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Fluid-attenuated Inversion Recovery Now with Another Acronym: "KRISP FLAIR"

Over the years, numerous MR pulse sequences have been described and discussed in the literature, but few have had the immediate and lasting impact of fluid-attenuated inversion recovery (FLAIR). As is well known by all involved in clinical neuroradiology, FLAIR provides T2-weighted images while suppressing the signal from CSF by use of an inversion pulse. The ability to discern high-signal abnormalities, particularly those adjacent to the ventricles, is improved, and by virtue of a widened, dynamic range, FLAIR frequently allows detection of what otherwise would be subtle findings on conventional spin-echo T2-weighted images. This pioneering work was first described and published by Graeme Bydder and his associates when the technique was originally coined ''PIETIR'' (prolonged inversion and echo time inversion recovery).

Despite the many advantages of FLAIR, a frequently annoying finding is the presence of unsuppressed CSF, particularly in the basal cisterns. Over the years, schemes have been published to diminish or eliminate this unwanted high signal. In this issue of the *AJNR*, Herlihy and colleagues (page 896) describe the implementation of a technique with the acronym, KRISP (k-space reordered by inversion time at each slice position) to improve FLAIR imaging even further.

In general, using selective inversion pulses that are thicker than the slices being imaged provides adequate CSF suppression. With this method, the CSF outside the slice is also inverted; hence, if the volume of the inverted CSF stays within the slices being imaged during the inversion time period, which is typically 2000 ms, the CSF signal is nulled. One of these methods employs an inversion pulse that is twice the thickness of the slice being imaged. The disadvantage of this method is that one has to use a 100% interslice gap, because the inversion pulse is twice the slice thickness of the images. To overcome this problem, interleaved acquisition has been proposed whereby the odd-numbered slices are acquired first, followed by acquisition of the even-numbered slices. With this technique, the inversion pulse used is twice the thickness of the slices being imaged to adequately suppress the CSF, and the imaged slices are contiguous. The disadvantage with the interleave acquisition method is that the total scanning time is doubled; however, by using fast spin echo as a data acquisition method, the total scanning time can be reduced. Both of the above-mentioned methods rely on the fact that the bolus of the inverted CSF stays within the slice being imaged during the inversion time period. There may be instances when the CSF flow is so fast that uninverted CSF enters the slice during the inversion time period. This could result in spurious signal from the inflowing CSF.

Another approach is to use a non-selective inversion pulse. With this method, the entire CSF signal is inverted; thus, the problem of uninverted CSF flowing into the slice being imaged is overcome. This is followed by data acquisition of multiple selective slices. The disadvantage with this method is that each of the slices will have a different inversion time; hence, the slices that are farthest away from the inversion time will have partial signal from the CSF. Also with this method, the number of slices that can be acquired is limited because the long echo times used for acquisition of T2-weighted images would result in inversion times being different than the optimum value.

The use of a non-selective inversion pulse provides the optimum method for suppression of CSF signal and it does not suffer from the inflow effect of the unsuppressed CSF that leads to spurious signals when using selective inversion pulses. Herlihy et al use non-selective inversion pulses to suppress the signal from the CSF; however, rather than using conventional data acquisition methods, the authors have proposed a data acquisition scheme that is similar to the fast spin-echo method whereby the effective echo time is at the center of k-space data from which contrast is determined. The authors have proposed to acquire the center of k-space data when the effective inversion time is optimal to suppress the CSF signal and the outer k-space data are acquired at much shorter or longer inversion times. The resultant images do not suffer from unsuppressed CSF signals. In theory, a ''krisper'' image should be obtained.

All of the above methods do not take into account the RF inhomogeneity that leads to partial inversion of the CSF signal. It is very severe at the edge of the RF transmitter, where CSF may experience a tip angle that is much less than 180°, and the resulting image will have signal from partially inverted CSF. One approach to overcome the problem of RF inhomogeneity is to use adiabatic inversion pulses. The adiabatic RF pulse alters the phase of the spins being excited such that the spins at the edge of the RF transmitter, which experience a smaller excitation tip angle, will be totally inverted at the end of the pulse. The adiabatic RF pulses invert all the CSF through the transmitter regardless of the RF inhomogeneity. These RF pulses can be designed to be selective or non-selective. When using selective excitation, one still has to take into account the inflow effects of the uninverted CSF, as described above.

It is certain many new schemes will be developed to effectively suppress the CSF. Recent developments have improved the suppression of the CSF signal on FLAIR images considerably. Maybe in the near future we will see a combination of nonselective adiabatic inversion pulses combined with k-space reordered acquisition, as described by Herlihy and colleagues. With this combination, one would overcome the problem of unsuppressed CSF flowing into the slices being imaged, as well as the RF inhomogeneity problem of the transmitter that leads to spurious signal from CSF in FLAIR imaging.

