

Yale CANCER
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answers

WNPR Connecticut Public Radio



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An Update on Brain Tumors

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Barber I am Bruce Barber and on this week's Yale Cancer Center Answers our hosts, Dr. Edward Chu and Dr. Ken Miller, will discuss the treatment of brain tumors. Dr. Chu is Deputy Director and Chief of Medical Oncology at Yale Cancer Center and a leading expert in cancer drug development. Dr. Miller, a Medical Oncologist, is the Director of the Connecticut Challenge Survivorship Clinic at Yale Cancer Center and specializes in pain and palliative care. Yale Cancer Center Answers is our way of providing you with the most up to date cancer information every Sunday evening on WNPR. Dr. Chu and Dr. Miller welcome some of the nation's leading oncologists and cancer specialists who are in the forefront of the battle to fight cancer. They wish to provide you with help and hope from Yale Cancer Center. They will also answer any of your questions. If you would like to submit a question about cancer to the show, please email them to canceranswers@yale.edu or call 1-888-234-4YCC. If you are interested in listening to past editions of Yale Cancer Center Answers, or if you would like to learn more about a specific kind of cancer, all of the shows are posted in audio and written formats on the Yale Cancer Center website, www.yalecancercenter.org. This evening, Dr. Chu and Dr. Miller will discuss brain cancer. Each year over 17,000 people in the United States are diagnosed with primary brain tumors. Our goal is to give you information on the detection, diagnosis and treatment of brain cancer.

Good evening doctors.

Chu Hello Bruce, I am Dr. Ed Chu.

Miller And I am Dr. Ken Miller.

Chu Today, Ken and I are joined by our colleague Dr. Joachim Baehring, Assistant Professor of Neurology and Medical Oncology here at Yale Cancer Center. Dr. Baehring directs the brain tumor program here at Yale and is a leading expert in his field. Joachim, thanks so much for being with us tonight on Yale Cancer Center Answers.

Baehring Thank you Ed. Thank you for your invitation.

Miller You are welcome. Let us begin by talking about the different types of tumors that can develop in the brain; both benign and malignant.

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- Baehring Generally, there are two major groups of brain cancer; primary brain cancer and what you consider metastatic or secondary brain cancer. Today, we will focus mostly on primary brain tumors. They again are divided into tumors that are derived from cells that I call glial cells, where the tumor is referred to as gliomas, and tumors that are less common, derived from nerve cells. The most common tumor amongst all of these is a tumor called glioblastoma multiforme. Unfortunately, it is also the most malignant type of brain cancer.
- Chu Is there a difference in the type of brain cancers depending upon the age of the patients?
- Baehring In general, as is the case for so many other types of cancer, brain cancer is usually a disease of the elderly. However, there are age-specific entities. The tumor that I just mentioned, glioblastoma multiforme, is a lot more common in the elderly population, patients above the age of 65, as opposed to other tumors that are a lot more common in childhood, such as medulloblastoma and related cancers.
- Miller What are the risk factors? I have heard people talking about cell phones and high-tension power lines being an issue. What are your thoughts on that?
- Baehring To this day there is no reliable population-based study that establishes a link between an environmental exposure, such as the ones you just mentioned, or certain toxins and brain cancer. Probably the only known link is exposure to high doses of radiation, but this only occurs in an industrial accident or something to that effect. There are multiple studies available now that try to see if there is a correlation between cell phone use and primary brain tumors. The vast majority of these studies do not point towards a link. There are few where a link was suggested, but to this day there is no clear established link between cell phone use and brain cancer. There has been no dramatic increase in brain tumors since cell phone use has become more common.
- Chu Is there any relationship between genetics and the development of brain cancer?
- Baehring Very few cases of brain cancer can be linked to a hereditary predisposition to cancer. It is in the order of less than 2 or 3 percent.
- Miller What are the signs and symptoms of a brain tumor?
- Baehring The early signs of a brain tumor are rather nonspecific. There is not one sign that would immediately lead to the suspicion of a brain tumor. Most types of brain cancer actually present with one of two symptoms; a headache or a seizure. A seizure is a lot more dramatic and patients immediately seek medical attention. With a headache, this is one of the most common complaints patients go to see their doctor

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for; this makes it a little more difficult. A headache that is new and that arises without any clear factors such as a lot of stress or a head or neck injury, and a headache that gets worse and worse week after week, should get the patients' attention and lead to a consultation with their family physician.

Chu Of that group of people who go and see their doctor for a headache, how common is it that you will find a brain tumor as opposed to other causes?

Baehring It is exceedingly rare. The most common causes of headaches are tension-type headaches, migraines and cluster headaches. Of all patients who present to a neurologist with a headache, a minute fraction, maybe less than one percent will end up having a brain tumor.

