NEW HORIZONS

Magnetic Resonance Spectroscopy

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Magnetic resonance (MR) imaging produces an image based upon the distribution and the physical-chemical state of water in tissues. The other focus of MR technology and research is based on using the magnetic properties of nuclei to yield data on the nature and concentration of metabolites within tissues. The fundamental theory remains the same for both MR imaging and Magnetic Resonance Spectroscopy (MRS) techniques(1).

Concepts : The basic concept of MRS is nuclear magnetism. Atoms whose nuclei possess an odd number of protons and neutrons are magnetic and are therefore NMR active. Most widely used and relevant nuclei for MR analysis are 1H and 31P.The other essential concept for MRS is of resonance. The differences in the resonance frequency of different nuclei, allow for specific selection of different nuclei for excitation and observation in MRS studies. Chemical shift is also a fundamental concept for MRS studies. The ability of MR to determine the chemical structure of compounds is dependant upon the phenomenon of chemical shift, which results from electron shielding. In spectroscopy, the net magnetic field is determined by the applied magnetic field and the magnetic field produced by the electron clouds that circulate each nucleus (1).

Metabolites in MR spectroscopy : At 1.5 tesla, a typical 31P spectrum obtained from the brain of a normal volunteer shows peaks originating from phosphomonesters (PME), inorganic phosphate (Pi), phosphodiesters (PDE), phosphocreatine (PCr) and the a, b and g phosphorus atoms of ATP. The compounds observable in proton spectra reveal major resonances from tetramethylamines especially choline- containing phospolipids (Cho), creatine (Cr) (either alone) or as phosphocreatine (PCr), N - acetylasparatate (NAA) and Lactate (LA). Choline increases in active demyelinating lesions because membrane phospholipids are released during active myelin breakdown. Many brain tumours are also associated with high signals from Cho, presumably associated with their increased cellular density and compression of sorrounding brain tissue. Total Cr concentration is used as an internal standard to which resonance intensities of other metabolites are normalized. NAA is the most important 1H MRS signal for the assessment of brain pathology. Decreases in relative NAA concentrations are observed in pathologies well known to involve neuronal loss or damage, e.g. degenerative disorders and stroke. Low NAA is also observed in multiple sclerosis. Brain neoplasms such as gliomas have increased concentration of LA because they have elevated relative rates of glycolysis, independent of the adequacy of oxidative metabolic pathways. LA tends to accumulate in the extra cellular environment of necrotic tissue and fluid-filled cysts, which act as "sinks" for LA (1).

Clinical Application : It provide information that cannot be obtained by any other MR imaging modality.

Brain Tumours : Gains in the sensitivity to detect tumours by conventional MR imaging have not been paralleled by gains in the specificity. 1H-MRS adds another dimension by which tumours can be differentiated by providing their chemical profile. Glioblastoma (GBM) shows spectra of low NAA, high LA, and persistent signals from lipids. Meningiomas show features consistent with destruction of neurons (low NAA) as well as resonance from alanine (Ala). Although alanine may be present in a number of tumour types, it is only clearly separate from LA in vivo in meningiomas. Additionally, GBMs, meningiomas and other tumours often show high choline, which likely reflects increased concentration of soluble compounds associated with the presence of tumour cells. Distinction between high-grade gliomas and solitary metastases using peritumoral 3-T magnetic resonance spectroscopy is possible because the

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choline to creatine ratio in the peritumoral regions of high-grade gliomas is significantly higher than in the metastases (2). MRS can be used to plan stereotaxic biopsies and selective tumour resections. Metabolic changes on chemical profile have also been used to predict chemosensitivity prior to therapeutic intervention as well as to monitor the response to drug and radiation therapy. Quantitation of taurine (Tau) concentrations with proton magnetic resonance spectroscopy improves the differentiation of primitive neuroectodermal tumors (PNET) from other common brain tumors in pediatric patients as taurine concentration was significantly elevated in PNETs compared to other tumors(3).MR spectroscopy can be used in the diagnosis of cerebral amyloid angiopathy presenting as a brain tumor (4).

Epilepsy : Both 1H-MRS and 31P-MRS are used to study epilepsy because of their ability to demonstrate altercations in energy metabolism. Because of intermittent nature of seizures, it is rarely possible to obtain spectra from actively seizing brain. However there is expected increase in signal from lactate whenever it is possible to obtain spectra of epileptic patients. In focal seizures, the increase in lactate persists for hours. In temporal lobe epilepsy, the traditional approach of lateralization of seizures has been modified by non-invasive and independent neuroimaging techniques that predict the hemisphere of origin of the epileptic signal. MR imaging demonstrates atrophy or changes in hippocampal T2-weighted signal intensity in 30% to 90% of patients. 1H-MRS reveals abnormal low resonance intensities of NAA/Cr with in one or both temporal lobes of patients of temporal lobe epilepsy, with greater reduction in intensities seen on the side from which the seizure originates (1).

