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Dual implantation of radiation seeds and chemotherapy wafers shows promise in treatment of recurrent, malignant brain tumor

Novel approach by UC brain tumor experts shown to be safe while extending survival rates for patients battling recurrent glioblastoma multiforme

CINCINNATI – In the battle against glioblastoma multiforme, a malignant brain tumor, concurrent implantation of radioactive seeds and chemotherapy wafers following surgery showed promising results in a study led by specialists at The Neuroscience Institute at the University of Cincinnati and University Hospital.

The study, published today in the February issue of the *Journal of Neurosurgery*, revealed that the simultaneous implantation of radioactive seeds and chemotherapy wafers following removal of glioblastoma multiforme (GBM) was well tolerated by patients and appears to provide longer survival compared with the implantation of seeds or wafers alone.

The study was the first ever to explore the combination treatment in patients suffering from recurrent GBM. The early-phase trial involved 34 patients, all of whom underwent the same treatment. None received a placebo. The study's purpose was to assess the safety and effectiveness of the highly localized, combination therapy.

The median survival was 69 weeks, and nearly a quarter of the study's patients survived two years. In comparison, patients with recurrent GBM who undergo conventional treatment (chemotherapy) have a median survival of approximately 26 weeks.

"Treatment of recurrent GBM presents a major challenge to neurosurgeons and neuro-oncologists," said investigator Ronald Warnick, M.D., Chairman of the Mayfield Clinic and professor of neurosurgery at UC. "Glioblastoma is an aggressive, highly malignant tumor with unclear boundaries. Because of its diffuse nature, surgeons are unable to remove it completely, and it regrows in the majority of patients. Our aim is to find a way to keep the infiltrating glioblastoma cells from growing into adjacent, healthy tissue."

Because most GBM tumors recur within 2 centimeters of the initial tumor margin, Dr. Warnick and his team have focused their efforts during the last several years on highly localized treatment.

Previously they studied the implantation of permanent, low-activity iodine-125 seeds following the surgical removal of the tumor. The seeds, housed in a titanium casing filled with iodine-125, are the size of grains of rice. They are left in the resection cavity permanently, and their radiation is delivered over a period of six months.

Other institutions have studied implantation of chemotherapy wafers, which are the size of a nickel. The wafers contain BCNU, a standard form of chemotherapy. The wafers are placed along the surface of the brain following removal of the tumor.

Combining radiation seeds and chemotherapy wafers was a logical next step, Dr. Warnick said. The combination of seeds and wafers "appears to provide longer survival" compared with studies of seeds and wafers alone, he said, and "disease progression also seems to be further delayed."

Dr. Warnick cautioned that the effectiveness of the combination therapy is not definitive, because the study did not include a control group.

In the most notable downside to the dual therapy, brain necrosis (tissue death) developed in nearly 25 percent of patients and appeared to be higher than in treatment with seeds or wafers alone. The necrosis was treated successfully with surgery or hyperbaric oxygen therapy, however, and did not affect survival.

Future studies will involve using a combination of seeds and wafers to treat patients newly diagnosed with GBM, Dr. Warnick said.

In addition to Dr. Warnick, study co-investigators included John Breneman, M.D., a radiation oncologist with The Neuroscience Institute and UC Radiology and a professor of radiology at UC; Robert Albright, M.D., a neuro-oncologist who practices in Cincinnati and Northern Kentucky, and Borimir Darakchiev, M.D., a former resident in the UC Department of Neurosurgery.

The Neuroscience Institute, a regional center of excellence at UC and University Hospital, is dedicated to patient care, research, education, and the development of new treatments for stroke, brain and spinal tumors, epilepsy, traumatic brain and spinal injury, Alzheimer's disease, Parkinson's disease, disorders of the senses (swallowing, voice, hearing, pain, taste and smell), and psychiatric conditions (bipolar disorder, schizophrenia and depression).

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