Evaluations of Inhomogeneous Shimming in ^{1}H MR Spectroscopy

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In this study, we investigate the effects of poor shimming on quantitative measurement of ratios of metabolite levels by proton magnetic resonance spectroscopy (^{1}H MRS). Coefficient of variation (COV) of metabolite ratios for point resolved spectroscopy (PRESS) and stimulated-echo acquisition mode (STEAM) spectra was evaluated from a phantom containing *in vivo* levels of metabolites using a conventional whole body 1.5T MR system and conventional acquisition and analysis protocol. A statistical P-value was also calculated from a linear regression for relationship of metabolite ratios. N-acetylaspartate (NAA)/ creatine (Cr) and NAA/ choline (Cho) had low COV values for the long and short TE spectra (29.1 and 27.5 %; 23.8 and 12.6 %), whereas Cho/Cr and Cr/Cho had high COV values (50.0 and 68.6 %; 27.5 and 29.3 %). A linear relationship between NAA/Cr and Cho/Cr, and between NAA/Cho and Cr/Cho revealed the statistical significance in the long and short TE spectra, respectively ($P < 0.0001$ and $P < 0.0001$; $P = 0.015$ and $P = 0.005$). There was no significant relationship between Cho/NAA and Cr/NAA in the measurement ($P = 0.159$; $P = 0.910$). The present study suggested that NAA/Cr and NAA/Cho could be useful for data with poor shimming in ^{1}H MR spectroscopy. In conclusion, statistical significance of metabolite ratios indicated that the Cr and Cho levels could be interpreted as a significant alteration factor in the long and short TE spectra, and then should be used with care to provide precise metabolite quantification.

Key words: metabolites; poor shimming; magnetic resonance spectroscopy (^{1}H MRS)

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Introduction

Quantitative analysis of the brain metabolites using proton magnetic resonance spectroscopy (^{1}H MRS) stems from the fact that the area under a collected peak is directly proportional to the number of spins contributing to the peak. Thus, under appropriate conditions in MRS evaluation, assessment of metabolite concentrations can be reduced to calculate peak areas that are able to aid in the interpretation of clinical MRS data (1, 2). The most refined approach to peak area calculation requires spectral curve fitting that is widely used in reporting clinical MRS results. Since the absolute quantification of poorly separated peaks in clinical low-field spectra poses much more formidable problems (3, 4), the ratio method on the basis of metabolite peak area is currently used in the most clinical MRS studies because it provide the simplest quantitative assessment (5). The ratio method is calculated from a spectrum of lesion and then compared to the corresponding ratios from contralateral normal region, if available, otherwise may be compared to normative values from healthy volunteers. In order to improve accurate quantification, one of the measured metabolites must fulfill the requirement of a reference that does not vary with the physical conditions and/or diseases. In general, the ratio method relies on the assumption that the metabolite of creatine (Cr) of the brain is stable enough to use as an internal reference in reporting relative concentrations of other metabolites such as N-acetylaspartate (NAA) and choline (Cho). However, recent reports suggest that this assumption should be used with care (6, 7). In reality, a stable internal reference may be unavailable for some pathophysiological conditions. Nevertheless, knowledge of biochemical processes with MRS techniques has contributed to the successful utilization of ratios in the interpretation of clinical MRS data (8, 9).

^{1}H MRS is to detect signals from small concentration of metabolites in the presence of the large concentration of water contained in a small volume over a narrow frequency range. Thus, it is critical to secure practical and precise localization techniques, the best field homogeneity possible and the effective water suppression. Specifically, the optimized homogeneity of the magnetic field within the volume of interest (VOI) directly improves the MR spectral resolution, signal to noise ratio (SNR) and smaller peaks. On the other hand, the field inhomogeneities such as a poor shim in the VOI degrade the water signal suppression significantly, decreasing the spectral quality of the resultant proton spectra. Thus, the incomplete water suppression and the residual water peak consequently affects the MRS signals and hence the calculation of peak area.

