CMR IMAGING OF INFILTRATIVE CARDIOMYOPATHIES

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INFILTRATIVE CARDIOMYOPATHIES

- A unique group of myocardial diseases characterized by deposition of abnormal substances within the myocardium
- Myocardial infiltration can be extracellular or intracellular (myocardial storage disorder)
- Infiltrative cardiomyopathies cause systolic dysfunction, diastolic dysfunction, or both, and can lead to heart failure and premature death
- Endomyocardial biopsy historically was considered the gold standard for diagnosis. However, due to its associated risks and limited sensitivity in diseases with patchy involvement, biopsy has been gradually replaced by cardiac imaging for the initial diagnosis, risk stratification, and guidance of therapeutic decisions

Cottam et al Circulation 2023

INFILTRATIVE CARDIOMYOPATHIES

- **Iron Overload Cardiomyopathy**
- **Cardiac Amyloidosis**
- **Anderson Fabry Disease**
- **Cardiac Sarcoidosis**
- **Danon disease**
- **Friedreich ataxia**
- **Pompe Disease, PRKAG2 syndrome, and the various types of mucopolysaccharidosis**

PATHOPHYSIOLOGY

- Myocardial infiltration typically generates an **inflammatory response** that can progress to **fibrosis**
- Infiltrative diseases frequently result in **increased wall thickness**, although not always
- Increased wall thickness, along with inflammation and fibrosis eventually lead to **impaired systolic and diastolic function**, **microvascular dysfunction**, decreased coronary flow reserve and **ischaemia**
- Reduced ventricular compliance causes significantly elevated left ventricular (LV) filling pressure, **atrial dilation**, and **pulmonary and systemic venous congestion**
- Infiltration is not necessarily limited to the ventricular myocardium but can also involve **the atrial wall and valves**, thereby causing atrial stiffness and valvular dysfunction

Cottam et al Circulation 2023

CMR Protocol

Anatomy	→	Cardiac structure
Ventricular function & wall thickness (cines)	→	Systolic dysfunction, Volumes, RWMA, Hypertrophy, Atrial Size, Valve function
T2* mapping	→	Iron loading, hemorrhage
T2-STIRS	→	Oedema/inflammation
T2 mapping	→	Oedema/inflammation
T1 mapping	→	Fibrosis
Perfusion	→	Myocardial blood flow/ischaemia
EGE	→	Filling defects (thrombus, mass)
LGE	→	Fibrosis
ECV mapping	→	Extracellular volume increase

Diagnosis
Phenotype
Risk stratification & prognosis
Follow up

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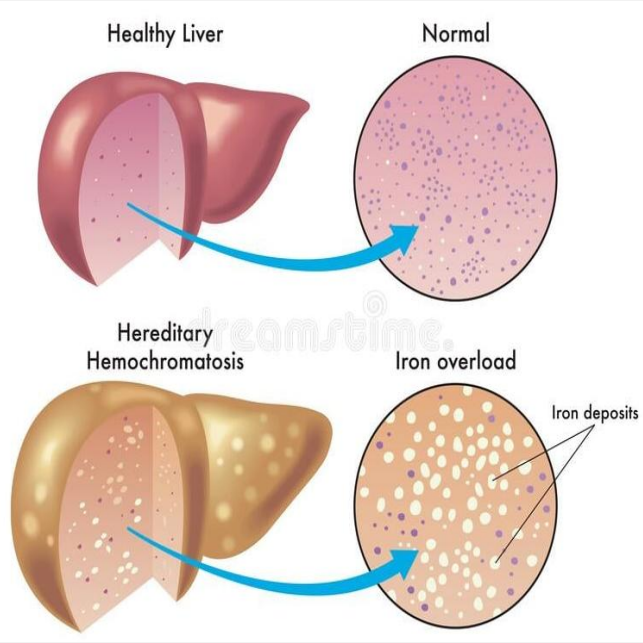
IRON OVERLOAD CARDIOMYOPATHY

- Excess iron deposition to the tissues (intracellular lysosomes of liver, spleen, bone marrow, and myocardim)
- **Causes:**

  -primary: Hemochromatosis

  -secondary: Transfusion-related, liver disease, increased adsorption
- **Cardiac dysfunction** typically presents with a nondilated restrictive clinical phenotype, which then advances to systolic dysfunction with LV dilation
- Heart failure and associated arrhythmias had been the predominant cause of death
- **Treatment**: Early identification of iron overload with **CMR T2* mapping** and iron chelation therapy to excrete iron from the body



Kottam et al, Circ Cardiovasc Imaging 2023

Iron Overload Cardiomyopathy

Anatomy

Volumetric analysis & wall thickness

T2* mapping

T2-STIRS**

T2 mapping**

T1 mapping*

EGE

LGE

ECV mapping**

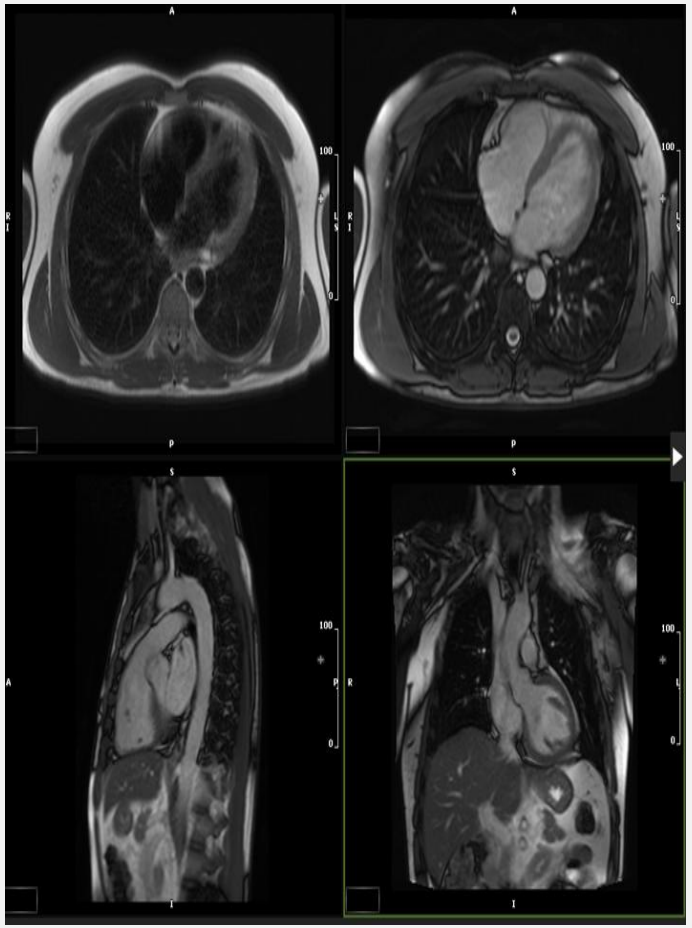
***not routinely done*

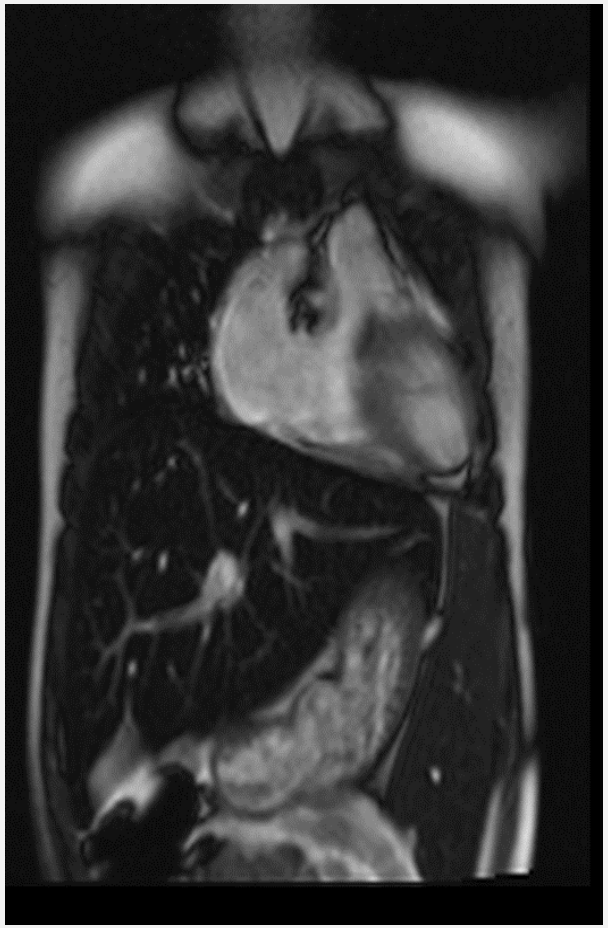
HASTE

- Half-Fourier-Acquired Single-shot Turbo spin Echo **Transaxial Black blood imaging**
- acquisition of high-resolution **T1-weighted** images

TruFISP

- True fast imaging with steady state precession uses a fully balanced gradient waveform
- **Transaxial/Coronal/Sagittal White blood**
- Very sensitive to the inhomogeneities in the magnetic field.





Iron Overload Cardiomyopathy

Anatomy

Volumetric analysis & wall thickness

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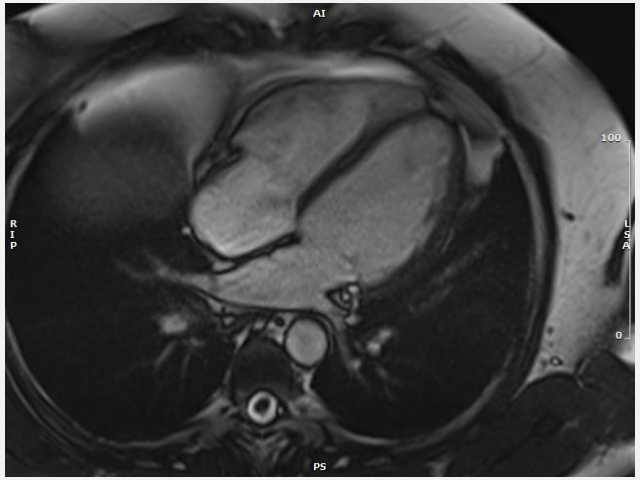
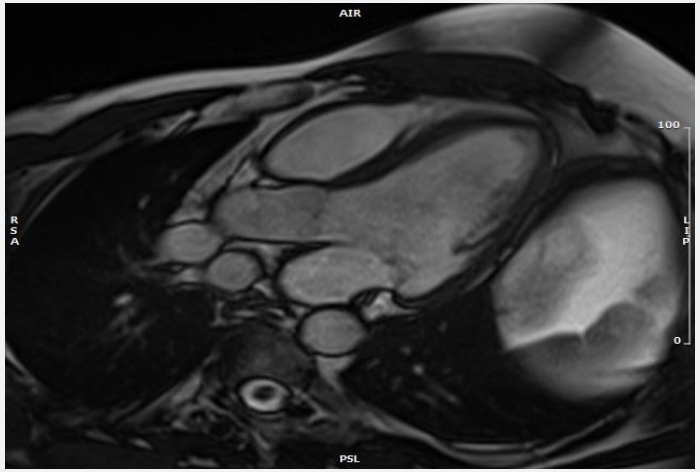
SSFP cines

4-chamber

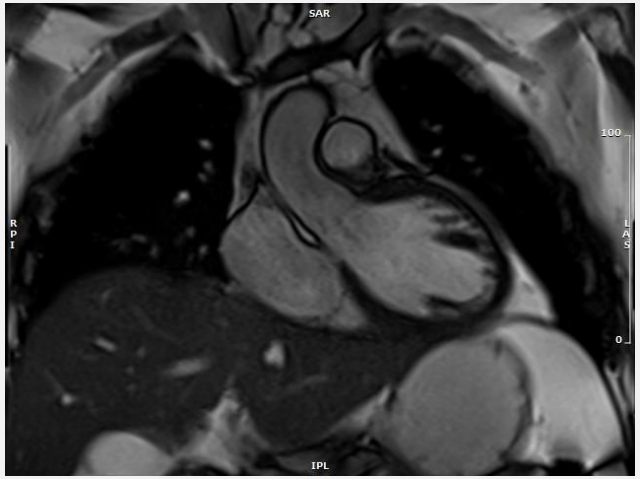


2-chamber

3-chamber



LVOT



Iron Overload Cardiomyopathy

Anatomy

Volumetric analysis & wall thickness

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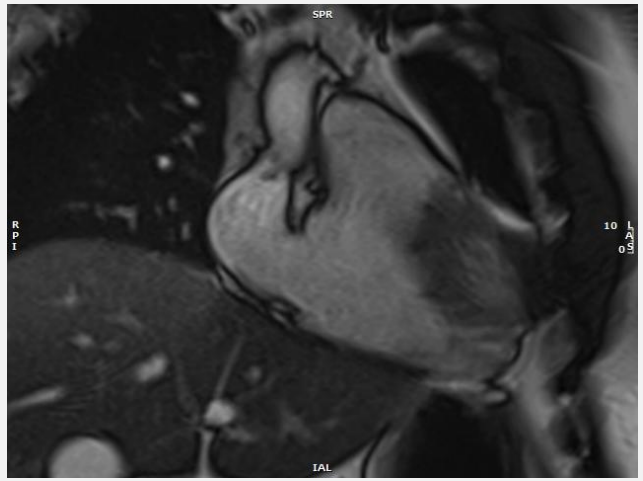

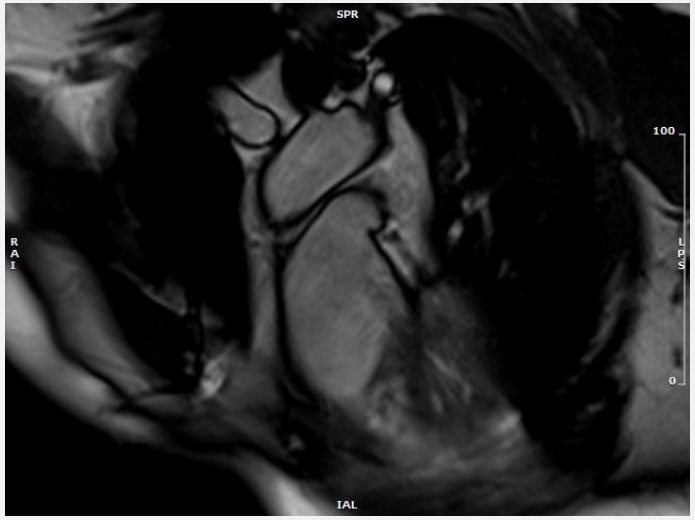

Iron Overload Cardiomyopathy

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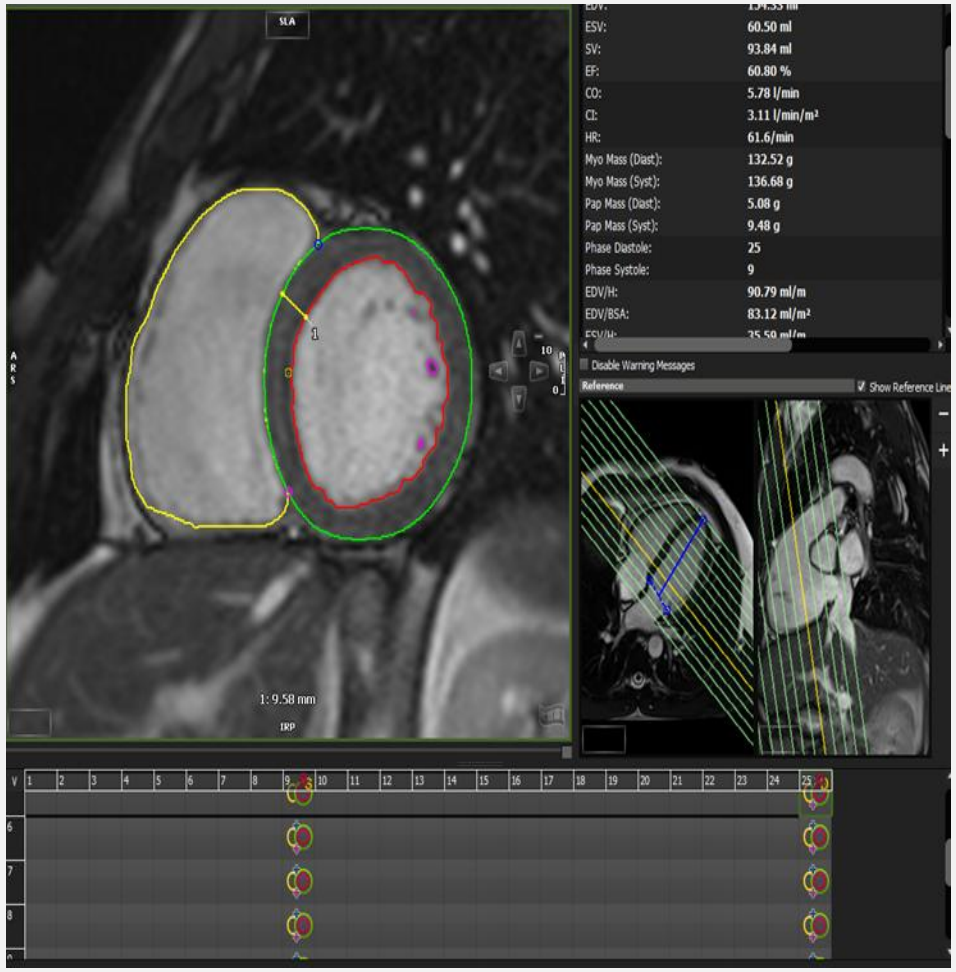
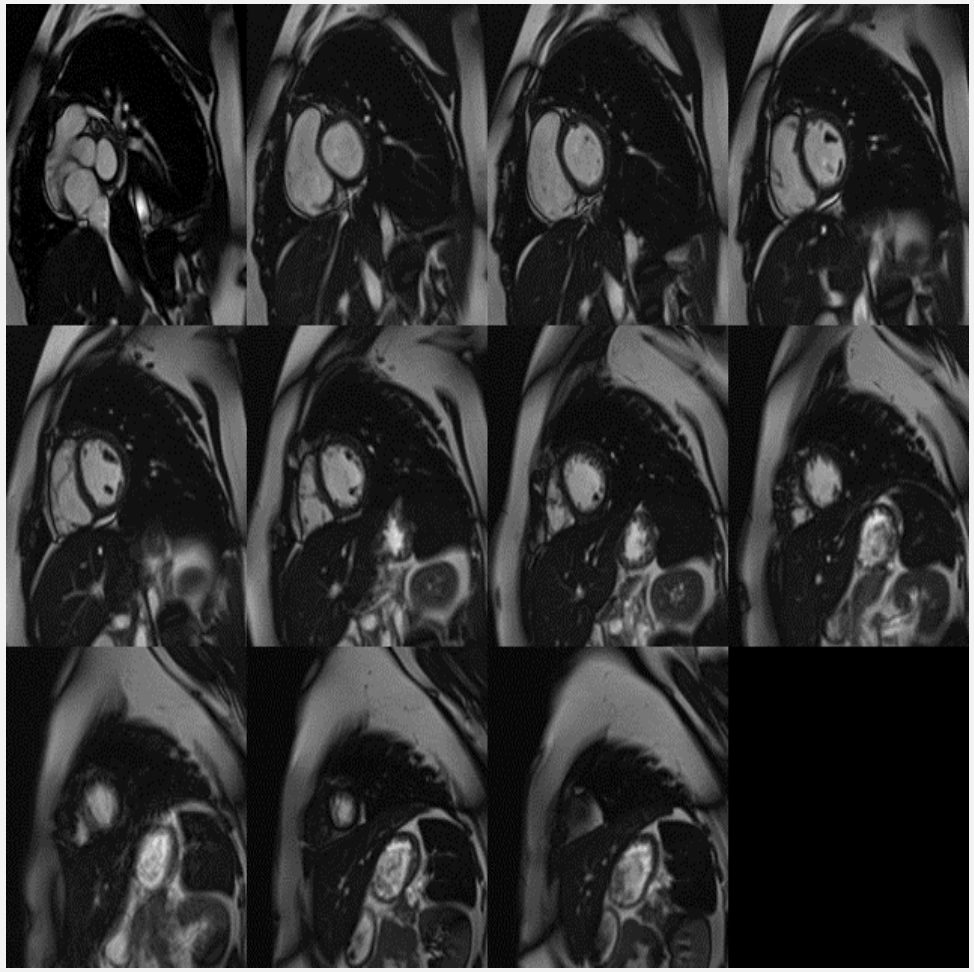




