Award ID:
RP130427

Project Title:
Clinical MR spectroscopy development of 2-hydroxyglutarate as a specific biomarker for malignant gliomas

Award Mechanism:
Individual Investigator

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Mutation of the gene, isocitrate dehydrogenase (IDH) in over 70% of patients with grade 2 and 3 malignant gliomas and 10% of glioblastoma, has created a great deal of interest in the biology of these difficult to treat primary brain tumors. Since the mutation is not found in other brain cancers, the presence of the gene makes the diagnosis of glioma. Moreover, presence of the mutation is associated with a better prognosis for the patient. The gene is important in cell metabolism and, when mutated, leads to accumulation of an abnormal metabolite, 2hydroxyglutarate (2HG). We have developed a method to identify 2HG by a brain MR scan. Thus, tumors that are found to have 2HG by MR scan are able to be classified as a glioma and the levels of 2HG are correlated with tumor grade. Low grade (grade 2) gliomas predominantly affect young patients and often have a period of years without tumor growth. The standard clinical management is observation with serial MR imaging after surgery has established the diagnosis, and treatment is initiated only at the point that there is clear progression of disease or transformation into glioblastoma. However, tumors are frequently located in areas of the brain where even a biopsy is associated with the risk of permanent neurological injury. Therefore, one of the most important clinical applications of 2HG detection is the ability to make the diagnosis and give prognosis without the need for surgery. We have also shown that 2HG levels rise when the tumor is progressing, thus following 2HG levels with MR scans will guide decision making about the timing of treatment. The overarching goal of the proposed research is to translate 2HG imaging and analysis to clinical MR scanners from the major vendors (Phillips and GE) so that it can be incorporated into standard clinical use, as quickly as possible. It will have a profound impact on patient management.