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Breath-hold spin echosequence for assessing liver iron content

Justin Cheng-Ta Yang [a,b,c,d], Meng-Yao Lu [e], Fu-Shan Jaw [a], Steven Shinn-Forng Peng [b,d,*], Tiffany Ting-Fang Shih [b,d,f]

[a] Institute of Biomedical Engineering, College of Engineering and the College of Medicine, National Taiwan University, Taipei, Taiwan
[b] Department of Medical Imaging, National Taiwan University Hospital, Taipei, Taiwan
[c] Department of Radiology, National Taiwan University Hospital, Chu-Tung Branch, Hsinchu, Taiwan
[d] Department of Radiology, National Taiwan University College of Medicine, Taipei, Taiwan
[e] Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan
[f] Department of Medical Imaging, Taipei City Hospital, Taipei, Taiwan

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ABSTRACT

Objective: To compare a multiple breath-hold, multiecho, multiplanar spin-echo (BHMEMPSE) magnetic resonance (MR) sequence with a TR of 300 ms with a traditional multiecho, multiplanar spin-echo (MEMPSE) MR sequence for assessing liver iron content.
Materials and methods: This study was approved by the institutional review board; informed consent was waived. Liver R2 measurement was derived from the mono-exponential model by BHMEMPSE and MEMPSE MR sequences of a 1.5 T MR machine in 30 thalassemia patients (9men, 21women, aged 27.7 ± 6.8 years). Hepatic iron contents were estimated using Ferriscan in all patients. The inter- and intra-observer agreement of the 2 MR sequences was also evaluated.
Results: MEMPSE R2 values significantly correlated with Ferriscan iron content values ($r = 0.895$, $p < 0.001$) and serum ferritin concentration ($r = 0.661$, $p < 0.001$). BHMEMPSE R2 values significantly correlated with Ferriscan values ($r = 0.914$, $p < 0.001$) and serum ferritin concentration ($r = 0.608$, $p < 0.001$). The distribution of MEMPSE R2 values against BHMEMPSE R2 values revealed an excellent linear relationship ($r = 0.978$, $p < 0.001$). The inter- and intra-observer agreement of the 2 MR sequences was excellent, with an interclass correlation coefficient exceeding 0.9. The distribution of Ferriscan against BHMEMPSE R2 values revealed a curvilinear relationship ($r = 0.935$, $p < 0.001$).
Conclusions: The BHMEMPSE sequence exhibited comparable estimation for assessing liver iron content, comparable repeatability and a shorter acquisition time compared with the MEMPSE sequence. The BHMEMPSE sequence can serve as an adjunctive sequence to assess liver iron content.
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1. Introduction

Iron overload is a major complication of several hematological disorders, including thalassemia major. The body iron burden is a major determinant of clinical outcomes in iron-overloaded patients, irrespective of whether the iron overload results from increased dietary iron absorption, transfusion therapy, or both. Therefore, a non-invasive assessment of the body iron load is crucial for monitoring tissue iron concentrations. Liver iron concentration (LIC) can provide an estimate of total body iron burden in thalassemia patients [1].

Several methods are available for measuring LICs, including chemical assay of liver biopsy specimens, biomagnetic liver susceptometry using superconducting quantum interference device (SQUID) technology [2,3], and magnetic resonance imaging (MRI) techniques [4–11]. Various MRI techniques have been described, including: (1) method measuring signal intensity ratio based on T2-weighted (spin-echo) [12] or T2*-weighted (gradient-echo) [5,13] sequences,(2) relaxometry methods based on the measurement of R2 [6,10] or R2* [9,14]. Iron-mediated signal decay can be characterized by a half-life time constant. The half life is T2 (spin-echo) or T2* (gradient-echo). Sometimes the signal decay is described as a rate: R2 (spin-echo) or R2* (gradient-echo). The relaxation rate is the reciprocal of the time constant; that is: $R2 = 1000/T2$, $R2^* = 1000/T2^*$. The factor of 1000 is used because R2 and R2* are expressed in 1/s while T2 and T2* are expressed in ms.

For measuring R2, the spin-density-projection-assisted (SDPA) method [6,15] (also known as FerriScan) is a widely used method. SDPA R2-MRI has been clinically proven to have high sensitivity and specificity for LIC measurement in clinical practice [6,15]. However,

* Corresponding author at: Department of Medical Imaging, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, Taiwan. Tel.: +886223562570; fax: +886223562811.
E-mail address: sfpeng@ntuh.gov.tw (S.S-F. Peng).

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Table 1
MR sequences in calibrated phantom study and human subjects.

	MEMPSE	BHMEMPSE	Gradient-echo	MEMPSE (8TE)	FIESTA
TR (ms)	1000	300	28.3	1000	4 ~ 5
TE (ms)	6, 9, 12, 15, 18	3, 5, 8, 12, 18, 30	1.8, 4.8, 7.7, 10.7, 13.7, 16.6, 19.6, 22.5	6, 9, 12, 15, 18, 21, 24, 27	1.8 ~ 2.5
Flip angle (degree)	-	-	20	-	60
Slice thickness (mm)	6	10	10	6	6
Space between slice (mm)	5	5	0	5	1
Bandwidth (Hz)	41.67	62.5	62.5	41.67	83.33
Field of view (cm)	38	48	38	38	38
Matrix	256 × 192	64 × 64	224 × 128	256 × 192	320 × 192
Slice number	11	8	-	-	26
Scanning time	24.5 ± 8.3 min	3.8 ± 0.6 min	-	-	24.1 ± 2.6 s

