Would Magnetic Resonance Spectroscopy (MRS) Benefit My Patient?

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Current Technology
Over the course of the past decade, Magnetic Resonance Spectroscopy (MRS) has evolved from the realm of esoteric experimentation to that of common clinical application. This is due in part to the ever-increasing power and speed of the computers that drive our imaging machines, and in part to the development of ever-faster gradients that drive our magnets. These improvements have made MRS more accessible and applicable than ever before.

MRS combines the sciences of Nuclear Magnetic Resonance Spectroscopy (NMR) and Magnetic Resonance Imaging (MRI) to uncover clinically relevant information about a lesion or region of interest within the brain. In MRI, 2-dimensional images are created based on the type and amount of hydrogen protons at different points in 3-dimensional space. NMR, on the other hand, looks only at a specific point in 3-dimensional space and generates a spectrum that displays the many different chemical compounds that are found at that point in space, but only at that point in space. Instead of a 2-dimensional image, a 1-dimensional line is displayed. The line is the MR spectrum. The relative amounts of the different chemical compounds that are present within the 3-dimensional region of interest are measured by the height of each peak (or area under each peak) in the spectrum. Peaks for the various chemical compounds appear in predictable locations in the spectrum. After first studying many normal brains, the normal MR spectrum was established. This concept has since been refined to include the normal MR spectra throughout the brain, which vary in a consistent manner. For example, the MR spectrum of normal white matter is different from that of the normal basal ganglia. Figure 1 shows the MR spectrum of normal white matter.

MRS can be used to investigate a specific lesion or a diffuse process. In the case of a focal lesion, there is a limit to how small the lesion can be. Generally, lesions less than 10 mm in diameter are difficult to evaluate with confidence. By contrast, in the investigation of diffuse processes such as Alzheimer's Dementia, a standardized volume of brain tissue in a standardized location is examined. Figure 2 shows the typical voxel placement for evaluation of dementia. Figure 2 (continued on page 2)

What Are We Measuring And Why?

The chemical compounds which we measure in clinical MRS are mostly brain metabolites and neuropeptides. The most commonly encountered are N-acetyl aspartate (NAA), Creatine (Cr), Choline (Cho), Myoinositol (MI), Lipid, and Lactate.

N-acetyl aspartate (NAA) is essentially a marker of neuronal health. Earlier, it was thought that NAA was a marker of neuronal volume because it is decreased in traumatic lesions and demyelinating plaques. When this was shown to be reversible, the concept was changed to that of a marker of neuronal health. High NAA is therefore desirable.

Choline (Cho) is found in cell walls. As cells replicate, Choline increases. This is especially evident in the case of tumor growth, in which cells grow without normal inhibitory regulation. While increased Choline may be seen transiently with acute infarction and demyelinating disease due to release from cells during cell breakdown, only tumors demonstrate consistently elevated Choline. High Choline is therefore an undesirable finding, especially when NAA is low. This typically indicates the diagnosis of tumor.

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The Myo-inositol (MI) peak is most often used in the diagnosis of Alzheimer’s Dementia. Many patients with Alzheimer’s Dementia will exhibit the combination of elevated Myo-inositol and low NAA on MRS. The MRS is performed on a single voxel of brain tissue, in a standardized location, that includes white and gray matter in medial aspect of both parieto-occipital lobes (Figure 2).

Creatine (Cr) is the reference metabolite. Fortunately, the amount of Creatine remains more or less constant throughout the normal state and most pathologic conditions. This provides a benchmark against which the other metabolites are measured. The amounts of NAA, Cho, and MI are measured in terms of a ratio, in which each is the numerator, and the amount of Creatine is the denominator.

Lipid and Lactate share a similar location on the spectrum and are both markers of tissue necrosis, thus they are often lumped together as the “lipid-lactate peak.”

Current Clinical Applications

MRS is used to further characterize lesions of uncertain etiology seen on MRI. Specifically, MRS is most useful in distinguishing tumor from other lesions that can look like tumor on MRI. For example, recurrent enhancing tumor can be indistinguishable from radiation necrosis on a contrast-enhanced MRI. There is no reliable way to distinguish these two entities by imaging, yet these diagnoses require diametrically opposed treatments. PET (positron emission tomography) was once touted to serve this function, but was later shown to be unreliable. MRS, on the other hand, is often diagnostic in these cases. This often eliminates the need for brain biopsy.

