Journal of the Korean Magnetic Resonance Society 1997, 1, 7-20

T_2 Relaxographic Mapping using 8-echo CPMG MRI Pulse Sequence

E.-K. Jeong*, S.-H. Lee†, J.-S. Suh Y.-Y. Kwak‡, S.-A. Shin‡, and Y.-K. Kwon§, Y. Huh§

Department of Diagnostic Radiology,Yonsei University, Seoul, Korea
†Department of Physics ,Yonsei University, Seoul, Korea
‡Department of Physics, Ehwa Women's University
§Applied Superconductivity Lab.,
Korean Electrotechnology Research Institute
Received March 3, 1997

Abstract: The mapping of the spin-spin relaxation time T2 in pixel-by-pixel was suggested as a quantitative diagnostic tool in medicine. Although the CPMG pulse sequence has been known to be the best pulse sequence for T2 measurement in physics NMR, the supplied pulse sequence by the manufacture of MRI system was able to obtain the maximum of 4 CPMG images. Eight or more images with different echo time TEs are required to construct a reliable T2 map, so that two or more acquisitions were required, which easily took more than 10 minutes. 4-echo CPMG imaging pulse sequence was modified to generate the maximum of 8 MR images with evenly spaced echo time TEs. In human MR imaging, since patients tend to move at least several pixels between the different acquisitions, 8-echo CPMG imaging sequence reduces the acquisition time and may remove any misregistration of each pixel's signal for the fitting of T2. The resultant T2 maps using the theoretically simulated images and using the MR images of the human brain suggested that 8 echo CPMG sequence with short echo spacing such as 17~20 msec can give the reliable T2 map.

INTRODUCTION

Magnetic resonance image (MRI) is one of the major imaging modalities in diagnosing the diseases in medicine, owing to its superior soft tissue contrast and non-destructive nature to other imaging techniques such as X-CT and ultrasonography. The signal intensities across the obtained plane are functions of many scanning parameters such as repetition time TR, echo time TE, slice thickness, receiver bandwidth, etc. The discrimination among different organs or between normal and abnormal tissues is visually accomplished via the difference in the signal intensities (contrast) among them on T_1 and T_2 weighted images.[1] When there would be any disease proceeding in certain tissue, the chemical and physical environment surrounding the water protons alters the local magnetic field, and results in changing the proton relaxation times. The MR images look different for different parameters and for different vendor's MR system, but the relaxation times T_1 and T_2 should stay the same as long as the field strength and the temperature of the subject remain the same.

The quantification of the relaxation time by mapping their values has been considered to give the more precise tissue characteristics for certain abnormality.[2-5] The T_2 relaxation time has been used in medical imaging by measuring the average value for a specific region of interest, in medicine. Lately, the mapping of the relaxation times (T_1 and T_2) in pixel-by-pixel was suggested as a new contrast technique for the quantitative analysis. R. Grunewald reported the possible application of the T_2 relaxography in determining the seizure foci for the hippocampal epilepsy.[6] G.P. Liney applied the T_2 mapping method to the human prostate.[7] In medical imaging of the human organ, T_2 relaxogram represents the magnetic environment of the protons in the water molecules in tissues. However the reliability and the accuracy of the resulting T_2 maps depend very much upon how the MR image data are acquired, so that the absolute quantification of certain tissue may be very difficult. However, the in-site quantification using the common scanning parameters may be used as a clinical tool.

The major sources of the error for the resulting maps is the random noise and the inconsistent registration of the signal in space due to the inconsistent patient position while being imaged. The noise tends to enlarge the fitted T_1, which requires the non-linear curve fitting.[8]

CPMG pulse sequence is commonly used to acquire a series of MR images with different TEs, and the obtained data set is used to fit the spin-spin relaxation time T_2. Even though 100 or more CPMG echoes are acquired in the in-vitro NMR system to measure T_2 value, it is not practical in MR imaging of human body to acquire that many echoes. The minimum echo-spacing is typically 10msec or longer in today's most update MRI system, so that the most of the transverse magnetization will be decayed off after 1 few tens of echoes.

At least 8 or more images are required with the same scanning parameters including possibly the long repetition time TR, except for the echo times TE. The echo time TEs are to be distributed over the expected T_2, with evenly spaced. T_2 relaxogram can then be calculated in pixel-by-pixel, by mathematically fitting the signal intensities of the series of MR images using the suitable linear least square algorithm.[10,11] In general, single T_2 component is assumed for each pixel, which is a good approximation to the real component for fat-suppressed image.