Iron Overload Cardiomyopathy
T2* Value

Anatomy

Volumetric analysis & wall thickness

T2* mapping

T2-STIRS**

T1 mapping**

EGE

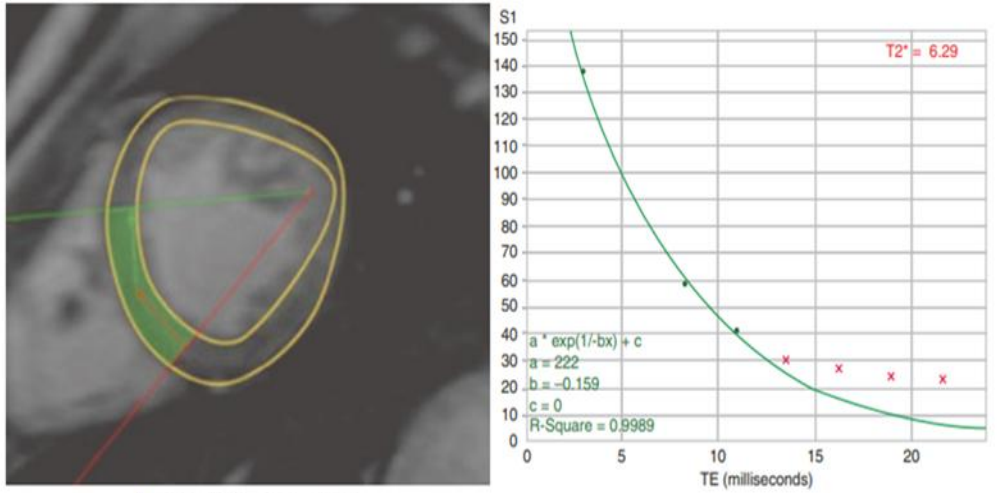
LGE

ECV mapping**

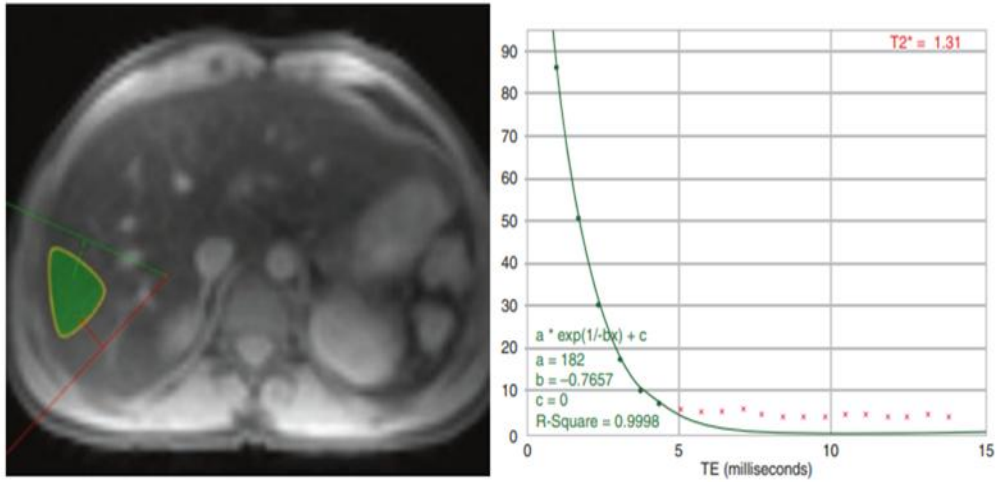
***not routinely done*

- T2* imaging for assessment of myocardial and liver iron loading
- The relation between cardiac iron deposition and T2* value was verified by several postmortem studies.

Myocardial T2* (ms)	Degree of iron overload
≥20	Absent
14–20	Mild
10–14	Moderate
≤10	Severe
Hepatic T2* (ms)	Degree of iron overload
≥15.4	Absent
4.5–15.4	Mild
2.1–4.5	Moderate
≤2.1	Severe



Myocardial iron overload



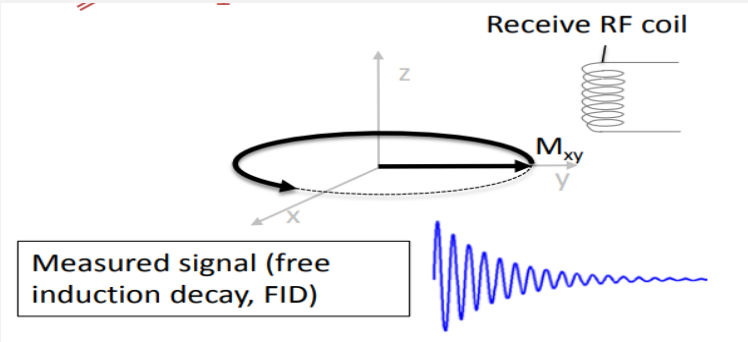
Hepatic iron overload

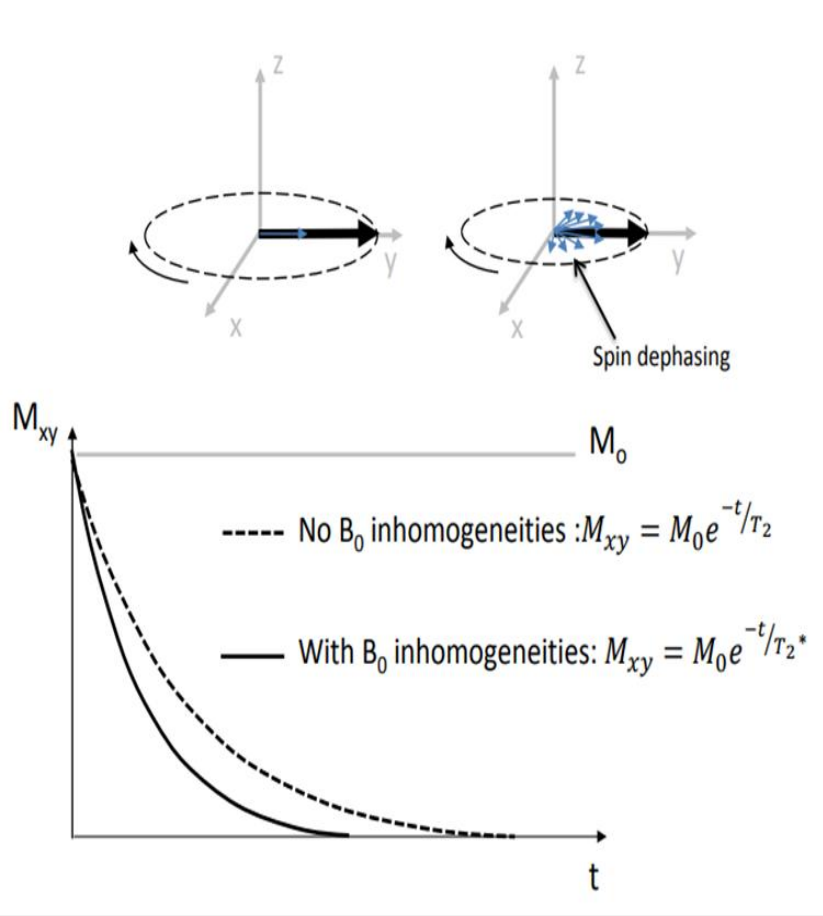
Sven Plein et all, 2011

T2* RELAXATION TIME

- Loss of coherence of the rotating proton spins due to spin spin interactions of the neighboring magnetic moments. This has a **time constant** and is known as **T2 relaxation**.

- Loss of coherence between rotating spins due to magnetic field inhomogeneity. This together with T2 relaxation leads to a more rapid decay with a combined time constant, T2* and is known as T2* relaxation

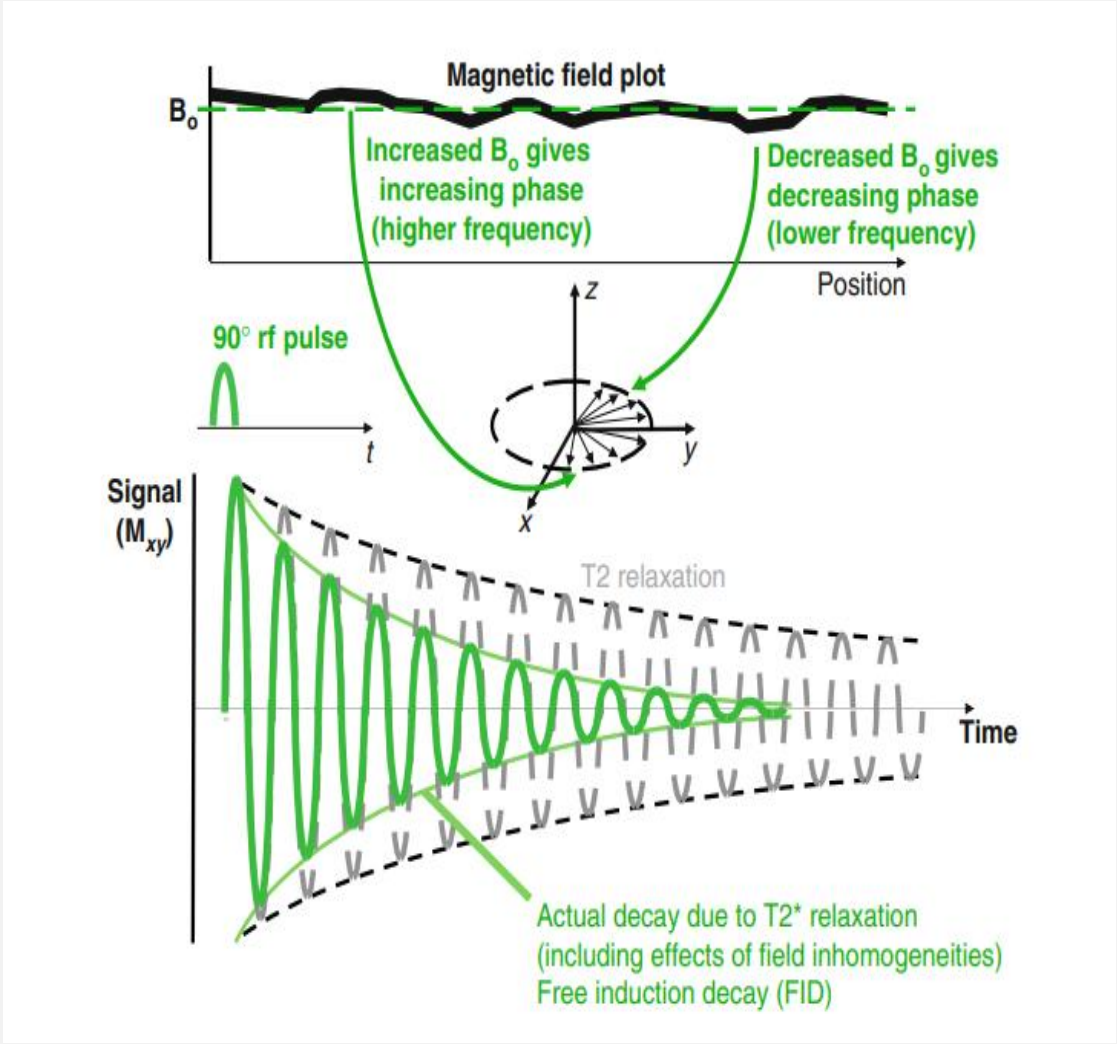




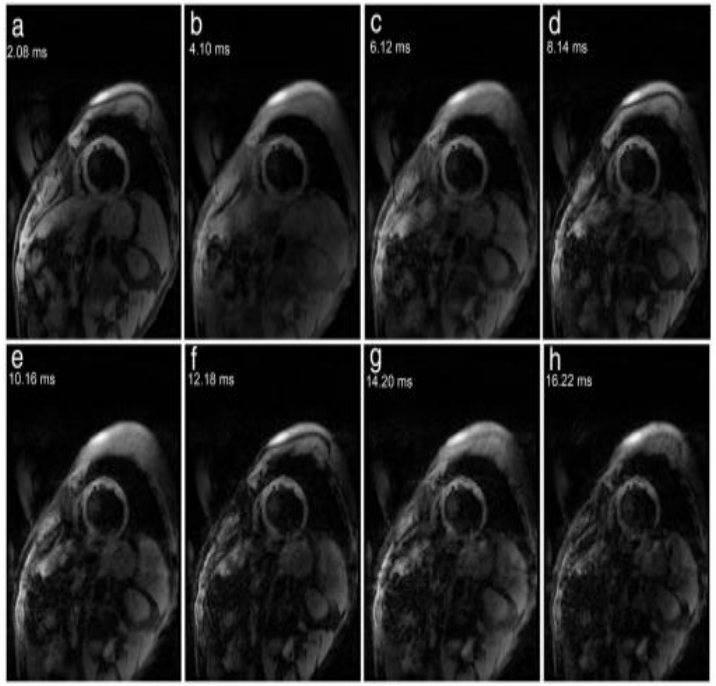
Sven Plein et all, 2011

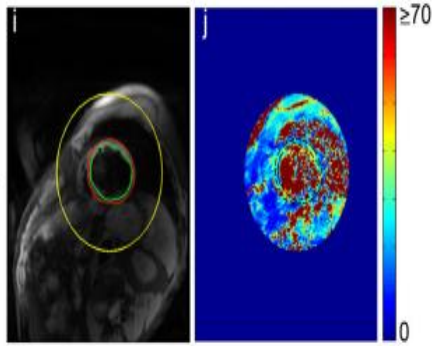
T2* RELAXATION TIME

- T2* [ms]: Time constant representing the decay of transverse magnetization in the presence of local field inhomogeneities
- T2* is progressively reduced with increasing levels of iron in tissues
- The T2* is predominately determined by hemosiderin
- T2* relaxation is a variation of T2 relaxation that accounts for additional factors contributing to signal decay, such as magnetic field inhomogeneities and susceptibility effects caused by variations in tissue composition or the presence of paramagnetic substances. These additional factors cause a faster decay of the MRI signal compared to pure T2 relaxation

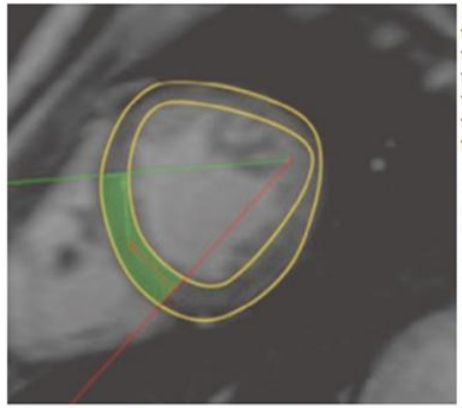


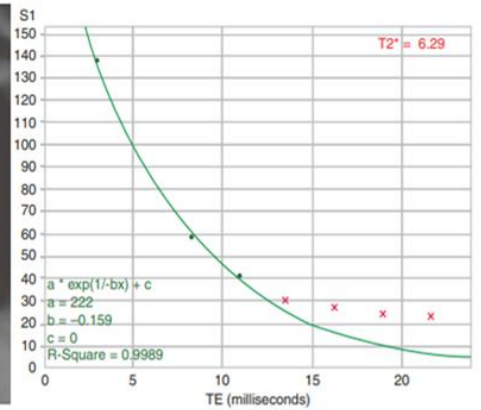
T2* MAPPING



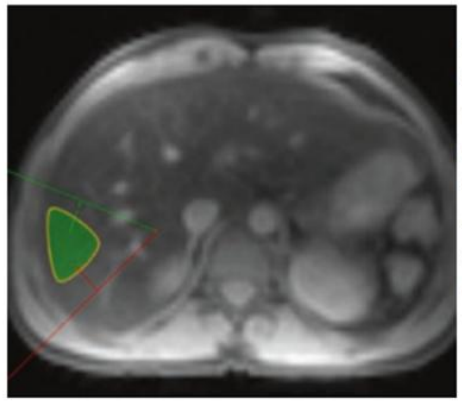


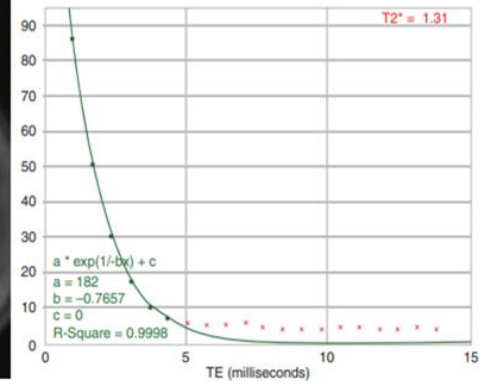
$$y = Ke^{-TE/T2^*}$$





Myocardial iron overload

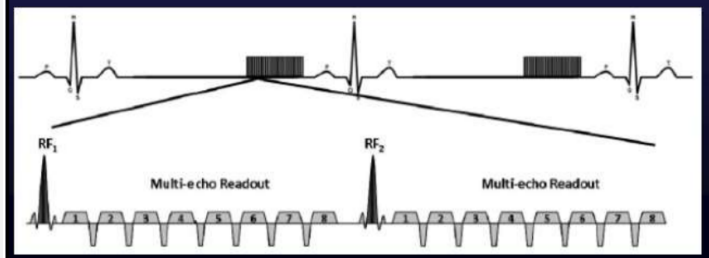




Hepatic iron overload

T2* mapping

Capture the signal decay after each RF excitation, sensitive to paramagnetic compounds.
Typically run at R-wave before heart walls move far, or in diastasis after dark-blood DIR prep.
Segmented imaging (at RBH). Typically approx 14 RR cycles BH. Why only forward echoes?

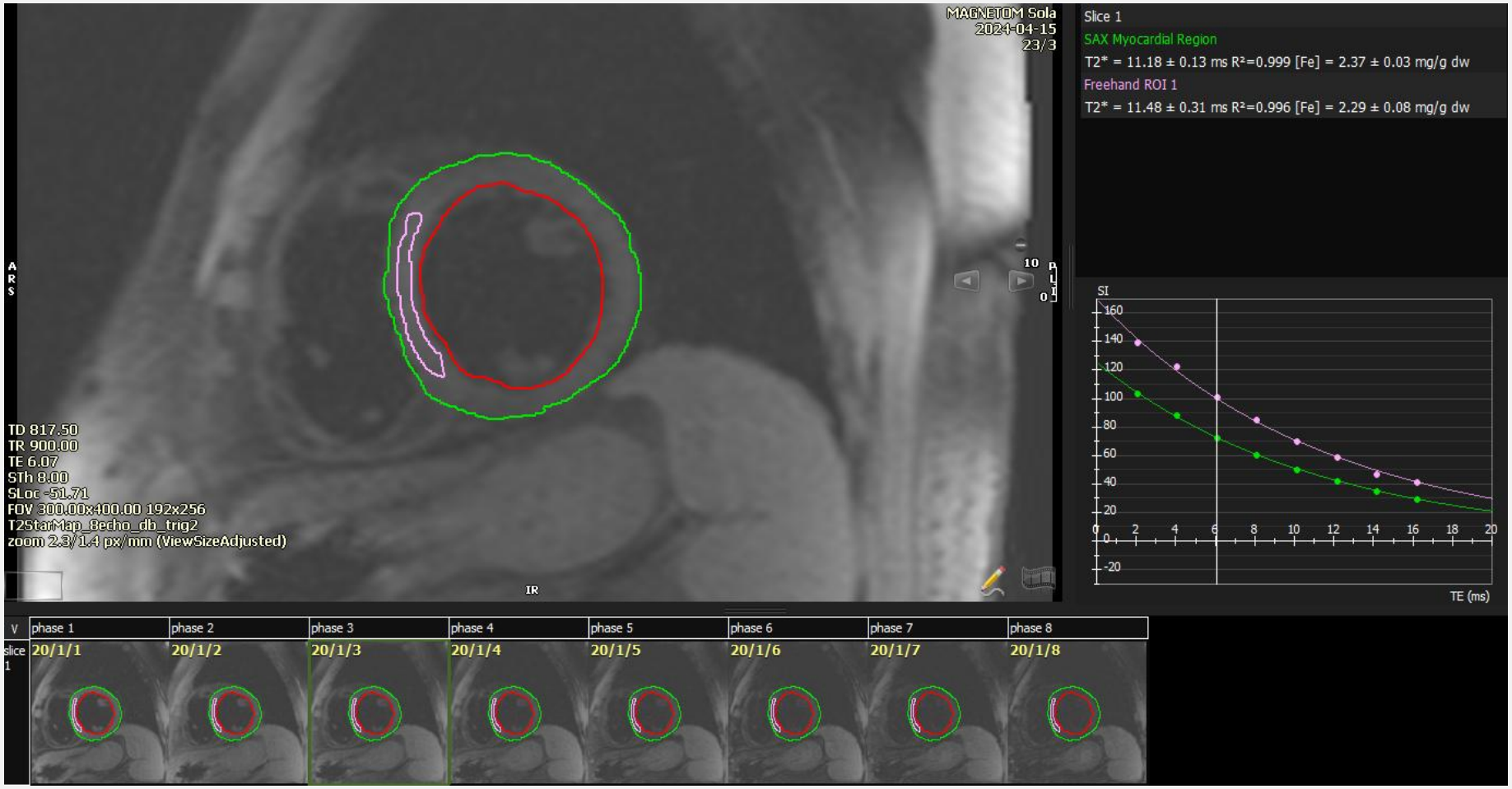


MYOCARDIAL T2* MAPPING

- **1,5 T scanner**
- a black-blood gradient echo sequence to generate pixelwise T2* mapping is recommended to improve the contrast between myocardium and its surroundings
- 8 different echo times ranging from 2 to 18 ms
- mid-ventricular short axis slice
- a homogeneous ROI is defined encompassing both sub-epicardial and subendocardial regions, as iron is preferentially stored in the sub-epicardial compared with the sub- endocardial layers
- The analysis is restricted to the septum to reduce susceptibility artifacts (in contrast to the inferolateral wall where they are common due to the proximity to the great cardiac vein)

