Localized Single Voxel $^1$H MR Spectroscopy Toward Routine Clinical Use

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Purpose: To evaluate the automated $^1$H magnetic resonance spectroscopy ($^1$H-MRS) method for a routine clinical use, various regions of the normal human brain were examined for regional variations, the reproducibility, and the quality control of the spectral data.

Materials and Methods: Localized $^1$H-MRS was performed in a GE 1.5T SIGNA MRI/MRS system using the automated method (PROton Brain Exam: PROBE). Six regions of the human brain from normal volunteers ($N=25$, age $=23–65$) were examined: occipital gray matter, parietal white matter, frontal white matter, pons, cerebellum, and basal ganglia regions. STEAM was used as the localization method with the following parameters: $TE=30$ msec, $TR=3.0$ sec, $AVG=48$ AVG, $NEX=2$, Spectral Width (SW) = 2500 Hz, Size (SI) = 2048 points (2K), and the size of voxel = 7–9 ml. The reproducibility and the quality control of the spectral data were evaluated.

Results: For the 6 regions, the regional variation by the spectral patterns and the metabolites ratios relative to creatine was well demonstrated. Rates of the auto prescan success and the percentages of obtaining the acceptable quality spectra were high in the parietal white matter, occipital gray matter, and basal ganglia regions, and low in the frontal white matter and pons regions.

Conclusion: PROBE is a highly practical as well as reliable method to produce reproducible quality spectra that represent the regional metabolic variations in the human brain. PROBE can be used as a single spectroscopic exam or as an additional series to a routine brain MRI exam, which takes less than 10 minutes for acquisition of one spectrum. In order to obtain good quality spectra, a good quality control scheme of the MR instrument is mandatory.

Index Words: Magnetic resonance (MR), spectroscopy

INTRODUCTION

Proton magnetic resonance spectroscopy ($^1$H-MRS) has gained remarkable attention for clinical uses from many fields of medicine over the last few years. It is a powerful technique for accessing metabolic information of a volume of interest (VOI) as a noninvasive tool of biochemical assay. It also provides additional diagnostic value to the magnetic resonance imaging (MRI) by presenting the metabolic information of the anatomically abnormal regions (1–3). Recent investigations have proved that clinical $^1$H-MRS can be used as one of the important diagnostic tools for a number of diseases. Hypoxic encephalopathy, hepatic encephalopathy, metabolic disorders in infants, Alzheimer disease, temporal lobe epilepsy, and hypernatremia are such examples (4–9).

Despite its usefulness, its practical use as a part of routine brain MR exam was limited due to the technical difficulty and impractical temporal resolution for the data acquisition. It suffered from the operator dependent spectral quality, a lack of reproducibility, and a prolonged time for the data acquisition. Therefore, clinical $^1$H-MRS was used in a few research institutions for research, and also, run only by extensively trained professionals, which rendered its clinical utility to very limited.
limited occasions. However, recent development in \textsuperscript{1}H-MRS has made the data acquisition all automatic and improved the temporal resolution dramatically (10). With the automated \textsuperscript{1}H-MRS method, the acquisition parameters can be adjusted in 2–5 minutes including the adjustments of the offsets of x, y, and z shim coils, transmitter radiofrequency (RF) powers, receiver gains, on-resonance frequency, and RF powers used for suppression of the water signal. They used to be adjusted manually with the conventional method consuming more than 30 minutes. The automated \textsuperscript{1}H-MRS method can also post-process the data immediately, and display the spectrum in the screen right after the acquisition is finished. The total elapsed time for 1-voxel spectroscopy from loading a patient to displaying the spectrum has been reduced approximately from 1 hour to 10 minutes. The operator dependent spectral quality, a lack of reproducibility, a prolonged time for the data acquisition are no longer problems, which offer the use of clinical \textsuperscript{1}H-MRS as a part of the

![Image of brain with spectra](image)