For the standard T_2 mapping of brain, the spatial resolution is typically 0.781mm/pixel, which is far smaller than the physiological motion, so that any physiological motion during imaging can easily spread the signal intensity of a pixel across the several pixels. This can cause the severe error in fitting T_2 values near the interfaces among different organs and between the normal and abnormal tissues, where their signal intensities vary abruptly.[8,12] The pulse sequence provided by the MR manufactures typically acquires the maximum of 4 CPMG echoes, which yields the maximum of 4 MR images with different echo times, so that two or more separate acquisitions are necessary for the reliable results. 8-echo CPMG imaging pulse sequence was developed and the advantage of 8-echo CPMG over 4-echo pulse sequence was examined.

The effect of random noise will be reported in this article. Artificial images, which were simulated from an MR image for different TEs and with some fraction of random noise introduced, were used to evaluate the noise effect on T_2 fitting. The random noise, artificially introduced into the simulated images, has the gaussian distribution with the mean value of zero and the standard distribution of one.

METHOD AND MATERIALS

Phantoms

A mixture of 44 % glycerin and distilled water was prepared in the 2cm OD/10 cm length plastic bottle. The T_1 relaxation time of protons of this concentration was about 700 msec. The obtain image was used for the simulation of images.

MR imaging

GE's Signa Horizon (General Electric Inc., Milwaukee, Wisconsin, USA)with 1.5T superconducting magnet and scanning software version 5.5 was used for imaging. The 4 echo spin-echo pulse sequence, i.e., 4 echo CPMG, supplied by the manufacture was modified to yield 8 images with evenly spaced TEs. A proprietary software EPIC™ supplied by GE was utilized for the programming of pulse sequence. TEs for the T_2 mapping were ranged in 20 ~ 160 msec, with evenly spaced echo-spacing. Rf pulses including 90° and all refocusing 180° were slice selective, and their pulse width were 3.2 msec. 4 or more slices were imaged at the same time.

To study the effect of the echo-spacing, 20 and 40msec echo spacings were used for the same slice location and thickness of a human subject. The echo time TEs of the acquired images were extended as long as 160 and 320 msec for 20 and 40 msec echo spacings respectively. All 8 images used to calculate T_2 map for 20 msec echo-spacing. For 40 msec echo-spacing, two T_2 maps were constructed, one using all 8 images and the other using 5 selected images with TEs up to 200 msec.

The typical imaging parameters, which is used for patient imaging, were followings: TR = 2500 ms, slice thickness = 4 mm, receiver bandwidth = 16 kHz, and FOV = 20 or 16 cm. The GE's head coil (quadrature polarized birdcage coil) was used for imaging of both phantom and human head.

Simulation

An arbitrary MR image of the phantom was used as a theoretical proton density image, for generating of various images with different TEs, T_2, and noise. T_2s used for the simulation were 50, 100 msec, and the random noise of 1, 5, 10 % were embedded into each simulated image. For example, the signal intensity of a coordinate for an echo time TE, the transverse relaxation time T_2, and the noise R, is,

$$S\,(TE\,) = S_o e^{-TE\,/T_2} \left|1 + R\delta\right| \qquad [1]$$

where δ is a random number with gaussian distribution. 11 images whose echo times were 10, 20, 40, 60, 80, 100, 120, 140, 160, 200, 240 msec, were generated for every set of T_2 and the noise.

The simulated data sets were then used to fit T_2 values by the linear-least-square fit (LLS) in pixel-by-pixel, and the mean value and the standard deviation were measured for some region of interest (ROI) from the fitted T_2 maps. The measured T_2 values were then compared with the theoretical T_2 values, which was used for the simulation of data sets.

These simulated data sets were fitted to the T_2 decay equation, and T_2 and χ^2 maps were generated. The algorithm and the threshold value were kept fixed for all noises and T_2 values.