Triadyaksa et all, J. MAGN. RESON. IMAGING 2020
Messroghli et all, JSCMR 2017

MYOCARDIAL T2* MAPPING



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≥20	Absent
14–20	Mild
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Hepatic T2* (ms)	Degree of iron overload
≥15.4	Absent
4.5–15.4	Mild
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LIVER T2* MAPPING

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10–14	Moderate
≤10	Severe
Hepatic T2* (ms)	Degree of iron overload
≥15.4	Absent
4.5–15.4	Mild
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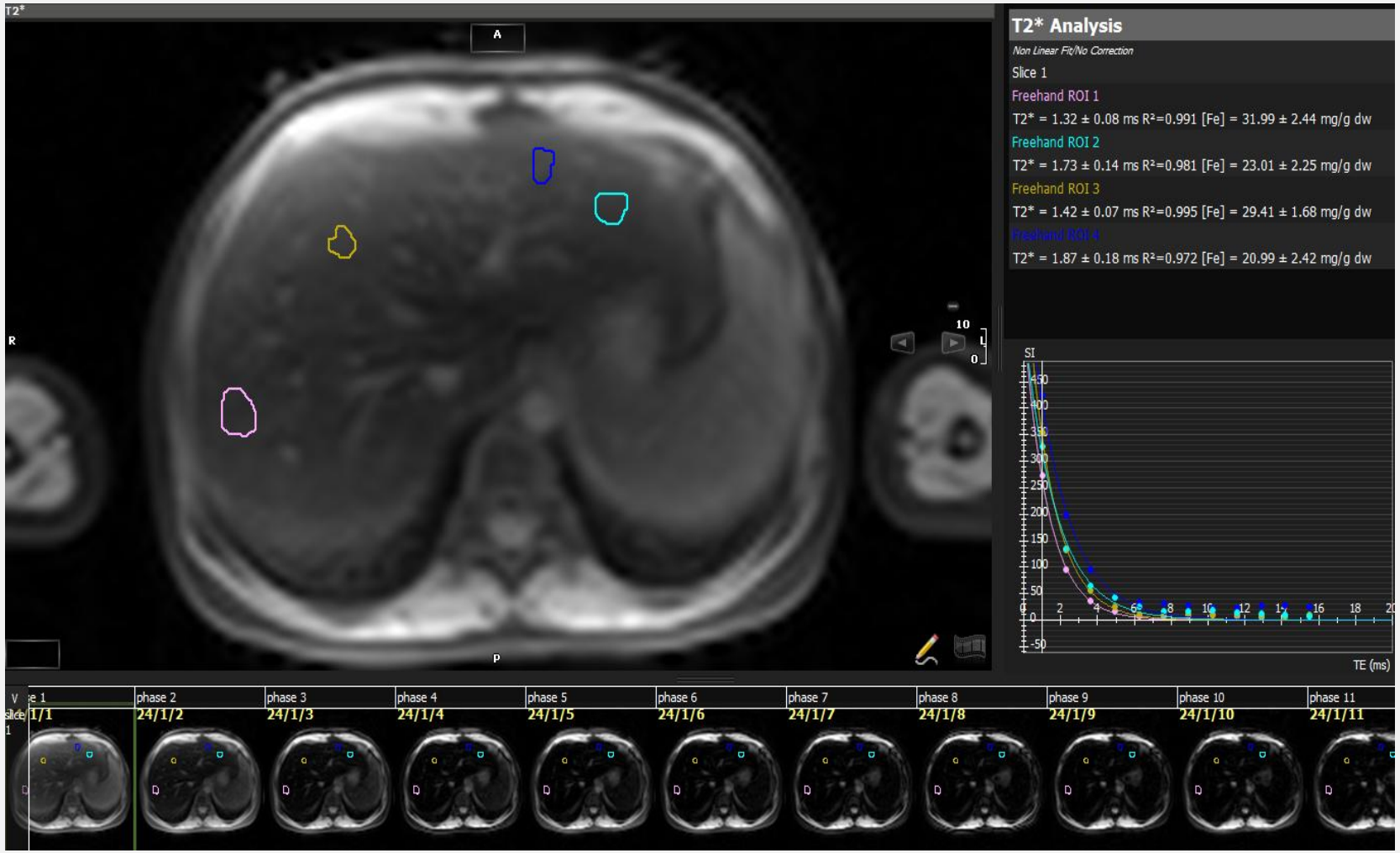
THALASSEMIA WITH MONTHLY TRANSFUSIONS



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Iron Overload Cardiomyopathy

Anatomy

Volumetric analysis & wall thickness

T2* mapping

T2-STIRS**

T2 mapping**

T1 mapping**

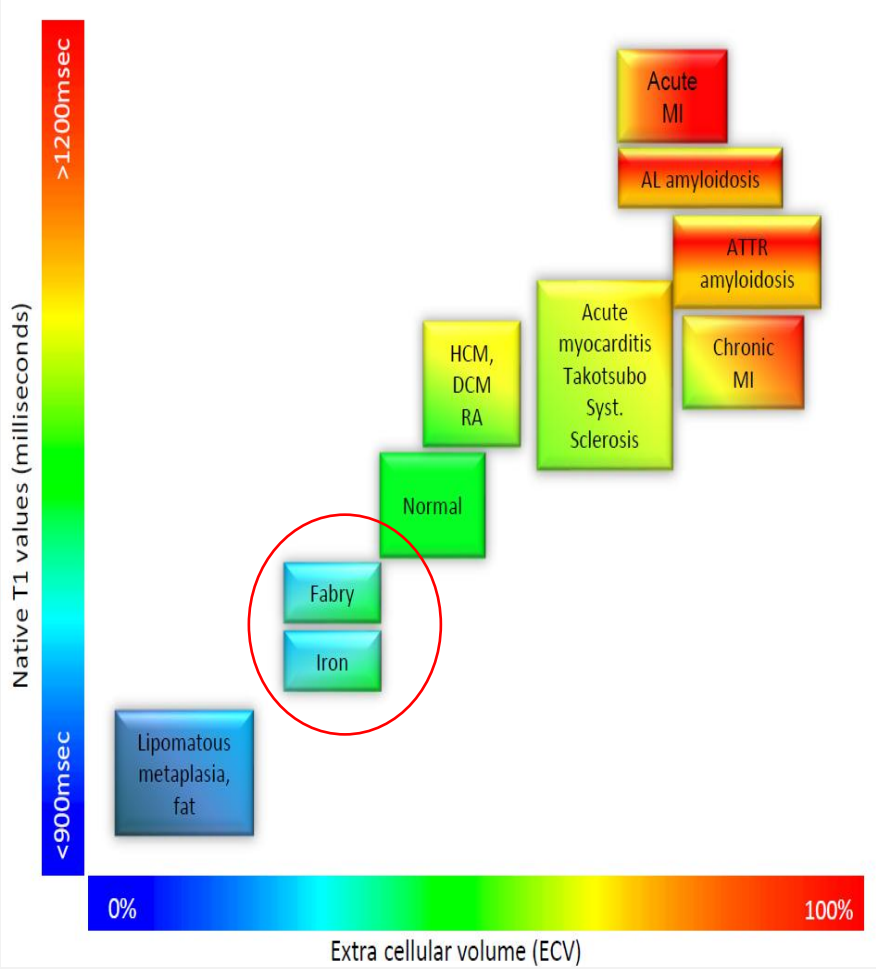
EGE**

LGE**

ECV mapping**

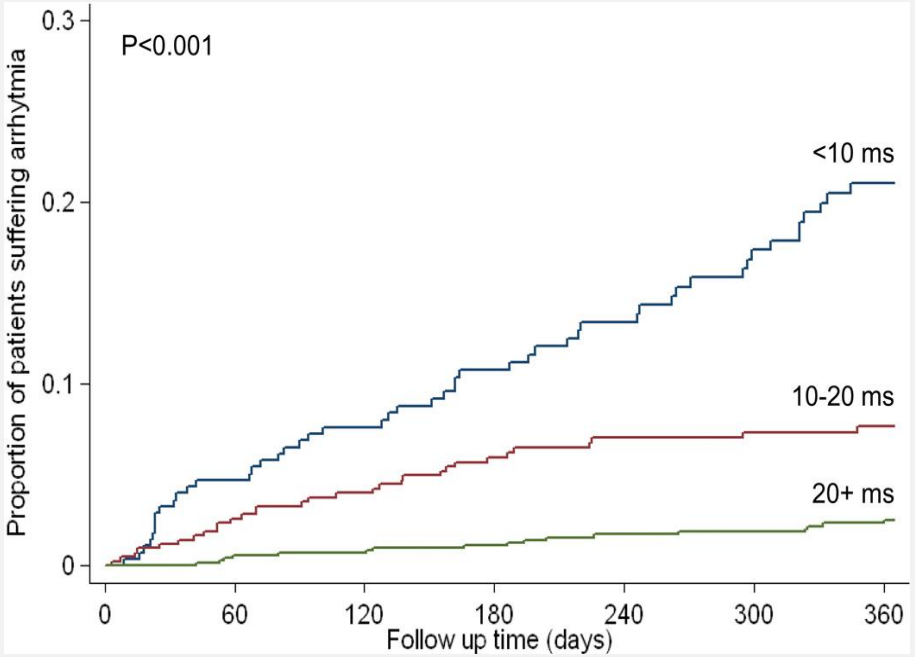
***not routinely done**

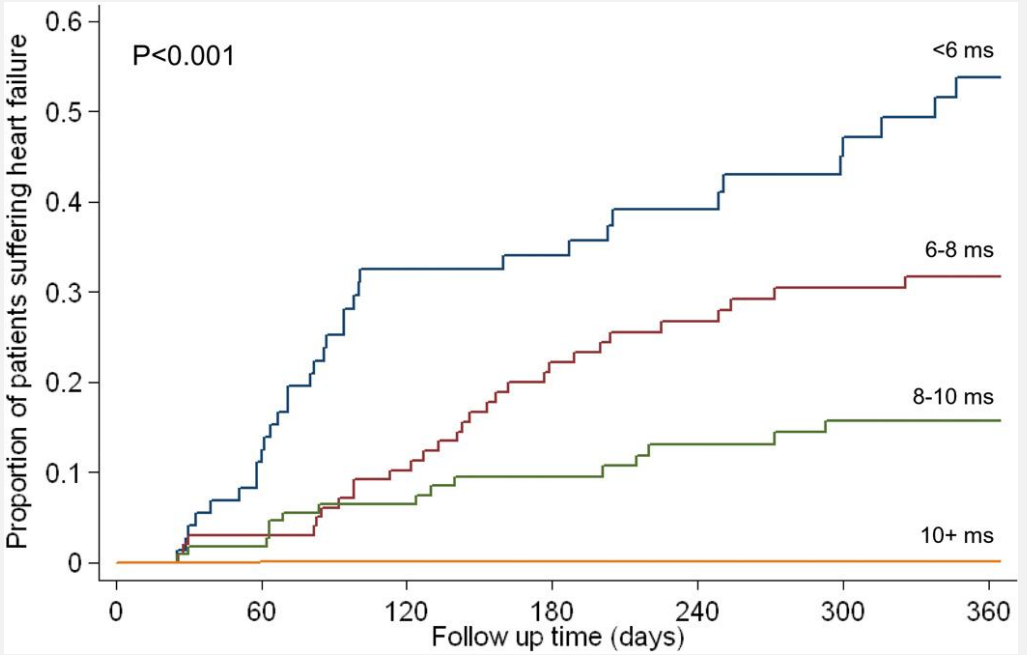
- In patients with only mild increases of cardiac iron, T1 mapping showed superior reproducibility as compared to T2* measurements (Iron deposition dominates the relaxation process in the myocardium which directly affects both transverse and longitudinal relaxation)
- Combined use of both segmental native T1 and T2* could improve the sensitivity for detecting myocardial iron.
- ECV may be increased in patients with thalassemia major and may potentially reflect diffuse interstitial myocardial fibrosis.
- <u>It is currently unknown whether ECV has a role in the management of cardiac siderosis patients</u>



IRON OVERLOAD CARDIOMYOPATHY

- Decades before the introduction of T2* CMR, heart failure and associated arrhythmias had been the predominant cause of death
- This was likely contributed to by the under-detection of myocardial iron overload

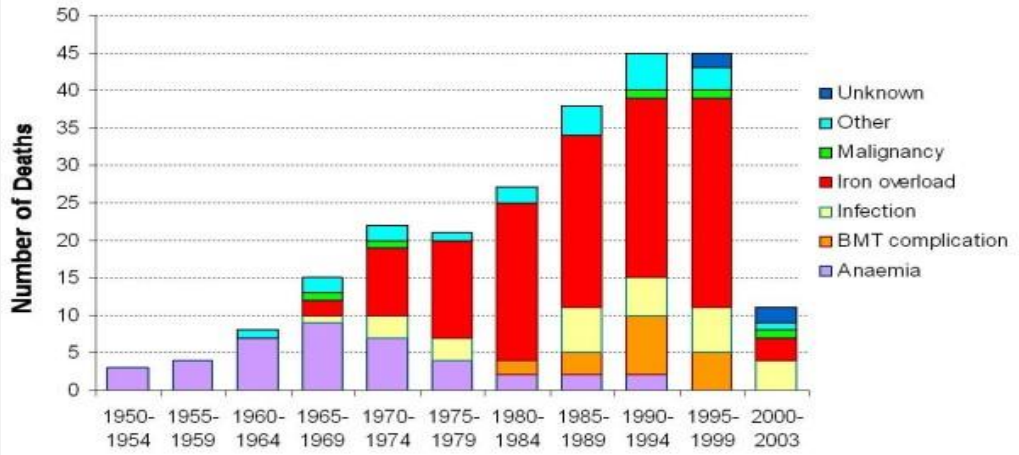


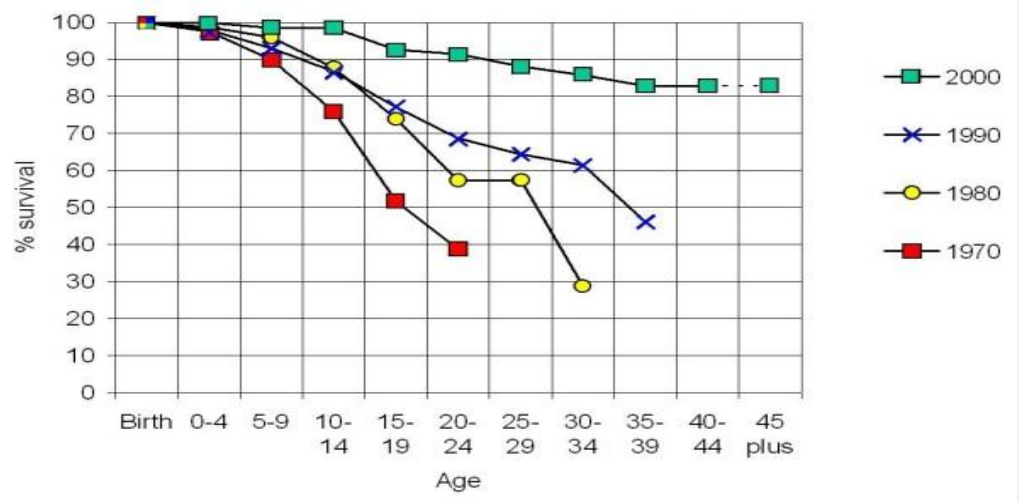


Kirk et all, Circulation 2009

IRON OVERLOAD CARDIOMYOPATHY

- After the introduction of T2* imaging to quantify myocardial iron load in United Kingdom in the late 1990s, resulting in the use of iron chelator therapy tailored to the heart iron concentration, the cardiac mortality fell by 71% in 2003
- **Similar information cannot be provided by other imaging modalities**





Pennell, Modell et all, JSCMR 2008

INFILTRATIVE CARDIOMYOPATHIES

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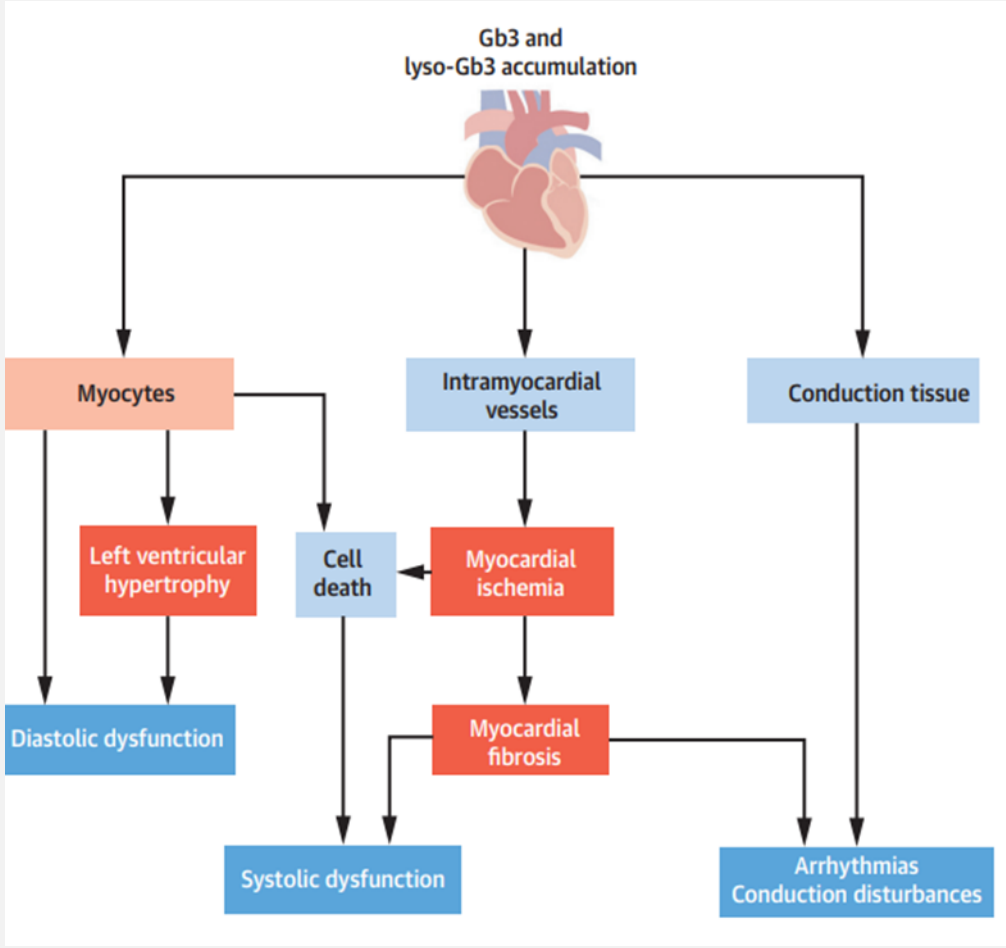
Anderson Fabry Disease

- Fabry disease is a X-linked lysosomal storage disorder characterized by accumulation of intracellular **glycosphingolipids** in different organs, including the heart
- Cardiac involvement is the leading cause of mortality and is characterized by progressive myocardial glycosphingolipid deposition, hypertrophy, inflammation, and fibrosis
- More than 30% of patients experience dyspnea, angina, palpitations, syncope, or peripheral edema
- Electrocardiographic features include short PR interval, LVH, and intraventricular conduction delay
- The diagnosis rests on genetic testing of mutations in α-galactosidase A
- CMR plays an important role in establishing a diagnosis of FD, risk stratifying patients, and monitoring disease progression or regression of LV wall thickness with therapy

Cottam et al Circulation 2023

CMR FINDINGS

- LVH
- High regional T2 in keeping with inflammation
- Low native T1 values
- Mid-wall basal inferolateral LGE