**Fig. 1.** Image guided \textsuperscript{1}H MR STEAM-spectra of the 6 selected regions (TE=30 msec, TR =3.0 sec, AVG=48, NEX=2, and Volumes=7–9 ml): Localization was performed on a) the frontal white matter region on the transverse T1-weighted MR image and b) the corresponding \textsuperscript{1}H MR spectrum of the frontal white matter region, c) \textsuperscript{1}H MR spectrum of the parietal white matter region, d) \textsuperscript{1}H MR spectrum of the occipital grey matter region, e) \textsuperscript{1}H MR spectrum of the basal ganglia region, f) \textsuperscript{1}H MR spectrum of the pons region, and g) \textsuperscript{1}H MR spectrum of the cerebellum region.
In this work, we examined the use of the automated proton brain exam (PROton Brain Exam: PROBE) which is a commercially available software package implanted on a GE 1.5T SIGNA MRI/MRS System (Milwaukee, WI, USA) as a part of the routine brain MR exam. This study was purposed to evaluate the clinical utility of PROBE as a routine brain MR exam for clinical diagnosis, and the following questions were examined: a) does PROBE produce regionally different spectral patterns for various regions of the human brain?, b) what is a set of acquisition parameters for the localization method which offers the acceptable and reproducible spectral sensitivity, and the temporal and spatial resolutions?, and c) how does the quality control have to be followed in order to produce the reproducible quality spectra? This study presents that PROBE can be implemented as an additional series in a routine brain MRI exam, and can also produce regionally different spectral results that are also reproducible for important regions of the human brain. A promising future of clinical 'H-MRS as a new diagnostic tool in the modern medicine is manifested throughout this study.

Table 1. Concentrations of the Brain Metabolites Relative to Creatine (Total N=25).

<table>
<thead>
<tr>
<th>Regions</th>
<th>NAA/Cr (N=5)</th>
<th>Cho/Cr (N=15)</th>
<th>ml/Cr (N=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal White*</td>
<td>1.70 ± 0.2</td>
<td>1.10 ± 0.1</td>
<td>0.56 ± 0.13</td>
</tr>
<tr>
<td>Parietal White</td>
<td>1.50 ± 0.11</td>
<td>0.74 ± 0.068</td>
<td>0.54 ± 0.088</td>
</tr>
<tr>
<td>Occipital Grey</td>
<td>1.30 ± 0.12</td>
<td>0.61 ± 0.093</td>
<td>0.59 ± 0.085</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>1.20 ± 0.14</td>
<td>0.78 ± 0.1</td>
<td>0.43 ± 0.068</td>
</tr>
<tr>
<td>Pons*</td>
<td>1.50 ± 0.14</td>
<td>1.10 ± 0.11</td>
<td>0.60 ± 0.21</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>0.97 ± 0.11</td>
<td>0.77 ± 0.13</td>
<td>0.59 ± 0.17</td>
</tr>
</tbody>
</table>

Note: Due to the small numbers of data points in frontal white and pons regions, ANOVA tests involving these regions give p-values greater than 0.05.

Table 2. Rates of the APS Success and Obtaining Acceptable Spectral Quality (N=25).

<table>
<thead>
<tr>
<th>Regions</th>
<th>APS Success</th>
<th>Acceptable Spectra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frontal White</td>
<td>17 (68%)</td>
<td>5 (20%)</td>
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<tr>
<td>Parietal White</td>
<td>19 (76%)</td>
<td>15 (60%)</td>
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<tr>
<td>Occipital Grey</td>
<td>23 (92%)</td>
<td>19 (76%)</td>
</tr>
<tr>
<td>Basal Ganglia</td>
<td>25 (100%)</td>
<td>16 (64%)</td>
</tr>
<tr>
<td>Pons</td>
<td>19 (76%)</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>Cerebellum</td>
<td>19 (76%)</td>
<td>11 (44%)</td>
</tr>
</tbody>
</table>

Fig. 2. Examples of unacceptable spectra: a) due to the heavy eddy current, the resonance peaks are asymmetrically shaped (arrows). In this situation, it is difficult to phase the spectrum and errors are introduced in integrating the areas of the peaks, b) contamination from the outside of the VOI can be detected (arrows), c) the baseline is severely distorted, which introduces errors for integrating the areas of the peaks, and d) inappropriate suppression of the water signal effects the intensities of the resonance peaks near the water signal at 4.8 ppm. In this case, the excess amount of the RF power for the suppression was applied, and consequently, the myo-Inositol peak near the water peak (3.3–4.4 ppm region, marked with *) was within the noise level.
MATERIALS and METHODS

Subjects and Selected Regions
Normal volunteers (N=25, age=23—65) were employed for this study. Six regions were selected: occipital gray matter, parietal white matter, frontal white matter, pons, cerebellum, and basal ganglia. Each volunteer was examined for the 6 regions at the time of examination, and one volunteer was examined for 4 times over a period of 4 months for the reproducibility test. Clinically diagnosed patients of hepatic encephalopathy, brain tumor, and temporal lobe epilepsy administered in Asan Medical Center were also examined, and their spectral results were compared with the published results (1).