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MR Perfusion Imaging of Hyperacute Stroke

Hypoperfusion is the proximate cause of all ischemic stroke, and it stands to reason that perfusion imaging should be useful in the evaluation of acute ischemic stroke. Patients presenting with neurologic symptoms on an ischemic basis should manifest regional hypoperfusion, and the distribution of observed hypoperfusion with respect to known vascular distributions should be diagnostically informative. In principle, perfusion imaging should provide the greatest sensitivity for stroke detection because hypoperfusion occurs in advance of metabolic and subsequent structural changes. Unfortunately, imaging of perfusion at high spatial resolution is challenging, and as yet no perfusion imaging method can approach the structural resolution of conventional MR. Nonetheless, over the past several decades, a variety of methods have been used to image cerebral perfusion in acute stroke. They include positron emission tomography, single-photon emission CT, xenon CT, and MR imaging with dynamic susceptibility (exogenous) contrast enhancement or arterial spin labeling (endogenous) diffusible tracer.

Information about regional perfusion obtained using these methods has contributed to our understanding of stroke pathophysiology, often in combination with metabolic information. It remains unclear which method provides the best compromise between image quality, convenience, cost, and time, and the capabilities of each technique are constantly being improved. In the case of MR, diffusion imaging provides a contrast mechanism thought to be sensitive to cytotoxic edema, a relatively early structural abnormality in brain ischemia. Diffusion contrast is simple to obtain from MR imaging, and has already been incorporated into most commercial scanning software. Perfusion MR imaging is somewhat more complicated to perform, minimally requiring dynamic scanning during contrast injection and postprocessing to produce maps reflecting hemodynamic parameters (many of which are not strictly related to classical perfusion, which is expressed in units of milliliters of blood flow per gram of tissue per unit time). For these reasons, diffusion MR has preceded perfusion MR for widespread use in stroke imaging.

Sunshine and colleagues in this issue of AJNR (page 915) find that perfusion MR imaging provides greater accuracy than does diffusion MR imaging for categorizing the vascular distribution of ischemia in patients scanned within 6 hours of ischemic onset. These findings are based on a retrospective analysis of patients presenting with acute stroke symptoms who underwent ultrafast MR scanning assessed by correlation with other clinical and imaging data that were subsequently collected. Patients showing hypoperfusion in a large vessel distribution on perfusion MR images were included. Of 62 such patients, perfusion MR imaging provided the best evidence of large artery distribution ischemia in 16 cases, with many of these patients showing no diffusion abnormality or diffusion changes in small vessel distributions. These findings support the concept that perfusion changes occur in advance of metabolic and structural changes and are also consistent with previous results showing that perfusion MR imaging correlates better with clinical severity than does diffusion MR imaging (1).

Although these findings support the general value of perfusion MR imaging in stroke assessment, the study population in Sunshine et al's article was biased toward perfusion, because patients were selected for inclusion on the basis of the presence of large artery abnormalities on perfusion MR images. Only a prospective study can truly eliminate this type of bias. Furthermore, in many cases large artery involvement was confirmed on the basis of angiographic abnormalities. However, the presence of large artery stenosis does not in and of itself necessarily indicate ischemia throughout that vascular distribution, because perfusion can be maintained by autoregulatory vasodilation and through collateral sources of blood flow. Large artery stenosis can also delay the time-to-peak susceptibility after contrast bolus, the parameter chosen as the surrogate for perfusion in this study, producing apparent hypoperfusion. Accounting for regional variations in arterial transit time and contrast-induced susceptibility effects remains a major challenge for the interpretation and quantification of dynamic susceptibility contrast perfusion MR imaging. A better understanding of pathophysiological effects on the measured parameter of time-to-peak is required for correct interpretation of dynamic susceptibility

contrast studies. It is, therefore, likely that experimentally determined thresholds of ischemia made using classical perfusion methods will not translate directly to related hemodynamic measures such as time-to-peak.

Despite some methodological shortcomings, this study clearly shows that a negative diffusion-weighted MR image does not exclude the presence of clinically significant ischemia. In addition, positive findings on diffusion MR images are clearly useful in stroke evaluation (2); eg, lesions in multiple vascular distributions suggesting an embolic etiology. However, the diagnosis of acute ischemic stroke ultimately remains a clinical one. Indeed, there remains great controversy concerning the real value of diffusion imaging in acute stroke management (3), particularly because the pathophysiological basis for diffusion changes remain incompletely characterized and are not entirely specific to ischemia. Several recent reports now also describe diffusion-negative ischemic symptoms. Arguably, the absence of any imaging lesion at all should provide the greatest impetus for urgent stroke evaluation, because the opportunity for prevention is greatest in that situation.