Fitting program

The measured signal intensity for the obtained MR image data was assumed to satisfy the following equation with a single T_2 and T_1; $S(TE,TR) = S_o e^{-TE/T_2}(1-e^{-TR/T_1})$. The T_1 recovery term in the parenthesis was neglected by long TR = 2500 msec. The fitting procedure returned two values for each pixel: T_2 values that minimized χ^2 and the resultant χ^2. These two values formed two separate images, T_2 map and χ^2 map. The program was tested by applying to a simulated data set with no noise, and gave the exactly same value as the simulation.

The image data were converted by logarithmic function *ln* (= log_e) for the simplicity, since *lnS(t)* is linear with the echo-time *TE*. T_2 fitting routine was programmed using a popular linear-least-square fitting algorithm in IDL (Interactive Data Language, Research System Inc., Boulder, Colorado, USA), and in C.[11]

RESULTS

T_2 values measured from a ROI of the calculated T_2 maps were listed in Table 1, with respect to the theoretical T_2 and the noise fraction embedded into the simulated data. TEs were same for all T_2s, ranging 10 ~ 240 msec. The area of the ROI was about 50 % of the whole phantom image, in most homogeneous region.

Table 1: Caculated T_2 Values (in msec) Measured from the T_2 maps for Different Noise and T_2 used for the Simulation of the Data Sets.

Noise / T_2 (msec)	1%	5%	10%
50	52.3±1.10	58.8±4.46	65.7±8.38
100	102.3±1.38	111.7±6.52	121.5±12.7

Table 2. Means and Standard Deviations(msec) for ROI 1 and 2 of Maps in Fig. 1.

Image # / ROI #	*a*	*b*	*c*
ROI 1	54.2±3.70	66.6±6.90	72.4±11.4
ROI 2	56.8±5.60	69.4±8.31	72.3±15.7

Fig. 1 displays T_2 maps of the echo-spacings (a) 20 and (b,c) 40 msec. All the MR imaging parameters were fixed for the source images of (a) and (b,c), except for the echo spacings. The source images for the T_2 map (c) include several noisy images with long TEs, such as 240, 280, 320 msec. The map (b) was constructed with 5 selected images from 8 images used for the T_2 map (c), whose TEs were 40, 80, 120, 160, and 200 msec.

The mean T_2 values and the standard deviations for ROI 1 and ROI 2 were measured for all three maps in Fig. 1, and listed in Table 2.

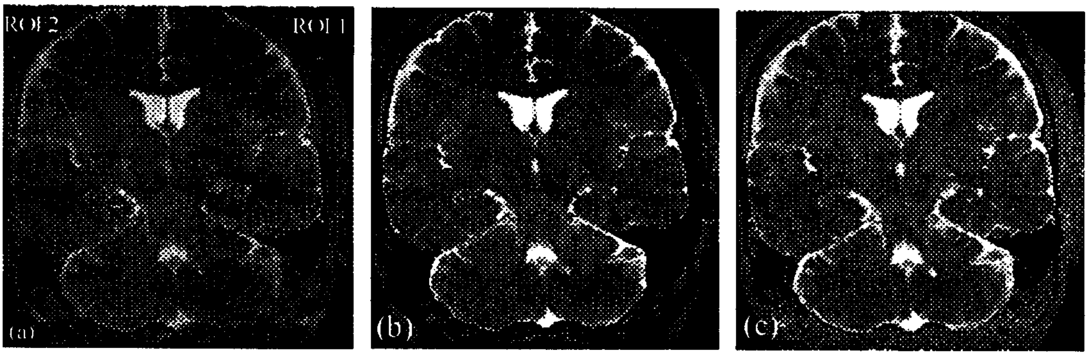


Fig. 1. T_2 maps of a normal volunteer. The echo spacings are (a) 20 and (b,c) 40 msec. 5 images with TEs of 40, 80, 120, 160, and 200 msec were used to generate the T_2 map (b), while all 8 images, whose TEs extend up to 320 msec, were used for (c). The mean T_2 values and the standard deviations for ROI 1 and 2 are listed in Table 2.