MR Spectroscopy
Localized in vivo 1H MR spectroscopy was performed on a GE 1.5T SIGNA MRI/MRS System equipped with the shielded gradients (Milwaukee, WI, USA, version 5. 4). The automated 1H-MRS method (PROBE) (Milwaukee, WI, USA, version 5. 4. 1) was used as a single spectroscopic exam or as an additional series in a routine brain MRI exam protocol. For the latter case, image guided localization was performed on any image acquired in the MRI series.

STEAM (Stimulated Echo Acquisition Method) (11, 12) was primarily used as the localization method in this study, and PRESS (Point Resolved Spectroscopic Sequence) (13) was also occasionally used. Sizes of the voxels for STEAM and PRESS were 7—9 ml and 1—3 ml, respectively. Suppression of the water signal was performed by using 3-pulse CHESS sequence (14, 15) for both methods. Offsets of the higher order and linear shim coils were adjusted by the auto prescan menu (APS) for optimization of the homogeneity of the total volume and the localized volume of the brain, respectively. Strengths of the transmitter RF power, receiver gains, and 3 RF pulses for suppression of the water signal were also adjusted by the APS. The total time for the APS was 2 minutes and 3 seconds. The measured full-width-half-maximum (FWHM) of the H2O signal after shimming was usually 1—3 Hz, which gave 98—99% of the suppression factor. Rates of the APS success for each region were noted. Image guided STEAM-spectra were obtained with TE of 30 msec, TR of 3.0 sec, 48 AVG, and 2 NEX. Image guided PRESS-spectra were obtained with TE of 135—270 msec, TR of 3.0 sec, and 96 AVG. For both localization methods, SW=25000 Hz and SI=2K were used. The factor for SQUEEZE which controls the slice profiles, and the choice of RF pulses, and the factor for SHARP which controls timing of the pulse sequences, and RF and gradient pulse timing, were also adjusted according to TE values selected. The total acquisition time for a spectrum was 5 minutes and 2 seconds.

Postprocessing and Analysis of Spectral Data
Raw data acquired by PROBE were transferred to SUN Sparc-10 workstation (Sun Computer inc., Sunnyvale, CA, USA) and processed as described by Kreise et al. (4) with Spectral Analysis/General Electric (SA/GE) processing software package (Milwaukee, WI, USA). The processing consists of low frequency filtering of the residual water signal, correction of the heavy eddy current if needed, Lorenz-to-Gauss transformation, gaussian line broadening of 0.5 Hz, zerofil-

Fig. 3. 1H MR spectral pattern of overt hepatic encephalopathy. Decreased myo-Inositol (ml) and Choline (Cho) are generally observed for hepatic encephalopathy.
Fig. 4. 1H MR spectral pattern of meningioma. Increases Choline (Cho) and decreased N-acetylacepartate (NAA) are observed. There is also a significant increase in Lactate (Lac).
Fig. 5. 1H MR spectrum of temporal lobe epilepsy. In the left side of the hippocampus as compared to the right side, the significant decrease in N-acetylacepartate (NAA) and increase in Choline (Cho) are observed, which suggests the epileptogenic focus be in the left hippocampus. It was surgically confirmed.
ling of 8K, Fourier Transformation, and zero order phasing of the transformed spectrum. Any resulting spectra which contain the features of inadequate signal-to-noise ratio (SNR), outer volume contamination, distorted baselines, severe phase distortion due to the heavy eddy current, hardware artifacts, and/or inappropriate suppression of the water signal were regarded as unacceptable spectra (Fig. 3). These spectra were not included for the data analysis. Percentages of obtaining the acceptable quality spectra for each region were estimated. Peak areas were measured by Lorenzian-Gaussian fitting of the resonance peaks. Relative ratios of the brain metabolites to creatine were calculated. All data were expressed as mean ± SD. Data were tested for the 6-group homogeneity by ANOVA Kruskal-Wallis test and for the 2-group homogeneity by Wilcoxon rank sum test. P values less than 0.05 were considered significant.