Anderson Fabry Disease

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

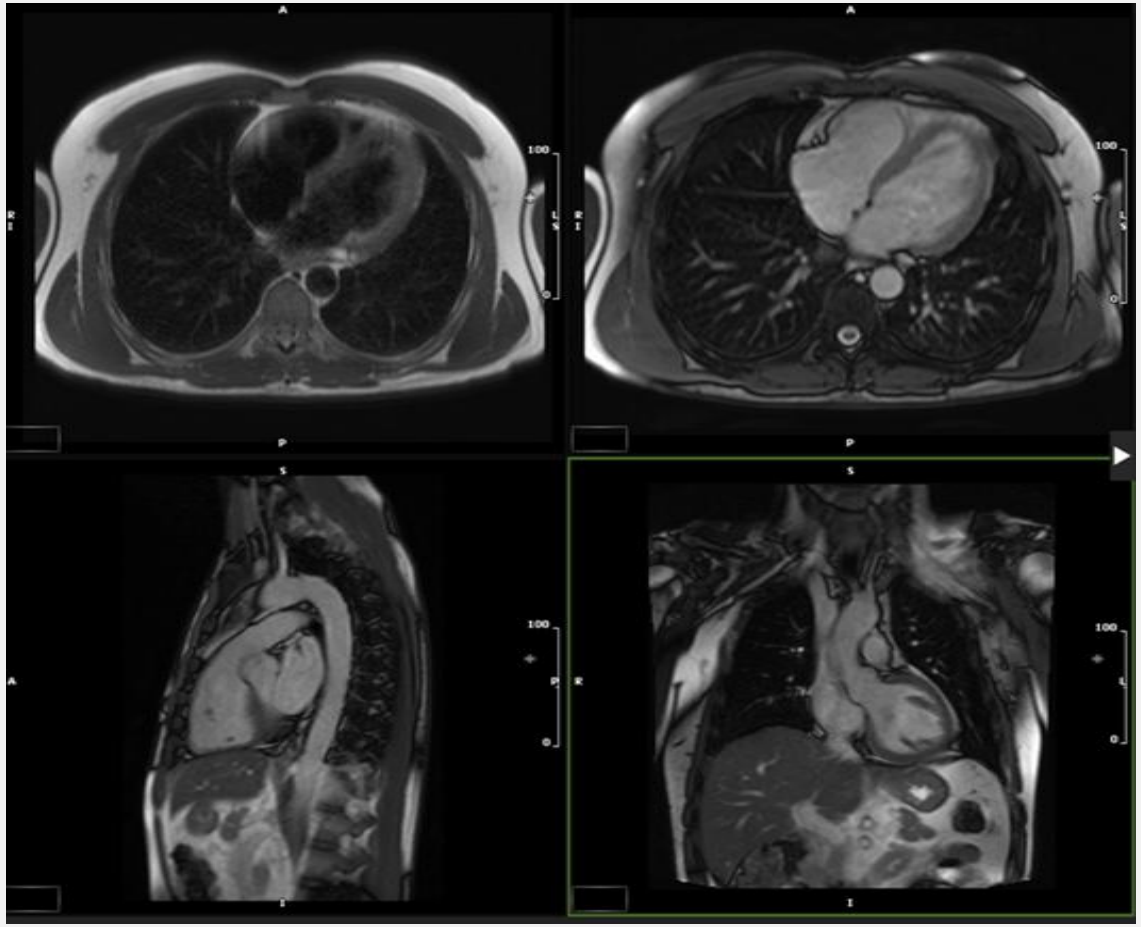
T1 mapping

Perfusion

EGE

LGE

ECV



Anderson Fabry Disease

Anatomy

Volumetric analysis & wall thickness

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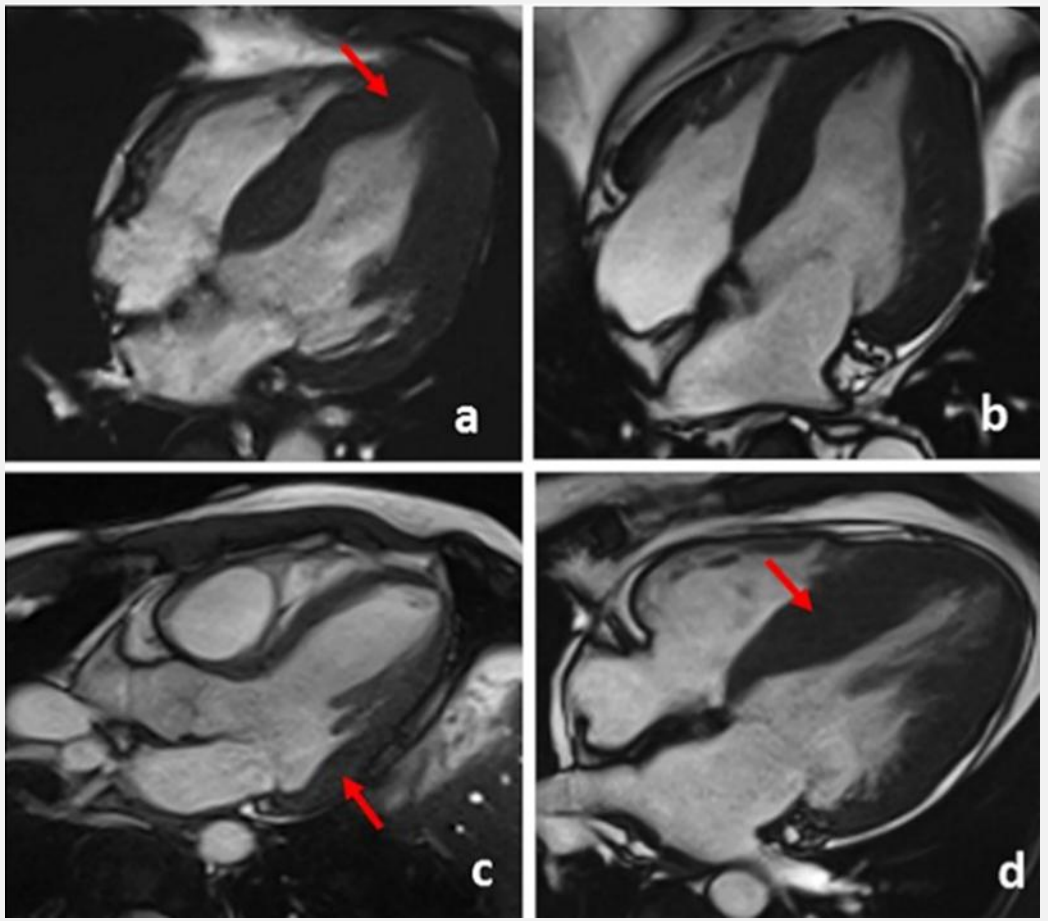
Perfusion

EGE

LGE

ECV

- Concentric LVH is the most common pattern
- Can also mimic the morphological characteristics of various subtypes of HCM, including asymmetric septal and apical variants
- Hypertrophy of the papillary muscles is also characteristic of FD and can mislead to the diagnosis of HCM
- **LVH is strong predictors of adverse cardiac events**



Anderson Fabry Disease

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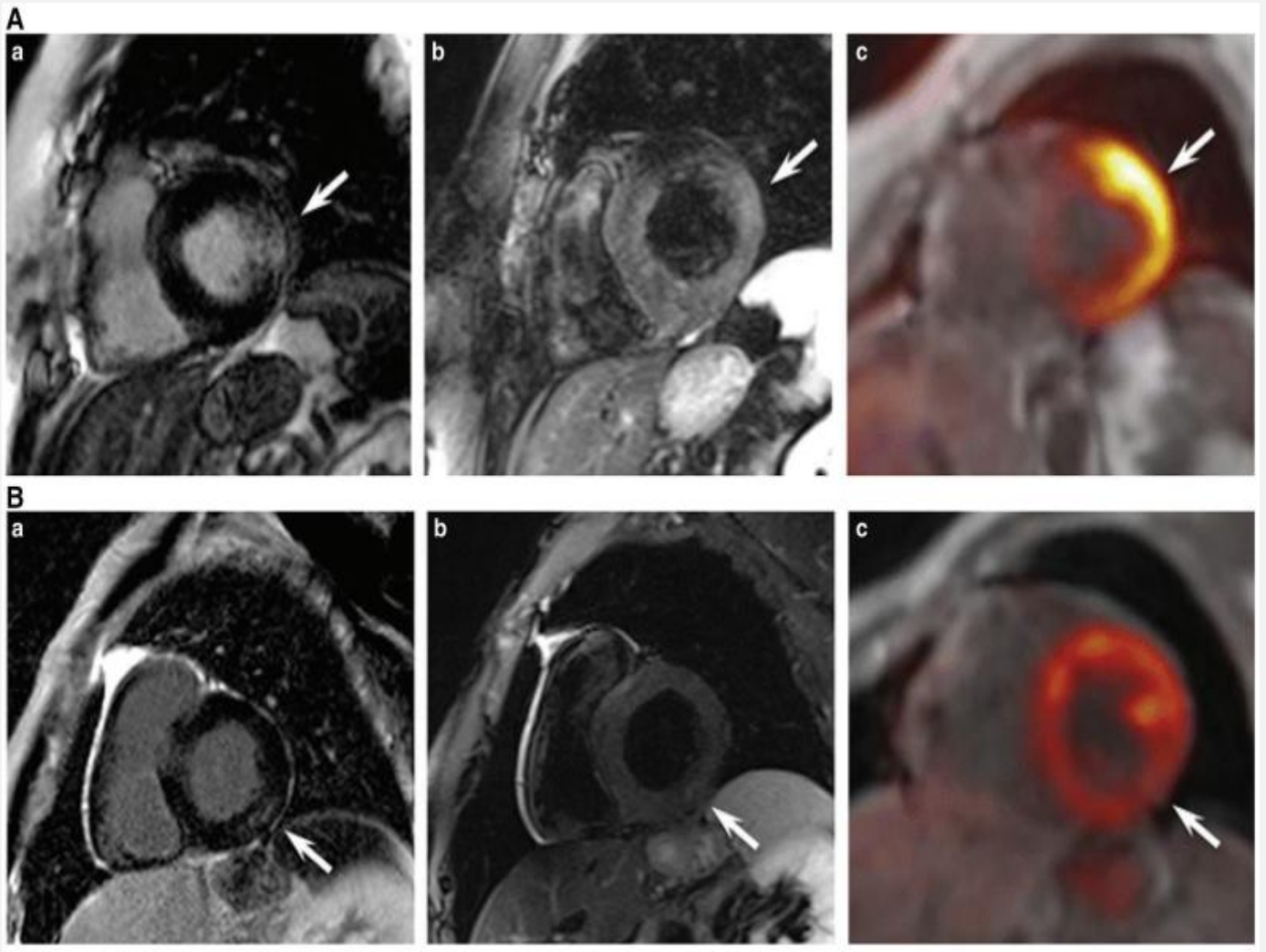
ECV

- Elevated myocardial signal suggesting edema/inflammation

T2-STIR



Anderson Fabry Disease

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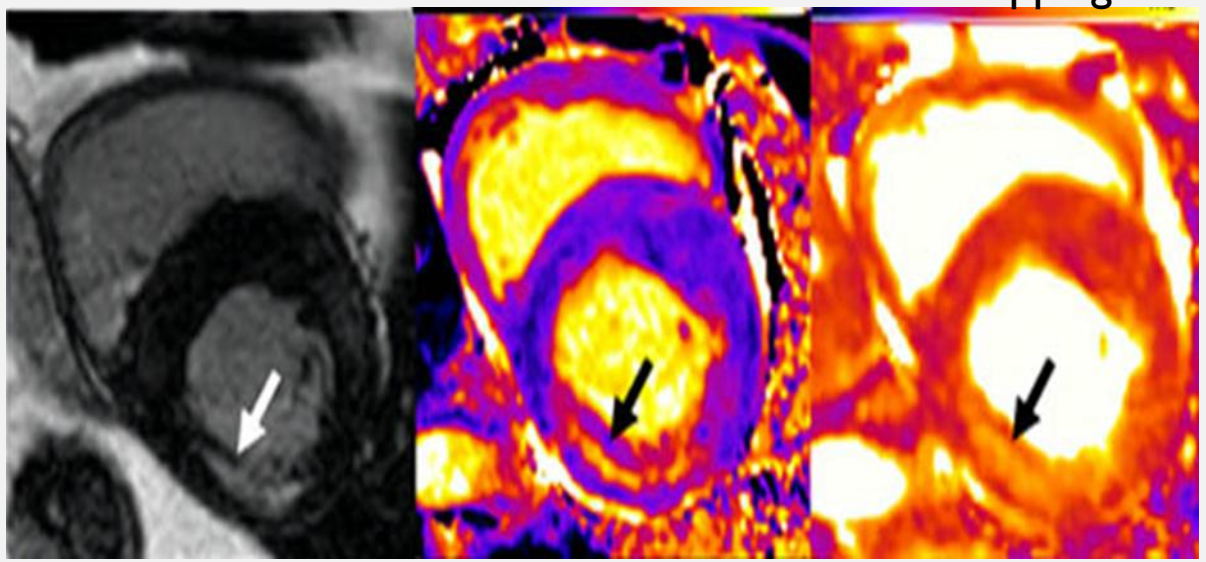
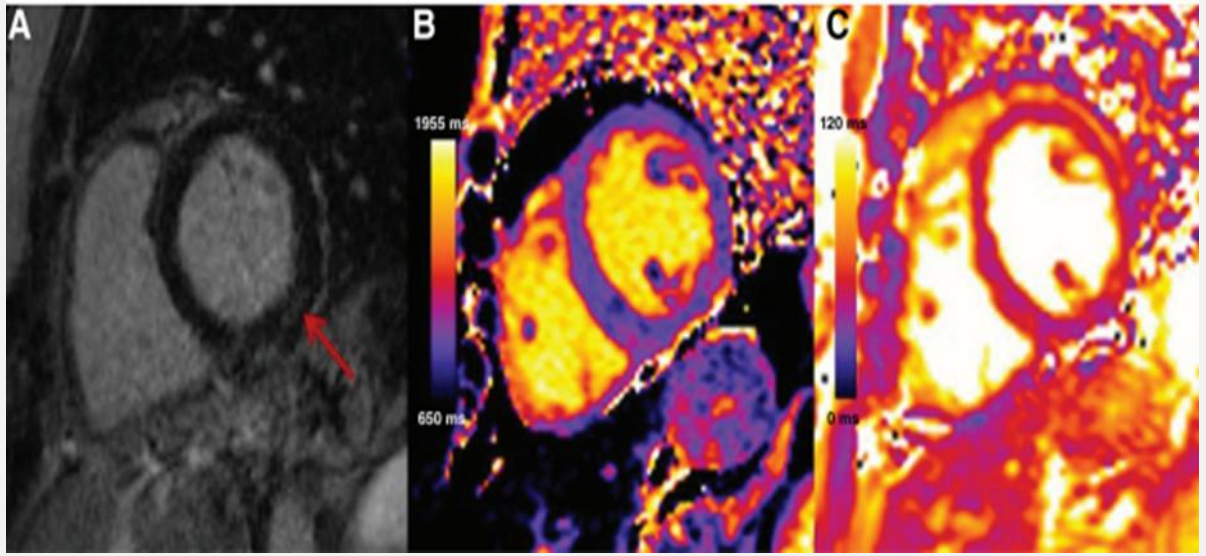
ECV

- High regional T2 values in keeping with inflammation

T2 mapping





Anderson Fabry Disease

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T1 mapping

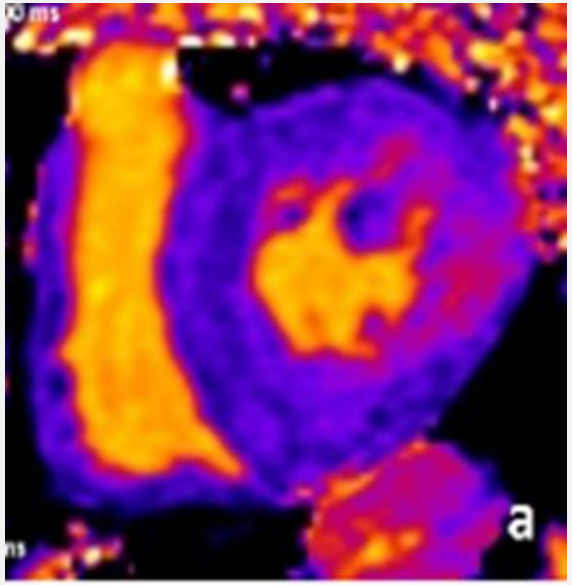
Perfusion

EGE

LGE

ECV

- Due to intracellular nature of glycosphingolipid accumulation, Native T1 values are substantially lower
- patients who have FD without LVH, lower native T1 values are associated with clinical disease worsening
- ECV is often normal in early stages (intracellular storage disease) but can be increased in later stages, particularly in areas of fibrosis



Fabry Disease
T1= 890 ms

Anderson Fabry Disease

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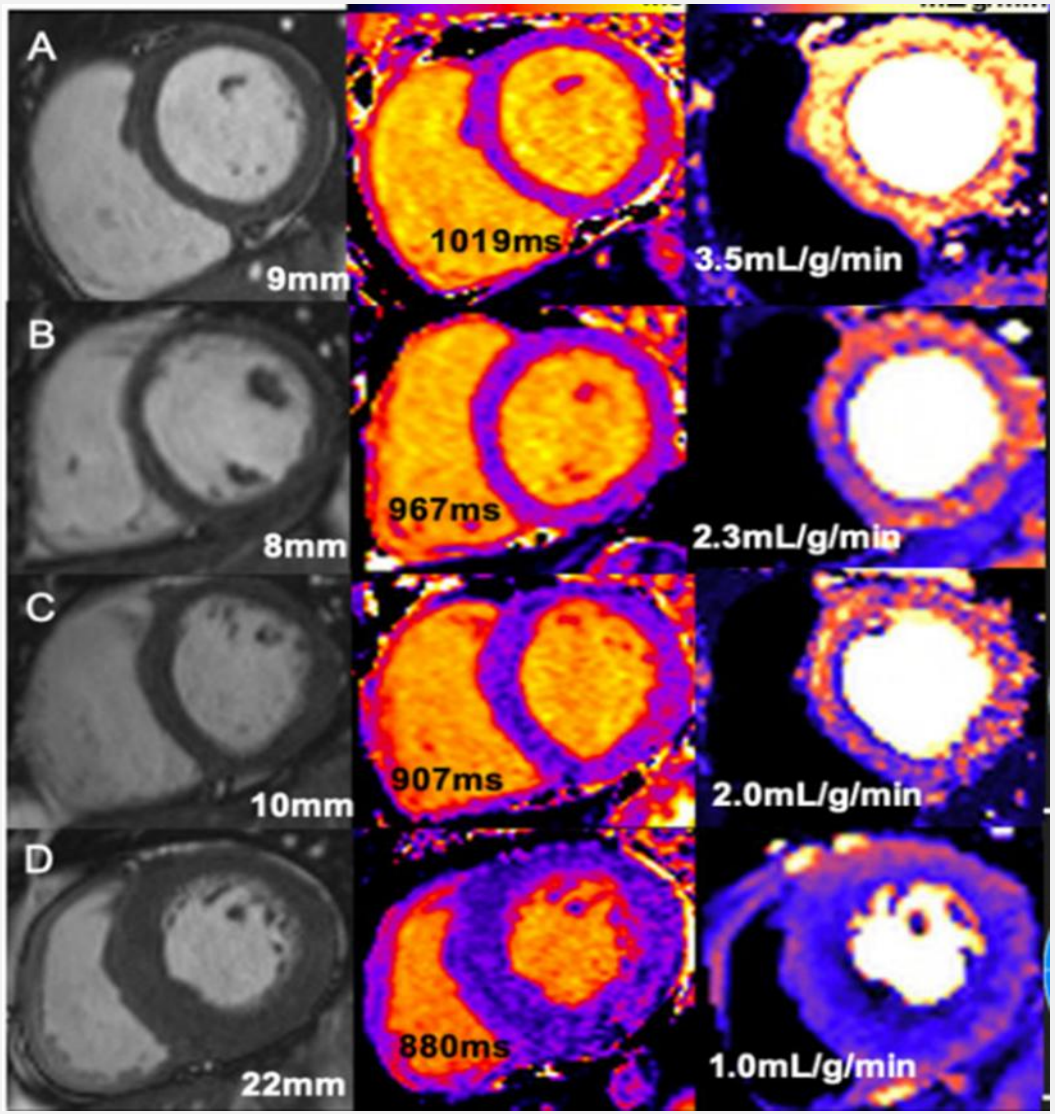
EGE