Multiple Sclerosis (MS) : MRS studies of acute MS lesions show that NAA is substantially reduced in these lesions, and these decreases in NAA usually show partial recovery over time. Acute lesions also show large increases in Cho resonance and moderate increase in LA while transient increase in Cr is seen during the hyperacute phase. MRS studies of brain of patients with chronic MS lesions show persistent decreases in NAA in the T2-weighted lesions. NAA in normal appearing white matter (NAWM) decreases progressively over time in MS patients with relapsing remitting MS and these changes in NAA in the NAWM correlate with the disability much more strongly than changes in the T2-weighted lesion volume. MRS of normal-appearing cervical spinal cords in multiple sclerosis patients shows reduced N-acetyl aspartate within the cervical spinal cord (5).

Cerebrovascular Injury : MR spectra from infarcted tissue consistently show high LA and Low NAA resonance intensities and these abnormalities may have predictive value as to whether tissue will survive or not. In the pediatric population, 1H-MRS has been used to study neonatal hypoxia during delivery, hypoxic encephalopathy following near drowning, and following various other acute CNS insults. In the adult population, a similar pattern of low NAA and high LA is seen following acute infarction. Levels of NAA continue to fall up to a week post infarction, suggesting that the window for salvage of damaged neurons may be greater than expected and provides a potential surrogate for monitoring therapeutic intervention in the acute stroke period. Low levels of NAA and high levels of LA correlate with and predict impaired neurological function and 1H-MRS may be used as a clinical tool for monitoring chronic ischaemia (1).

Neurodegenerative Diseases : Amytropic lateral sclerosis (ALS):- 1H-MRS imaging has demonstrated decreased cortical NAA, indicative of loss or dysfunction of upper motor neurons in patients with ALS (1).

Alzheimer disease (AD) : These patients show a significant decrease of NAA in Mesial-temporal structures including hippocampus as well as in various areas of cerebral cortex. A combination of Mesial-temporal NAA and atrophy measures may help discriminate AD from normal aging, but apparently not from subcortical ischaemic vascular dementia. An increase in myo-isositol (ml) associated with decreased NAA has been found by a number of investigators in the cortex of patients with AD (1).

Metabolic Disorders : Inspite of the extremely large number of inherited and acquired metabolic disorders that affect the brain, only some of which are currently diagnosable.MRS can diagnose hepatic encephalopathy. Increase in the glutamate-glutamine/creatine ratio and a decrease in choline/creatine and inositol/creatine ratios helps in diagnosis of patients with minimal liver cirrhosis patients who do not show overt clinical cirrhosis-associated neurological deficits (6).

Miscellaneous conditions : Proton magnetic resonance spectroscopy is used in the differential diagnosis of ring-enhancing intracranial cystic mass lesions (7). Single enhancing brain lesions , mostly as a result of neurocysticercosis or tuberculosis, are a common cause of seizures. Tuberculomas have a high peak of lipids, more choline, and less N-acetylaspartate and creatine. The choline/creatine ratio is also greater than 1 in all tuberculomas but not in cysticerci (8). Differentiation of cerebral degenerating cysticerci from

anaerobic abscesses is possible on proton MR spectroscopy due to higher succinate levels in degenerating cysticerci (9). Differentiation of tuberculous from pyogenic brain abscesses is done by proton MR spectroscopy (10).MR spectroscopy is also useful as additional diagnostic modality for differentiating brain abscesses from cystic or necrotic brain tumors (11).1H-MRS is able to detect decreases in NAA and increases in Choline in human immunodeficiency virus associated neurological disorders even before manifestation of clinical symptoms and the detection by MR imaging. Low NAA in hippocampus has been found most frequently in schizophrenia, even though MRS findings are inconsistent. MR spectroscopic imaging in Creutzfeldt-Jakob disease reveals marked asymmetric decrease of normal metabolites (12). Proton MR spectroscopy in Sturge-Weber syndrome reveals decreased N-acetyl aspartate and increased choline peaks (13). Proton magnetic resonance spectroscopy can also be performed in utero to diagnose fetal brain injury (14). The addition of proton MR spectroscopy adds to the diagnostic power of MRI in the setting of post-infectious demyelinating disorders of the CNS and may obviate the need for biopsy (15). Preliminary results suggest that MR spectroscopy has the potential to contribute to an accurate and early prediction of tumor behavior and response to treatment in squamous cell carcinoma of the head and neck region (16). In future, Radiation-induced proctitis during and after radical radiotherapy for prostate cancer could be decreased by reducing target volumes by both CT/MRI co-registration and dose painting using MR spectroscopy of choline and citrate in the prostate (17).

Conclusion

MRS rewards the sensitivity that is simply unavailable from any water based imaging technique and therefore there is continuous & dramatic increase in the utilization of MRS in the clinical settings. MRS will hold the key in future because of greater reliance on noninvasive neuroradiolgy.

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