Ultrafast Magnetic Resonance Imaging for Iron Quantification in Thalassemia Participants in the Developing World

The TIC-TOC Study (Thailand and UK International Collaboration in Thalassaemia Optimising Ultrafast CMR)

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Thalassemia is the most common monogenetic disorder worldwide, with 60 000 infants with thalassemia major born annually.[1] Survival often depends on regular blood transfusions to correct anemia and to reduce ineffective erythropoiesis, but these transfusions can result in iron overload and organ failure unless chelation therapy is undertaken. Serum ferritin levels continue to be used as a guide to chelation but are unreliable, and the availability of cardiovascular magnetic resonance (CMR) T2* imaging has transformed patient management by allowing organ-specific quantification of iron content.[2,3]

Countries with a high prevalence of thalassemia major have CMR, but magnet time is expensive and analytic expertise lacking. The aim of TIC-TOC (Thailand and UK International Collaboration in Thalassaemia Optimising Ultrafast CMR) was to investigate whether ultrafast CMR mapping could provide reliable immediate diagnoses of heart and liver iron content, eliminating the need for complex analysis, thus reducing costs to a level within local resources. The research received approval by the Institutional Review Board of the Faculty of Medicine at Chulalongkorn University. All participants provided written informed consent.

One hundred participants with thalassemia major were recruited by the local support group at the King Chulalongkorn Memorial Hospital in Bangkok, Thailand. Eleven healthy volunteers not on cardio-active medication were recruited through local hospital advertising to confirm normal ranges. All participants underwent magnetic resonance imaging scans with a 1.5-T scanner (Aera, Siemens) calibrated with the T1MES (T1 Mapping and ECV Standardisation in CMR) phantom.[4] The scan consisted of 10 breath holds: localizer and pilot images, myocardial and liver T2* and T1 mapping, anatomic half-Fourier acquisition single-shot turbo spin echo stack, and long-axis left ventricular steady-state free-precession cines with an optional short-axis cine stack (2 breath holds) if abnormal, but none were. Both modified look-locker inversion recovery (MOLLI) and shortened MOLLI (MyoMaps, Siemens) T1 mapping sequences were implemented. T2* and native T1 maps were performed on the same mid left ventricular short-axis slice. The black-blood T2* sequence consisted of 8 or 12 echoes (2.68–20.11 milliseconds; 2.49-millisecond increments for the heart; 12 in the transverse plane for the liver; minimum echo time, 0.99 millisecond). Images were analyzed as they were acquired, providing assessment of myocardial and liver iron, function, and extracardiac anatomy.

For the myocardial maps, a single septal region of interest was manually traced. For the liver T2* maps, a large region of interest was traced, avoiding vasculature. Liver T1 values were obtained from the myocardial short-axis images. The 11 healthy volunteers all had normal scans. The lower limit of normal for T1 was taken as 2 SD below the mean and 20 millisecond for myocardial T2*.[2,3]

Ferritin and hemoglobin blood levels were measured. One-year average ferritin values were calculated from a minimum of 3 values per patient.

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Of the 100 participants invited, 97 were scanned; 2 participants were unwell and 1 patient consented but was claustrophobic (Table). Visual left ventricular function assessment on long-axis cines was normal in all participants, including those with cardiac iron. In total, including test-retest, 123 scans were performed in 2 days (12-hour working days). Mean scan duration was 8.3±2.4 minutes with complete analysis within 1 minute of the last image acquisition.

Fifteen participants had myocardial iron loading by T2* (10 severe, 2 moderate, 3 mild). There was good correlation between myocardial T2* and T1 maps (T2* versus MOLLI, r^2=0.81; T2* versus shortened MOLLI, r^2=0.83; both P<0.0001). All participants with low myocardial iron T2* had low T1 values. Thirty participants with normal T2* had low T1 MOLLI values (<982 milliseconds). Ninety-six participants had liver iron by T2*(46 severe, 33 moderate, 17 mild); only 1 patient had a normal liver T2* value. Liver T2* mapping correlated with T1 mapping (T2* versus MOLLI, r^2=0.33; T2* versus shortened MOLLI, r^2=0.36; P<0.0001).

There was a weak correlation between myocardial and liver T2* maps and mean ferritin values (r^2=0.17 and r^2=0.15, respectively; both P<0.0001). There was no correlation with ferritin in severe myocardial and liver iron.

TIC-TOC demonstrated the clinical and economic advantages of ultrafast magnetic resonance imaging protocols, scanning 6 participants per hour for two 12-hour days, reducing scanning costs by a factor of ≈4. Mapping analysis took minimal training, required <1 minute, and was reliable (data not shown). Mapping revealed a 15% prevalence of abnormal cardiac iron content by T2* and 45% by T1. High liver iron was detected in 99%. This study has demonstrated that ultrafast scanning is achievable with the use of sequences available on commercially available CMRs and scanners. Thus, widespread adoption of this approach is feasible and currently being investigated by the Global-AID project, which is endeavoring to distribute this technology to multiple countries to confirm applicability and cost-effectiveness and to investigate potential changes in outcomes.

Table. Participant Baseline Characteristics

Characteristics	Value
n	97
Age, y	34.1±12.1
Sex, M/F	31/66
Height, m	1.57±0.08
Weight, kg	50.7±9.2
BSA, m^2	1.48±0.16
Chelation	
DFO, n	13
DPO, n	63
Deferasirox, n	6
DFO+DPO, n	5
DPO+deferasirox, n	2
None, n	8
MRI scanning duration, min	8.3±2.4
Myocardial T2*, ms	29.5±7.9
Myocardial iron by T2* <20 ms (participant frequency, %)	15 (15.5)
Liver T2*, ms	2.5±1.4
Liver iron by T2* <6.3 ms (participant frequency, %)	96 (98.9)
Average ferritin, μg/L	3533±2897
Hemoglobin, g/dL	8.03±1.24

Average ferritin over 1 year. Data are presented as mean±SD when appropriate. BSA indicates body surface area; DFO desferrioxamine; DPO, deferiprone; and MRI, magnetic resonance imaging.

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DISCLOSURES

None.

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FOOTNOTES

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