^{31}P T_1 measurement using ISIS with simultaneously measured spin-echo and stimulated-echo (ISIS-sSESTE)

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INTRODUCTION: Creatine Kinase (CK) is widely present in human tissues such as brain and skeletal muscle. It catalyzes the transfer of a phosphate group between phosphocreatine (PCr) and adenosine diphosphate (ATP) which is described by formula: $PCr^{2-} + ADP^{-} + H^{+} \overset{CK}{\Leftrightarrow} Cr + ATP^{2-}$, whereas ATP is an energy source for normal brain functioning. Thus CK reaction rate constant (k_f) is an indicator of the neuronal activity in brain. The measurement of k_f can provide some insight about the brain chemistry, which may be an important biomarker to understand the neuropathology in patients with mental disorder. A recently revised method using ISIS and a saturation recovery process [1] provides accurate measurement of CK reaction rate constant within 40 min data acquisition, which is mostly spent to measure the apparent T_1 relaxation time. Although magnetization-transfer ^{31}P-MR spectroscopy may be a powerful tool to evaluate the high-energy phosphate (HEP) activity in the brain, the long acquisition time prevents its routine application in clinical setting. To shorten the acquisition time, rapid measurement of T_1 of PCr is required. Typically ^{31}P MRS uses a large voxel to improve the signal to noise ratio with an expense of increased RF field inhomogeneity within the voxel. Although RF field inhomogeneity on proton imaging with smaller voxel size has been successfully corrected by employing the SESTEPI technique [2], RF inhomogeneity correction on larger voxel is still a major challenge to researchers on single voxel ^{31}P MR spectroscopy. In this report, a new pulse sequence "ISIS with simultaneous spin echo and stimulated Echo (ISIS-sSESTE)" is developed to rapidly measure the T_1 relaxation time of phosphorus compound in ^{31}P MR spectroscopy.

METHOD: The hard 90^o RF excitation pulse in the ISIS was replaced by three 90^o RF pulses to simultaneously measure a spin-echo (SE) and a stimulated-echo (STE), as shown in Fig. 1a. OVS and ISIS inversion indicate the outer-volume-suppression and three phase-cycled adiabatic inversion pulses with 4 kHz bandwidth for the voxel localization, respectively. If the second RF pulse is perfect 90^o, one half of the transverse magnetization, which undergoes dephasing during between the first two RF pulses, is restored along the longitudinal direction, and other half is used to form a spin-echo at TE. The third 90^o pulse flips the longitudinal magnetization, which is a mixture of the restored magnetization that experiences T_1 decay and the freshly recovered magnetizations during the mixing time TM. Two crusher gradients that are applied just before the second RF pulse and after the third RF pulse, respectively, play the crucial role to selectively form a STE from the restored magnetization while spoiling the freshly recovered magnetization. The relationship between the signal intensities of SE and STE satisfies $S_{STE} = S_{SE} \cdot e^{-TM/T_1}$ under the assumption of perfect 90^o RF pulses, from which T_1 can be determined by $TM/\ln(S_{SE}/S_{STE})$. However, due to RF field spatial inhomogeneity, RF flip angle may spread out around 90^o in the volume of interest (VOI), particularly with large voxel size. Simulation on T_1 relaxation time with respect to the actual RF flip angle without RF field inhomogeneity correction has been performed based on the paper [2]. The plot is shown as Fig.1c, where intrinsic T_1 value is assumed to be 4 second. T_1 measurement was conducted on a spherical phantom filled with a phosphate solution (Braino phantom by General Electric, Waukesha, WI) to measure the T_1 relaxation time using the ISIS-sSESTE with either B_1-independent-rotation (BIR4) [3] or hard RF pulses. Spectroscopic voxel was chosen at the center and edge of the phantom with dimensions of 8x8x8 cm^3 and 4x4x4 cm^3. Protocol parameters for ISIS-sSESTE pulse sequence are TR 20 s, TE 6.56 ms, TM 2.5 s, receiver bandwidth 2.5 kHz, and vector size 1024. T_1 was also measured using saturation recovery method [1]. Protocol parameters for saturation recovery method are receiver bandwidth 2.5 kHz, vector size 1024, TE 6.56 ms, and various saturation duration times (t_{sat}=0.5, 1, 2, 4, 8, and 16 second). All studies were performed on a 3 T clinical MRI system (Trio-Tim, Siemens Medical Solutions, Erlangen, Germany) with Avanto gradients (40 mT/m strength and 150 T/m/s slew rate) using a ^{31}P/^{1}H double-tuned volume head coil (Clinical MR Solutions, LLC, Brookfield, WI, USA). All FID data are preprocessed using a home-made software programmed in MatLab, with 5 Hz Lorenzian line broadening, zerofilling, FFT, and. the zero-order phase correction. The integral of the PCr peak was used as the PCr signal intensity.