The successful validation of intravenous thrombolytic therapy for patients presenting within several hours of ischemic onset presents more specific challenges for hyperacute stroke imaging. Intravenous thrombolytic therapy is far from universally effective, and six to eight patients must be treated for one to benefit (4). The efficacy of intravenous thrombolytic therapy could be improved through better selection of patients that might benefit and elimination of patients at risk of hemorrhagic complications. The presence of a large perfusion-diffusion mismatch currently represents a reasonable working model for selecting patients for thrombolytic therapy, perhaps even beyond the current 3-hour window. Regions with severe hypoperfusion or a particularly low apparent diffusion coefficient may potentially represent regions of early necrosis and therefore be at high risk for hemorrhage. Finally, patients with normal perfusion might be spared the risk of thrombolytic therapy, because they have presumably reperfused spontaneously and have an excellent prognosis if untreated (5). However, the utility of these imaging criteria must be carefully validated in a prospective trial. In addition, because time to thrombolysis has been shown to be a major determinant of outcome from thrombolytic therapy (6), any delays in therapy due to imaging and image processing must be factored into the equation.

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References

1. Baird AE, Lovblad KO, Dashe JF, et al.**Clinical correlations of diffusion and perfusion lesion volumes in acute ischemic stroke.** *Cerebrovasc Dis* 2000;10:441–448
2. Albers GW, Lansberg MG, Norbash AM, et al.**Yield of diffusion-weighted MRI for detection of potentially relevant findings in stroke patients.** *Neurology* 2000;54:1562–1567
3. Powers WJ. **Testing a test—a report card for DWI in acute stroke.** *Neurology* 2000;54:1549–1551
4. NINDS rt-PA Stroke Study Group.**Tissue plasminogen activator for acute ischemic stroke.** *N Engl J Med* 1995;333:1581–1587
5. Marchal G, Furlan M, Beaudouin V, et al.**Early spontaneous hyperperfusion after stroke. A marker of favorable tissue outcome.** *Brain* 1996;119:409–419
6. Marler JR, Tilley BC, Lu M, et al.**Early stroke treatment associated with better outcome: The NINDS rt-PA Stroke Study.** *Neurology* 2000;55:1649–1655

Tuning in on Tumor Activity with Proton MR Spectroscopy

Proton MR spectroscopy's role in the clinical evaluation of human brain tumors has been receiving increased attention from neuroradiologists, neurosurgeons, and radiation and medical oncologists. Good-quality proton MR spectra can be obtained on most clinical 1.5-T MR imaging systems fitted with commercially available automated software that allows acquisition of single-volume MR spectra. More recently, multi-volume proton MR spectroscopic techniques have become available that allow exploration of multiple-volume elements as small as 0.5 cc within a slice as quickly as 10 minutes. Additionally, in multi-volume MR spectroscopic studies, processing software programs are available that can display the relative level of the proton metabolites within the spectroscopic voxels. Zones of colors of varying intensity or shades of gray can be overlaid onto an MR image to show the distribution and level of the metabolic group within the anatomic image slice, known as either spectroscopic or chemical shift imaging. Because of these advances, we and others have integrated the proton spectroscopic technique into the routine clinical evaluation of brain tumors, because it provides greater information concerning tumor activity and characterization of the tumor tissue than what is possible with contrast-enhanced MR imaging techniques alone.

Clinical studies have shown the value of proton MR spectroscopy for the differentiation of recurrent or residual brain tumor activity from necrotic and cystic tumor processes (1–3). The differentiation of these processes is based on comparison of the proton spectral peak patterns and peak area determinations from normalized spectra for the intracellular brain metabolites choline (3.2 ppm), creatine (3.0 ppm), *N*-acetyl aspartate (2.0 ppm), lactate (1.3 ppm), and lipids (0.8–1.5 ppm). Increases in choline levels relative to creatine and *N*-acetyl aspartate measured on pretreatment MR spectra have been shown to correlate with the proliferative capacity of gliomas (4). Medium-to-high choline lev-

els, relative to creatine, have been used as a marker for the presence of actively proliferating tumor cells, whereas decreases in the overall levels of choline, creatine, *N*-acetyl aspartate, and increases in lipid/lactate proton resonances between 0.8–1.5 ppm indicate necrotic processes. These changes in brain metabolite levels/patterns have been used to monitor and assess the effects of therapy on brain lesions (5).

