Radiology-2013
OMICS Group Conferences
Accelerating Scientific Discovery
International Conference on
Radiology and Imaging
August 14-16, 2013 Chicago, USA

Chemical exchange saturation transfer (CEST) enhanced molecular imaging

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Abstract

Chemical exchange saturation transfer (CEST)[1-6]based magnetic resonance (MR) methods are widely used to probe chemical exchange phenomenon in both model systems as well as in biological tissues *in vivo*. These methods probe exchanging spin dynamics and provide endogenous molecular contrast, which among other MR parameters depends on the concentration and pH of the solute spins.

CEST methods require slow to intermediate exchange on the NMR time scale (chemical shift (**Δω)**> exchange rate (*k*)), and they primarily probe longitudinal magnetization exchange. The major advantage of the CEST method is that, depending upon the rates of exchangeable spins,itinherently hasanorder of magnitude or greatersensitivity advantage over conventional magnetic resonance spectroscopy (MRS) methods. CEST has been exploited to assess pH in biological tissues in vivo[7], to quantifyglycogen in liver[8], glycosaminoglycans[9] in cartilage, myoinositol (MI)[10]and glutamate (Glu) [11,12]in brain,creatine (Cr)[13]in brain, skeletal muscle[14]and myocardium[15]as well as in studying gene expression[16], and differentiation between gliomas and radiation necrosis [17]. Recently,some preliminary results demonstrating the feasibility of measuringpH based cell viability[18]andglucose [19]as a biodegradable MRI contrast agent have been described

Given the broad spectrum of exchange rates of amide, amine and hydroxyl protons on biologically important molecules, higher static magnetic field strengths allow awider range of exchange rates to be probed. Consequently, the advent of whole body 7T MRI scanners has reinvigoratedresearch activity in CEST mediated molecular imaging andexpanded the range of the metabolitesable to be probed*in vivo*.In addition, there is a separate class of exogenous agents, known as PARACEST agents[3,4], that combine exchangeable protons capable of providing CEST with a paramagnetic metal ion.Since PARACEST agents create larger chemical shifts between exchangeable protons,CEST experiments involving these agents have significantly reduced direct water saturation effects.

In this presentation,a brief outline ofthe basic principles, technical requirements, sensitivity advantages and recent developments of CEST methods, and their implementation in measuringendogenous metabolites in biological systems will be provided.Some representative examples of detecting endogenous metabolites in pathological conditions such as tumors and Alzheimer's diseasewill be described. In addition, advantages and potential challenges of CEST MRI in quantifying the metabolites under *in vivo* environments will be discussed.