Below is a list of some of the most common uses of MRS:

1. Distinguishing recurrent tumor from radiation necrosis
2. Distinguishing high-grade tumor from active demyelinating disease (MS) or tumefactive multiple sclerosis
3. Distinguishing low-grade tumor from chronic demyelinating disease or other nonspecific causes of elevated T2 signal when there is no enhancement
4. Distinguishing tumor grade (high vs. low)

In addition to the characterization of lesions, MRS can be used in the evaluation of Alzheimer’s Dementia (AD). While a normal spectrum does not exclude the diagnosis, a characteristic spectrum is highly suggestive of AD.

As you can imagine, by now just about every form of central neuropathology has been evaluated with MRS to look for characteristic patterns that may help in future diagnosis of the entity in question. Below is a list of some of the pathologic entities for which specific abnormal MR spectra have been demonstrated:

1. Huntington’s Chorea
2. Anoxia/Stroke
3. Canavan’s Disease
4. Alexander’s Disease
5. Lymphoma
6. Progressive Multifocal Encephalopathy (PML)
7. Mesial Temporal Sclerosis
8. MELAS
9. Toxoplasmosis
10. Cryptococcus
11. Renal failure
12. Diabetes
13. Herpes encephalitis
14. Hyponatremia

Unlike the question of tumor versus non-tumor, the neuropathologic entities listed above are less well established in terms of sensitivity and specificity. As with Alzheimer’s Dementia, the findings should be viewed as a piece of the diagnostic puzzle, not the “be all, end all” of the diagnostic work-up. In other words, a positive result supports the clinically suspected diagnosis. Likewise, a negative result does not exclude it. Aside from Alzheimer’s Dementia, there is, as yet, no clinical role for MRS in the evaluation of mental illness. The role of MRS in various psychiatric diagnoses is, however, currently being investigated.

“It’s a Matter of Interpretation”

Although this all may seem quite straight forward, the interpretation of MR Spectroscopy involves more than just plugging in the numbers. First and foremost is attention to quality. There are many confounding factors that can distort and disrupt the acquisition of the spectrum. Some are obvious, but others can be subtle. Without meticulous attention to technique by experienced MR technologists, and direct supervision by a radiologist with appropriate subspecialty training, the results have the potential to be misleading.

How To Get It Done

With the exception of cases in which Alzheimer’s Dementia (AD) is suspected, MRS is rarely requested by the ordering physician at the outset. In most instances, MRS is recommended by the radiologist who interprets the patient’s brain MRI, upon discovery of a lesion that requires further clarification. The recommendation for MRS will appear in the patient’s brain MRI report.

At Wake Radiology, we believe it is imperative that a radiologist with subspecialty expertise in MRS be present to supervise the study. This radiologist verifies the validity of the indication, determines the placement of the voxel(s), supervises the study, and ensures appropriate quality. This is one reason why these cases are only scheduled during times when a radiologist experienced with MRS is physically present at the facility where the patient is being imaged.

Scheduling is handled in the same manner as the MRI. If contrast was not administered during the initial brain MRI, the addition of contrast-enhanced imaging is recommended. This is because the presence or absence of enhancement is invariably important in the evaluation of any brain lesion. Although brain MR studies are often ordered “with contrast if necessary,” there is no option to order an MRI “with MRS if necessary.” This is because the time it takes to perform MRS of a specific lesion is significant, and scheduling constraints do not allow for MRS to be added “on the fly.”

If it were, the remainder of the patients to be scanned that day would be significantly delayed. Furthermore, at Wake Radiology, we make every effort to schedule MRS only on days when a radiologist with MRS experience is present at the facility. Currently, we offer MRS at our Raleigh MRI Center on Merion Drive, our West Raleigh Office on Lake Boone Trail, and at WakeMed Hospital on New Bern Avenue. Despite the proven utility of MRS and the potential cost savings from avoiding unnecessary biopsies and inappropriate treatment, Medicare and Medicaid do not currently reimburse for the procedure. Some third party payers do, however, reimburse for some indications.

In cases of cognitive decline or suspected AD, the MRS interpretation is usually brief and included in the “findings” section of the brain MRI report. This information may also appear in the “impression” section of the report. In cases where MRS is ordered separately and used in the evaluation of a specific lesion, the report is more detailed. In these cases, you will receive information about the procedure, the quality of the study (i.e. the reliability of the findings), the specific values and ratios of the various metabolites and neuropeptides, an interpretation of the findings, and an impression or conclusion pertaining exclusively to the MRS study. Ultimately, our objective is to provide a diagnosis with a level of confidence that greatly exceeds that which could be attained with MRI alone, and rivals that of a biopsy.

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