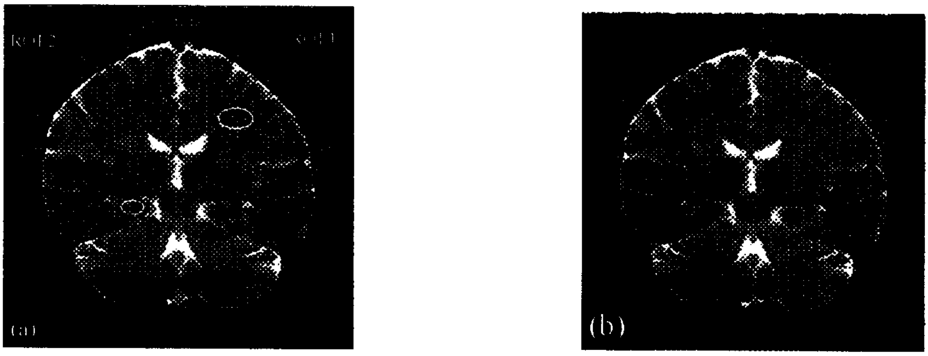
Table 3. Means and Standard Deviations of two ROIs in Fig. 2.

Image # / *ROI #*	*(a)*	*(b)*
1	62.3±2.74	73.9±2.60
2	65.2±5.21	84.0±6.89

Images (a) and (b) in Fig. 2 represent the T_2 maps of a volunteer, for the same slice location. Image (a) was constructed from 8 echoes with TEs of 20~160 msec with 20 msec echo-spacing. Image (b) was constructed from 8 echoes, which were selected from 12 images obtained by three consecutive data acquisitions with 4-echo CPMG pulse sequence. The TEs for image (b) were 17, 39, 68, 78, 92, 117, 138, 156 msec, which were selected as close to those of 8 echo CPMG. The total scanning times for the data set (a) and (b) were about 5 and 17 minutes respectively for 128 phase-encoding matrix with 1 NEX (number signal averages).

Table 3 listed the means and the standrad deviations of the selected ROIs in the

T_2 maps (a) and (b) of Fig.2.



T_2

Fig. 2. T_2 maps of a volunteer: (a) was constructed with 8 images obtained using 8-echo CPMG, and (b) with 8 images selected from three different consecutive acquisitions.

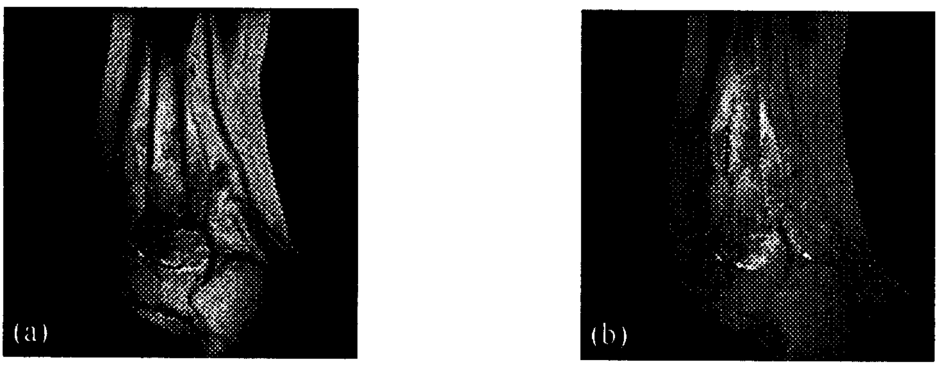


Fig. 3. (a) T_2 weighted image and (b) T_2 map of a patient with the osteosarcoma. Image (a), which was one of the source images for calculating T_2 map (b), was obtained with TR/TE = 2500/80 msec. The T_2 map (b) may be used for characterizing the local pathologic information in the tumor area.

Images in Fig. 3 are, (a) a T_2 weighted image with TR/TE = 2500/80 msec, and (b) the T_2 map calculated using 8 images including the image (a), of a patient with osteosarcoma. The patient was treated with chemotherapy. The tumor showed the necrotic regions and the area with the viable tumor cell. Although the T_2 weighted image (a) is one of the popular method for visual discrimination of the abnormality, the T_2 map may be used to obtain the information about the tissue characteristics.