LGE

ECV



(A) Healthy control, no LVH, normal T1, MBF

(B) FD with normal T1 and without LVH; MBF is mildly reduced

(C) FD with low T1 and without LVH, low MBF

(D) FD with LVH; T1 is low, MBF are significantly impaired

Augusto EHJ 2021

Anderson Fabry Disease

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

Perfusion

EGE

LGE

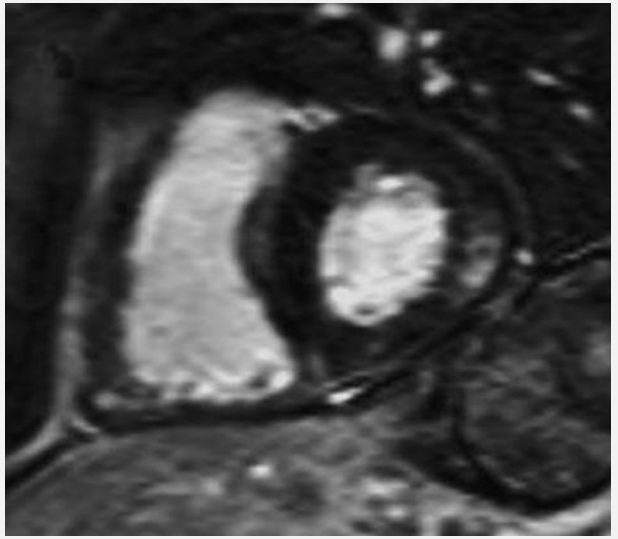
ECV

- Basal inferolateral wall LGE

De Cobelli et al, AJR 2009

- 50%

- Inferolateral LGE: pseudonormalisation native T1 normal/↑ possible if the effects of replacement fibrosis exceed the fatty-related T1 decrease



Anderson Fabry Disease

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

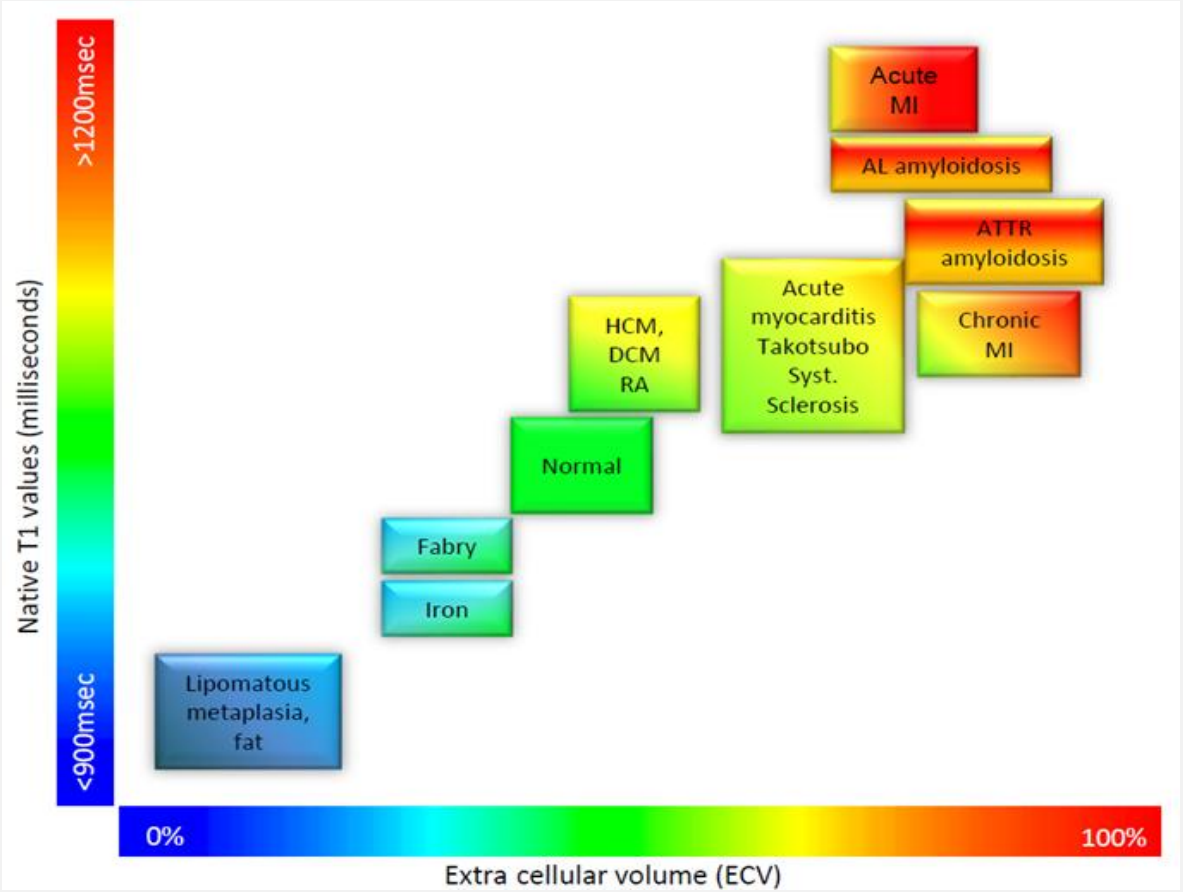
Perfusion

EGE

LGE

ECV

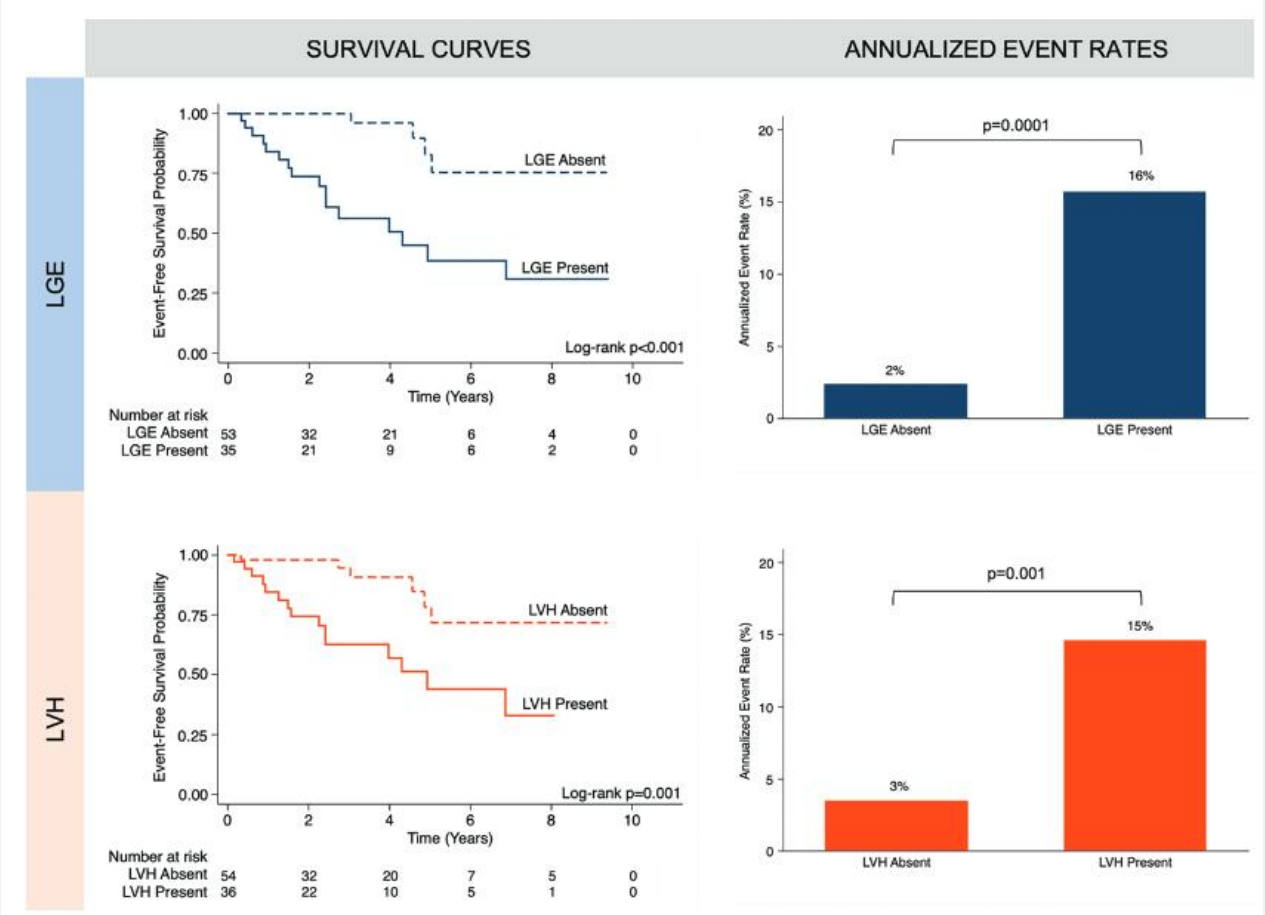
- ECV is often normal in early stages but can be increased in later stages, particularly in areas of fibrosis and LGE



Deva et al, JACC 2016
Karur Radiology 2018

Anderson Fabry Disease

Cardiac MRI findings of left ventricular hypertrophy and late gadolinium enhancement can be used to identify patients with Fabry disease who are at high risk of adverse cardiac events (composite end point: ventricular tachycardia, bradycardia requiring device implantation, severe heart failure or cardiac death)



Hanneman et all, Radiology 2020

Anderson Fabry disease 3-phase model

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

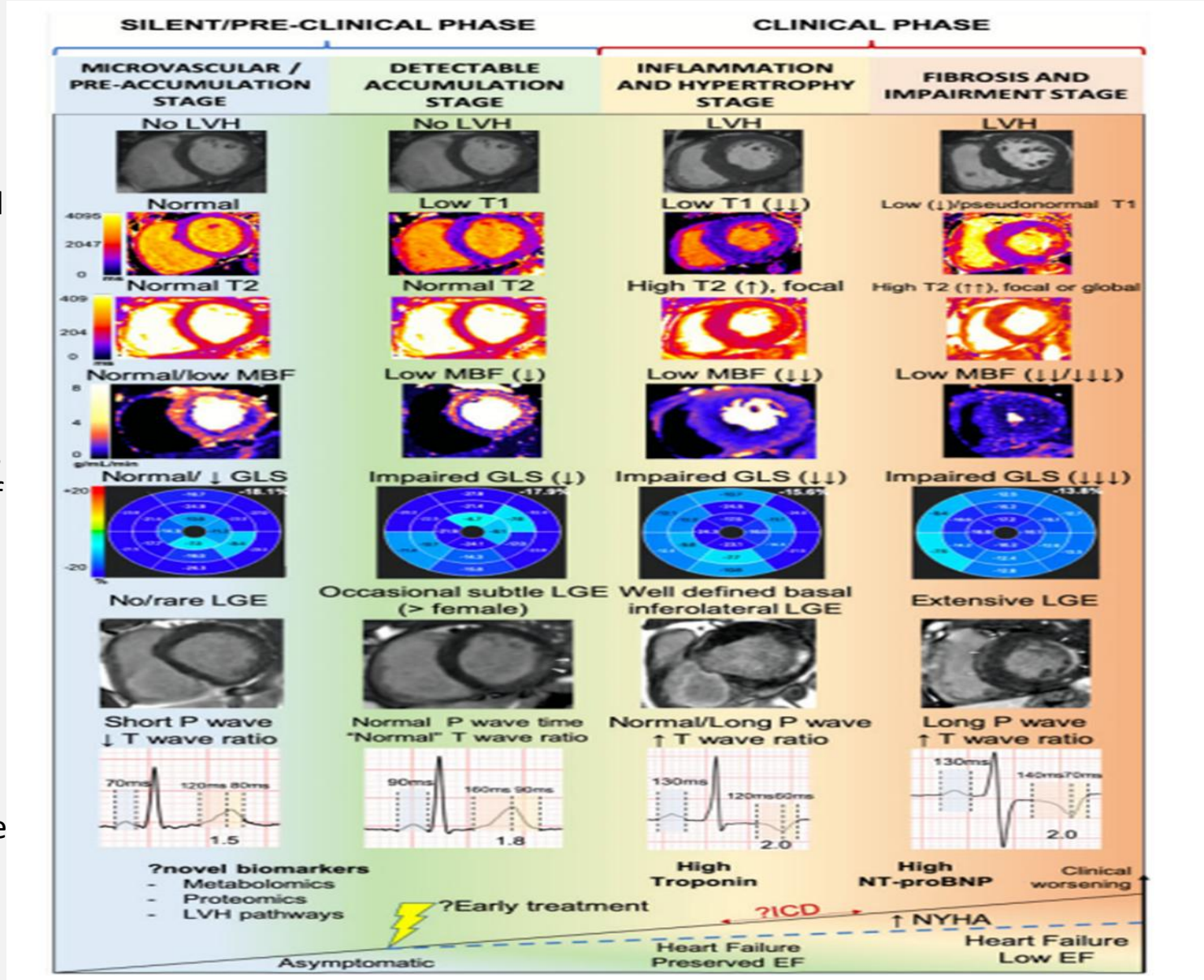
T1 mapping

EGE

LGE

ECV

- accumulation, starting in childhood and characterized by progressive lowering of T1 with no LVH or LGE
- inflammation and/or hypertrophy, with low T1, initial LVH (mostly in males), and T2 mapping evidence of inflammation in the basal inferolateral segment associated with LGE
- fibrosis and/or impairment, with increasing T1 values (pseudo-normalization) and LGE with wall thinning in the basal inferolateral segment



INFILTRATIVE CARDIOMYOPATHIES

- Iron Overload Cardiomyopathy
- Anderson Fabry Disease
- Cardiac Amyloidosis
- Cardiac Sarcoidosis
- Danon disease
- Friedreich ataxia
- Pompe Disease, PRKAG2 syndrome, and the various types of mucopolysaccharidosis

CARDIAC AMYLOIDOSIS

- Amyloidosis is characterized by extracellular deposition of misfolded or misassembled proteins
- Several types of amyloids can involve the heart (AL, ATTR, AA)
- Treatment is dictated by the type of amyloid and the degree of involvement
- Early detection and accurate classification are essential
- A substantial number of patients with heart failure with preserved ejection fraction have undiagnosed cardiac amyloidosis
- Advanced stages of CA usually present as restrictive cardiomyopathy, typified by dyspnea on exertion, elevated jugular venous pressure, hepatomegaly, ascites, and peripheral edema

Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS**

T2 mapping**

T1 mapping

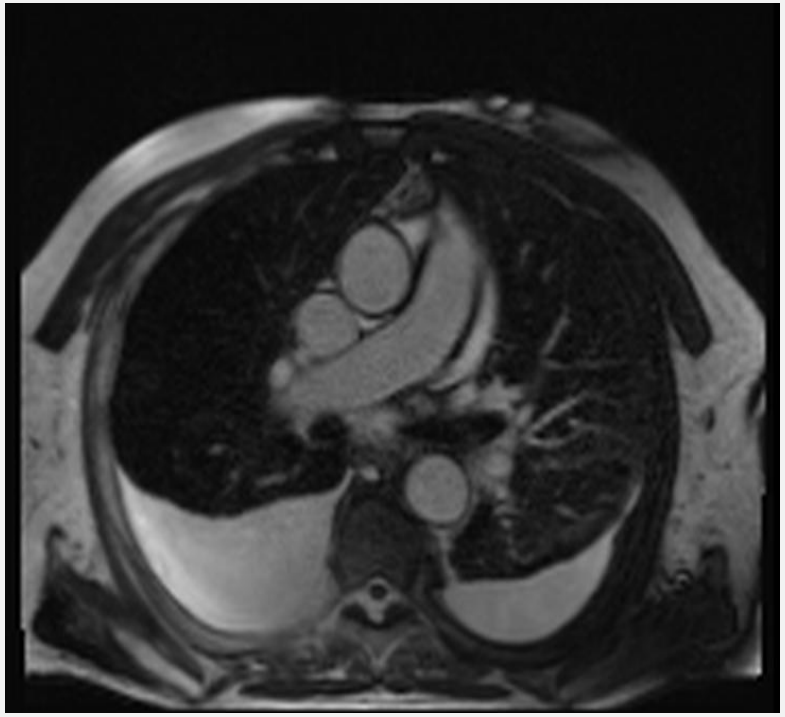
Perfusion**

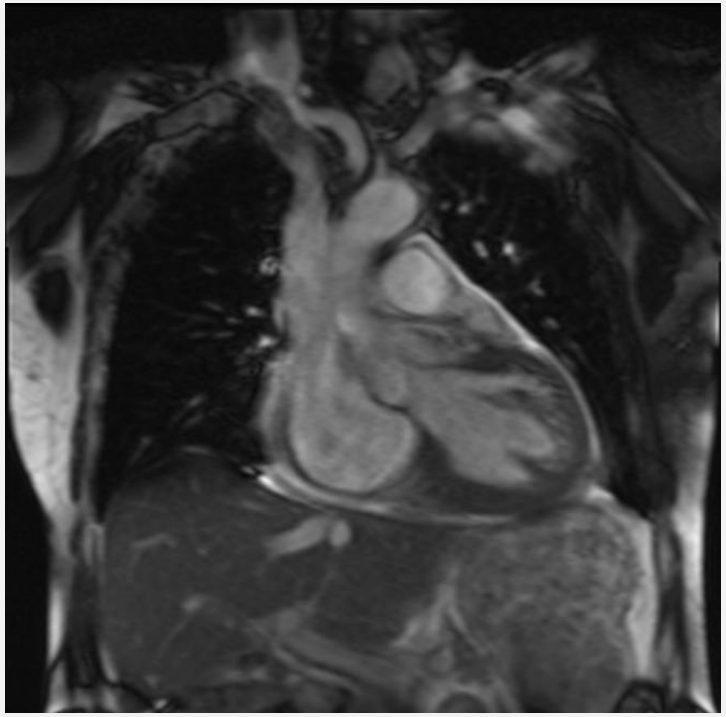
EGE

LGE

ECV mapping

*** not routinely done***





Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS**

T2 mapping**

T1 mapping

Perfusion**

EGE

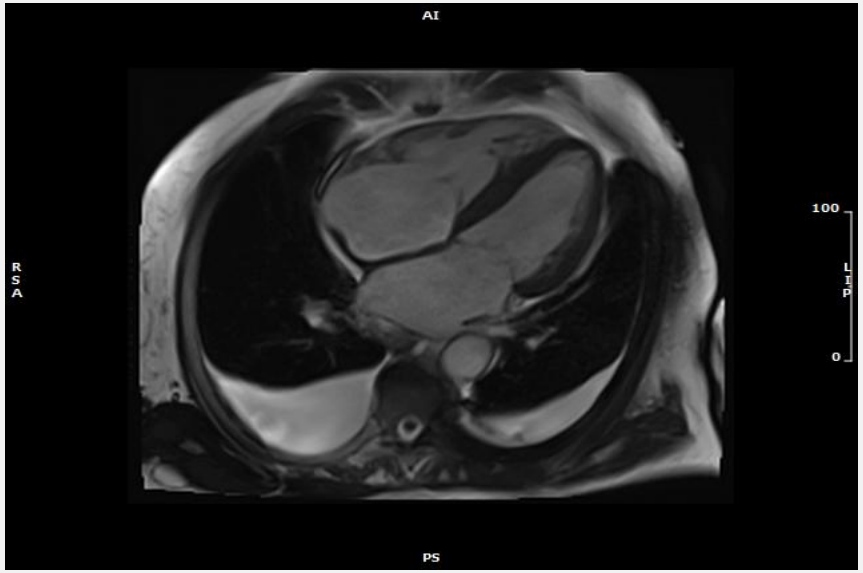
LGE

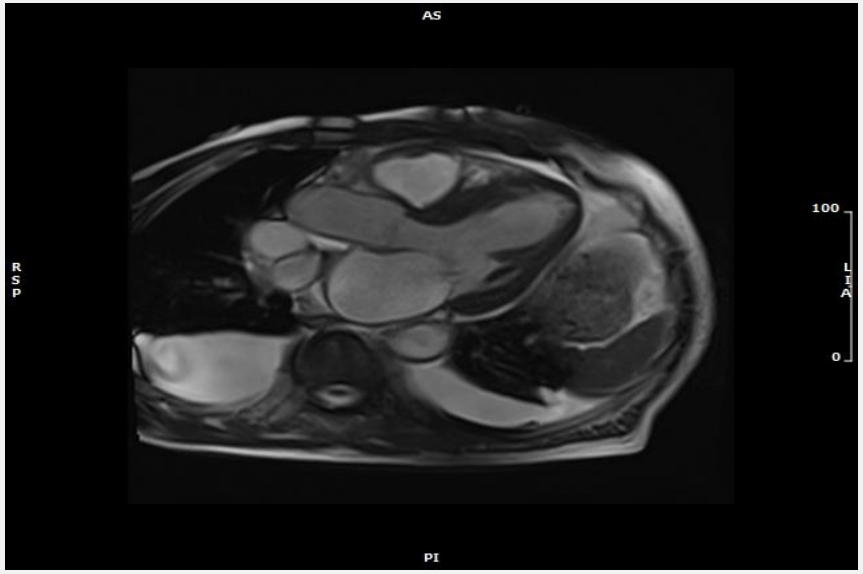
ECV mapping

*** not routinely done***

Cine images typically demonstrate:

