The Effect of Nuclear Overhauser Enhancement in Liver and Heart ^{31}P NMR Spectra Localized by 2D Chemical Shift Technique

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Purpose : To investigate the signal enhancement ratio by NOE effect on in vivo ^{31}P MRS in human heart muscle and liver. we also evaluated the enhancement ratios of different phosphorus metabolites, which are important in 31P MRS for each organ.

Materials and Methods : Ten normal subjects (M:F = 8:2, age range = 24-32 yrs) were included for in vivo ^{31}P MRS measurements on a 1.5 T whole-body MRI/MRS system using ^{1}H-^{31}P dual tuned surface coil. Two-dimensional Chemical Shift Imaging (2D CSI) pulse sequence for ^{31}P MRS was employed in all ^{31}P MRS measurements. First, ^{31}P MRS performed without NOE effect and then the same 2D CSI data acquisitions were repeated with NOE effect. After postprocessing the MRS raw data in the time domain, the signal enhancements in percent were estimated from the major metabolites.

Results : The calculated NOE enhancement for liver ^{31}P MRS were : α-ATP (7%), β-ATP (9%), γ-ATP (17%), Pi (1%), PDE (19%), and PME (31%). Because there is no creatine kinase activity in liver, PCr signal is absent. For cardiac ^{31}P MRS, whole body coil gave better scout images and thus better localization than surface coil. In ^{31}P cardiac multi-voxel spectra, DPG signal increased from left to right according to the amount of blood included. The calculated enhancement for cardiac ^{31}P MRS were : α-ATP (12%), β-ATP (19%), γ-ATP (30%), PCr (34%), Pi (20%), PDE (51%), and DPG (72%).

Conclusion : Our results revealed that the NOE effect was more pronounced in heart muscle than in liver with different coupling to 1H spin system and thus different heteronuclear cross-relaxation.

Index words : NOE, ^{31}PNMR, Liver, Heart

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I. Introduction

Magnetic resonance spectroscopy (MRS) is a unique, non-invasive tool with which to probe tissue metabolism (1-3). Because many pathologic processes are accompanying metabolic changes, MRS is potentially sensitive to such metabolic processes. MRS is therefore an attractive complementary method to characterize many diseases and to evaluate the outcome of therapeutic treatment. Although a variety of nuclei (^{1}H, ^{31}P, ^{19}F, ^{23}Na) and a variety of magnetic field strengths are available today, the clinical applications of MRS on a standard clinical 1.5 T scanner are focused on ^{1}H and ^{31}P MRS techniques. In vivo application of ^{31}P MRS demonstrated that signals from various phosphates involved with energy metabolism could be detected from muscle, liver, heart, and brain (4-7). Compared to ^{1}H MRS, phosphorus has a larger chemical shift range and a much lower sensitivity. Solvent suppression schemes are not required in ^{31}P MRS, but lower spatial resolution and increased examination times are required to achieve adequate signal-to-noise ratio (SNR).

Whereas the increase of SNR can be achieved by increasing magnetic field strength, the increase in field strength causes more patient safety problem. One way to increase SNR without increasing magnetic field strength is so-called "Nuclear Overhauser Enhancement (NOE)" effect (8-10). This principle states that if the spin under observation is coupled to another spin and this coupling is removed by saturation or decouping techniques, the spin under observation may undergo "cross-relaxation", in which the relaxation rate and the signal amplitude of the observed spin will be modified due to the irradiation of the secondary spin. This NOE effect in biological system is observed in ^{1}H decoupled-^{13}C observation or ^{1}H decoupled-^{31}P observation and can result in significant increase in signal amplitude. That is, irradiation of the tissue at the ^{1}H MR frequency prior to ^{31}P MRS data acquisition can produce substantial increase in phosphorus metabolite signals by means of the nuclear Overhauser enhancement effect. This new technique becomes recently available on clinical 1.5 T MRI/MRS unit.

The purpose of this study is twofold. First, we evaluate the signal enhancement ratio by NOE effect on in vivo ^{31}P MRS in human heart, and liver. Second, we estimate the enhancement ratios of different phosphorus metabolites, which is important in ^{31}P MRS for each organ.

Materials and Methods

Ten normal subjects (M:F = 8:2, age range = 24-32 yrs) for ^{31}P liver MRS and eight subjects (M:F = 7:1, age range = 22-28 yrs) for ^{31}P cardiac MRS were included in this study.