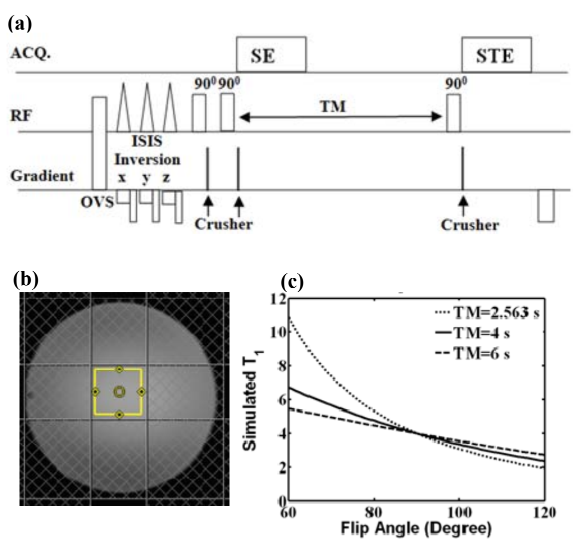

Table 1. List of measured T_1 relaxation time (second) of PCr in Braino phantom.

Technique	Saturation Recovery method		ISIS-sSESTE	
90^0 RF Pulse Type	Hard	BIR4	Hard	BIR4
Voxel size 4x4x4 cm^3 at Braino Center	3.55	3.93	11.57	5.00
Voxel size 4x4x4 cm^3 at Braino Edge	3.64	4.08	9.54	4.33
Voxel size 8x8x8 cm^3 at Braino Center	3.74	3.81	13.56	4.77

Figure 1: (a) ISIS-sSESTE pulse sequence diagram: OVS band is followed by phase cycling ISIS inversion to localize the voxel position. PCr is selected as reference compound in 31P MR spectroscopy. (b) Location of voxel and OVS band. (c) Simulated T_1 without RF field inhomogeneity correction based on SESTEI method. Assume intrinsic T_1 is 4 second, 90^0 RF Flip angle shows consistent simulated T_1 with different TM.

RESULT & DISCUSSIONS: Fig.1c shows the theoretical predication of T_1 underestimation or overestimation with various RF flip angle without RF field inhomogeneity correction. Measured T_1 is overestimated for the smaller flipangle with all values of TM. It is severely over-estimated with small TM and small actual flipangle. Table 1 lists the measured T_1 values of phantom PCr with saturation recovery method and ISIS-sSESTE. In saturation recovery method, measured T_1 are similar with hard or BIR4 excitation and can be regarded as intrinsic T_1 (~4 second) of PCr in Braino phantom. T_1 calculated from ISIS-sSESTE with Hard RF pulse shows heavy deviation from 4 s. Relatively BIR4 RF pulse application shows great improvement of T_1 measurement accuracy. To further improve the accuracy of T_1 value, the RF homogeneity may need to be improved using alternative BRI4 RF pulses with different B_1 amplitude.

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REFERENCES: [1] EK Jeong et al. NMR in Biomed. In press. [2] XF Shi et al. Magn. Reson. Med. 2010(64):734-742. [3] Matlab code to generate BIR4 waveform was provided by Dr. Ouwerkerk at Johns Hopkins University.