In this issue of the *AJNR*, Martin et al (page 959) have extended the use of proton MR spectroscopy in assessing brain lesions. In this article, the authors have used proton MR spectroscopy in conjunction with MR imaging to intraoperatively guide them in selecting areas for biopsy within the tumor that have the greatest activity as judged by the level of choline relative to the disease-free area of the brain. The rationale for the use of proton MR spectroscopy to target the region for biopsy is that the selection of the biopsy target normally is based on the tumor's anatomic appearance and its enhancement properties. However, in patients who have heterogeneous lesions or who have been treated with radiation, the CT or MR imaging findings ''may be insufficient for defining an optimal target for pathologic assessment''. Addition of a technique that will give information about tumor metabolic activity at the intended biopsy site clearly is desirable to help define the optimal site from which to obtain a needle biopsy specimen.

A proton turbo spectroscopic imaging technique was used in conjunction with non-contrast MR imaging to select and position the needle sites for biopsy in 26 patients. Of these patients, 16 had received prior radiation treatment for their tumor, nine were being assessed for the first time, and one had undergone a hemispherectomy 11 years prior to the present study. Both the spectroscopic imaging data sets were used to determine an appropriate target site. Metabolic images were created that could be overlaid onto the anatomic images. The choline spectroscopic imaging maps were used extensively to locate focal regions of relatively high levels of this metabolite. After selecting the target from the combined spectroscopic and anatomic image and creation of a burrhole, the patient was repositioned in the MR unit and the introduction of the biopsy needle into the brain was monitored using real-time snapshot MR images to position the needle precisely at the desired target. The patient was then removed from the magnet and the tissue was harvested by means of the needle.

Of the 26 patients, only 17 manifested focal MR spectra with regions of increased choline and had histologically confirmed tumor. In the remaining nine patients, proton MR spectroscopy did not show any regions that had major increases in choline levels and had spectra suggestive of necrosis. Of these nine patients, five had histologically proven necrosis, whereas in the remaining four patients (two glioblastoma multiforme, one lymphoma, and one germinoma), the presence of tumor along with necrosis was histologically confirmed. In one histologically confirmed glioblastoma multiforme with a choline level less than or isointense to the reference volume, the observed spectral pattern was suspicious for the presence of tumor (see Figure 7 [page 967]). However, even though the investigators felt that this area was suspicious, they felt that they could not include this in their MR spectroscopic/histologic positively correlated patient data set. We consistently find similar MR spectral patterns among patients who have glioblastoma multiforme in which volume contains a large level of necrosis (both treated and untreated) and classify volume containing such spectral patterns as positive for active tumor. If this patient is included, in which the proton MR spectroscopic findings correlated with the histologic findings, then only three of 26 or approximately 10% of the areas that underwent biopsy gave false-negative results.

In this preliminary study, it appears that proton MR spectroscopy in conjunction with MR imaging will be highly useful in defining areas for the stereotactic biopsy of brain lesions. Nonetheless, despite the encouraging results from this study, there are several limitations. The major one is that most institutions do not have intraoperative MR suites in which these studies can be performed. Another limitation is that the spectroscopic method used in this study was a 2D and not a 3D MR spectroscopic technique (3). Thus, not all of the tumor could be examined. A 3D MR spectroscopic technique would have allowed visualization of metabolic activity throughout the entire tumor and surrounding regions. Additionally, if 3D metabolic spectra can be obtained, the possibility exists for the incorporation of this data set in 3D MR/CT imaging-guided surgery devices now used at many institutions to obtain fused anatomic and spectroscopic images that can be used for both biopsy and surgical planning. This may obviate the need for these studies to be performed in a dedicated MR intraoperative suite.

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References

1. Castillo M, Kwock L. **Clinical applications of proton magnetic resonance spectroscopy in the evaluation of common intracranial tumors.** *Top Mag Res Imaging* 1999;10:104–113
2. Taylor JS, Langston JW, Reddick WE, et al. **Clinical value of proton magnetic resonance spectroscopy for differentiating recurrent or residual brain tumor from delayed cerebral necrosis.** *Int J Radiation Oncology Biol Phys* 1996;36:1251–1261
3. Vigneron DB, Nelson SJ, Kurhanewicz J. **Proton chemical shift imaging of cancer.**In: Higgins CB, Hricak H, Helms CA, eds. *Magnetic Resonance Imaging of the Body*. 3rd ed. New York: Lippincott-Raven Press; 1997:205–220
4. Shimizu H, Kumabe T, Shirane R, Yoshimoto T. **Correlation between choline level measured by proton MR spectroscopy and Ki-67 labeling index in gliomas.** *AJNR Am J Neuroradiol* 2000; 21:659–665
5. Preul MC, Carmano Z, Villemur J-G, et al.**Using proton magnetic resonance spectroscopic imaging to predict in vivo response of recurrent malignant gliomas to tamoxifen chemotherapy.** *Neurosurgery* 2000;46:306–318