To evaluate the effects of poor shimming on quantitative measurement of ratios of metabolite levels by proton magnetic resonance spectroscopy (^{1}H MRS), the present study investigated quantitatively a coefficient of variation (COV) when field inhomogeneities were introduced by a linear shim current offsets. A linear relationship between metabolite ratios was evaluated in order to determine the variation of major metabolites such as NAA, Cho, and Cr.

Materials and Methods

Phantom

A phantom containing *in vivo* levels of metabolites at concentrations in the adult human brain was used to study *in vitro* ^{1}H MRS. The

homemade phantom (liquid brain) contains 12.5 mM of NAA, 10.0 mM of Cr + PCr, 3.0 mM of Cho, 7.5 mM of myo-inositols (Ins), 12.5 mM of glutamate (Glu), 5.0 mM of Lactate (Lac), 50.0 mM KH_2PO, 0.1% sodium azide and 0.1% Gd-DTPA, although three major peaks such as NAA, Cr, and Cho are considered here.

Data Acquisition

All localized ^{1}H MRS studies were performed on a 1.5T MRI/MRS system (Vision plus, Simense, Erlangen, Germany) with a quadrature transmit and receive high pass birdcage head coil for all measurements. The point resolved spectroscopy (PRESS) and stimulated-echo acquisition mode (STEAM) pulse sequences (10, 11), followed by water suppression with three chemical shift-selective saturation (CHESS) pulses and dephasing gradients were then used to obtain water-suppressed metabolite spectra. Spectral parameters in the PRESS (or, STEAM) were TE 135 ms, TR 1500 ms (20ms, 2000ms), acquisition averages 128, spectral width 2500 Hz and data points 2048. A localized voxel size (6mL) was prescribed from an axial localizer at isocenter.

Poor shimming

It is often necessary to distinguish compounds that differ in chemical shift by only a fraction of a part per million (ppm). Thus, it is important to emphasize the homogeneity of the magnetic field since the homogeneity directly affects the spectral resolution, SNR and peak area for each metabolite. In particular, it is crucial for *in vivo* ^{1}H MRS because poor shimming degrades the water signal suppression and produces the bad quality of the resultant spectra. Consistent field *homogeneity for a series of similar in vivo* studies is alsó an important asset for accurate metabolic quantification (12). Thus, in general, a local shim is applied over a selected VOI for local homogeneity improvement before water suppression in MRS experiment (13). In the present study, however, poor shim due to linear shim current DC offsets was specifically applied for optimum shim values as shown in Table 1. Typical full width at half maximum (FWHM) of water peak was 1Hz. The field inhomogeneities introduced by the poor shim affected peak broadening and/or baseline distortions of spectrum due to incomplete water suppression. Thus, the incomplete water suppression and the residual water peak affected the MRS signals and hence peak area for each metabolite. The calculated peak area included possible errors for each metabolite concentration. Therefore, the poor shimming influenced on the MRS signals and hence the calculation of peak area for each metabolite.

Data Analysis

All MRS raw data were processed using a software package supplied by the manufacturer of the system (Siemens NUMARIS data analysis package) running on a SUN workstation (Vision plus, Simens, Erlangen, Germany). Metabolite spectra were phase-corrected using measurements from the water spectra, and residual water signal suppressed by a low-frequency filter using window convolution. This window convolution has a negligible effect on the metabolite signals of interest. Data were zero filled to 4096 points and line broadened to 3 Hz prior to Fourier transformation. Phased absorption spectra were reported with baseline corrections or resolution enhancement. All of the ^{1}H MRS spectra were plotted and analyzed in the absorption mode and fitted to Lorentzian lineshapes. Proton resonance

Table 1. Field inhomogeneities introduced by linear shim current DC offsets within a localized volume of interest along the X, Y and Z directions, respectively.