- **Restrictive LV pattern** (non-dilated ventricles, preserved LV function, restrictive filling pattern, enlarged LA / RA) and concentric LV hypertrophy
- **Bi-atrial dilation**
- **Atrial septal hypertrophy** of >6mm (in <20% of the cases)
- **Pericardial and pleural effusion are common**





Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS**

T2 mapping**

T1 mapping

Perfusion**

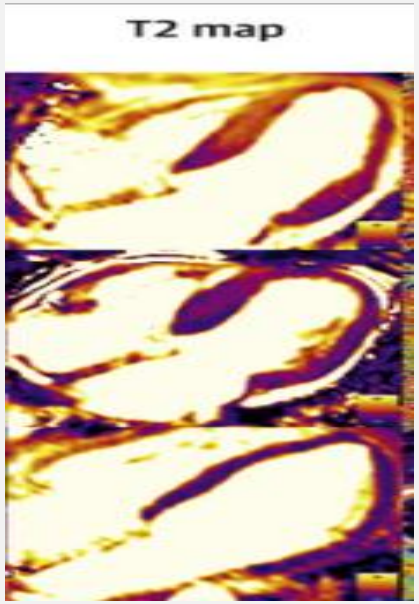
EGE

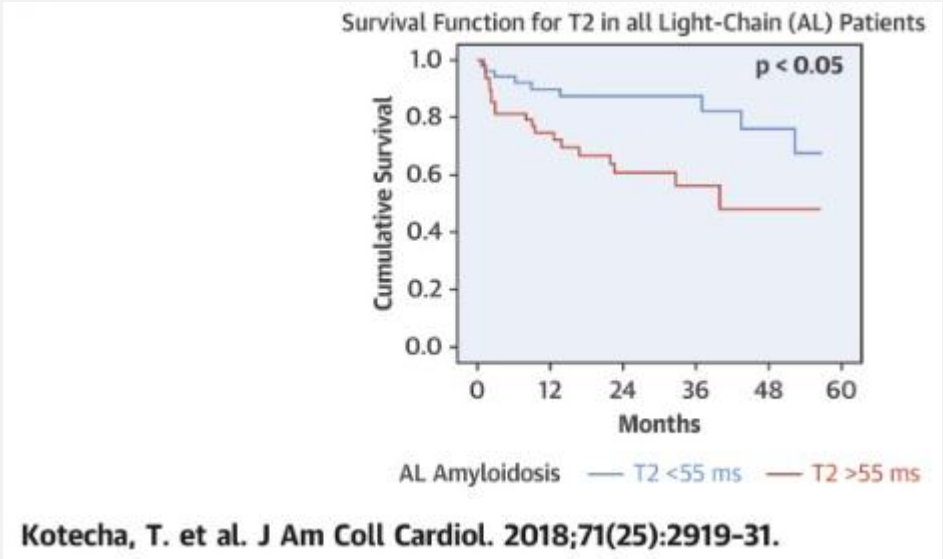
LGE

ECV mapping

*** not routinely done***

- There are also conflicting data on the presence and significance of myocardial edema in cardiac amyloid, with elevated T2 values reported in some studies, whereas others have demonstrated normal T2 values both in patients with active amyloidosis and those in remission
- Myocardial edema is present in cardiac amyloidosis by histology and cardiovascular magnetic resonance T2 mapping.
- T2 is higher in untreated AL amyloidosis compared with treated AL and ATTR amyloidosis and is a predictor of prognosis in AL amyloidosis. This suggests mechanisms additional to amyloid infiltration contributing to mortality in amyloidosis.





Kotecha, T. et al. J Am Coll Cardiol. 2018;71(25):2919-31.

Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS**

T2 mapping**

Native T1 mapping

Perfusion**

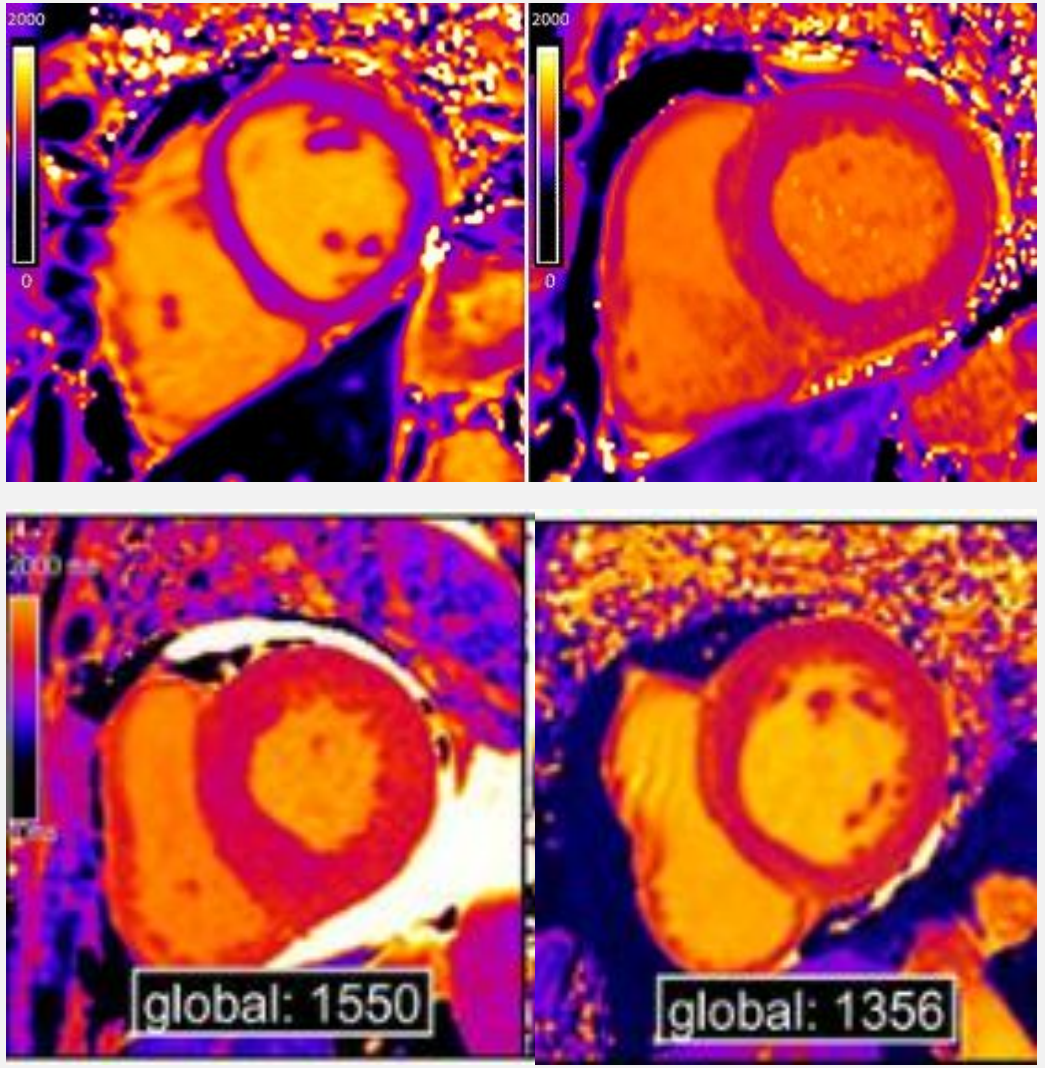
EGE

LGE

ECV mapping

*** not routinely done***

- Native T1 values (pre-gadolinium contrast) are higher in areas of amyloid deposition compared with normal tissues
- the native T1 values provide a combined signal from myocyte and extracellular space and reflect changes in either or both of those tissue compartments



Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS**

T2 mapping**

T1 mapping

Perfusion**

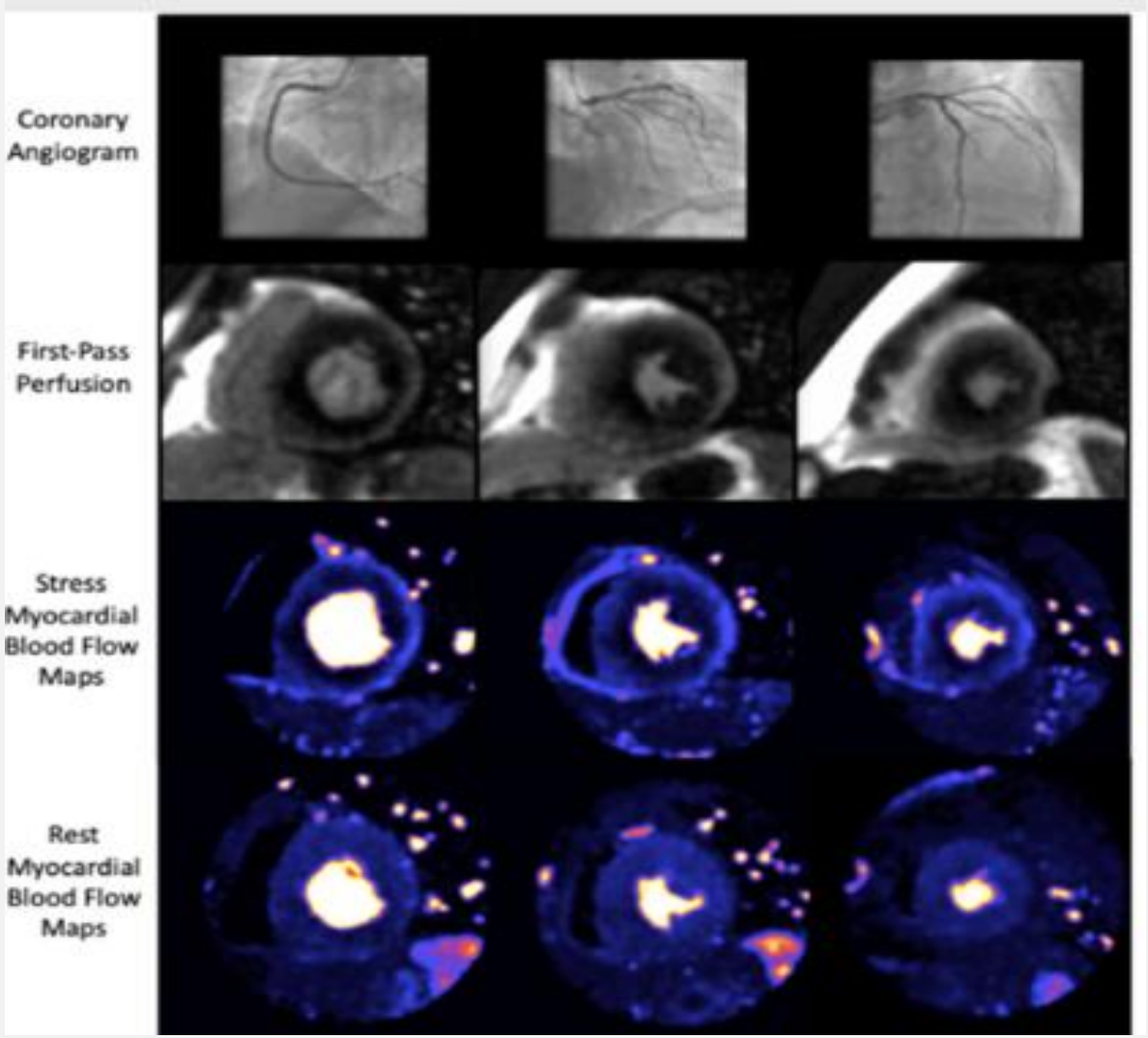
EGE

LGE

ECV mapping

***** *not routinely done***

Cardiac amyloidosis is associated with severe inducible myocardial ischaemia demonstrable by CMR stress perfusion mapping



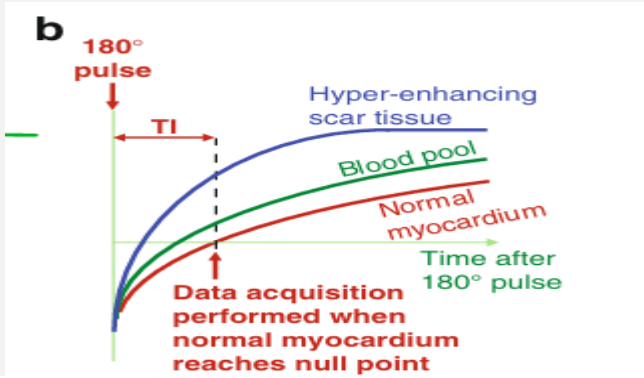
stress myocardial perfusion maps show extensive global ischaemia

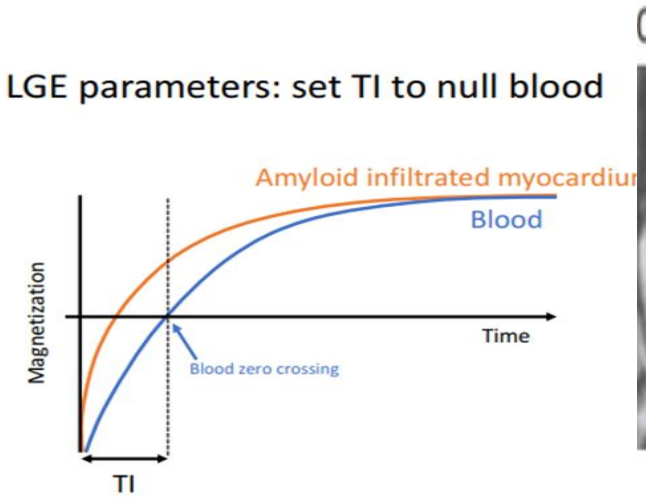
Cardiac Amyloidosis

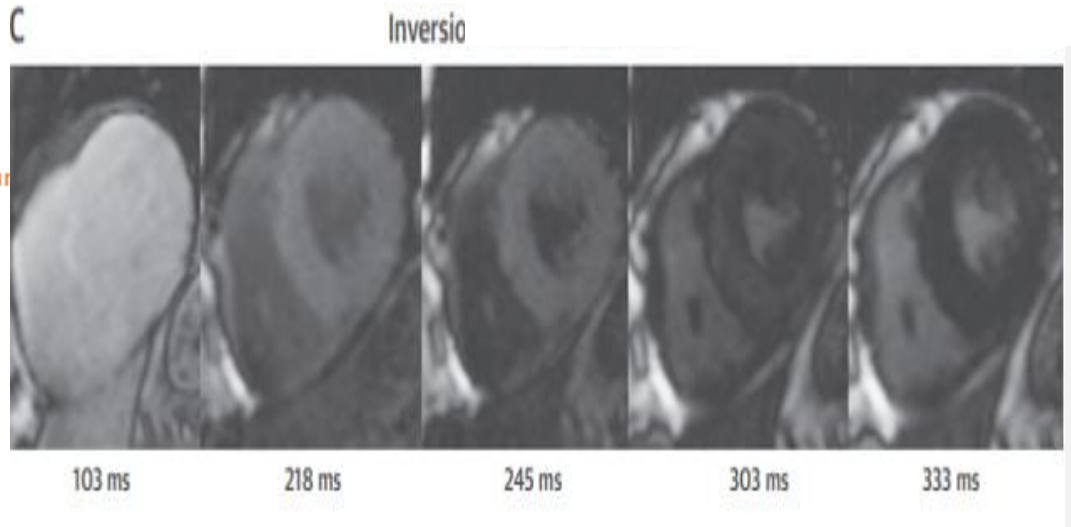
- **Anatomy**
- **Volumetric analysis & wall thickness**
- **T2-STIRS**
- **T2 mapping**
- **T1 mapping**
- **Perfusion****
- **EGE**
- **LGE**
- **ECV mapping**

** ***not routinely done***

- determined the null point, which is the inversion recovery time at which the normal myocardium appears black or "nulled."







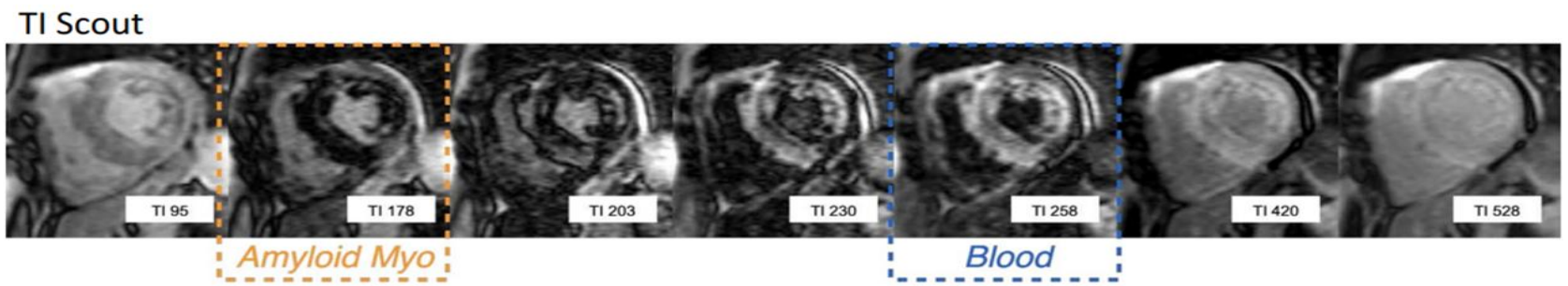


Fig. 12 Cardiac amyloidosis. Top: Inversion recovery curves for the subset of patients with cardiac amyloidosis markedly altered gadolinium kinetics (left). Selection of the TI in this subset can often be confusing because, effectively, all the myocardium is abnormal and the null time for myocardium is shorter than blood. In this scenario, selecting an inversion time that null blood highlights the amyloid infiltration, and the regions with greater involvement have higher image intensity (right). Bottom: A TI scout can be used to quickly identify the presence of markedly altered gadolinium kinetics and to aid in the selection of the initial TI selection to null blood

Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

Perfusion**

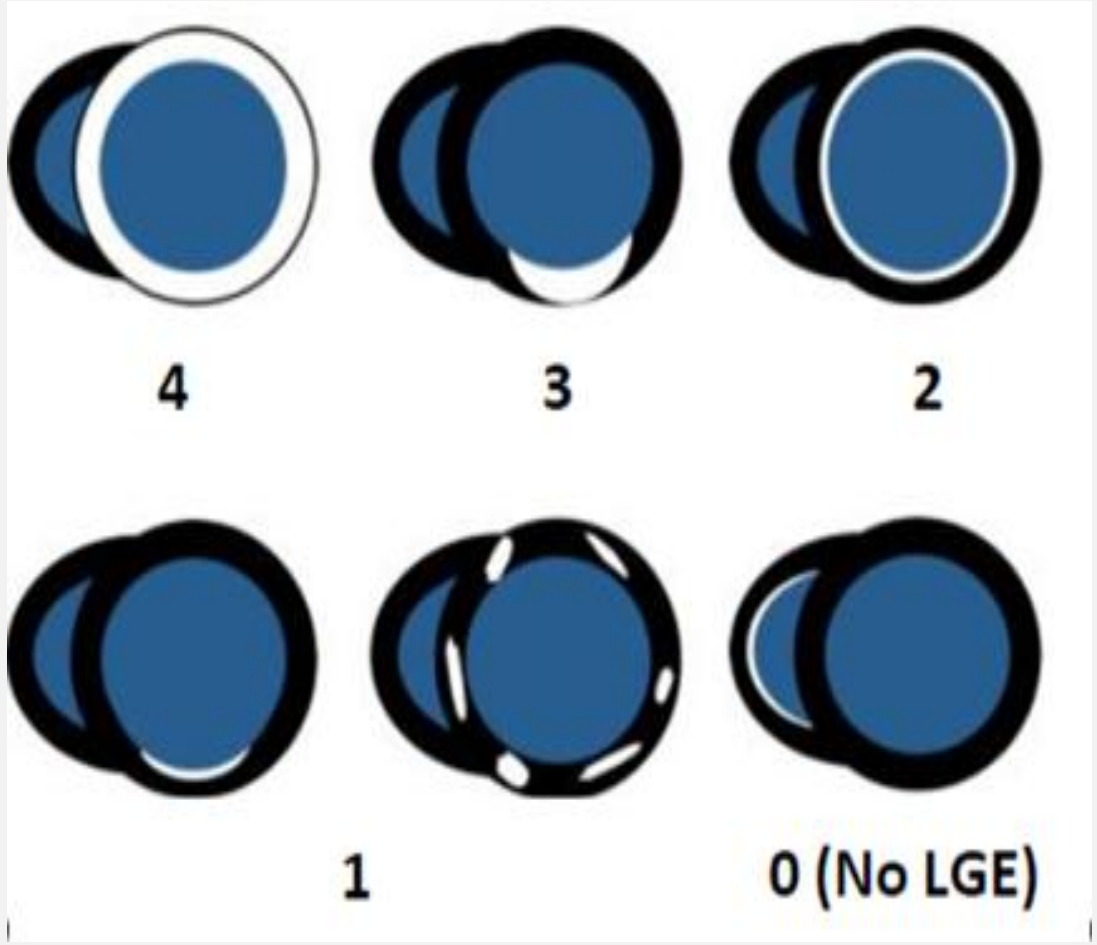
EGE

LGE

ECV mapping

*** not routinely done***

- Global subendocardial enhancement, transmural LGE, and to a lesser degree, a focal, patchy LGE, are all features of CA with a sensitivity of 86% and specificity of 92%
- LGE is highly prevalent and more common in ATTR than AL CA
- LGE is a significant predictor of mortality in AL, ATTRv, and ATTRwt ($p < 0.001$) (52), and in patients with transmural LGE, overall survival at 24 months is worse for AL (45%) than for ATTR CA