**Reproducibility and Quality Control Tests**

Reproducibility of the spectral data was tested regularly in the institution to assure the quality of spectra. A phantom of 700 ml polyethylene bottle containing 25.7 mmoles, 17.5 mmoles, and 4.4 mmoles of N-acetylaceptate, creatine, and choline-chloride (Sigma Chemical Co., St. Louis, MO., USA), respectively, dissolved in water, and the occipital gray matter region in the brain of one volunteer were examined. Resolution and sensitivity of the phantom spectrum were estimated. Degrees of the phase distortion due to the eddy current of the head coil were also estimated by acquiring transaxial image guided STEAM-spectra of a sphere phantom containing acetone (CH₃CH₂OH) at the center (x₀, y₀) and the periphery (x₄₀, y₄₀) of the head coil.

**RESULTS**

Representative ¹H MR spectra of the 6 selected regions are shown in Fig. 1. The relative ratios of the major brain metabolites to creatine are tabulated in Table 1. Variations in the spectral patterns of the 6 selected regions are well demonstrated. Regional variations were significant as tested by the ANOVA tests. Rates of the APS success and the percentages of obtaining the acceptable quality spectra were shown for each region in Table 2. The parietal white matter, occipital grey matter, and basal ganglia regions were highly successful regions, whereas the frontal white matter and pons were difficult regions with PROBE.

Unacceptable quality spectra due to the heavy eddy current, distorted baseline, outer volume contamination, and inappropriate H₂O suppression were shown in Fig. 2. Examples of clinical ¹H MR spectra of chronic hepatic encephalopathy, brain tumor, temporal lobe epilepsy, were shown in Fig 3—5, and their spectral patterns were consistent with the published results.

**DISCUSSION**

PROBE was simple to perform which took less than 10 minutes for acquisition of one spectrum from a single voxel accounting for 1°36' for acquisition of the localizer images, 2°03' for adjustment of the acquisition parameters by APS, and 5°02' for acquisition of one spectrum. The temporal resolution obtained with PROBE (8°41') is a remarkable improvement over the conventional method which consumes more than 30 minutes for the manual adjustment of the acquisition parameters alone. The spectra of the occipital grey and the parietal white matter regions were consistent with the previous reports (1—5) in their spectral patterns and qualities, and our results were also reproducible. Differences in the spectral patterns and the metabolite ratios of the selected regions were clearly demonstrated in Fig. 1 and Table 1.

Despite its high practicability, unacceptable spectra are often acquired as shown in Fig. 2, which can be devastating if repeating of the exam is not permitted due to a patient's condition. Effects of the heavy eddy current can be minimized by a periodic checking of the head coil with a sphere phantom followed by a proper adjustment of the instrument if necessary, and a careful handling of admitting patients. Degrees of the zero order phase correction less than 15 and 30 degrees for the phantom spectra acquired from the center and the periphery, respectively, of the head coil were the acceptable amounts of the phase corrections which seem to offer the acceptable quality spectra for the data analysis. With the PRESS localization method, outer volume contamination is often resulted, which is easily visible in the spectrum with small sections of noises near water and other metabolite signals (Fig. 2b). It is due to an inaccurate profile of the 180 degree pulse used in the pulse sequence and inappropriate spoiler gradient strengths used for suppressions of the water signal and the metabolite signals outside of the voxel (16). To avoid these effects in a simple way for the interpretation of the spectrum, it is best recommended to locate the voxel where the contamination does not alter the spectral result or to adjust the strength of the spoiler gradients. A periodic calibration of the transmitter/receiver RF powers and a proper adjustment of the spoiler gradient strength can also minimize the distorted baseline and inappropriate suppression of the water signal problems.

Using the automated proton brain exam method which is well supported by a proper maintenance scheme of the MR instrument, ¹H-MRS can now offer an improved clinical utility. However, its usage is still limited to regions of the brain which are effected low by the susceptibility effect. As shown in Table 1, rates
of the APS success and percentages of obtaining the acceptable quality spectra are low for those regions affected by the susceptibility effect such as for the frontal white matter and pons regions. For these regions, the APS performance needs to be improved by modifying the pulse sequence and/or the exam protocol (unpublished results in this institution).