Chu So if someone has a headache that does not resolve itself with the typical aspirin or Tylenol, that individual might seek attention first from their family care physician, and then if there is concern, refer to someone like yourself for further evaluation.

Baehring That would be the most reasonable approach. It depends also on how ill the patient is. Patients with a brain tumor can have a bleed in their brain into the tumor and those patients will present with a much more disabling headache. At that point it is probably best to go to the emergency room right away. But in general, patients are referred to me through a local family physician or a general neurologist.

Miller There are a lot of different forms of x-rays and imaging, CAT scans PET scans and MRIs, can you tell us a little about how you use them in terms of diagnosing a brain tumor and looking at the response to the treatment.

Baehring Once a strong suspicion of a brain tumor has been established, the most sensitive non-invasive test is a magnetic resonance imaging, an MRI, and in many cases that is the first step. A CAT scan is more of an emergency room tool, or a diagnostic tool for patients who cannot have an MRI due to a cardiac pacemaker or other reasons. The MRI gives us the first clue as to what the origin of the headache might be and if there is concern for a tumor or not.

Chu One of the issues with MRIs, and I have to say I never really appreciated this until I myself had to undergo an MRI, is the tight quarters in which the test is done. What do you suggest for patients who are perhaps claustrophobic?

Baehring Many patients who are claustrophobic still tolerate the MRI as long as they are premedicated. There are sedatives like lorazepam, just to mention one, that can be taken within half an hour of the examination and then patients can rest or even sleep during the examination. For patients who cannot go into a closed MRI scan even with medication can undergo an open MRI scan. It is not as anxiety provoking, and

although the image quality is not as high as with the closed MRI, it is still sufficient to rule out the possibility of a brain tumor.

- Chu Ken mentioned the use of PET to try to image the brain. Could you explain what a PET scan is and how the PET scan fits into the diagnosis of brain tumors.
- Baehring PET stands for a positron emission tomography. For the patient, it is rather similar to an MRI. While an MRI gives you an accurate anatomical picture, PET scanning is a metabolic picture of the brain using a lower resolution, but the areas that are particularly active and have a high demand for the metabolic substrates such as brain tumors, light up on a PET scan. The problem with PET scanning is that it is not very sensitive. This means that a large number of patients with brain cancer have a negative PET scan. Patients with low-grade brain tumors do not benefit from a PET scan because these tumors generally do not take up the tracer. It is a test that is useful in specific situations. For example, after exposure to radiation there can be some changes on an MRI scan which could reflect a growing tumor, but the changes could just be the effects of radiation. A PET scan can help to distinguish the two conditions.
- Miller If someone goes to the doctor with a headache, and they end up being in the small group of patients who have a brain tumor, what happens next in terms of making a diagnosis and then the first step in treatment?
- Baehring Although MRI scans are very good in detecting tumors, the vast majority of patients will require confirmation by retrieving a tissue specimen of the mass by a neurosurgeon. Many times this last diagnostic step is also the first therapeutic step. Many patients with a tumor that is considered resectable, meaning it can be removed at least in part by the neurosurgeon, will have this procedure performed. The pathologist takes a piece of that mass to identify the sub type of brain cancer. If the cancer is located in an area where major surgery would result in a patient's disability, then the procedure is limited to stereotactic biopsy, which is a lot less invasive and only serves the purpose of making a specific diagnosis.
- Chu Joachim, you and Dr. Piepmeier are the directors of the brain tumor center here at Yale. Can you explain what that means and at what point an individual would be referred to your center?
- Baehring We have established a multidisciplinary Brain Cancer Center at Yale and Dr. Piepmeier and I are only two of many members involved in this endeavor. We have radiation oncologists and neuroradiologist who are specialized in the diagnosis of brain cancer. We have neuro-pathologists and also a lot of administrative support. We have a clinical coordinator, Betsey D'Andrea, who is the first contact point who helps with the decision of which member of the team should be contacted first. These are the major components and we meet on a weekly basis to review the cases of the week to establish a diagnostic plan and a treatment plan for these patients.

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We evaluate patients for their eligibility in clinical trials and the meeting also serves as a platform for discussions with the basic scientists who are interested in brain cancer.

Miller Along those lines, if someone has a biopsy and they are told that they have a brain tumor, what role do second opinions have?

Baehring Second opinions can be very helpful in various circumstances. Sometimes you encounter a case that is truly challenging such as an exceedingly rare tumor; a tumor that in spite of all efforts is still undiagnosed as to the exact subcategory. In that case a second opinion is helpful to the medical team. Many times a second opinion is very helpful to the patient. They are facing a diagnosis of a rare disease with a rather poor prognosis. Obtaining a second opinion will inform them as to how other multidisciplinary centers would approach the case and what clinical trials might be available at other institutions. I think obtaining a second opinion at a multidisciplinary center is crucial. We are dealing with a disease where only 20,000 cases a year in total are encountered in the US. I strongly believe that patients benefit considerably from the input of specialists in multiple fields.

