

Fluorescent Cancer Cells to Guide Brain Surgeons

Malignant brain tumors grow with fine extensions which make them hard to distinguish from healthy brain tissue during surgery. Scientists of the German Cancer Research Center (Deutsches Krebsforschungszentrum) and the University of Heidelberg have developed a staining method that makes tumor cells glow in yellow-green. Thus, borders between tumor tissue and normal tissue become visible during the entire operation, which makes resection easier for brain surgeons.

Gliomas are malignant brain tumors that arise from glial (supporting) cells of the brain. Gliomas are often resistant to chemotherapy. These tumors grow fine extensions that infiltrate normal brain tissue and, in addition, individual tumor cells can form satellites in surrounding tissue. Therefore, it is almost impossible to remove the tumor tissue completely by surgery.

Yet, radical surgical removal of the tumor would substantially improve the prognosis of patients. Surgeons are confronted with the difficulty of discriminating between tumor tissue and healthy brain tissue during surgery. Dr. Eva Frei of DKFZ, collaborating with doctors and researchers of the Medical Faculty of Heidelberg University, has now developed a method to improve neurosurgery.

The scientists took advantage of the fact that tumors cover their increased energy needs, among other things, by taking up large amounts of the blood protein albumin. The researchers attached a fluorescent substance (5-aminofluorescein) to albumin, which is distributed throughout the body via the bloodstream and eventually accumulates in the brain tumor. Laser light causes the substance to glow and makes the fine extensions of the tumor visible.

“Other contrast agents often fade,” says Dr. Eva Frei, “for tumor resection can take five to six hours.” The fluorescence marker attached to albumin, however, is visible during the entire operation.

The scientists tested the albumin method in thirteen patients with malignant gliomas. In nine cases it was possible to remove the fluorescent tumor tissue completely thanks to the intensive yellow-green light signal. The researchers calculated that the probability of the glowing tissue being tumor cells is 97 percent.

“Staining is a tremendous help for the surgeon, because he or she can recognize the exact borders between tumor and normal brain tissue, which is normally very difficult,” explains Eva Frei. “Another problem is that the tumor often exerts pressure on the meninx so that, when it is opened for surgery, the tumor shifts or changes its shape.” The new method takes account of this ‘brain shift’ effect and makes the effort of intraoperative MRTs unnecessary. Further advantages of the new method are that it is tolerable, inexpensive and easy to apply.

Tolerability and effectiveness of the staining method will be validated next year in a larger study involving several hospitals. The scientists will monitor in a long-term study whether the prognosis of patients will improve as a result of the new method.

Paul Kremer, Mahmoudreza Fardanesh, Reinhard Ding, Maria Pritsch, Saida Zoubaa and Eva Frei: Intraoperative fluorescence staining of malignant brain tumors using 5-

aminofluorescein-labeled albumin. Neurosurgery 2009,
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The German Cancer Research Center (Deutsches Krebsforschungszentrum, DKFZ) is the largest biomedical research institute in Germany and is a member of the Helmholtz Association of National Research Centers. More than 2,000 staff members, including 850 scientists, are investigating the mechanisms of cancer and are working to identify cancer risk factors. They provide the foundations for developing novel approaches in the prevention, diagnosis, and treatment of cancer. In addition, the staff of the Cancer Information Service (KID) offers information about the widespread disease of cancer for patients, their families, and the general public. The Center is funded by the German Federal Ministry of Education and Research (90%) and the State of Baden-Württemberg (10%).

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