Opinion

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Noninvasive Detection of Metabolic Alterations through *In Vivo* Magnetic Resonance Spectroscopy: A New Technology in Current Molecular Medicine

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Opinion

As the prevalence of obesity explosively increases worldwide, the rise in the population with metabolic diseases is of great concern. Metabolic alterations can be assessed by typical medical techniques (e.g. tissue biopsy, etc.), however, noninvasive *in vivo* detection in living tissue was not forthcoming. Magnetic resonance spectroscopy (MRS), which is similar to magnetic resonance imaging (MRI) first appeared in medicine in 1970's, can detect metabolic changes *in vivo* noninvasively [1].

MRS functions without ionizing radiation by detecting stable isotopes (^{1}H, ^{31}P, ^{13}C and others), in contrast to other imaging modalities, such as X-ray computed tomography (CT) or position emission tomography (PET). With its noninvasive nature, ^{1}H, ^{13}C and ^{31}P MRS are actively utilized in clinical and preclinical studies. Quantification of lipids and important metabolites in living tissue are the forte of this technique. The data obtained by MRS offer a critical piece of metabolic information in animals and humans, and often serve as a very useful biomarker. For example, ^{1}H MRS can quantify lipid content in liver and other metabolites in the brain and body, such as 2-hydroxyglutarate (2-HG), *in vivo*. A recent report indicated that the levels of 2-HG in tumors quantified by ^{1}H MRS can be utilized as a biomarker to differentiate wild-type from mutated isocitrate dehydrogenase (IDH1 and IDH2) gliomas [2]. Of interest, the mutations in IDH1 and IDH2 were recently found to be most among human World Health Organization (WHO) grade 2 and 3 gliomas. Thus this new technique, ^{1}H MRS opens up a new way to aid the clinical management of patients with gliomas, particularly for follow-ups after treatment.

Furthermore, many studies have indicated that hepatic and intramyocellular lipid content quantified by ^{1}H MRS is correlated with insulin resistance. Thus noninvasively measured lipid content can be utilized as a biomarker for insulin resistance, which is the best predictor for the clinical onset of type 2 diabetes. In addition, highly sensitive and specific ^{1}H MRS technique can help accurately evaluate the efficacy of a new drug in clinical trials for quantifying the content of liver fat without tissue biopsy. This accurate method also can aid to expedite the drug development process by providing robust and statistically significant data from a modest pool size of patients [3]. Therefore this can be a good way to effectively cut cost in both preclinical studies and clinical trials.

Furthermore, employing other stable isotopes, such as ^{13}C MRS, hepatic glycogen synthesis and breakdown can be directly detected in real time, and altered glycogen metabolism was detected in type 1 and type 2 diabetes mellitus. In addition, ^{31}P MRS can provide *in vivo* ATP synthesis rates and/or *in vivo* ATP content in living tissue [1].

This technique provides not only comfort to patients, but also a unique means to detect metabolites *in vivo,* including intermediates, which can be easily oxidized or reduced in ambient air (e.g., *in vivo* ATP content). Though the high cost of MRI equipment can be a potential limitation, this cutting-edge MRS technology can deliver a new avenue to noninvasively study molecular and cellular medicine *in vivo*.

References

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