents that we use for systemic melanoma? Are you using those for the eye?

Materin No, again those are clinical trails only just starting, but not today.

Foss Is there anything that can be done to decrease the toxicity of radiation when a patient is undergoing radiation therapy? Are there any agents or anything that is done to try to alleviate that toxicity?

Materin Radiation, first of all, will not affect the other eye and it will not affect the brain of the patient. It is a very localized treatment. There are different methods that are under investigation trying to prevent or to cure vision loss from the radiation, from laser, injections, eye drops, but to my knowledge, and after today there could be cases that succeed, but there is not a standard of care for those patients trying to prevent vision loss.

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Foss After a patient has completed say radiation therapy, how often do you screen that patient and what kinds of tests do you do to look for a metastasis?

Materin Excellent question, and another controversial topic. Here at Yale, I work together with the melanoma group and depending on the risk for these patients they are going to have two or three times a year surveillance exams. In other institutions, they could do it more often and in other institution there is no systemic treatment available. Sometimes they do not even do any tests.

Foss Do you do PET scans or CAT scans to look at the liver?

Materin The recommendation, in general, that we prefer is physical exam and blood work for liver function tests two or three times a year, and a chest x-ray, and a liver MRI once or twice a year for the first three years.

Foss Can you tell us a little bit about some of the other kinds of tumors of the eye? You mentioned initially that there are metastases that can appear in the eye from other kinds of solid tumors as well. Could you go through that a little bit with us?

Materin The most common metastatic cancer to the eye, is in women. It comes from breast cancer. The most common metastatic disease to the eye in men comes from lung cancer. Now, we need to also keep in mind that the eye might be the first site of a known metastasis from a primary tumor. What I am trying to say is that it can be the first manifestation of a systemic metastasis. Sometimes patients do not know that they have a primary cancer somewhere else and because these patients usually do provide symptoms, we are the first one telling them something is wrong.

Foss Miguel, we are almost at the end of our show, but I just had another question and I am sure this is on a lot of people's minds, and that is, if you know that you have another kind of cancer, should you be getting regular ophthalmologic exams just to make sure that you do not have metastasis there?

Materin From my point of view, that is a great idea. I do not know if that should become the standard of care. What I can say is that in general, and this is not because of an eye cancer or a systemic cancer, in general, every person should have an eye exam once a year or once every other year for many reasons, not only for this.

*Dr. Miguel Materin is Assistant Professor of Ophthalmology and Director of Ocular Oncology at Yale School of Medicine. If you have questions or would like to share your comments, visit [yalecancercenter.org](http://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 on the Connecticut Public Broadcasting Network.*