# T2\* mapping tables

**Table 3c-iii.1: Correlation of T2\* mapping indices with histological substrates.** Agreement expressed as Pearson r-coefficient, linear R2 regression index or area under the curve (AUC). mb – multiple breath-hold, GRE – gradient echo, BB – black blood, I/R – ischaemia – reperfusion model

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| --- | --- | --- | --- | --- | --- | --- |
|  | **N** | **Population** | **Sequence** | **Histological correlation** | **Agreement** | |
| **Cardiac iron loading** | | |  |  |  | |
| Carpenter[1] | 12 | ExVivo Hearts | T2\*GRE(BB) | Iron content | Native R2\* (=1/T2\*) | R2=0.91 |
| Anderson[2] | 30 | Liver biopsy | mbT2\*GRE(BB) | Iron Content | Loge 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 R2=0.9; p<0.001  Chronic vs. ex vivo, R2=0.9; p<0.001  Chronic vs. histology, R2=0.7, p<0.001 |
| Kali[5] | 20 | Canines (I/R injury) | T2\*GRE(BB) | Histology | Native T2\* (ms) | R2=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

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| --- | --- | --- | --- | --- | --- |
| **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.

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| --- | --- | --- | --- |
| **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.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **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.

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| --- | --- | --- | --- | --- | --- | --- |
| **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.

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| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **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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