Noninvasive assessment of isocitrate dehydrogenase mutation status in cerebral gliomas by magnetic resonance spectroscopy in a clinical setting.


Abstract

OBJECTIVE Mutations in the isocitrate dehydrogenase (IDH) genes are of proven diagnostic and prognostic significance for cerebral gliomas. The objective of this study was to evaluate the clinical feasibility of using a recently described method for determining IDH mutation status by using magnetic resonance spectroscopy (MRS) to detect the presence of 2-hydroxyglutarate (2HG), the metabolic product of the mutant IDH enzyme. METHODS By extending imaging time by 6 minutes, the authors were able to include a point-resolved spectroscopy (PRESS) MRS sequence in their routine glioma imaging protocol. In 30 of 35 patients for whom this revised protocol was used the lesions were subsequently diagnosed histologically as gliomas. Of the remaining 5 patients, 1 had a gangliocytoma, 1 had a primary CNS lymphoma, and 3 had nonneoplastic lesions. Immunohistochemistry and/or polymerase chain reaction were used to detect the presence of IDH mutations in the glioma tissue resected. RESULTS In vivo MRS for 2HG correctly identified the IDH mutational status in 88.6% of patients. The sensitivity and specificity was 89.5% and 81.3%, respectively, when using 2 mM 2HG as threshold to discriminate IDH-mutated from wildtype tumors. Two glioblastomas that had elevated 2HG levels did not have detectable IDH mutations, and in 2 IDH-mutated gliomas 2HG was not reliably detectable. CONCLUSIONS The noninvasive determination of the IDH mutation status of a presumed glioma by means of MRS may be incorporated into a routine diagnostic imaging protocol and can be used to obtain additional information for patient care.

KEYWORDS: 2HG = 2-hydroxyglutarate; AUC = area under the curve; CRLB = Cramér-Rao lower bound; FWHM = full width at half maximum; GBM = glioblastoma; IDH = isocitrate dehydrogenase; IDH mutations; MR spectroscopy; MRI; MRS = MR spectroscopy; MS = multiple sclerosis; PCNSL = primary CNS lymphoma; PCR = polymerase chain reaction; PRESS = point-resolved spectroscopy; ROC = receiver operating characteristic; STEAM = stimulated echo acquisition mode; TE = echo time; glioma; isocitrate dehydrogenase; oncology; ppm = parts per million

PMID: 28298040 DOI: 10.3171/2016.10.JNS161793