Miller We would like to remind you to email your questions to us, and to Dr. Baehring, at canceranswers@yale.edu. We are going to take a short break for a medical minute. Please stay tuned to learn more information about the treatment of brain tumors with Dr. Joachim Baehring from the Yale Cancer Center.

Barber This medical minute is brought to you as a public service by Yale Cancer Center.

Breast cancer is the second most common cancer in woman. In Connecticut alone approximately 3000 women will be diagnosed with breast cancer this year. But there is new hope for these women; early detection, noninvasive treatments and novel therapies provide more options for patients to fight breast cancer. In 2007, more women are learning to live with this disease than ever before. Now women should schedule an annual mammogram beginning at age of 40 or earlier if they have risk factors associated with the disease. With screening, early detection and healthy lifestyle, breast cancer can be defeated. Clinical trials are currently underway at federally designated comprehensive cancer centers such as the Yale Cancer Center, to make innovative new treatments, which have not yet been approved by the food and drug administration available to the patients. For more information, visit www.yalecancercenter.org.

Miller Welcome back to Yale Cancer Center Answers. This is Dr. Ken Miller. I am here with my co-host Dr. Ed Chu and our guest, Dr. Joachim Baehring from the Yale Cancer Center. He is one of the directors of the brain tumor center. Joachim, let's start this second portion of the program by talking about treatment for brain tumors. What are some of the surgical options for someone who has a glioblastoma?

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- Baehring The first step of therapy for the vast majority of patients is indeed surgical intervention. The goal of surgery is to remove as much of the tumor as possible. However, the patient should not be put at risk of suffering neurological disability as a result of the procedure. We know that we cannot cure a glioblastoma multiforme surgically, so there is no benefit to the patient if a tumor is overly aggressive. Relieving the mass that the tumor exerts on the brain frequently results in complete resolution of the patient's symptoms. This is the rationale for trying to take out as much as possible.
- Chu Obviously there are a lot of very vital pathways and structures in the brain. How does the neurosurgeon know that normal brain tissues are not involved and that there won't be consequences after the surgery?
- Baehring There are now numerous tools available to the neurosurgeon to plan the surgical procedure ahead of time. Most of these are imaging procedures that can be done while the patient is being prepped for surgery. One of them is a procedure that is MRI based called fiber tracking MRI. It tells the surgeon where important functioning areas of the brain are such as language, and can also point out the connections of these important functioning centers on the surface of the brain with deeper structures and their relationship to the tumor. Then the surgeon in the operating room can use the procedure called electrical stimulation, where an electrode is put on the surface of the brain to get a better feel for where important areas are located.
- Miller There is talk about gamma knife and CyberKnife, what are these?
- Baehring These are all new treatment modalities that have become available over the past 10 years. The terminology implies that it is a surgical procedure, but it actually isn't. Both gamma knife and CyberKnife are primarily radiation therapies. Gamma knife is a procedure where the patient's head is placed into a large shielding device that contains a large number of bur holes; outside of that shielding device is a radiation source. These bur holes can be directed towards the target within the brain, let's say a deep-seated brain tumor. The major advantage of this technique is that by having the radiation beam come from multiple directions, normal brain tissue surrounding these lesions can be spared more so than with conventional radiation treatment modalities. Gamma knife requires a small surgical procedure. A head frame is fixed to the patient's head which is crucial for planing and targeting the lesion. This is done under local anesthesia.
- CyberKnife is quite similar in that it also delivers a focused beam of radiation to a specific target such as a brain cancer. The difference is that a head frame is not necessary. Plain x-rays help the radiation therapist to target the x-ray beam to the intended lesion. Also CyberKnife is not only applicable to brain cancer; it can be used for cancer anywhere in the body.
- Chu Joachim, we presently have a gamma knife facility here at Yale correct?

