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A Brain Tumor Q&A

*A Conversation with Ronald Warnick, MD,
Chairman of the Mayfield Clinic
And the AANS/CNS Section on Tumors*

CINCINNATI -- Ronald Warnick, M.D., Chairman of the Mayfield Clinic and Professor of Neurosurgery at The Neuroscience Institute at the University of Cincinnati and University Hospital, has emerged as one of America's leading experts in the treatment of brain tumors. He is currently serving his second year as Chairman of the American Association of Neurological Surgeons/Congress of Neurological Surgeons Section on Tumors. Dr. Warnick's term will come to a close this spring.

Dr. Warnick is a co-investigator in nine clinical trials with UC's Department of Neurosurgery, which in 2005 ranked 13th nationally among public medical schools and 25th nationally among all medical schools in funding from the National Institutes of Health (NIH). In 2004 Dr. Warnick was co-investigator of the first study [insert link http://www.mayfieldclinic.com/PR_04Jul13.htm] to involve combining implantable radioactive seeds and chemotherapy wafers with the surgical removal of tumor mass to prevent recurrence of glioblastoma multiforme. The new therapy nearly tripled the survival rate of patients with recurring glioblastoma, a lethal type of brain tumor resistant to conventional therapies.

Dr. Warnick is Co-Director and a developer of the Precision Radiotherapy Center in West Chester, Ohio, which has brought state-of-the-art radiotherapy technologies for fighting cancer to the Greater Cincinnati/Northern Kentucky area.

During a recent interview, Dr. Warnick discussed current treatments for brain tumors and new developments on the horizon.

Question: Dr. Warnick, you are completing your term as Chairman of the AANS/CNS Section on Tumors, which has given you a global view of progress in brain tumor research and treatment. What have you seen?

Answer: Keep in mind that in order to become Chairman, I have been involved in the Section on Tumors' leadership for about 10 years, working my way through the organization. This organization represents all the brain tumor surgeons in the United States, and we really determine the guidelines and the advancements in the field. I would say the two most exciting new strategies for brain tumor care are immunotherapy and, in

particular, stem cell therapy. Stem cell therapy is looking at the stem cells within the patient that are responsible for the growth of the tumor. Think of it this way: the stem cells are like the queen bee of the hive. They produce the worker bees, and the worker bees grow and change and the tumor grows and affects the patient. For the past 20 years we have focused our treatment on the worker bees, so to speak. We've treated them with surgery, radiation, and chemotherapy. But we have not been able to touch the queen bee, which has different qualities. And these stem cells that are within, for example, the most malignant tumor – the glioblastoma – are not sensitive to treatments such as radiation and chemotherapy. So if we can identify these stem cells and determine their characteristics and devise therapy that is specific for them, that's the most exciting thing in neuro-oncology right now. There have been some recent advances showing, for example, that the stem cells in glioblastoma are particularly sensitive to radiation if you manipulate them in certain ways. And if you can extinguish the cancer stem cells, the rest of the tumor falls apart.

Question: Normally, we hear about trying to harness the growth of stem cells. In the case of glioblastoma, you're talking about destroying stem cells.

Answer: The same processes that are involved with the development of the brain and the fetus are also responsible for the development of the tumor. Unfortunately, in the case of the tumor, it's a deranged growth, and that's why we apply the same kind of investigations. There are two aspects to stem cells in the brain. One is identifying the stem cell that produces the tumor and killing it, eliminating it. The other is to take stem cells from the patient's bone marrow and to use them as targeted missiles against the deranged stem cells in the glioblastoma. If you can get a stem cell from the bone marrow to act like a cancer stem cell, then maybe you can load it with a toxin, for example, that would act like the other stem cells, congregate within the tumor, and take its toxin in with it. So we want to both harness stem cells and also kill stem cells in a very selective fashion.

Question: When might these new treatments become available?

Answer: It typically takes five to seven years to bring a new finding from the laboratory to the clinic and have it FDA-approved. Unfortunately, many of the strategies will not work. That's why you must have multiple, parallel strategies to be successful. Because you don't want to wait seven years and then start a new project. So multiple investigators at multiple institutions are working on different aspects of stem cells, with the hope that in five to seven to 10 years we will have a new treatment for glioblastoma.

