## T2 weighted imaging

**Table 3b-ii.1: Validation studies with T2 weighted imaging (T2W**). IR – ischaemia-reperfusion model. T2-TSE - double-inversion black blood fast-spin-echo, SI – signal intensity, ECV – extracellular volume, AAR – area-at-risk, TTC -Triphenyltetrazolim chloride-stained, T2W(STIR) - triple-inversion black blood (short tau) fast-spin-echo, CNR – contrast to noise ratio, T2-SFFP – steady-state free precession.. \*Histological diagnosis of myocarditis include histological, immunohistological, and molecular pathological analyses diagnosing myocardial inflammation and viral infections [1]. Edema ratio described in [2].

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | **N** | **Disease model** | **Validation approach** | **Sequence** | **Time-points** | **Correlation/Agreement or Accuracy(95%CI)** | | |
|  | | | |  |  | | | |
| **Animal studies** | | |  |  |  | **T2W** | **R** | **P value** |
| **Higgins** [3] | 8 | IR (Dogs) | Water content | T2-TSE | 24h | T2W SI | 0.90 | <0.001 |
| **Garcia-Dorado** [4] | 21 | IR (ex vivo pig heart) | Water content | T2-TSE | (time-point not available) | T2 time | 0.76 | p< 0.001 for all |
|  |  |  |  | T2W SI | 0.83 |  |
|  |  | Histological ECV |  |  | T2 time | 0.58 |  |
|  |  |  |  |  | T2W SI | 0.59 |  |
|  |  | Histology (Fluorescein) |  |  | AAR- T2W (%LV) | 0.96 |  |
| **Aletras** [5] | 17 | IR (Dogs) | Microspheres (TTC staining of infarction) | T2-TSE | 2 days after the  coronary artery occlusion 90min /reperfusion | AAR- T2W (%LV) | 0.84 | <0.001 |
| **Tilak** [6] | 14 | IR (Dogs) | First pass contrast enhanced perfusion | T2-TSE | Day 0 and 2 after the  coronary artery occlusion 90min /no reperfusion | AAR- T2W (%LV) | 0.91 | P<0.001 |
| **Abdel-Aty**[7] | 15 | IR (dogs) | Water content | T2-STIR |  | T2-CNR | 0.77 | 0.04 |
| **Payne** [8] | 15 | IR (pig) | Histological haemorrhage | T2-SSFP | 0, 3, 10, 60 days | AAR- T2W (%LV) | Sens 98(94-100)  Spec 90(83-98) | |
| **Fernandez-Jimenez** [9] | 25 | IR (pig) | Water content |  | T2-TSE | T2 time | 0.87 | |
|  |  |  |  |  | T2 mapping | T2 time | 0.85 | |
| **Human studies** | | |  |  |  |  | | |
|  | | |  |  |  |  | | |
| **Lurz** [10] | 132 | Myocarditis | Histological diagnosis of myocarditis\* | T2-STIR |  | T2W(STIR) – Edema ratio | 59(51-67) | |
|  |  | Acute (n=70) |  |  |  | 63(53-76) | |
|  |  | Chronic (n=62) |  |  |  | 55(41-66) | |
| **Krieghoff** [11] | 93 | Heart transplant (n=73) | Histological diagnosis of Grade ≥ 1B rejection\* | T2-STIR |  | T2W(STIR) – Edema ratio | Sens: 63, Spec: 75 | |
| **Gutberlet** [12] | 49 | Chronic myocarditis | Histological diagnosis of myocarditis\* | T2-STIR |  | T2W(STIR) – Edema ratio | 68 | |
| **Francone** [13] | 57 | Acute myocarditis | Histological diagnosis of myocarditis\* | T2-STIR |  | T2W(STIR) – Edema ratio | Sens: 27-81 | |

**Table 3b-ii.2. Correlations with other relevant parameters for T2W-AAR.** AMI – acute myocardial infarction, STEMI – ST-elevation myocardial infarction, SPECT –single photon emission computed tomography, ESL-LGE – endocardial surface length.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **AMI-AAR** |  | |  |  | Correlations/Agreement | |
| **Berry** [14] | 50 | AMI | 1.5 | T2 SSFP | Approach-AAR | 0.78 |
|  |  |  |  |  | DUKE Jeopardy | 0.39 |
| **Carlsson** [15] | 16 | STEMI | 1.5 | T2-STIR | SPECT | 0.70 |
| **Wright** [16] | 108 |  |  |  | ESL-LGE | 0.77 |
| **Fuernau** [17] | 197 | STEMI | 1.5 | T2-STIR | Approach-AAR | 0.87 |
|  |  |  |  |  | ESL-LGE | 0.56 |

