T2* mapping tables

Table 3c-iii.1: Correlation of T2* mapping indices with histological substrates. Agreement expressed as Pearson r-coefficient, linear R^2 regression index or area under the curve (AUC). mb – multiple breath-hold, GRE – gradient echo, BB – black blood, I/R – ischaemia – reperfusion model

	N	Population	Sequence	Histological correlation	Agreement	
Cardiac iron loading						
Carpenter[1]	12	ExVivo Hearts	T2*GRE(BB)	Iron content	Native R2* (=1/T2*)	R^2=0.91
Anderson[2]	30	Liver biopsy	mbT2*GRE(BB)	Iron Content	Log_e liver native T2*	R=0.93
Acute MI – intramyocardial haemorrhage						
Ghurge[3]	8	Pigs (I/R injury)	T2*GRE(BB)	Histology	Native T2* (ms)	Qualitative
Kali[4]	20	Canines (acute I/R and chronic MI, day 56)	T2*GRE(BB)	Histology	Native T2* (ms)	Acute vs. ex vivo R^2=0.9; p<0.001 Chronic vs. ex vivo, R^2=0.9; p<0.001 Chronic vs. histology, R^2=0.7, p<0.001
Kali[5]	20	Canines (I/R injury)	T2*GRE(BB)	Histology	Native T2* (ms)	R^2=0.7; p<0.001
House[6]	2	Human (transfusion iron overload)	T2*GRE(BB) (R2* map)	Synchrotron	Tissue iron map content	Correlation plots

Table 3c-iii.2. Correlation of myocardial native T2* mapping with other imaging biomarkers. §T2*<20msec; δT2*<10 msec.
mb – multiple breath-hold, GRE – gradient echo, BB – black blood, SWI – susceptibility weighted imaging; HPF – high pass filter. CNR – contrast-to-noise ratio

Myocardial native T2*	N	T2 mapping sequence	Population	Imaging biomarker	Outcome/Agreement
Cardiac iron loading					
Anderson[2]	109	mbT2*GRE(BB)	Thalassemia major	Liver T2*	R=0.15, p=0.11
				§LV EF (%)	R=0.61, p<0.001
				§LV ESVi(mL/m2)	R=0.50, p<0.001
				§LVmassi (g/m2)	R=0.40, p<0.001
Westwood[7]	67	T2*GRE(BB)	Thalassemia major	§E/A ratio	R=-0.62, p<0.01
				§A-wave	R=0.49, p<0.001
Tanner[8]	65	T2* GRE(BB)	Thalassemia major	δLV-EF (%)	R=0.67, p<0.001
Marsella[9]	776	T2* GRE(BB)	Thalassemia major	LV-EF(%)	R2*: R= -0.327, p<0.0001
Carpenter [1]	31	T2*GRE(BB)	Hemochromatosis	§LV-EF(%)	R=0.57, 0.049
Acute MI – intramyocardial haemorrhage					
O'Regan[10]	15	T2*GRE(BB)	STEMI	T2WI-STIR LGE	Qualitative analysis
O'Regan[11]	50	T2*GRE(BB)	STEMI	T2WI-STIR	Qualitative analysis
Zia[12]		T2*GRE(BB)	STEMI	T2WI-STIR	Qualitative analysis
Kandler[13]	151	T2*GRE(BB)	STEMI	T2WI-STIR	T2* mapping had superior diagnostic accuracy vs. T2W-STIR (16% false negative, 24% false positive).
Kidambi[14]	49	T2*GRE(BB) SWI	STEMI	T2W-STIR	SW MRI had sensitivity of 93% and specificity of 86%
Carrick[15]	245	T2*GRE(BB)	STEMI	T2 map	T2* mapping had superior diagnostic accuracy vs. T2 map
Durighel[16]	30	T2*GRE(BB) SWI	STEMI	T2WI-STIR HPF	CNR with SWI was higher than other methods
Bulluck[17]	48	T2*GRE(BB)	STEMI	T1 map T2 map	T2* hypointense core is taken as the reference dataset

Table 3c-iii.3. Intra, interobserver and interstudy variability reported for native T2* using various sequences and field strengths. Studies reported if included interstudy reproducibility. CoV%(coefficient of variation); mb – multiple breath-hold, GRE – gradient echo; BB – black blood.