In conclusion, PROBE is a practical as well as a reliable method to produce the quality spectra for the 6 selected regions. PROBE can be used as a single spectroscopic exam or as an additional series to the routine brain MRI exam, which takes less than 10 minutes for acquisition of one spectrum. Although the spectral results are quite satisfactory, the rates of the APS success for every region of the brain still need to be improved. And, in order to obtain a good quality spectrum without an ambiguity for the data analysis, a good quality control scheme of the MR instrument is mandatory.

Acknowledgment
The authors express their sincere thanks to Sam Sung Medical System for a good maintenance of the GE 1.5T SIGNA MRI/MRS System in the Department of Diagnostic Radiology at Asan Medical Center, especially to Jong Hyun Yeon and his colleagues. And, the MR chief technician, Yong-Mun Lee, and all other MR technicians in the institution are greatly appreciated for their supports, interests, generosity for this study. The authors also thank to many physicians in the institution, especially Dr. Young Sang Lee, Dr. Dong Wan Seo, Dr. Jung Gyo Lee, and Dr. Ki Soo Kim for sending his patients for the MRS exams, and many residents and staff members for participating as volunteers.

REFERENCES
체적선택기법을 이용한 수소 자기공명분광법의 일상적인 임상응용1

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2 울산대학교 의과대학 서울중앙병원 진단방사선과

이정희1·최충곤2·김상태1·김진서2·문처웅1·서대철2·임태환1,2·오용호2

목 적: 자동화된 수소 자기공명분광법의 일상적인 임상에의 응용도를 측정하기 위하여, 정상인의 뇌의 여러부위에서 분광정보(spectrum)를 얻어 부위별 차이(the regional variation)와, 분광정보의 재현성(the reproducibility) 및 질조절(quality control)을 검사하였다.

대상 및 방법: 체적선택기법(Localization method)을 이용한 수소분광정보는 GE 1.5T SIGNA MRI/MRS 기기에서 PROBE (PROton Brain Exam)라고 하는 자동화된 분광기법을 사용하였다. 6개의 부위를 정상인 (N=25, age=23-65)의 뇌에서 정하였다: 후두부회질, 전두부백질, 두정부백질, 소뇌백질, 기저핵. STEAM을 이용한 체적선택기법을 아래의 조절치(parameter)와 함께 사용하였다: TE=30msec, TR=3.0sec, AVG=48, NEX=2, Spectral Width (SW)=2500 Hz, Size(SI) =2048 points (2K), the size of voxel=7-9 ml.

결 과: 본 연구에서 선정한 6개의 부위에서는, 부위별 차이가 분광정보상의 패턴의 차이와 대사물질간의 상대적인 비율의 차이로 명확하게 관찰되었다. 오토프리느캔(APS) 성공률과 우수한 질의 분광정보를 얻을 수 있는 비율은 두정부백질, 후두부회질, 기저핵 부위에서 우릴하였으며, 반면에 전두부백질과 뇌교부위에서는 낮았다.

결 론: PROBE를 이용한 수소 자기공명분광법은 매우 현실적이고 재현이 가능한 우수한 분광정보를 얻을 수 있는 신뢰있는 방법이다. PROBE는 한개의 분광정보를 얻는데 10분 이하의 시간을 들여 단독적으로나 일반적으로 사용되고 있는 자기영상법(MRI)의 추가 series로써 사용되어 질 수 있다. 우수한 질의 분광정보를 얻기 위하여서는 MR기기의 관리와 유지가 절대적으로 요구된다.
제18차 진단방사선과 전문의 연수강좌 안내

일 시 : 6월 22일(토)
장 소 : 용평리조트 드래곤 벨리 호텔
주소 : 강원도 평창군 도암면 용산리 130 (우) 232-950
전화 : 서울사무소 (02)561-6271 Fax (02)561-6272
용평사무소 (0347)35-5757
주 제 : 전산화단층촬영술
사전 등록 비 : 20,000원 (현장등록시 30,000원)
사전 등록 마감 : 1996년 4월 30일까지
사전 등록 처 : 본학회 사무국
전화 : (02)578-8003 Fax : (02)529-7113

일 정
6월 22일(토)

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