**Table 3b-ii.3. Proof of concept studies using T2W imaging in health and disease.** Studies included if n>25 subjects per patients’ group. Number of participants per group, mean values (mean±SD, or standard error (SE)) are reported for disease entity, the type of sequence and field strength, including effect size as a measure of dispersion observed in healthy subjects, as well as the Cohen’s d index. The order relates to the order referencing.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | **N** | **Disease model** | **Field Strength** | **Sequence** | **Health vs disease** | | |
|  | | |  |  | **Controls** | **Patients** | **Cohen D** |
| **Myocarditis** | |  |  |  |  |  |  |
| **Friedrich** [18] | 44 | Acute (suspected) | 1.5 | T2W STIR (body coil) | 1.36±0.2(SE) | 1.6±0.2 (SE) | 0.6 |
| **Abdel-Aty** [19] | 25 | Acute (suspected) | 1.5 | T2W STIR (body coil) | 1.7±0.4 | 2.3±0.4 | 1.5 |
| **Puntmann** [20] | 34 | Acute (suspected) | 1.5 | T2W STIR | 2.5±1.1 | 4.9±2.4 | 1.3 |
| **Mavrogeni** [21] | 71 | Suspected | 1.5 | T2W STIR | 1.57±0.13 | 2.6±0.9 | 1.6 |
| **Mavrogeni** [22] | 32 | H1N1 | 1.5 | T2W STIR | 1.56 ± 0.12 | 1.9 ± 0.16 | 0.81 |
| **Ferreira** [23] | 50 | Acute (suspected) | 1.5 | T2W STIR | 1.56±0.15 | 1.73±0.27 | 0.55 |
| **Radunski** [24] | 104 | Chronic (suspected) | 1.5 | T2W STIR | 2.3(2.1-3.0) | 2.5(2.2-2.9) | 0.44 |
| **Hinojar** [25] | 128 | Acute (suspected, n=61) | 1.5/3.0 | T2W STIR | 1.3 (1.1–1.6) | 2.3 (1.5–3.5) | 1.6 |
|  |  | Chronic (suspected, n=67) |  |  |  | 1.4 (1.1–2.3) | 0.22 |
| **Von Knobelsdorff-Brenkenhoff**[26] | 18 | Acute (suspected) | 1.5 | T2W STIR | 1.6 (1.5–1.7) | 2.2(2.0–2.3) | 3.6 |
| **Systemic inflammatory conditions** | | |  |  |  |  |  |
| **Mavrogeni** [27] | 50 | Lupus | 1.5 | T2W STIR | 1.9±0.1 | 24±0.4 |  |
| **Puntmann** [28] | 33 | Lupus | 3.0 | T2W STIR | 1.7±0.5 | 1.9±0.7 | 0.33 |
| **Ntusi** [29] | 55 | Rheumatoid arthritis | 1.5 | T2W STIR | 1.5±0.1 | 1.7±0.3 | 0.89 |
| **Ntusi** [30] | 103 | HIV | 1.5 | T2W STIR | 1.49±0.13 | 1.55±0.23 | 0.32 |
| **Luetkens** [31] | 28 | HIV | 1.5 | T2W STIR | 1.4±0.3 | 1.6±0.3 | 0.67 |

**Table 3b-ii.4** **Outcome studies for all-cause mortality or major adverse cardiac events (MACE)**. PPCI – primary percutaneous coronary intervention, MSI – myocardial salvage index, HR – hazard ratio, NSTEMI – non ST-elevation myocardial infarction.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | |  |  |  |  | Univariate | Multivariate |
|  | Study type | Patient population (n),  follow-up (months) | Sequence | Field Strength  (Tesla) | Myocardial T1 index | HR (95%CI), p-value) | HR (95%CI), p-value |
| **Eitel** [32] | Observational, single centre | STEMI (PPCI),  48 (27-73), n=208 | T2W-STIR | 1.5 | MSI | 0.95(0.93-0.97) | 0.93(0.91-0.96) |
| **Raman** [33] | Observational, single centre | NSTEMI, 6-months, n=88 | T2W-STIR | 1.5 | Oedema | 4.47(1-20.3) |  |
| **De Waha** [34] | Observational, single centre | STEMI (PPCI),  48 (27-73), n=438 | T2W-STIR | 1.5 | MSI | 0.93(0.92-0.95) | 0.92(0.90-0.95) |

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