Question: How are you currently treating glioblastoma?

Answer: We're approaching glioblastoma in a couple of different ways. One of our recognized areas of expertise is the use of local implant therapy. We think that the best time to treat a glioblastoma is at the time of removal. You have the least number of cells, and the surgeon is there already and can place certain implants at the site of surgery to

eradicate tumor cells. So we started many years ago by placing low-radioactivity, permanent iodine 125 seeds into the cavity after the removal of the glioblastoma. That worked. We already knew that chemotherapy wafers, such as Gliadel, work from some investigations done at other institutions. So we decided some years ago to combine radiation seeds and chemotherapy wafers together at the time of surgery, after the removal of the tumor, and we had spectacular results. We had survivals that were lasting five or more years in patients that normally die within six months. It has been our most effective therapy to date, and we're continuing our work in this area and hope this will become a standard treatment in the near future.

Are the seeds and wafers left behind permanently?

Answer: The wafers are about the size of a Necco wafer, or about the size of a nickel. And they are a polymer that has been filled with BCNU, a very standard form of chemotherapy. We usually place eight wafers along the surface of the brain when we remove the tumor. We also place seeds, which are about the size of a grain of rice. They're in a little titanium casing filled with iodine 125, and we place anywhere from 40 to 60 seeds. We leave them in. The polymers dissolve over several weeks, giving off the chemotherapy. The casings of the seeds remain forever, but the radiation is nearly gone in six months. So essentially we have overlapping therapies that are distributing treatment to wherever the remaining tumor cells are.

Question: How does the Precision Radiotherapy (PRT) Center fit in with brain tumor eradication?

Answer: The PRT Center is a full-therapy radiation center in West Chester, Ohio. PRT houses two different types of technology: the Novalis, which is mainly for brain radiation, and Tomotherapy, which is mainly for the body. So for brain tumors we're mainly interested in the Novalis. This allows us to shape the beam of radiation to treat irregular tumors and to almost shrink-wrap them with radiation. So we're able to treat brain tumors, and spine tumors, with a single dose when appropriate or multiple doses over several weeks at a time. We can treat benign tumors and malignant tumors.

Question: In summary, how has brain tumor survival changed in recent years?

Answer: This is both an uplifting and frustrating topic. On the uplifting side, our biggest changes and improvement of survival have occurred with metastatic brain tumors. It used to be a death sentence if a patient with lung cancer or breast cancer developed a brain metastasis. That was before stereotactic radiosurgery, which we do at PRT. Now we can control 90 to 95 percent of those patients through a combination of surgery, implant therapy (radiation seeds), and radiosurgery. That's where the biggest changes have occurred. As those patients are living longer from their primary disease, they have a higher likelihood of brain disease, which we can control most of the time.

We have not been as successful, however, in the area of glioblastoma, which we've talked about with regard to neural stem cells. And the overall survival rate for people

with that tumor has not changed in 20 years. There has been a select subset of patients who have benefited from implant therapy, however. Those are patients who are generally a little bit younger and who have a single spot of tumor that can be removed. For those patients implant therapy has led to a “tail” of survivors, as we call it. About 20 to 25 percent of those patients will go on to be cured of their tumor with implant therapy. So there is a subset of patients with glioblastoma who have done well and whose survival rate has improved over the years. But as a whole, nothing has changed in that area.

Question: What are your future goals?

Answer: Our goal is to further advance our center by recruiting additional researchers in the area of stem cells and immunotherapy. Over the past 16 months, all of the brain tumor specialists at the University of Cincinnati and the Mayfield Clinic have worked on a weekly basis to put together a strategic plan and business plan to allow us to expand our center. We’ve identified various recruitment needs, technology needs, to prepare us for the next 10 years. Now that we’ve finished that work, we’re in the process of working with the various hospitals and foundations to see how we can fund these initiatives. Essentially, we need more basic researchers and additional medical neuro-oncologists to provide the innovative clinical trials that are necessary.