PRESS (or, STEAM) Optimum Shim Value (X = -8 (-4), Y = 282 (3), Z = -137 (-4))		
X_{yz} SC DC Offsets	Y_{zx} SC DC Offsets	Z_{xy} SC DC Offsets
	(-60)	
(-50)	(-50)	(-50)
(-40)	(-40)	-15 (+40)
(-30)	(-30)	-10 (+30)
(-20)	(-20)	-5 (+20)
0 (-10)	0 (-10)	0 (+10)
+5 (0)	+5 (0)	+5 (0)
+10 (+10)	+10 (+10)	+10 (-10)
+15 (+20)	+15 (+20)	+15 (-20)
+20 (+30)	+20 (+30)	+20 (-30)
+25 (+40)	+25 (+40)	+25 (-40)
+30 (+50)	+30 (+50)	
+35 (+60)	+35 (+60)	

Note. X_{yz} SC DC offsets are independent of only X axis shim current (SC), when Y and Z shim current components are fixed. Y_{zx} and Z_{xy} SC DC offsets like X_{yz} are adjusted through starting shim values and gradient hardware.

Table 2. Mean and standard deviation of quantitative measurement of metabolite ratios by the long TE PRESS and the short TE STEAM techniques

Metabolic Ratio	Cr Ref.		Cho Ref.		NAA Ref.	
	NAA/Cr	Cho/Cr	NAA/Cho	Cr/Cho	Cho/NAA	Cr/NAA
COV1	14.6	27.8	14.2	26.3	24.1	14.4
COV2	29.1	50.0	27.5	68.6	28.5	30.7
COV3	23.8	27.5	12.6	29.3	13.9	24.9

Note. coefficient of variation (COV) = 100% × standard deviation / mean, NAA = N-acetylaspartate, Cr = creatine, Cho = choline-containing compounds, Ref. = reference. COV1 and COV2 are given as the percentage for an optimum and poor shim with the long TE PRESS spectra, and COV3 are depicted for a poor shim with the short TE STEAM spectra.

in the spectra was assigned on the basis of prior assignment (1). Resonance peak assignments of major proton metabolite were 1.25 and 1.35 ppm of Lac, 2.0 ppm of NAA, 2.35 ppm of Glu, 3.0 ppm of Cr, 3.2 ppm of Cho and 3.55 ppm of Ins. From these values, NAA/Cr, Cho/Cr, NAA/Cho, Cr/Cho, Cho/NAA and Cr/NAA ratios were determined. A relative error was characterized by a coefficient of variation (%COV = 100 times standard deviation/mean). A COV value was determined for the effects of poor shim on quantitative measurement of ratios of metabolite levels by the PRESS and STEAM pulse sequences. Optimum shim with re-shimming the magnet was also characterized by the percentage value as shown in Table 2. In additional data analysis method, a linear relationship between metabolite ratios was used to determine the degree of variation of Cr, Cho, and NAA metabolites. Statistical analysis was performed using Origin (Origin for Windows, Version 6.0, Microcal Software, Inc.). The P value was obtained from the ANOVA for linear regression (the P value for the t-test of the slop=0).

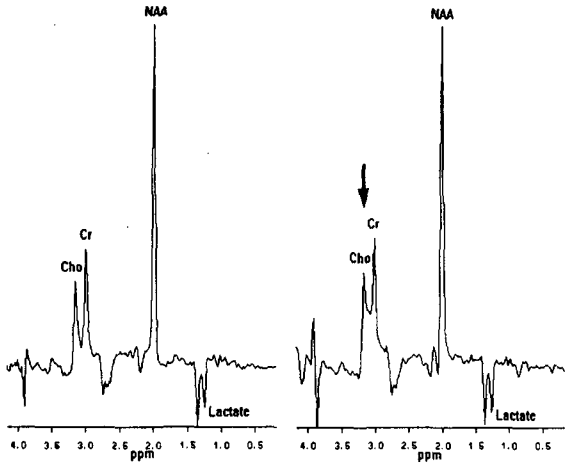

Figure 1. Spectra obtained from a localized volume of interest centered on the phantom containing major brain metabolites under an optimum (left) and poor (right) shim, or moving the phantom in ^{1}H MRS with the long TE PRESS pulse sequence. The poorly separated peak was observed when field inhomogeneities were introduced.

