Metabolite

Metabolites are the intermediates and products of metabolism. The term metabolite is usually restricted to small molecules. Metabolites have various functions, including fuel, structure, signaling, stimulatory and inhibitory effects on enzymes, catalytic activity of their own (usually as a cofactor to an enzyme), defense, and interactions with other organisms (e.g. pigments, odorants, and pheromones). A primary metabolite is directly involved in normal “growth”, development, and reproduction. Ethylene is an example of a primary metabolite produced in large-scale by industrial microbiology. A secondary metabolite is not directly involved in those processes, but usually has an important ecological function. Examples include antibiotics and pigments such as resins and terpenes etc. Some antibiotics use primary metabolites as precursors, such as actinomycin which is created from the primary metabolite, tryptophan. There are also examples of sugars that are metabolites, and example of this would be fructose or glucose in the metabolic pathways.

Findings have indicated that the metabolite characteristics of the lesion are valuable for the investigation of underlying differences in malignancy.

In vivo metabolite imaging provides a unique opportunity for the evaluation of spatial and temporal changes in the lesion and surrounding tissue that can be used to direct tissue sampling at the time of resection, as well as for the selection and monitoring of therapy. The lesion-wide data obtained using this approach are synergistic with recent results from genome-wide sequencing and informatics-driven analyses that identify different subtypes of glioma with genetic characteristics.

The ability to infer the mutational status of isocitrate dehydrogenase (IDH) genes through non-invasive MRSI of D-2 (hydroxyglutarate dehydrogenase) is an example with strong prognostic implications. This is a significant breakthrough in the realm of cancer diagnostics [1) 2)].

Metabolite Quantification

Metabolite quantification is always required when the metabolite is toxic or pharmacologically active or when the concentration of metabolite reaches or exceeds the parent drug concentration in plasma.

In Vivo Absolute Metabolite Quantification

Absolute quantification of metabolites in MR spectroscopic imaging (MRSI) requires a stable reference signal of known concentration. The Electronic REference To access In vivo Concentrations (ERETIC) has shown great promise but has not been applied in patients and 3D MRSI. ERETIC hardware has not been integrated with receive arrays due to technical challenges, such as coil combination and unwanted coupling between multiple ERETIC and receive channels, for which we developed mitigation strategies.

Purpose: To develop absolute quantification for whole-brain MRSI in glioma patients.

Study type: Prospective.

Population: Five healthy volunteers and three patients with isocitrate dehydrogenase mutant glioma (27% female). Calibration and coil loading phantoms.

Field strength/sequence: A 3 T; Adiabatic spin-echo spiral 3D MRSI with real-time motion correction, Fluid Attenuated Inversion Recovery (FLAIR), Gradient Recalled Echo (GRE), Multi-echo Magnetization Prepared Rapid Acquisition of Gradient Echo (MEMPRAGE).

Assessment: Absolute quantification was performed for five brain metabolites (total N-acetyl-aspartate [NAA]/creatine/choline, glutamine + glutamate, Myo-inositol) and the oncometabolite 2-hydroxyglutarate using a custom-built 4x-ERETIC/8x-receive array coil. Metabolite quantification was performed with both EREIC and internal water reference methods. ERETIC signal was transmitted via optical link and used to correct coil loading. Inductive and radiative coupling between ERETIC and receive channels were measured.

Statistical tests: ERETIC and internal water methods for metabolite quantification were compared using Bland-Altman (BA) analysis and the nonparametric Mann-Whitney test. $P < 0.05$ was considered statistically significant.

ERETIC could be integrated in receive arrays and inductive coupling dominated (5-886 times) radiative coupling. Phantoms show proportional scaling of the ERETIC signal with coil loading. The BA analysis demonstrated very good agreement (3.3% ± 1.6%) in healthy volunteers, while there was a large difference (36.1% ± 3.8%) in glioma tumors between metabolite concentrations by ERETIC and internal water quantification.

The results indicate that ERETIC integrated with receive arrays and whole-brain MRSI is feasible for brain metabolites quantification. Further validation is required to probe that ERETIC provides more accurate metabolite concentration in glioma patients [3].

1)
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