T2* mapping (msec)	Anderson[2]	Westwood[18,19]	Tanner[20]
Magnetic field	1.5	1.5	1.5
N	10	10	39
Population	Thalassemia major	Thalassemia major	Thalassemia major
Centres	1	1	6
Sequence	mbT2* GRE (BB)	T2* GRE(BB)	T2* GRE(BB)
No of echo images	9	9	9
Interobserver V	Heart 6.4% Liver 4.5%		
Intraobserver V			
Interstudy V	Heart 5.0% Liver 3.3%	Heart 5.3% T2*<20: 2.3% T2*>20: 9.3%	Heart 5.8% Liver 4.4%
Inter-centre V		Heart 9.4% Liver 7.9%	Heart 5.0% Liver 7.1%

Table 3c-iii.4: Normal values for myocardial and liver native T2* reported for different sequences and magnetic fields.
Mean native T2 values±SD or 95%CI in single mid-ventricular slice, expressed in ms. Septal ROIs, § global (average measurement of 3 short axis slices). mb – multiple breath-hold, GRE – gradient echo; BB – black blood; WB – white blood.

	N	Age (years, range)	Sequence	Native T2*(msec)			
				1.5 T		3.0 T	
				Myocardium	Liver	Myocardium	Liver
Anderson[2]	15	32(26-39)	mbT2*GRE(BB)	52±16	33±7		
Westwood[18]	10	49±26	mbT2*GRE(BB)	30.1±7.1	26.6±4.7		
			T2* GRE(BB)	33.3±7.8	26.7±4.2		
Rammazotti[21]	5	35±10	T2* GRE(BB)	39±7.3 §36±5	23±3.6		
Alam[22]	20	35(26-33)	T2* GRE(WB)	32.3(28.9-36.7)	25.8(23.1-28.0)	20.5(18.3-24.3)	17.3(14.8-21.4)
Carrick[15]	50	54±13 years 26 (52%) male	T2*GRE(BB)	31.0 ± 2.1			

Table 3c-iii.5. Proof of concept studies with T2* indices differentiating between health and disease.
The table reports mean values±SD for each disease entity, sequence type, T2* index, and field strength; includes effect size as a measure of dispersion observed in healthy subjects. Native T2* values are expressed in msec. § global (average measurement of 3 short axis slices). deferoxamine (DFO), deferiprone (DFP), combined regime (DPO+DFP). HR(95%CI): hazard ratio, 95% confidence interval. mb – multiple breath-hold, GRE – gradient echo, BB – black blood.

Disease model	**Sequence**	**Health** **Average T2* in ms (n)**	**Disease** **Average T2* in ms (n)**
Thalassemia major		1.5 T	1.5 T
Anderson[23]	mbT2*GRE(BB)	/	11.4 (treatment with DFO; n=30) 34.0 (treatment with DFP; n=15)
Anderson[2]	mbT2*GRE(BB)	/	Cardiac T2* predictive of the need for cardiac medication with (HR (95%CI): 0.81 (0.71-0.93), p=0.003; n=109)
Tanner[8]	T2* GRE(BB)	/	11.4 (treatment with DFO; n=30) 32.0 (treatment with DFO+DFP; n=15)
Rammazotti[21]	T2* GRE(BB)	39±7.3 (n=5)	24 (n=5)
Casale[24]	T2* GRE(BB)	/	34 (n=107) §38.8 (n=107)
Alam [25]	T2*GRE(BB)	30.8(29.0-34.4) (n=20)	28.1 (n=53)
Hemochromatosis			
Carpenter[26]	T2*GRE(BB)	/	34.8 (genetically confirmed hemochromatosis, n=31)
Acute myocardial infarction			
O'Regan[11]	T2*GRE(BB)		Affected - haemorrhage 15.4 ± 5.7 ms Affected – no haemorrhage 47.2±13.8 ms
Zia [12]	T2*GRE(BB)		Day 2 Affected – 32.4 ms Remote – 37.4 ms 3 weeks Affected – 37.7 ms Remote – 38.4 ms 3 weeks Affected – 37.3 ms Remote – 38.2 ms

