A Breathhold Technique for T2 Quantification Utilizing Echo Sharing for Efficient Sampling

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Introduction: Chronic transfusion therapy is used in patients with sickle cell disease to avoid further complications of the disease. However, repeated red blood cell transfusions lead to iron accumulation in key tissues such as the heart and the liver, interfering with normal tissue function in a progressive manner that may be life-threatening. Monitoring iron content in the body is critical for management of the iron chelation therapy. While liver biopsy is still the gold standard for iron assessment, there have been tremendous efforts over the past decade to develop accurate and reliable, non-invasive methods for serial quantification of body iron burden based on MR relaxometry. The first method used in clinical studies was developed by Clark and St. Pierre [1] and is based on R2 quantification of liver tissue: several spin echo images are acquired at different echo times (TE) and are used to calculate T2; the acquisition time of about 20-30 min leaves this method susceptible to motion artifacts, image misregistration, reduced patient tolerance and leads to the quest for alternative methods. R2* quantification is now commonly used for iron quantification in heart and liver due to its acquisition within a single breathhold [2]. T2* relaxation times in iron-overloaded organs may however not only be increased by iron deposition, but also be affected by imperfect shimming, local field inhomogeneities, susceptibility gradients etc. These contributions introduce uncertainty to the R2* based iron evaluation in patients. Thus, recent work has focused on the development of multiple TE breathhold Turbo Spin Echo (TSE) sequences for improved T2 quantification in moving organs such as the liver and the heart [3]. This work presents our first results with a further methodological development of this technique, which by means of echo sharing [4] allows for a more time efficient sampling of the relaxation curve and thus has the potential to provide a higher accuracy of T2 values for early diagnosis and treatment of iron loading.

Methods: A novel multi-echo turbo spin-echo sequence with echo sharing (ES-TSE) was implemented on a clinical 1.5T system (Magnetom Avanto, Siemens AG, Erlangen, Germany). In this implementation, the number of shared echoes m depended on the number of k-space segments per image n and can be expressed by m=(n-1)/2. The sequence allowed for a maximum of 32 images (i). The echo train length (ETL) is therefore ETL=(i-1)*(m+1)+n, in contrast to ETL=n*i in a conventional multi-echo TSE experiment. Unlike conventional TSE imaging, this sequence applied non-slice selective, rectangular refocusing pulses and thus allowed for more accurate T2 evaluation [5]. 3, 5 or 7 could be selected as values for n. The reordering scheme was optimized such that increments in k-space were minimized. As an example, the ES-TSE sampling scheme for n=7 and ETL=15 is as follows: 2, 1, 3, 4, 6, 7, 5, 4, 2, 1, 3, 4, 6, 7, 5, where 1 denotes the first segment of k-space, 4 the center segment, and 7 the last segment. In this case, 3 different TE images can be reconstructed.
The T2 measurements were validated by measuring a series of tubes filled with aqueous solutions of Manganese Chloride ($MnCl_2$); concentrations ranged from 0.1mM to 0.7mM and were varied in steps of 0.1mM. T2 maps calculated from an ES-TSE experiments (n=5, i=32) which generated 32 images at different TE (TE 15-484ms, TR 5s, matrix 256x256, TA 4:21min) were compared to T2 maps obtained from a set of 22 SE sequences with increasing TE in the range of 5–1000ms (TR 5s, matrix 128x256, TA 22*11:17min) which served as gold standard. T2 values were calculated on a pixel-by-pixel basis by fitting an exponential curve to the signal intensities in the tubes in the series of increasing TE images. Regions of interest (ROI) covering almost the whole area of the respective tubes were defined and the T2 value within this area was determined as the average over the fitted pixel values.
To test the feasibility of this technique in a clinical setting, healthy volunteers were examined after informed consent had been obtained. In this case the ES-TSE sequence was carried out in a single breathhold. T2 maps were calculated as described above and compared to T2 maps obtained with a slightly modified SE technique which is widely used for in vivo quantification of T2 [6]. In vivo imaging parameters for ES-TSE were as follows: n=5, i=32, TE 12-376ms, TR 2.5s, matrix 51x128, TA 25sec. SE parameters were TE 6,9,12,15,18ms, TR 2.5s, matrix 96x256, TA 5*4:18min. Axial liver images were obtained and a ROI was outlined on each T2 map. ROIs of similar location and size in ES-TSE and SE images were chosen, while avoiding obvious breathing artifacts and vessels. The $MnCl_2$ phantoms were placed on the table underneath the patient as external T2 references. ROIs were selected in the phantoms as well and analyzed as described above.

