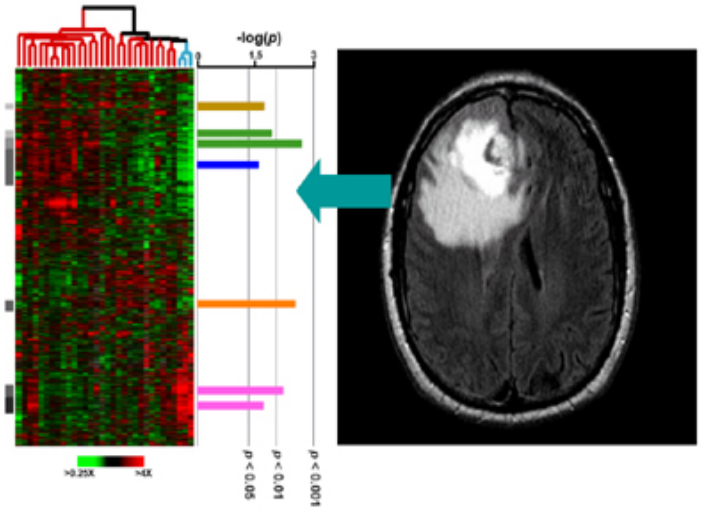
UC San Diego Health

Non-Invasive Imaging Provides Window Into Genetic Properties of Brain Tumors

March 24, 2008 |

Doctors diagnose and prescribe treatment for brain tumors by studying, under a microscope, tumor tissue and cell samples obtained through invasive biopsy or surgery. Now, researchers at the University of California, San Diego (UCSD) School of Medicine have shown that Magnetic Resonance Imaging (MRI) technology has the potential to non-invasively characterize tumors and determine which of them may be responsive to specific forms of treatment, based on their specific molecular properties. The study will be published on line by the *Proceedings of the National Academy of Science* (PNAS) the week of March 24.



"This approach reveals that, using existing imaging techniques, we can identify the molecular properties of tumors," said Michael Kuo, M.D., assistant professor of interventional radiology at UCSD School of Medicine. Kuo and colleagues analyzed more than 2,000 genes that had previously been shown to have altered expression in Glioblastoma multiforme (GBM) tumors. They then mapped the correlations between gene expression and MRI features.

The researchers also identified characteristic imaging features associated with overall survival of patients with GBM, the most common and lethal type of primary brain tumor.

The researchers discovered five distinct MRI features that were significantly linked with particular gene expression patterns. For example, one specific characteristic seen in some images is associated with proliferation of the tumor, and another with growth and formation of new blood vessels within the tumor– both of which are susceptible to treatment with specific drugs.

These physiological changes seen in the images are caused by genetic programs, or patterns of gene activation within the tumor cells. Some of these programs are tightly associated with drug

targets, so when they are detected, they could indicate which patients would respond to a particular anti-cancer therapy, according to the researchers.

"For the first time, we have shown that the activity of specific molecular programs in these tumors can be determined based on MRI scans alone," said Kuo. "We were also able to link the MRI with a group of genes that appear to be involved in tumor cell invasion –a phenotype associated with a reduced rate of patient survival."

Laboratory work that relies on tissue samples is routinely used to diagnose and guide treatment for GBM. However, the biological activity shown may depend on the portion of the tumor from which the tissue sample is obtained. The researchers have shown that MRI could be used to identify differences in gene expression programs within the same tumor.

"Gene expression results in the production of proteins, which largely determine a tumor's characteristics and behavior. This non-invasive MRI method could, for example, detect which part of a tumor expresses genes related to blood vessel formation and growth or tumor cell invasion," said Kuo. "Understanding the genetic activity could prove to be a very strong predictor of survival in patients, and help explain why some patients have better outcomes than others."

Kuo also led a study, published in *Nature Biotechnology* in May 2007, correlating CT images of cancerous tissue with gene expression patterns in liver tumors. "In the new study, we were able to take a different imaging technology, MRI, and apply it to a totally different tumor type," he said, noting that the studies open up promising new avenues for non-invasive diagnoses and classification of cancer.

Contributors to the paper include first author Maximilian Diehn, UCSD Department of Radiology and Department of Radiation Oncology at Stanford University School of Medicine; Christine Nardini and David S. Wang, UCSD Department of Radiology; Susan McGovern and Kenneth Aldape, Department of Neuropathology, University of Texas M.D. Anderson Cancer Center, Houston; Mahesh Jayaraman, Department of Radiology, Brown University; Yu Liang, UCSF Brain Tumor Research Center, and Soonmee Cha, Department of Radiology, UCSF Medical Center.

The research was funded in part by the National Institutes of Health.

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