In vivo ^{31}P MRS measurements were performed on a 1.5 T whole-body MRI/MRS system (Siemens Vision Plus, Siemens Medical, Erlangen, Germany) using ^{1}H - ^{31}P dual tuned surface coil. This dual tuned coil was tuned to two RF fields (63.86 MHz for ^{1}H and 25.85 MHz for ^{31}P). T1-weighted ^{1}H MR images were first obtained for spectroscopic volume localization in three planes (axial, coronal, and sagittal plane) and the spatial localization was guided by axial MR images. Two-dimensional Chemical Shift Imaging (2D CSI) pulse sequence for ^{31}P MRS was employed in all ^{31}P MRS measurements. The sequence parameters were TR/TE = 323/2.3 msec, slice thickness = 40 mm and 8×8 phase encoding steps. This 2D CSI technique can therefore provide muti-voxel spectroscopic data within 20 minutes. For cardiac ^{31}P MRS, ECG gating was employed on both imaging sequence for scout images and 2D CSI for ^{31}P MRS. T1-weighted ^{1}H MR scout images were obtained using whole body coil instead of dual tuned surface coil for better image quality in cardiac MRS. First, ^{31}P MRS performed without NOE effect and then the same 2D CSI data acquisitions were repeated with NOE effect. After postprocessing the MRS raw data, the magnitude of signal was estimated

Table 1. The NOE enhancement ratio of major metabolites from liver and heart.

Metabolites	Chemical shift (ppm)	Liver	Heart
β-ATP	-16.3	9%	19%
α-ATP	-7.8	7%	12%
γ-ATP	-2.7	17%	30%
PCr	0	-	34%
PDE	2.6	19%	51%
Pi	4.9	1%	20%
PME	6.5	31%	-
DPG	6.3	-	72%

by measuring the peak area and the signal enhancements in percent were estimated from the major metabolites. The metabolites of interest are α-, β-, γ-adenosine triphosphate (ATP), inorganic phosphate (Pi), phosphocreatine (PCr), phosphodiester (PDE), and phosphomonoester (PME). The chemical shifts of metabolites are assigned following the values from the literature. For ^{31}P liver spectroscopy, PCr signal is absent due to no creatine kinase activity in liver. Diphosphoglycerate (DPG), which exhibits characteristic resonances at about 5.4 and 6.3 ppm relative to PCr, is often observed in ^{31}P cardiac MRS due to blood contamination.

Results

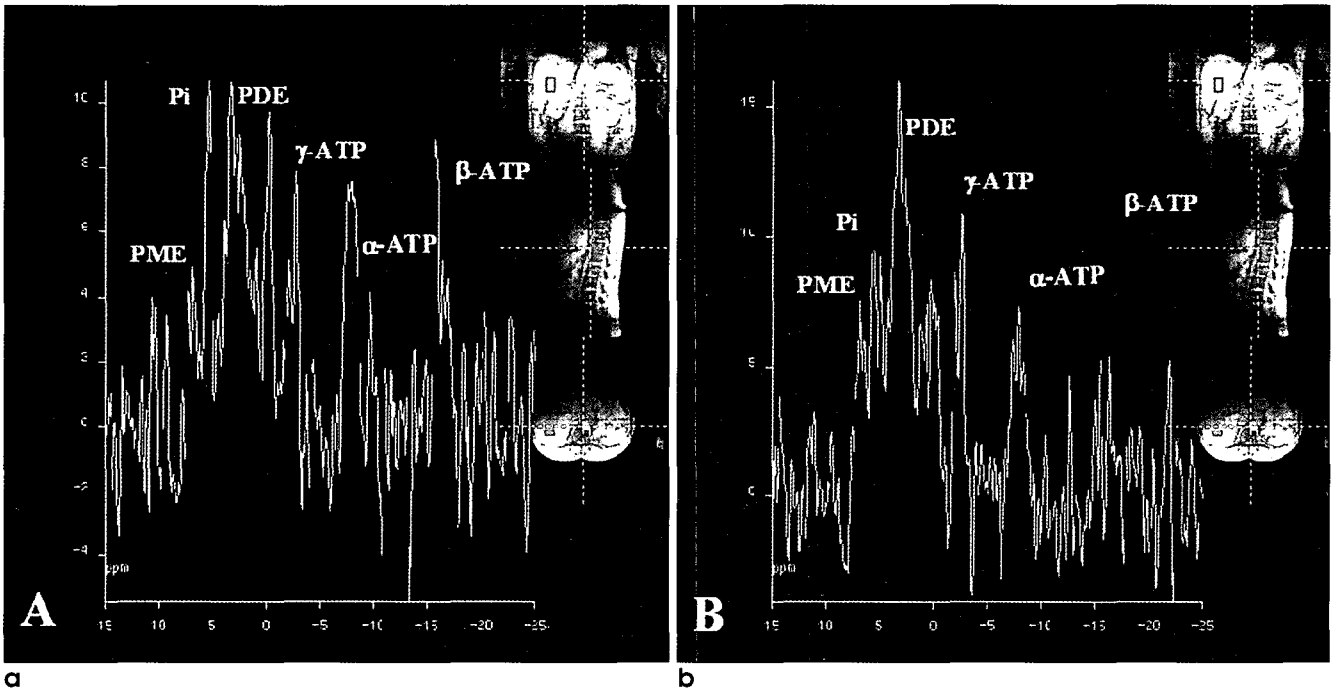
Figure 1 shows typical ^{31}P liver MR spectrum of normal volunteer with and without NOE effect. The significant signal enhancement was observed with NOE effect as seen in Figure 1. The calculated NOE enhancement for liver ^{31}P MRS were : α-ATP (7%), β-ATP (9%), γ-ATP (17%), Pi (1%), PDE (19%), and PME (31%). Because there is no creatine kinase activity in liver, PCr signal is absent. The signal enhancements of metabolites in two organs were summarized in Table 1.