Results: Table 1 summarizes the T2 values obtained with ES-TSE and variable TE SE-measurements in the series of $MnCl_2$ solutions. No artifacts due to echo sharing or k-space reordering have been observed in raw images of ES-TSE. Figure 1 shows T2 maps in a volunteer obtained with the standard technique and with the ES-TSE technique. Note the absence of motion artifacts in the map obtained in a breathhold. The T2 values obtained from ROIs in the liver of the volunteer were 37±13ms for the SE maps and 54.0±6.1ms for the ES-TSE maps. Due to the low resolution, the ROIs from the phantom could not be evaluated for all tubes. It should be noted however, that the obtained T2 values for concentrations lower than 0.6mM for the ES-TSE sequence were within 5% of the values obtained with the gold standard sequence in the phantom alone, whereas the SE sequence had wider deviations, especially with lower concentrations.

$MnCl_2$ (mM)	0.7	0.6	0.5	0.4	0.3	0.2	0.1
T2 (ms) SE	19	22	26	33	43	67	131
T2 (ms) ES-TSE	19	23	28	35	46	69	134
Difference	-2%	2%	5%	6%	6%	4%	3%

Table 1: T2 values in $MnCl_2$ solutions obtained with SE and ES-TSE.

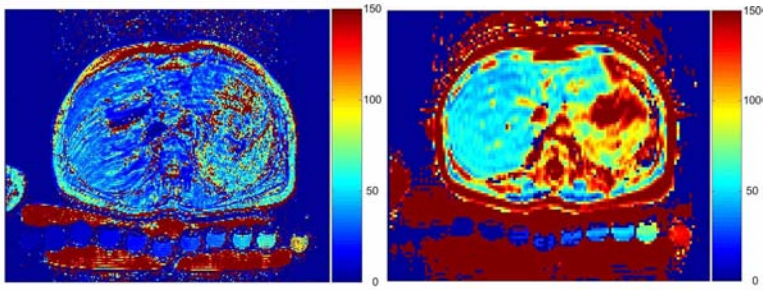

Fig 1: T2 maps of the liver of a healthy volunteer. On the left hand side the T2 map obtained with SE is shown. The T2 map obtained with ES-TSE in breathhold is depicted on the right.

Discussion: We have successfully implemented a technique that allows for accurate sampling of the T2 relaxation curve by echo sharing. Phantom and volunteer measurements showed that ES-TSE is very accurate. T2 values in human subjects can be determined with a lower error margin than with a standard SE technique. This is due to the fact that motion artifacts in the SE case negatively influence the T2 determination. A major advantage of the ES-TSE sequence is, that ES-TSE can be carried out in a breathhold and thus no motion correction or further post processing has to be applied. Echo sharing in addition has the advantage of sampling the T2 decay with a higher temporal resolution or allowing a faster acquisition while maintaining the temporal resolution compared to standard breathhold TSE [3]. Further investigations have to determine the origin of the difference in T2 times in vivo with the two techniques; our preliminary results show that the ES-TSE values seem to be closer to the 'real' values.

References: [1] Clark PR & St Pierre TG. Magn Reson. Imaging 18, 431-438 (2000). [2] Anderson LJ et al. Eur. Heart J. 22, 2171-2179 (2001).[3] He T. et al. J. Magn Reson. Imaging 24, 580-585 (2006).[4] Johnson,BA et al. AJNR 15, 667-673 (1994).[5] Majumdar S et al Magn Reson. Med. 3, 397-417 (1986). [6] St Pierre TG et al Ann. N. Y. Acad. Sci. 1054, 379-385 (2005).

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