Fontana Circulation 2015
Dorbala JACC 2020

Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

Perfusion**

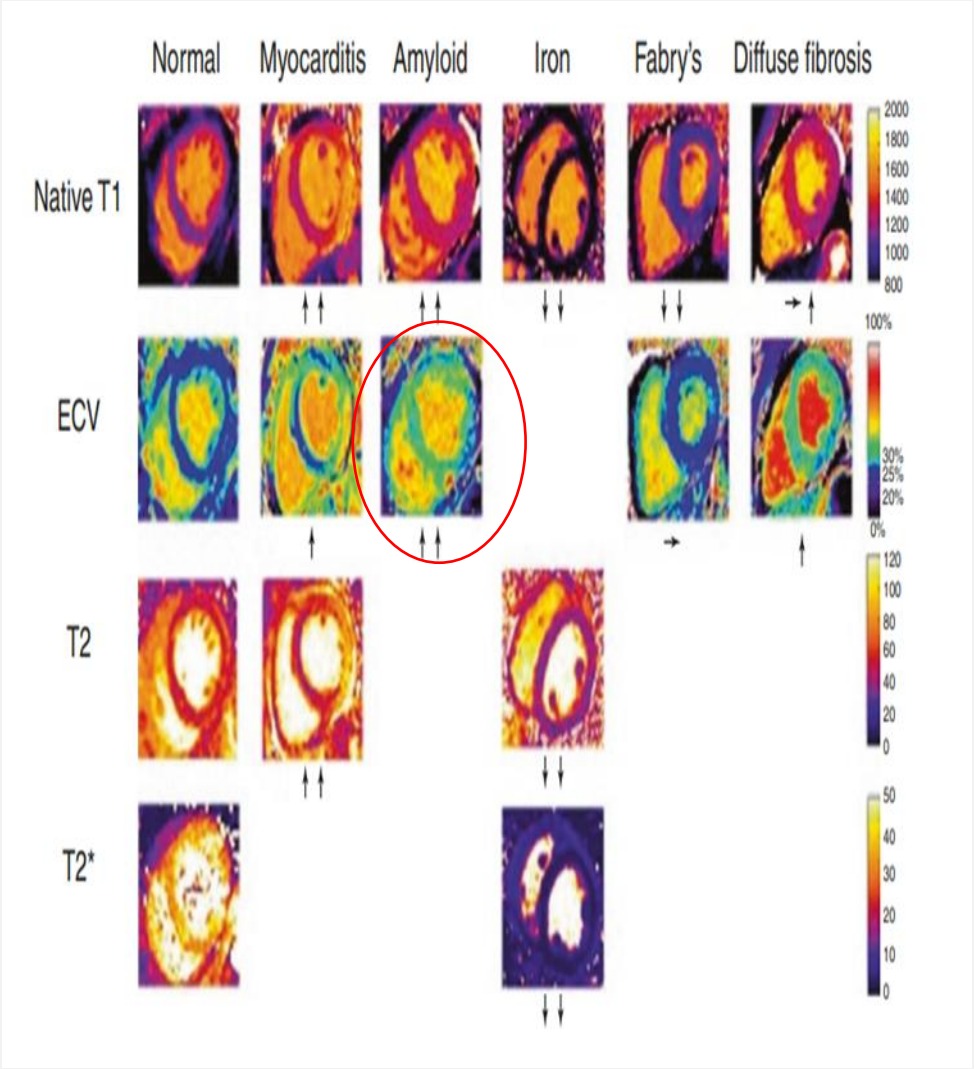
EGE

LGE

ECV mapping

***** not routinely done**

- Native T1 and ECV values are often dramatically elevated in CA due to expansion of the interstitial space from fibrillar deposits
- Mean native T1 and ECV values have been shown to differ between subtypes, with higher native T1 in AL and higher ECV in ATTR
- Total myocyte cell volume, derived from ECV and indexed LV myocardial volume, is higher in ATTR than AL amyloidosis, indicative of concomitant and potentially compensatory myocyte hypertrophy



Cardiac Amyloidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

Perfusion**

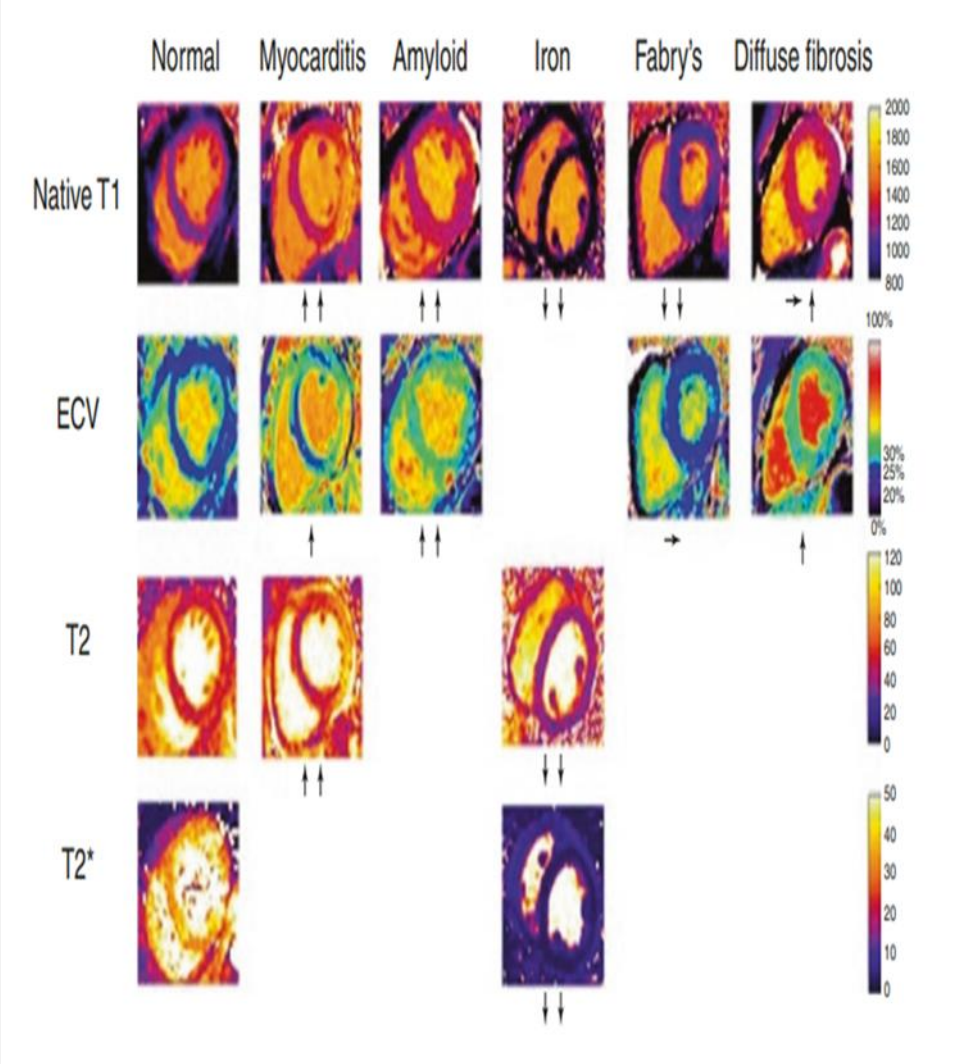
EGE

LGE

ECV mapping

***** not routinely done***

- Higher values of ECV are noted in areas of LGE, suggesting significant extracellular deposition of amyloid
- ECV has been shown to be a more robust marker of prognosis compared with native T1 or LGE in cardiac amyloidosis
- Furthermore, ECV may be useful for tracking disease burden and response to therapy, although some studies have demonstrated lower ECV in AL amyloid after treatment38 while others have not



Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

Perfusion**

EGE

LGE

ECV mapping

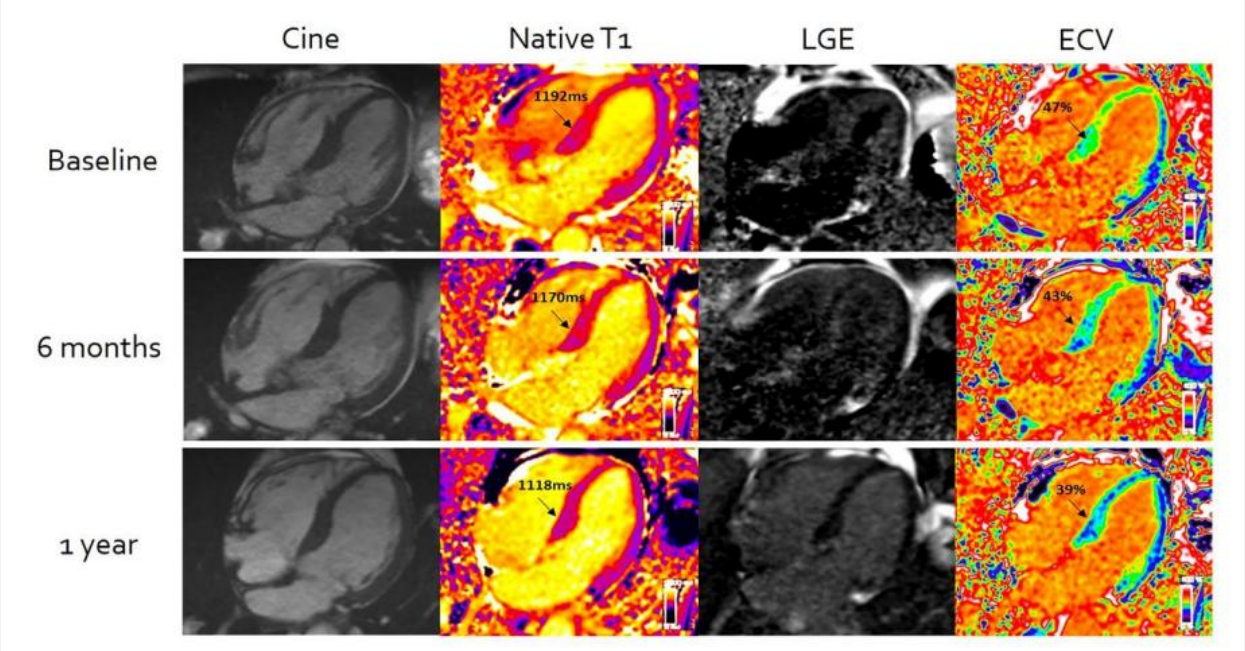
*** not routinely done***

AMYLOIDOSIS

	AL amyloidosis	ATTR amyloidosis
LV mass	• Mildly increased < 100 g/m²	• Markedly increased > 100 g/m²
Septum thickness	Septum AL < Septum ATTR	
LGE	• Less extensive LGE • Often (global) subendocardial pattern • QALE score < 13	• More extensive LGE • Often more diffuse and transmural pattern • QALE score ≥ 13
Native T1	> 1050 - 1150 ms Native $T1_{AL}$ > Native $T1_{ATTR}$	
ECV	>0.40 ECV_{AL} < ECV_{ATTR}	
Therapy	• Chemotherapy	• Novel TTR-specific treatment (Phase III)
Prognosis	• Worse (despite less extensive LGE)	• Better (despite more extensive LGE)

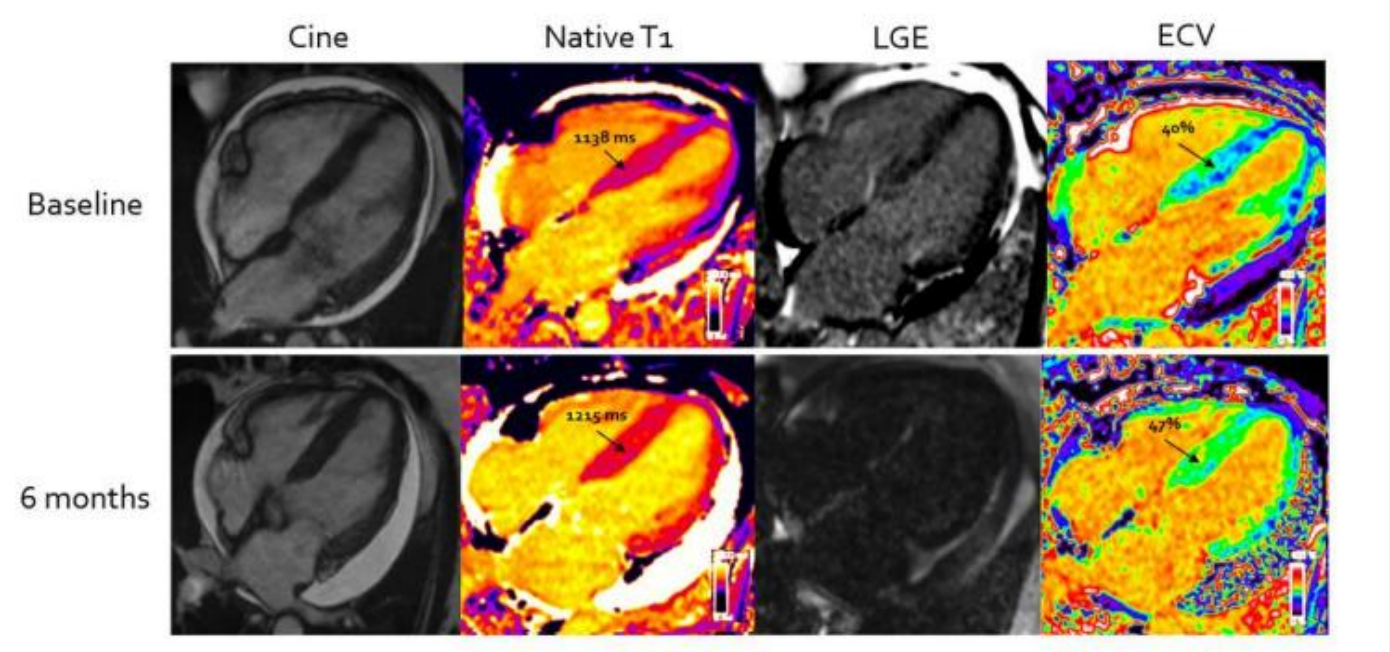
AMYLOID REGRESSION ON SERIAL CMR AFTER TREATMENT

Cardiac systemic light-chain amyloid regression on serial cardiovascular magnetic resonance scans at baseline (top row) and after treatment with chemotherapy at 6 months (second row) and 1 year (third row). Reductions in native T1, late gadolinium enhancement, and extracellular volume within the myocardium are demonstrated progressively over the course of treatment



AMYLOID PROGRESSION ON SERIAL CMR DESPITE TREATMENT

Cardiac systemic light-chain amyloid progression on serial cardiovascular magnetic resonance scans at baseline (top row) and after treatment with chemotherapy at 6 months (second row). Increase in native T1, late gadolinium enhancement, and extracellular volume within the myocardium are demonstrated after not achieving good response to chemotherapy at 6 months.



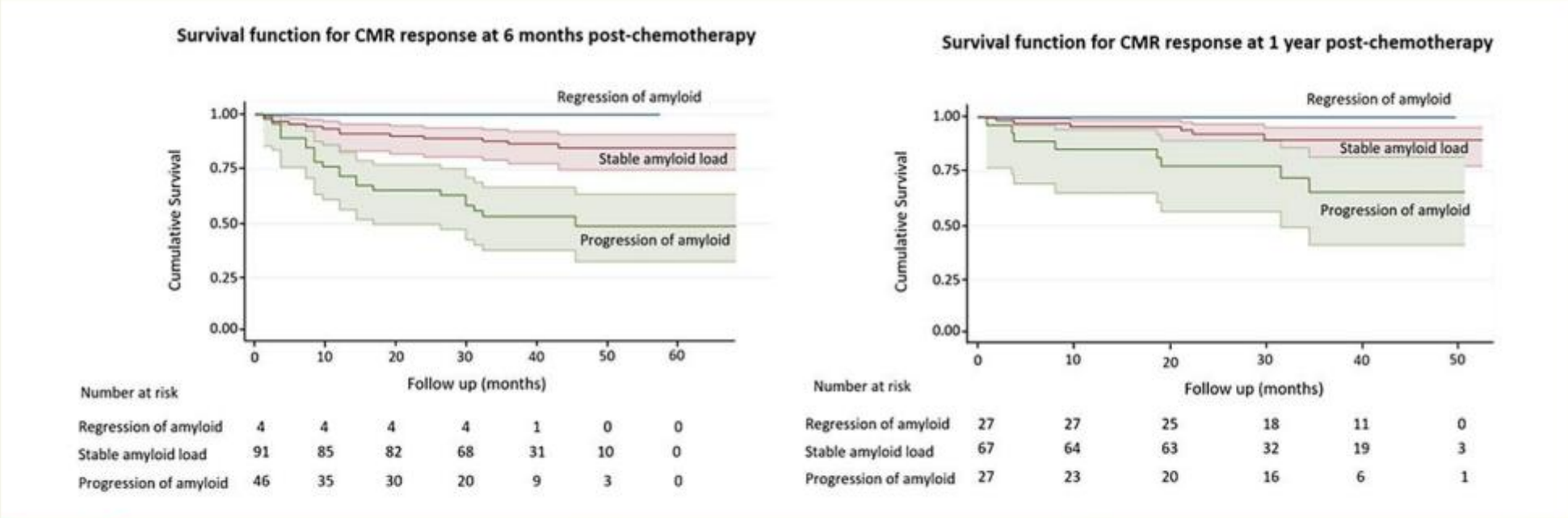
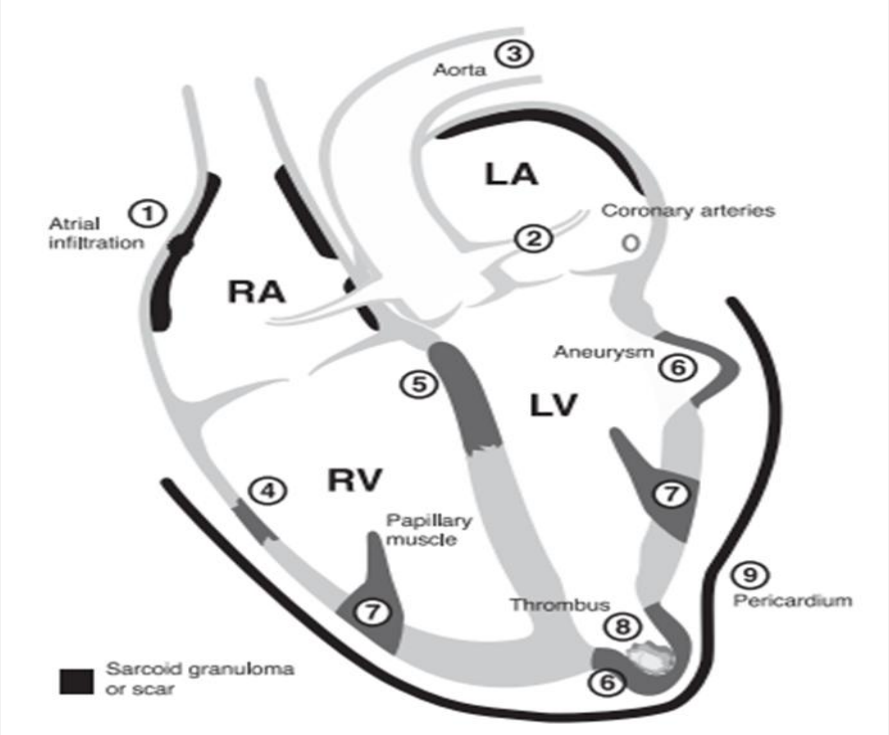


Figure 5 Kaplan–Meier survival curves, with shaded 95% confidence regions, displaying survival in all patients according to change in amyloid burden (measured by the change in extracellular volume on follow-up cardiovascular magnetic resonance) after 6 months (left panel) and 1 year of chemotherapy (right panel).