MEMPSE = multi-echo, multi-planar spin-echo sequence, BHMEMPSE = breath-hold, multi-echo, multi-planar spin-echo sequence, FIESTA = Fast Imaging Employing Steady-state Acquisition.

one limitation of the SDPA R2-MRI method is the time-consuming nature of this magnetic resonance (MR) sequence. Total scan time is approximately 30 min due to long repetition time [16]. A previous study by Pavitt [17] revealed that reducing repetition time from 2500 ms to 1000 ms exhibited no significant difference in LIC measurement. This 1000-ms multislice, single-spin echo sequence reduced total scan time to 20–30 min. In thalassemia patients with chronic liver disease, incorporating sequences for R2 measurement in routine MR pulse sequences places a heavy burden on the examination unit.

In this paper, we compare a new multiple breath-hold, multiecho, multiplanar spin-echo (BHMEMPSE) sequence with the 1000-ms multiecho, multiplanar spin-echo (MEMPSE) sequence for liver R2 measurement.

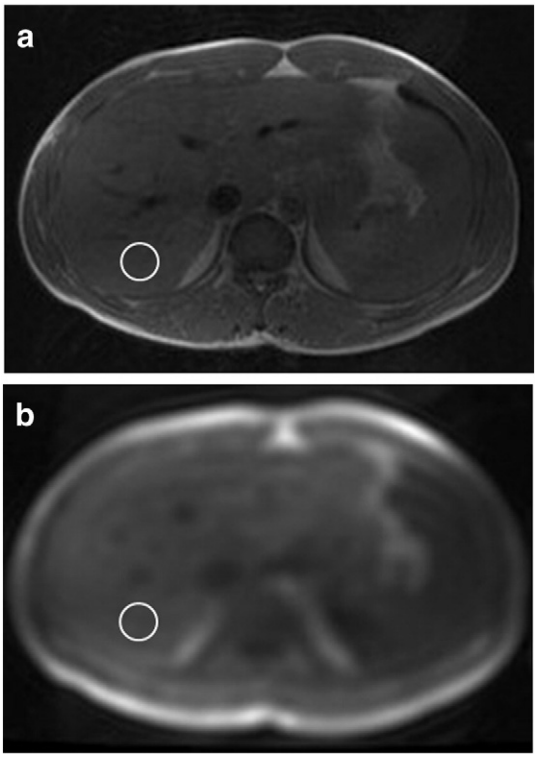

Fig. 1. Liver R2 measurement in a 26-year-old man with thalassemia. The ROI analysis were performed by drawing a circle (white) in the right posterior lobe of liver in both MEMPSE sequence (a) and BHMEMPSE sequence (b). MEMPSE R2, BHMEMPSE R2 and Ferriscan value of the patient were 36 1/s, 39 1/s and 1.8 mg/g dw, respectively. His ferritin and ALT levels were 891 ng/ml and 8 IU/dL, respectively.

2. Materials and methods

2.1. Phantom study

Weighted amounts of ferric chloride ($FeC1_3$) were dissolved in 30 ml distilled water (iron concentration 0.01, 0.02, 0.05, 0.1, 0.2, 0.5, 1 and 2 mg Fe/g). In order to avoid the sediment of the ferric compound, HCl (99% HCl, Sigma-Aldrich, St. Louis, MO, USA) was added into each test tube to keep pH < 2.

Calibrated phantom tubes received MRI examinations using a 1.5-T scanner (Signa Magnetom; GE Medical Systems, Milwaukee, WI, USA). MEMPSE with 5 TEs, BHMEMPSE, gradient-echo (T2*-weighted) and MEMPSE with 8 TEs (Table 1) were used to scan calibrated aqueous iron solutions with 10 times repetition. Comparison among MEMPSE, BHMEMPSE and gradient-echo sequences were made. Besides, MEMPSE with 5 TEs and 8TEs were compared as well.

2.2. Curve fitting models

Raw data of MEMPSE and BHMEMPSE sequences were analyzed by three different curve fitting models: mono-exponential, mono-exponential plus constant offset and bi-exponential curve fitting models. Comparison among three curve fitting models was made to determine the best fitting model.

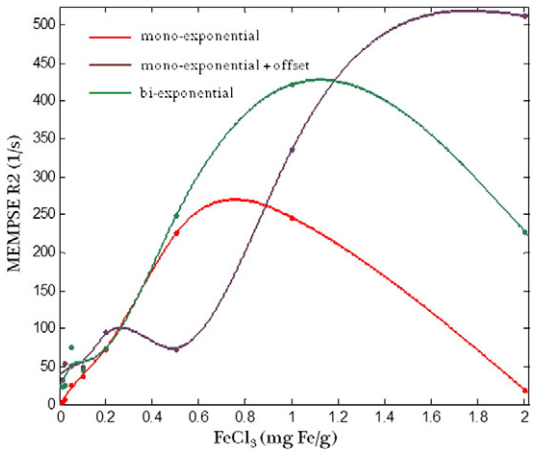

Fig. 2. Phantom R2 measurement of MEMPSE sequence against different concentrations of $FeCl_3$. Mono-exponential (red), mono-exponential plus constant offset (brown) and bi-exponential (green) curve fitting models were applied.

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