For cardiac ^{31}P MRS, whole body coil gave better scout images and thus better localization than surface coil (Fig. 2). The typical ^{31}P cardiac MR spectrum with NOE effect is shown in Fig. 3. In multi-voxel spectra, DPG signal increases from left to right according to the amount of blood included. Therefore, it is clear that DPG is the signal not from myocardium but from blood. The calculated enhancement for cardiac ^{31}P MRS were : α-ATP (12%), β-ATP (19%), γ-ATP (30%), PCr (34%), Pi (20%), PDE (51%), and DPG (72%). The most enhanced metabolite in heart was DPG signal.

In all ^{31}P MR spectra regardless of organ type, there is no change in chemical shift due to NOE effect. This shows that NOE effect dose not change intracellular pH, which can be estimated by the chemical shift of Pi.

Discussion and Conclusion

Phosphorus MR spectroscopy offers a unique opportunity to investigate cellular energy metabolism (11-13). ^{31}P MRS has been used to investigate energy metabolism in brain, muscle, liver, prostate and breast tumors. A distinctive feature of phosphorus spectra from organs other than brain and muscle is that they do not contain a PCr peak due to the absence of



a b

Fig. 1. The liver ^{31}P MRS. The spectrum without NOE (**A**) and with NOE effect (**B**) showed that the signals from major metabolites increased after 1H decoupling. Note the scale difference in (**A**) and (**B**).

creatine kinase activity. However, its low sensitivity compared to ^{1}H in biological system is often limiting factor of ^{31}P MRS in clinical use. Therefore, the motivation for increasing signal-to-noise ratio (SNR) of ^{31}P MR spectrum is apparent and so higher magnetic field strength is often prefered. The spectroscopic studies at higher magnetic field provide larger chemical shift (better spectral resolution) and higher signal amplitude. Beside of safety concern, however, high magnetic field is possibly problematic in organs such as liver and heart due to susceptibility artifact. Especially, liver has relatively high content of iron. Therefore, it is desirable to find a way to increase signal amplitude without increasing field strength.

The nuclear overhauser enhancement effect, which is a way to increase signal amplitude without increasing field strength, is resulting from heteronuclear cross-relaxation. That is, if a spin system is coupled to another spin system and this coupling is removed by saturation or "decoupling" techniques, the spin system under observation may undergo "cross-relaxation" in which the relaxation rate and the signal amplitude of the observed spin will be modified due to the irradiation of the secondary spin. It is observed in ^{1}H decoupled ^{13}C NMR or ^{1}H decoupled ^{31}P NMR studies and can result in a significant increase in signal amplitude, as much as 100% signal increase for the ^{31}P spins attached to the ^{1}H spins. Previous in vivo ^{31}P-^{1}H double resonance NMR studies on human skeletal muscle tissue revealed that ^{31}P MR signal enhancements of up to 70% by NOE effect (14). For maximizing NOE effect, the bandwidth of rf pulses and the energy distribution of the rf power throughout the range of frequencies used must be carefully adjusted to ensure all the coupling nuclei are properly excited. Often mismatch in the NOE preparation lead to less effective decoupling and thus to loss of signal-to-noise ratio in the resultant spectrum.