RESULT

Figure 1 illustrates two spectra acquired from the phantom under a good (left) and poor (right) shimming, or moving the phantom in ^{1}H MRS by the long TE PRESS pulse sequence. The mean and standard deviation of the areas for each of the metabolite signals were calculated, and a relative error was obtained by taking the ratio of the standard deviation to the mean. Table 2 shows COV value for effects of poor shim on quantitative measurement of ratios of metabolite levels. NAA/Cr and NAA/Cho showed the low

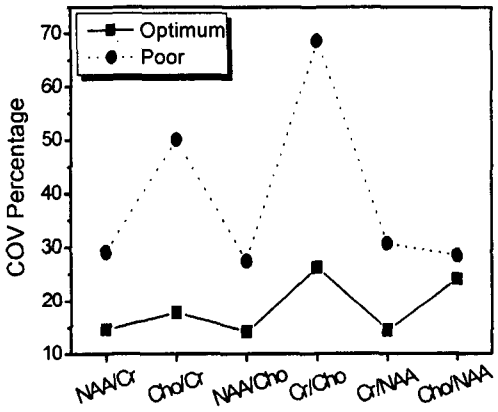

Figure 2. The calculated COV values for an optimum shim with re-shimming, and for a poor shim by the linear shim current DC offsets. Poor shim was statistically compatible to the optimum shim in the metabolite concentration variations possible in the measurements

COV values in the long TE spectra (29.1, 27.5 %), whereas those of Cho/Cr and Cr/Cho showed the high COV values (50.0, 68.6 %). The results for an optimum and poor shim studies are shown in Figure 2. A percentage COV value for the effects of poor shim in ^{1}H MRS by the short TE STEAM pulse sequence is also included in Table 2. NAA/Cr and NAA/Cho in the short TE spectra were observed in low COV values (23.8, 12.6 %), when compared with those of Cho/Cr and Cr/Cho (27.5, 29.3 %).

When a relationship between the metabolite ratios was analyzed as a linear regression model, we found an interesting result. The statistical P-value was used to determine the variation of Cr, Cho, and NAA metabolites when field inhomogeneities were introduced. Figure 3 illustrated that the relationship between NAA/Cr and Cho/Cr had the significance in the long and short TE spectra (r = 0.894, P < 0.0001; r = 0.883, P < 0.0001). Figure 4 showed a significant relationship between NAA/Cho and Cr/Cho in the