DISCUSSION

The signal intensity of a spin-echo image is a function of TE, TR, T_2, and T_1, as written in following equation.[1,9,13]

$$S(TR,TE) = S_o e^{-TE/T_2}[1 - e^{-(TR-TE_{max})/T_1}] \qquad [2]$$

where TE is the echo time, TE_{max} the echo time of the last echo, and TR the repetition time. As long as the TR is long enough, for example, 3 or 4 times of the T_1 of tissue water, the term in the square bracket may be neglected. Since the purpose of the T_2 relaxographic mapping is to obtain the threshold value of the normal/abnormal change and T_1 of the tissue with large water contents becomes larger than that of the normal tissue, long TR (at least 3 times of average T_1) was necessary. (NOTE: T_1 of the normal tissues ranges in 500~1000 msec.) But the long TR results in the long imaging time and the obtained images may be corrupted due to the patient's motion, so that 2500 msec TR was selected as a reasonably long TR. Then the equation above may be approximated as

$$S(TE:T_2) = S_o e^{-TE/T_2} \qquad [3]$$

neglecting the difference due to the different T_1 recoveries.

All T_2 maps were fitted to above equation (3), which became a linear equation after taking logarithmic conversion. The fitting process of an 8 echo images took about 2 minutes on a SPARC20 workstation (single 70 MHz SuperSPARC CPU and 64 MB RAM; SUN Microsystem, Mountain View, California, USA) using IDL. The calculation time may be reduced by programming in C, which requires more programming skill.

The fitted T_2 values and the errors increased as the noise in the images data increased. Since the image data sets used for the fitting were simulated with the identical T_2 value for all pixels, the errors in the fitted T_2 maps must come from the noise in the images. As for the non-linear curve fitting of T_1,[8] the more noise was acquired in the images data, the larger the fitted T_2 became. The amount of the noise in the image with the different TE remained the same, while the signal intensity decreased exponentially as in e^{-TE/T_2}, so that the SNR of a simulated image with the echo-time TE decreased e^{-TE/T_2}. This data sets reflected the noise of the MR images, since the source of the noise in the MR images, obtained at the same scan with 8-echo CPMG, remained the same in the actual scanning of a patient images.

T_2 maps (a), (b), and (c) in Fig. 1 show the significantly different appearance. Comparing the maps (a) and (c) which were constructed from 8 images with different echo-spacings, images with 40 msec echo-spacing gave noisier T_2 map. And the mean T_2 values of ROI 1 and 2 were about 40 % larger than those of 20 msec. By neglecting images with long TEs (TE = 240, 280, 320 msec), the resultant T_2 map had the mean T_2 closer to that of (a) and less standard deviation than that of (c). As for the T_2 maps of the simulated images in Table 1, the actual images with TE of 240 msec or longer has almost no signal left especially for the tissues with short T_2 but the amount of the noise was the same as the image with TE = 20 msec.

Since the longest echo time for the map (a) was 160 msec which was much longer the calculated T_2 of the selected region and the data set include a few images with relatively short TEs (20, 40, 60 msec) compared to T_2, T_2 map (a) may be considered as the closer to the true T_2 map than maps (b) and (c). As the result, the images with the short echo-spacing and with the several short TEs may be necessary for the accurate T_2 mapping.

The images (a) and (b) in Fig. 2 does not show any visible difference, but the quantitative measurements of ROI 1 and 2 listed in Table 3 showed the significant change. Even though the data sets for T_2 maps (a) and (b) had similar TEs, the mean T_2 of (b) for both ROIs are about 20 % larger than those of (a), with much larger standard deviation. Not only the imaging time is longer, but also the fitted result is less accurate with the 4-echo CPMG imaging pulse sequence than with the 8-echo CPMG.

CONCLUSION

The 8-echo CPMG imaging pulse sequence was developed for the clinical MR imaging system, and used for data acquisition of the T_2 mapping. The manufacture supplied pulse sequence was only able to obtain the maximum of 4 CPMG images. Eight or more images with the different TEs were required for the reliable T_2 mapping. Using the standard 4-echo CPMG pulse sequence, two acquisitions taking longer than 10 minutes were required, while 8-echo CPMG reduced the scanning time by half.

The 8 images with less echo-spacing gave more accurate T_2 map and less error than the longer echo-spacing. For applying T_2 mapping to the human subject, images with small echo spacing need to be required. This pulse sequence may be used for

MR characterization of the abnormal tissues for various anatomies, but before being applied for the routine diagnosis, more intensive study is yet to be performed.

Acknowledgements

This work was supported partly by a fund from Korean Electrotechnology Research Institute, a grant from Yonsei University, Basic Science Research Institute Program from Korean Ministry of Education (KOSEF through SPRC, 1996, Project No. 2424), and a fund from Samsung GE Medical System.

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