In this study, we evaluated the ^{31}P MR signal enhancements with NOE effect in liver and

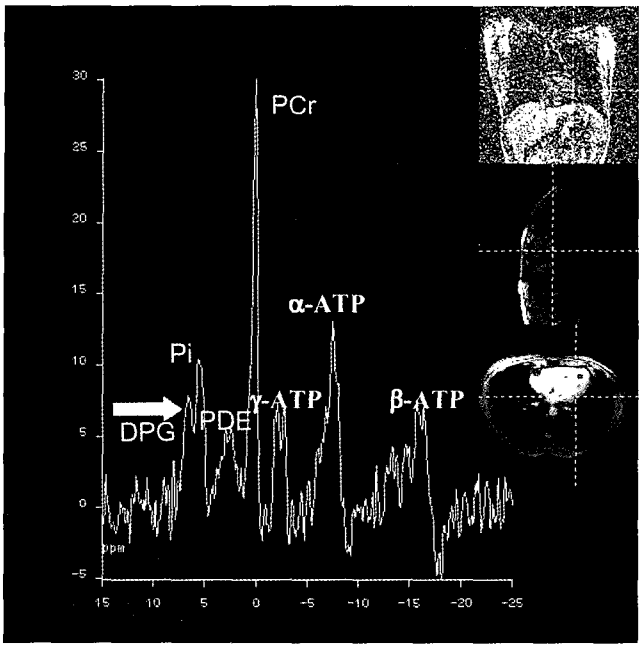


Fig. 3. The typical NOE enhanced ^{31}P cardiac MRS. The blood 2,3-diphosphoglycerate (DPG) signal is overlapped with PME signal.

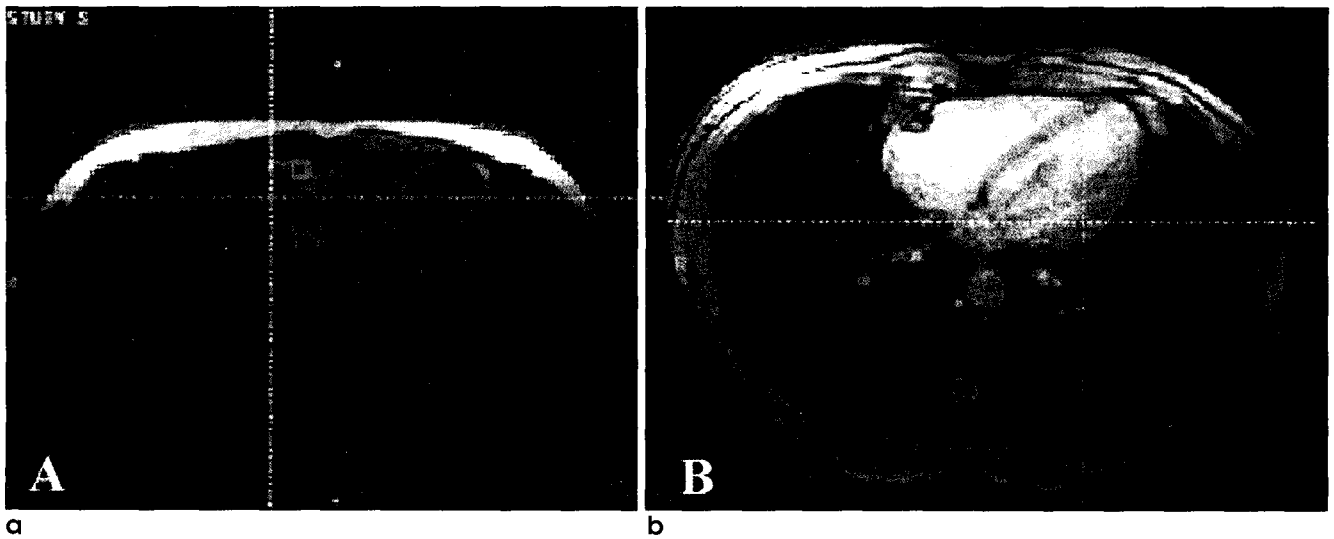


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Fig. 2. The scout image obtained with 31P-1H dual tune surface coil (**A**) and with whole volume coil (**B**).