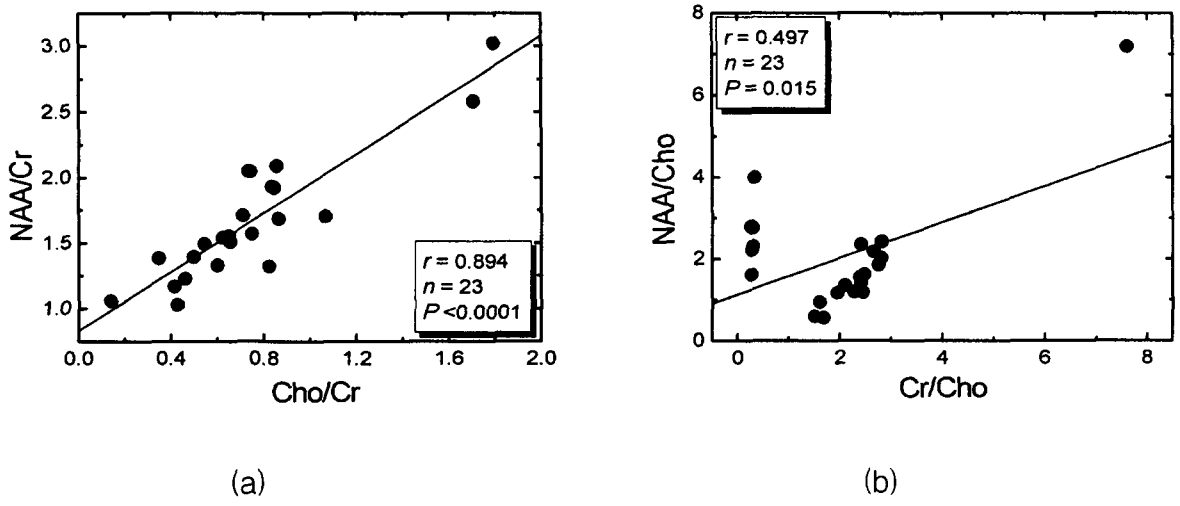

Figure 3. Relationship between NAA/Cr and Cho/Cr in ^{1}H MRS with the long TE PRESS (a) and the short TE STEAM (b) spectra.

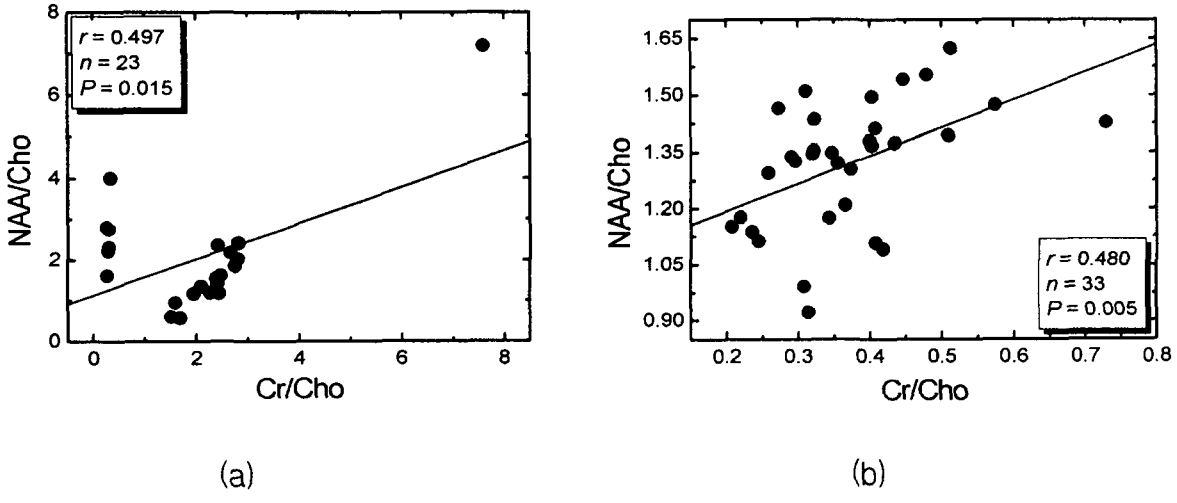

Figure 4. Relationship between NAA/Cho and Cr/Cho in ^{1}H MRS with the long TE PRESS (a) and the short TE STEAM (b) spectra.

shimming among these factors is to optimize the magnetic field homogeneity specifically over the