Kali[5]	T2*GRE(BB)		Affected - haemorrhage 15.9± 4.5 ms Affected – no haemorrhage 37.8±2.5 ms Remote - 35.2 ± 2.1 ms
Durighel[16]	T2*GRE(BB)		Affected - haemorrhage 33.5 ms [24.9 - 43] Affected – no haemorrhage 49.9 ms[44.6 - 67.6] Remote 44.9 ms [38.8 – 51.4]
Carrick[27]	T2*GRE(BB)	31.0±2.1	Table 3 & time course See below
Bulluck[17]	T2*GRE(BB)		Affected - haemorrhage 13.3 ms [24.9-43] Remote 33 ± 4 ms

Table 3c-iii.6. Outcome studies and treatment comparisons' studies using T2* indices.
deferoxamine (DFO), deferiprone (DFP), combined regime (DPO+DFP), GRE – gradient echo, BB – black blood, FMD – flow-mediated dilatation, RR – relative risk, mb – multiple breath-hold.

	Type	Population	N	Follow-up (months)	Sequence	Field Strength	Endpoint	Statistics
Tanner [20]	RCT multicentre	Thalassaemia major ➔ DFO and placebo ➔ DFO+DFP	65	12	T2* GRE(BB)	1.5T	Δcardiac T2*	Absolute percent difference: ~10% (95%CI 2-19%), p=0.02
							LV-EF	Absolute percent difference 1.17% (95% CI 0.0-2.35%), p=0.05
							Brachial FMD	Absolute percent difference: 5.9%(95%CI 0.99-10.8), p=0.02
Tanner [28]	Observational two centre open-label	Thalassaemia major: ➔ DFP+DFO	15	12	T2* GRE(BB)	1.5T	Δcardiac T2*	baseline 5.7±0.98ms 12 months: 7.9±2.47ms (p = 0.010)
							LV-EF	baseline 51.2±10.9% 12 months: 65.7±6.7% (p = 0.010)
Kirk [29]	Observational multicentre outcome	Thalassaemia major	652	12	T2* GRE(BB)	1.5T	Heart failure	T2*=10msec predictive of HF : ➔ sensitivity 97.5% (95% CI, 91.3-99.7) ➔ specificity of 85.3% (95% CI, 83.3-87.2). RR T2*<10 ms: ➔ 8 to 10 ms: 2.97 ➔ 6 to 8 ms: 3.48 ➔ <6 ms: 4.51 (p< 0.001)
							Arrhythmia	➔ T2*=20msec predictive of arrhythmia ➔ sensitivity 82.7% (95% CI 73.7-89.6) ➔ specificity of 53.5% (95% CI 50.8-56.2).

								RR T2*<20 ms: ➔ 15 to 20 ms : 2.21 ➔ 10 to 15 ms 3.23 ➔ 8 to 10 ms: 6.82 ➔ 6 to 8 ms: 7.5 ➔ <6 ms: 8.78 (p< 0.001)
Pepe [30]	Observational multicentre study	Thalassaemia major: stable treatment with: ➔ DFP ➔ DFO ➔ DFP+ DFO	164	18	T2* GRE(BB)	1.5T	Δ mean cardiac T2* between groups	The improvement in the global heart T2* was significantly higher in the DFP+DFO than the DFO group, without a difference in biventricular function
Pennell [31]	RCT multicentre	Thalassaemia major ➔ DFO ➔ DFP	61	12	mbT2* GRE(BB)	1.5T	Δcardiac T2*	DFO: 13% DFP: 27% (p=0.023)
							ΔLV-EF	DFO: 0.3% DFP: 3.1% (p=0.03)
Pennell [32]	RCT multicentre	Thalassaemia major ➔ DFO ➔ Deferasirox	197	12	mbT2* GRE(BB)	1.5T	Δcardiac T2*	DFO: 7% Deferasirox: 12% Non-inferiority criteria met
							ΔLV-EF	DFO: 0% Deferasirox: -0.6% P=0.54

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