myocardium. Our results showed that the NOE effect is more pronounced in heart muscle than in liver. That is, all metabolites in heart muscle showed the higher signal enhancement than the corresponding metabolites in liver. This results suggested that the same metabolite (for example, ATP) in different organs has different coupling to ^{1}H spin system and thus different heteronuclear cross-relaxation. Also, the different metabolites in the same organ showed different NOE effects. For liver, PME showed highest NOE enhancement among metabolites. This result again suggested that each metabolite has different coupling scheme between ^{1}H and ^{31}P spin system. Therefore, in addition to biochemical informations provided by ^{31}P MRS, the NOE measurement provides further information on metabolite activity and seems to extend our understanding on energy metabolism of human organ.

Another aspect of ^{1}H decoupled ^{31}P MRS technique is the spectral resolution. For in vivo MRS, metabolite line widths are broader (poorer resolution) than in vitro due to magnetic susceptibilities, subject motion, and gradient eddy currents. ^{1}H decoupling, although providing more biochemical information, also complicates spectra quantification. The phosphomonoesters (PME) and phosphodiesters (PDE) which are single peaks without ^{1}H decoupling become multiple peaks after decoupling. With a greater number of peaks in the decoupled spectrum and each with a lower SNR than the original sum, the quantification of the spectrum is more difficult than in coupled ^{31}P in vivo spectra. Therefore, in vivo proton decoupled phosphorous NMR spectra can pose a number challenges in the area of quantification.

In summary, we investigated the NOE effect in ^{1}H decoupled ^{31}P MR spectroscopy in liver and heart. Our results revealed that the NOE effect could provide one way to increase metabolites signal without increasing magnetic field strength. This increase in signal intensity will give better identification of each metabolites or reduce the number of acquisition (and so total scan time) without much loss of signal intensity. In addition, we also found that the NOE effect was more pronounced in heart muscle than in liver with different coupling to ^{1}H spin system and thus different heteronuclear cross-relaxation.

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대한자기공명의과학회지 8:94-99(2004)

이차원 화학변위 기법을 이용한 간 및 심장 ^{31}P 자기공명분광에서의 Nuclear Overhauser 효과에 대한 연구

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목적: 인체의 심근 및 간조직의 생체내 ^{31}P MRS에서 NOE 효과에 의한 분광신호 세기의 증가를 평가하고자 하였으며 또한 동일 장기에서 대사물질에 따른 NOE 효과의 차이를 알아보고자 하였다.

대상 및 방법: 열명의 정상 성인군(남:여 = 8:2, 연령분포= 24-32)을 대상으로 1.5T 자기공명영상/분광 장치에서 ^{1}H - ^{31}P 이중 튜닝 표면 코일을 사용하여 생체내 ^{31}P MRS를 시행하였다. ^{31}P MRS 측정은 이차원 화학변위영상기법을 사용하였으며 동일한 파라미터에서 NOE 효과 없이 그리고 ^{1}H decoupling 상태에서 NOE 효과에 의한 ^{31}P MRS 데이터를 획득하였다. ^{31}P MRS raw data의 postprocessing 후 얻어진 스펙트럼에서 주요 대사물질들의 신호증가를 비교하였다.

결과: 간조직의 ^{31}P MRS에서 NOE 효과에 의한 신호증가율은 α-ATP (7%), β-ATP (9%), γ-ATP (17%), Pi (1%), PDE (19%), PME (31%) 였다. 간조직의 경우 크리아틴 키나제가 없기 때문에 PCr 신호는 관찰되지 않았다. 심근의 ^{31}P MRS은 whole body 코일이 표면 코일보다 우수한 scout 영상을 제공하여 ^{31}P MRS의 localization에 유리하였다. ^{31}P 심근 다중 체적 스펙트럼에서, 혈액의 DPG 신호는 심근으로부터 멀어질 수록 증가하는 양상을 나타내었고 NOE 효과에 의한 신호증가율은 α-ATP (12%), β-ATP (19%), γ-ATP (30%), PCr (34%), Pi (20%), PDE (51%), DPG (72%) 였다.

결론: 간조직에 비해 심근의 경우 큰 신호증가를 보였고 이는 간조직 대사물질들의 ^{31}P가 심근과는 다른 ^{1}H coupling을 나타냄을 의미한다고 해석할 수 있다.

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