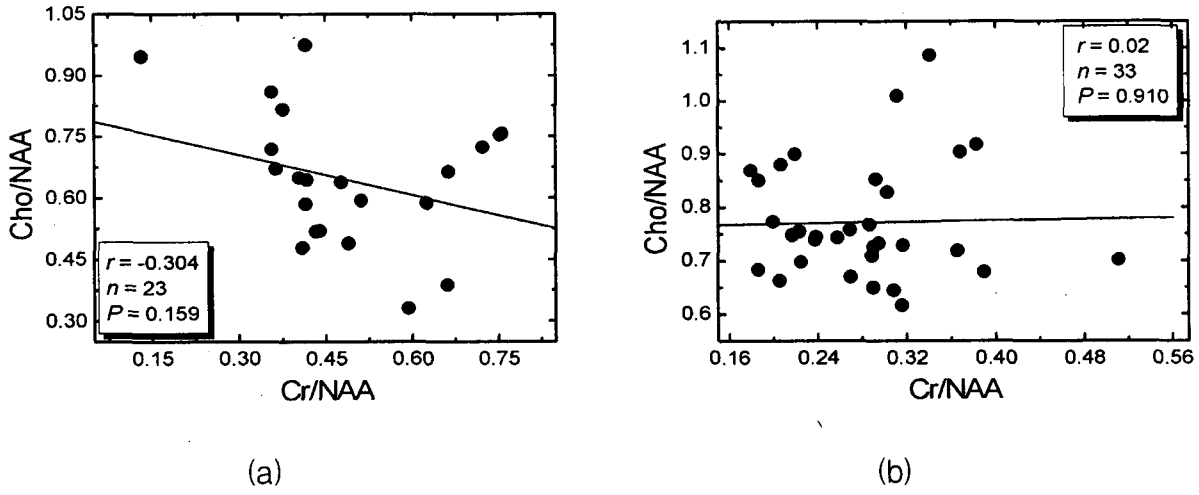

Figure 5. Relationship between Cho/NAA and Cr/NAA in ^{1}H MRS with the long TE PRESS (a) and the short TE STEAM (b) spectra.

long TE PRESS (r = 0.497, P = 0.015) and the short TE STEAM (r = 0.480, P = 0.005) pulse sequences. In case of NAA, however, there was no significant relationship between Cho/NAA and Cr/NAA ratios, with the use of a regression line (r = 0.304, P = 0.159; r = 0.02, P = 0.910) (Figure 5 (a) and (b)). Thus, NAA variation was not statistically significant in the measurement.

DISCUSSION

Successful MRS examination for quantitative results depends on a wide variety of different factors that include patient preparation, voxel shimming, water suppression, choice of acquisition parameters and post-processing. Each of these factors can contribute to possible deviations in the precision of the results. The local voxel selected VOI. A good local shimming procedure produces narrower and shaper metabolite peaks, hence better spectral resolution and improved SNR. In our experiment, however, we used an inappropriate shimming control that could degrade the water signal suppression and the quality of the resultant spectra. The poor or inadequate shimming in accordance with linear shim current DC offsets was applied for optimized good shim values specifically over the selected VOI. The shim current offset was adjustable through the shim values starting from the references and gradient hardware. All acquisition spectra were obtained from the physical environments. The peak area for each metabolite in MR spectra was affected by peak and/or baseline distortions of spectrum due to incomplete water suppression. Thus, the calculated peak area included a signal loss for each metabolite on the measurements, although the residual water peak area and the baseline were correctly defined in determining the peak areas.

Percentage COV value was calculated by finding the mean and standard deviation of the peak area variations to determine the effects of an optimum and poor shim in ^{1}H MRS by the long TE PRESS pulse sequence. In most cases the COV values of poor shim are mostly larger than the optimum shim when field inhomogeneities were introduced. The poor shim was comparable to the optimum shim as shown in Figure 2.

An interesting result was observed when we measured the effects of poor shim on quantitative measurement of ratios of metabolite levels by the PRESS and STEAM pulse sequences. NAA/Cr and NAA/Cho were observed in low COV values in the long and short TE spectra. These finding may indicate that two independent ratios (e.g., NAA/Cr and NAA/Cho) could be most useful for data with poor shim. Otherwise, Cho/Cr and Cr/Cho ratios with increased COV values could be explained confidently as a significant change on the measurement.

