

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-SFFP	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)
Kriehoff [11]	93	Heart transplant (n=73)	Histological diagnosis of Grade \geq 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 \pm 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.

	Study type	Patient population (n), follow-up (months)	Sequence	Field Strength (Tesla)	Myocardial T1 index	Univariate HR (95%CI), p-value)	Multivariate 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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