- Baehring Yes, we do.
- Chu We do not yet have a CyberKnife system though, but will shortly.
- Baehring We will have a system here soon for what you call image-guided stereotactic radiosurgery and I am quite excited about it. It will be a tool that we will frequently use for various types of cancer. For our neuro-oncology program, it will enable us to provide stereotactic focussed radiosurgery to patients with spine cancer.
- Miller After the surgery, what is the role of chemotherapy in the treatment of brain tumors?
- Baehring It depends a bit on the type of brain cancer that you are facing. Let us focus on the most common type of brain cancer, which is glioblastoma. A clinical trial was conducted and published about a year ago. It was a combined effort of neuro-oncology centers around the world. It firmly established the role of chemotherapy after tumor resection. It shows that chemotherapy with an alkylating agent called temozolomide, provided along with radiation therapy and followed thereafter, increases the survival of patients with glioblastoma multiforme.
- Miller I know you are an expert in the treatment of lymphoma of the brain. In those cases, is surgery the primary treatment or is chemotherapy?
- Baehring It is chemotherapy. Surgery is limited to a stereotactic biopsy. Lymphoma of the brain is an elusive target. This is not a single tumor. It is composed of lymphocytes. These are cells of the immune system that are supposed to traffic the entire body to eliminate agents or invaders such as bacteria that do not belong there, and the tumors reflect that behavior. They migrate throughout the nervous systems, so resecting a lymphoma would not really make much sense. In the vast majority of patients, surgery is limited to a biopsy and then the primary treatment modality is chemotherapy.
- Miller It has been very exciting having read some of your work and having seen some of your patients, realizing how effective chemotherapy can be for some of them.
- Baehring Yes, it is quite amazing. Lymphoma is a very sensitive chemosensitive tumor.
- Chu Along those lines, for the primary CNS lymphoma, which we are talking about, is there a particular age group in which you see this cancer in the brain?
- Baehring Again, like with the glioblastoma, it is usually a disease of the elderly. Most patients are actually older than 60 years of age, however, in the referral center we certainly see patients from the pediatric age group to 60 and above.

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- Chu For this type of brain cancer are there any specific risk factors that one can attribute to the disease?
- Baehring The risk of suffering brain lymphoma is markedly increased in patients whose immune system is compromised, possibly through an infection like the HIV virus or through pharmacotherapy such as the chronic use of steroids.
- Miller In terms of treatment, there is the a device that can be put right on the tumor or right in the brain that releases chemotherapy. Can you talk a little about that?
- Baehring Referring to the wafer?
- Miller Yes the wafer.
- Baehring There are wafers available that are impregnated with the chemotherapeutic agent. They have added this treatment modality to what a neurosurgeon can provide in terms of treatment for patients with malignant gliomas. It is also an FDA approved form of therapy for both the initial diagnosis and relapse disease. These chemotherapy impregnated wafers are placed into the wall of the resection cavity. They are about the size of a diamond and very thin. The surgeon attaches these wafers to the wall of the brain tissue that is left after resection of the tumor. Then over the next few days after surgery, the chemotherapeutic agent is released from the wafer and diffuses into the brain. It has shown to be effective and is certainly a reasonable form of therapy. It is not the cure for glioblastoma, which we unfortunately do not have, but it is one option that belongs in the armamentarium.
- Chu Joachim, you are playing a very active role in developing new clinical trials here at Yale Cancer Center. Can you quickly review with us some of the interesting studies that you are involved with.
- Baehring We have been involved in a large number of clinical trials and will open a large number in the near future. We currently have a clinical trial available that uses this standard of care, which as we discussed is a combination of radiation therapy and chemotherapy, with a form of therapy where the dose of the chemotherapy is escalated or intensified. Over the next couple of weeks, a trial will be available where the standard of care, again radiation and chemotherapy, is combined with a tumor-directed vaccine. The vaccine initiates an immune response targeting at certain receptors on the surface of glioblastoma cells. We are very excited about that clinical trial as well. We have been involved in a trial where a new compound was administered directly into the brain through infusion. That trial has been completed and we are awaiting the publication of the results.
- Miller If you have questions for Dr. Baehring, Dr. Ed Chu or myself, we encourage you to

go to our website, www.yalecancercenter.org for more information about cancer and the resources available to you. Again, you can listen to past editions of Yale Cancer Center Answers in audio and written format on the Yale Cancer Center website which is www.yalecancercenter.org.

Joachim, I want to thank you for being on the show and for telling us about some of the very exciting advances in terms of the treatment of brain tumors.

Chu Joachim, thanks so much for joining us. We look forward to having you on a future show to tell us the results of your very interesting clinical trials. Remember, tune in to WNPR every Sunday evening at 6 p.m. for Yale Cancer Center Answers for the latest information in cancer care and treatment. Our next program will feature a discussion on colorectal cancer. Until then, this is Dr. Ed Chu and Dr. Ken Miller from the Yale Cancer Center wishing you a safe and healthy week.

Bruce Thank you Dr. Chu and Dr. Miller. If you have questions for Dr. Baehring, I encourage you to go to www.yalecancercenter.org for more information about cancer and the resources available to you. You can also listen to past editions of Yale Cancer Center Answers in audio and written formats on the Yale Cancer Center website at yalecancercenter.org. Remember, tune in to WNPR every Sunday evening at 6 p.m. for Yale Cancer Center Answers for the latest information in cancer care and treatment. On our next week show Dr. Chu and Dr. Miller will discuss screening, detection, and treatment of colorectal cancer.