There was a compatible difference of percentage COV values between the long and short TE spectra for quantitative metabolite ratio levels. The long TE PRESS spectra were larger than those from the short TE STEAM spectra. This is a note-worthy result given that the PRESS spectra have twice the SNR of the STEAM spectra. Especially, Cho/Cr and Cr/Cho revealed significant COV values in the long TE spectra. In other studies, Brief E and coworkers (14) reported the significance of the difference between measurements to require knowledge of the precision of a single measurement. They characterized the effect of re-shimming the magnet and measured the variation of the peak area with re-shimming and re-positioning. In clinical studies, they found that the short TE spectra were comparable to the long TE PRESS spectra. And then, Cho/Cr could be interpreted confidently as a significant change in the patient. Sijens and coworkers (15) suggested that the resonance of Cho might be altered due to field inhomogeneities introduced by GD-DTPA contrast. It appeared that GD-DTPA caused T2 shortening of extracellular Cho-containing compounds. These alternations also appeared more pronounced with method using the long TE PRESS than those using short TE STEAM pulse sequence. Therefore, our finding might indicate that Cho/Cr and Cr/Cho could be explained as a significant alternation factor in the long TE spectra.

In Figures 3-5, the present study showed a relationship between metabolite ratios relative to Cr, Cho, and NAA. A significant relationship between NAA/Cr and Cho/Cr, between NAA/Cho and Cr/Cho, was observed in both the long TE PRESS and the short TE STEAM spectra. Thus, it suggested significant variation of Cr and Cho metabolites. These findings indicated that Cr and Cho levels could be interpreted as a significant change when field inhomogeneities were introduced by poor shim. Therefore, the Cr and Cho metabolites should be considered to be careful in the evaluation of absolute metabolite quantification. Moreover, non-significant relationship between Cho/NAA and Cr/NAA might reflect that NAA would be the least affected by poor shim.

In some special cases of psychiatric or pediatric patients and even patients with metallic dental supplements or surgical clips, we could not get the acceptable shimming results. In order to inevitably use ^{1}H MRS data under the inadequate or poor shimming conditions, NAA/Cr and NAA/Cho ratios based on low coefficients variation seem to be a relatively accurate quantification method. Furthermore, NAA peak is the most reliable resonance for rationing and the dominant peak in normal adult brain spectra. It

is also accepted as a neuronal and axonal marker whose physiological role is currently unknown. Thus, NAA/Cr and NAA/Cho may be generally a reliable ratio in interpreting many pathological MR spectra.

In conclusion, the present study suggested that NAA/Cr and NAA/Cho could be useful to evaluate the metabolite alterations acquired on the influence of poor shim in ^{1}H MR spectroscopy. The Cr and Cho metabolism could be interpreted as a significant alteration factor in the long and short TE spectra, and then should be used with care to provide accurate metabolite quantification. Further studies are in progress to establish whether there is the relationship between the metabolite peak area ratios for *in vivo* tissues.

REFERENCES

1. Frahm J, Bruhn H, Gyngell ML, Merboldt KD, Hanicke W, and Sauter R. Localized high-resolution proton NMR spectroscopy using stimulated echoes: Initial applications to human brain in vivo. Magn Reson Med 1989;9:79-93.

2. Michaelis T, Merbolt KD, Hanicke W, Gyngell ML, Bruhn H and Frahm J. On the identification of cerebral metabolites in localized ^{1}H NMR spectra of human brain in vivo. NMR Biomed 1991; 4: 90-98.

3. Christiansen P, Henriksen O, Stubgaad M, Gideon P, Larsson HB. In vivo quantification of brain metabolites by ^{1}H MRS using water as an internal standard. Magn Reson Imaging 1993;11:107-118.

4. Hennig J, Pfister H, Ernst T, Ott D. Direct absolute quantification of metabolites in the human brain with in vivo localized proton spectroscopy. NMR Biomed 1992;5:193-199.

5. Ross BD, Kreis R, Ernst T. Clinical tools for the 90s: magnetic resonance spectroscopy and metabolite imaging. Eur J Radiol 1992;14:128-140.

6. Negengank W. Studies of human tumors by MRS: a review. NMR Biomed 1992;5(5): 303-324.

7. Kreis R, Arcinue E, Shonk TK, Flores R, and Ross BD. Hypoxic encephalopathy after near-drowning studied by quantitative ^{1}H magnetic resonance spectroscopy. J Clin Invest 1996;97(5):1142-1154.

8. Auld KL, Ashwal S, Holshouser BA, Tomasi LG, Perkin RM, Ross BD, and Hinshaw DB. Proton magnetic resonance spectroscopy in children with acute central nervous system injury. Pediatr Neurol 1995;12:323-334.

9. Holshouser BA, Ashwal S, Luh GY, Shu S, Kahlon S, Auld KL, Tomasi LG, Perkin RM, and Hinshaw DB. Proton MR spectroscopy after acute central nervous system injury: Outcome prediction in neonates, infants, and children. Radiology 1997;202:487-496.

10. Frahm J, Merbold KD, Hanicke W. Localized proton spectroscopy using stimulated echoes. J Magn Reson 1987;72:502-508.

11. Ordidge RJ, Bendall MR, Gordon RE, Connelly A. Volume selection for in vivo spectroscopy. In: Govil G, Khetrapal CL, Sarans A, Eds. Magnetic resonance in biology and medicine. New Delhi, India: Tata-McGraw-Hill; 1985:387-397.

12. Hu J, Javaid T, Arlas-mendoza TF, Liu Z, McNamara R, and Brown TR. A fast, reliable, automatic shimming procedure using ^{1}H chemical

shift imaging spectroscopy. J Magn Reson Ser B 1995;108:213-219.

13. Schneider E and Glover G. Rapid in vivo proton shimming. Magn Reson Med 1991;18: 335-347.

14. Brief E, Whittall KP, MacKay AL, Li DKB. Precision of MRS Metabolite Peak Area Ratios in Human Brain at Short TE. Prc Intl Soc Magn Reson Med 1999: 7.

15. Sijens PE, Van den Bent MJ, Nowak PCJM, et al. ^{1}H chemical shift imaging reveals loss of brain tumor choline signal after administration of Gd-contrast. Magn Reson Med 1997;37:222-225.

자기공명분광에서 비균질 자장보정에 관한 평가

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최보영, 백현만, 서태석, 이형구, 전흥재, 신경섭

본 연구에서는 양성자 자기공명분광법을 이용하여 대사물질의 양적 비율 산출시 비균질한 자장보정의 영향을 정량평가하였다. 점분해분광법과 자극반향 획득법을 사용하여 대사비율의 변화상수를 전신 1.5T 자기공명장비, 기존 분석방법에 의해 평가하였다. 통계학적 분석방법으로 선형계측방법을 사용하여 P d값을 산출하였다. 결과로서 N-acetylaspartate (NAA)/ creatine (Cr)과 NAA/ choline (Cho) 비율은 긴 TE와 짧은 TE 값에 대해 낮은 COV 값은 나타낸 반면 Cho/Cr과 Cr/Cho 비율은 높은 COV 값을 나타냈다. NAA/Cr과 Cho/Cr 그리고 NAA/Cho과 Cr/Cho 비율은 긴 TE와 짧은 TE 값에 대해 상당한 긴밀한 P값을 나타냈다. ($P < 0.0001$ and $P < 0.0001$; $P = 0.015$ and $P = 0.005$). 반면 Cho/NAA과 Cr/NAA은 통계Gkr적 유의성이 발견되지 않았다. ($P = 0.159$; $P = 0.910$). 본 연구 결과에 의해서 NAA/Cr과 NAA/Cho 비율은 자기공명분광 비율산출에서 자기보정에 관계없이 가장 유용한 방법으로 나타났다. 결론적으로 Cr과 Cho는 정확한 정량측정시 가장 유용한 대사물질로 나타났다.

중심단어. 대사물질 비율, 비균질 자장보정, 양성자 자기공명분광