A. Martinez-Naharro et al, EHJ 2022

CARDIAC SARCOIDOSIS

- Sarcoidosis is a multisystem disease characterized by the development and accumulation of **noncaseating granulomas** in multiple organs including the heart
- Cardiac involvement affects at least one-quarter of patients with sarcoidosis.
- Cardiac sarcoidosis is associated with poor prognosis, with most deaths due to ventricular arrhythmias, high-degree heart block, or heart failure.



Smedema et al, 2020

Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

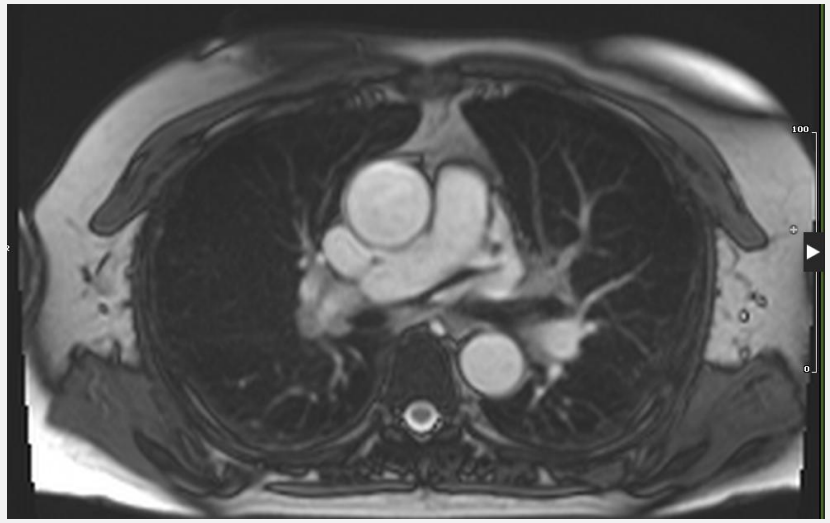
T2 mapping

T1 mapping

Perfusion

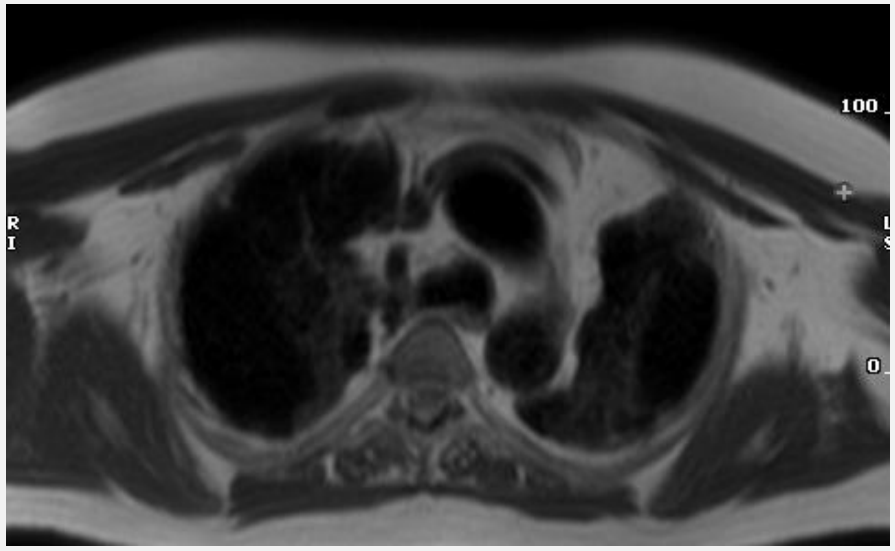
EGE

LGE



- Peri-hylar lymphadenopathy

- Bilateral lung changes



Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

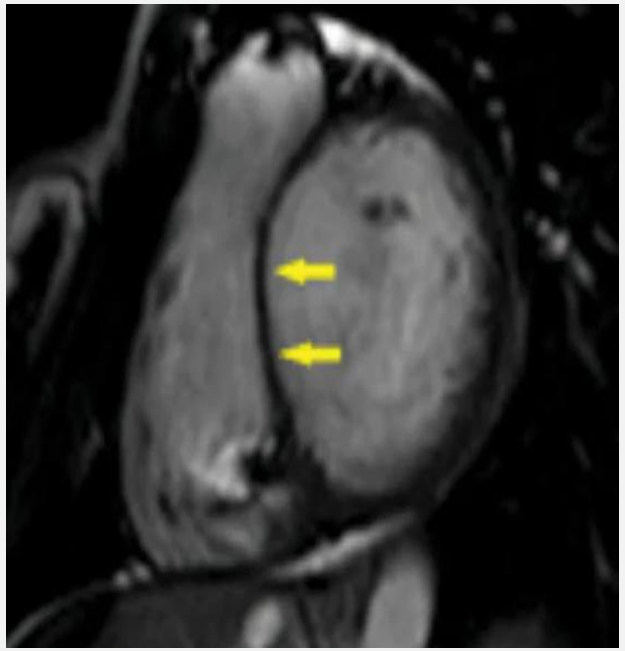
T1 mapping

Perfusion

EGE

LGE

- Increase wall thickness
- Segmental or global hypokinesia of the LV
  - septum and LV lateral wall most commonly affected
  - RWMA in noncoronary distribution
- Left ventricular dilatation
- Septal thinning (Ventricular aneurysms)
- Involvement of the Right ventricle



Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

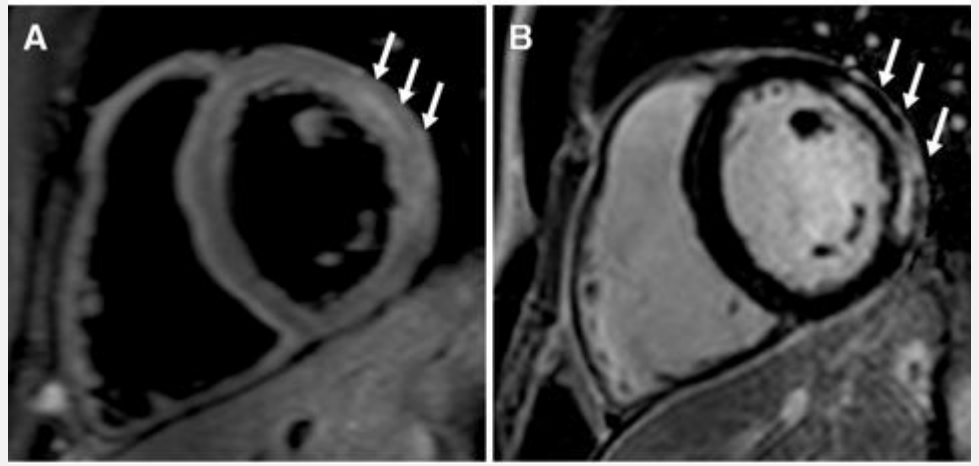
T1 mapping

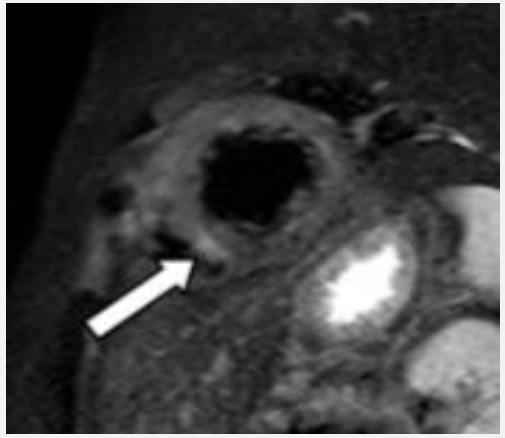
Perfusion

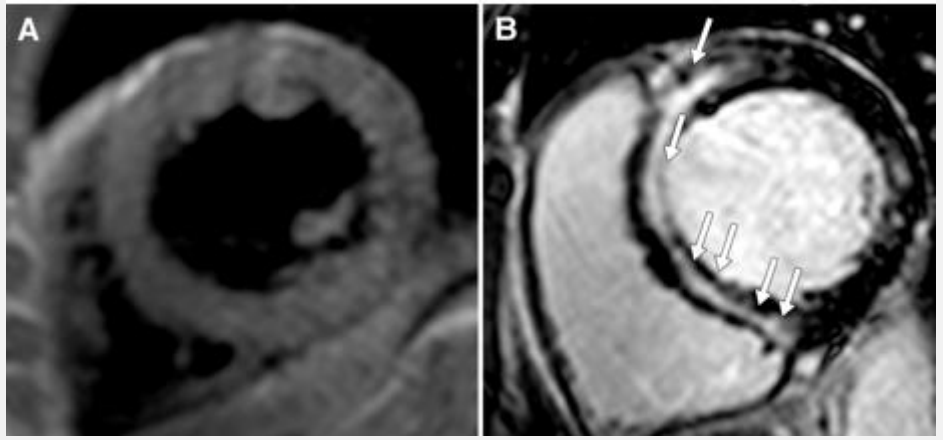
EGE

LGE

- Abnormal increased signal on T2-weighted imaging identifies areas of myocardial edema suggestive of active inflammation







Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

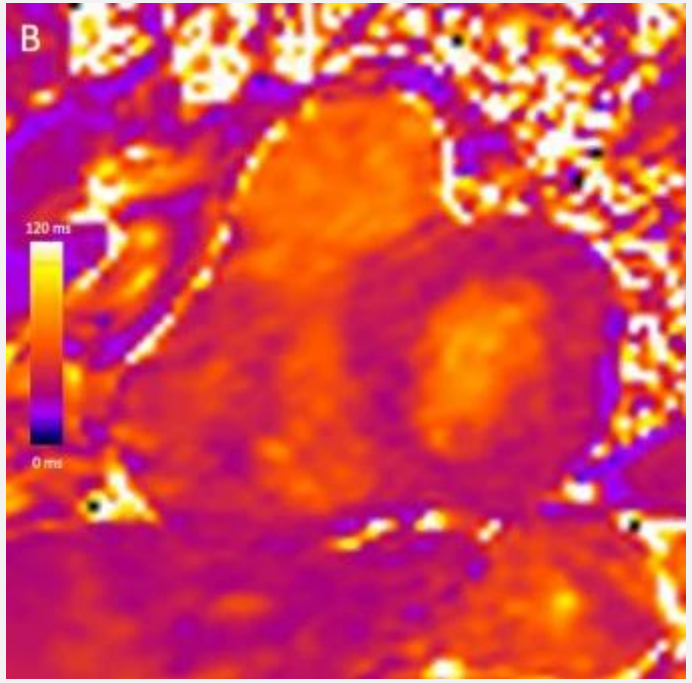
T1 mapping

Perfusion

EGE

LGE

Increased T2 values suggesting oedema/inflammation



Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

T1 mapping

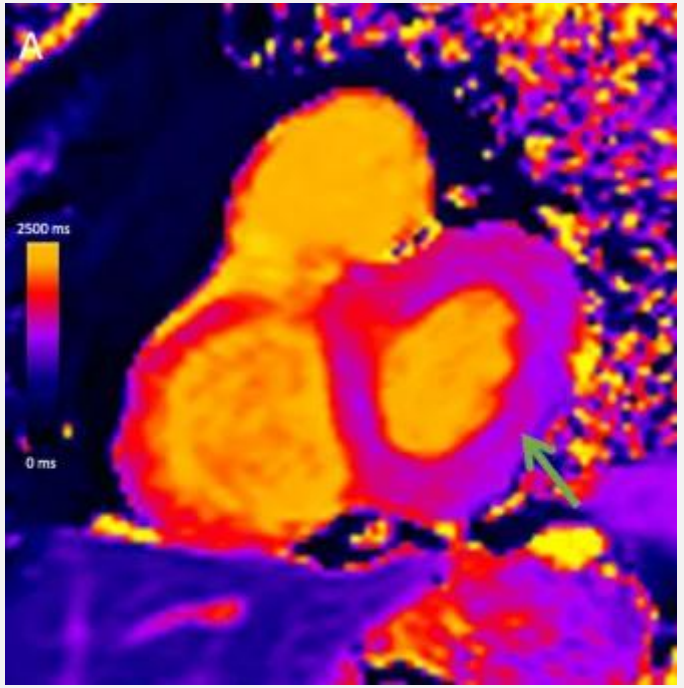
Perfusion

EGE

LGE

ECV

Increased T1 values



Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

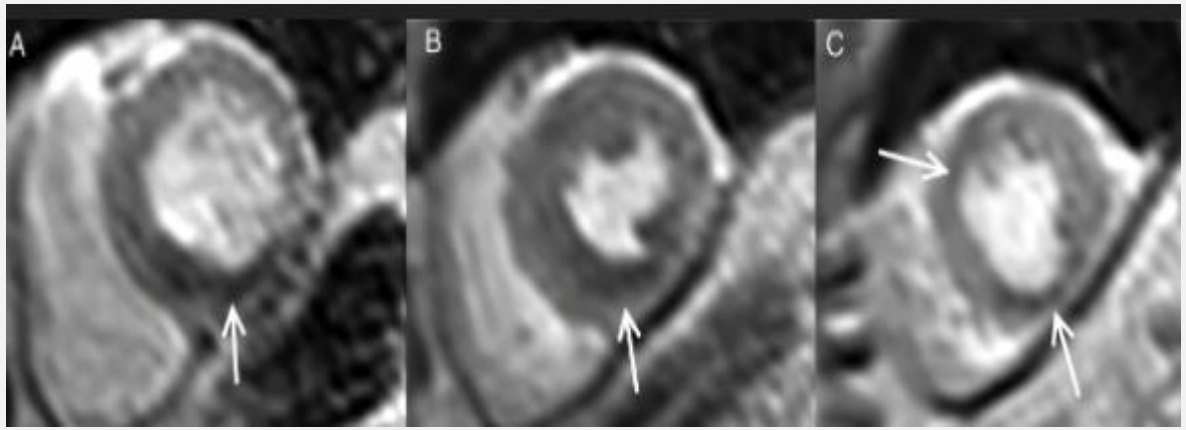
T1 mapping

Perfusion**

EGE

LGE

- Coronary infiltration leading to ischaemia



***not routinely done*

Cardiac Sarcoidosis

Anatomy

Volumetric analysis & wall thickness

T2-STIRS

T2 mapping

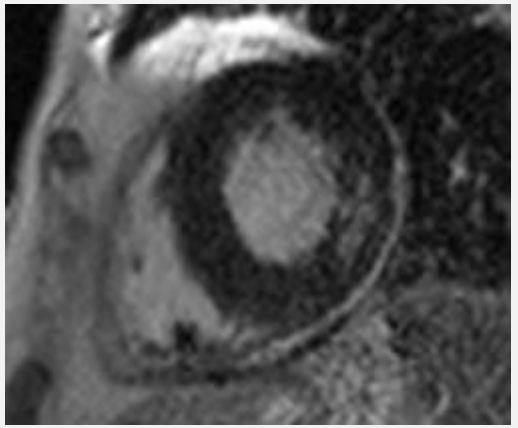
T1 mapping

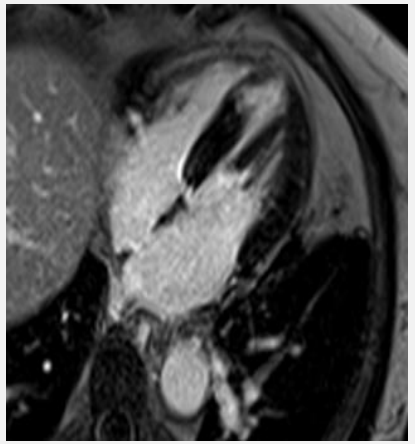
Perfusion

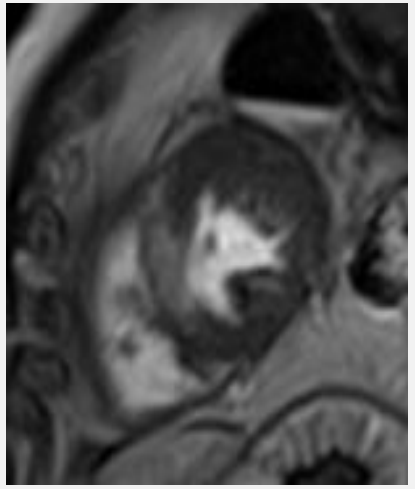
EGE

LGE

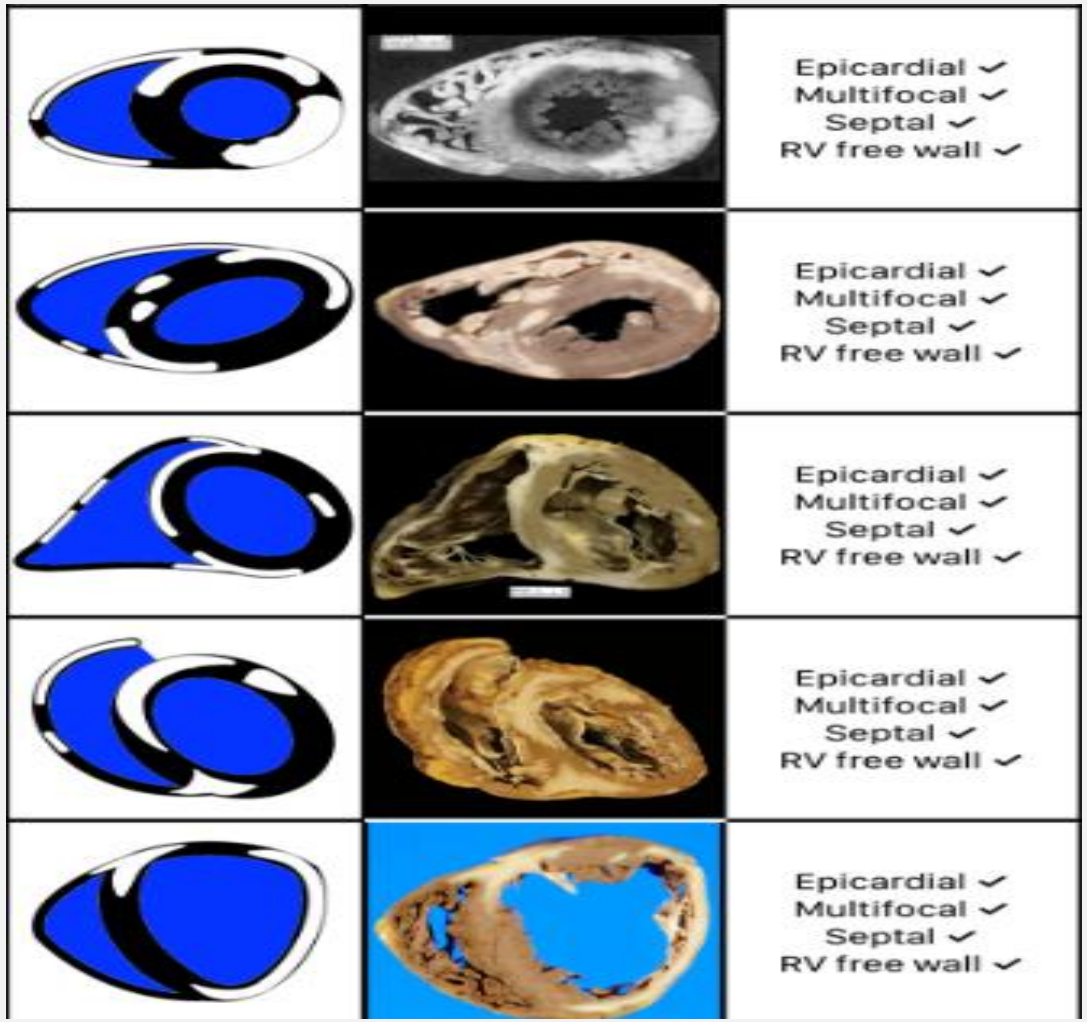
- Typical imaging findings on CMR include intense nodular or patchy LGE in a nonischemic distribution
- LGE can involve both left and right ventricles, often involving the subepicardial or midmyocardial layers with prominent involvement at the insertion points, and direct and contiguous extension, as well, across the basal interventricular septum into the right ventricle (the hook sign)







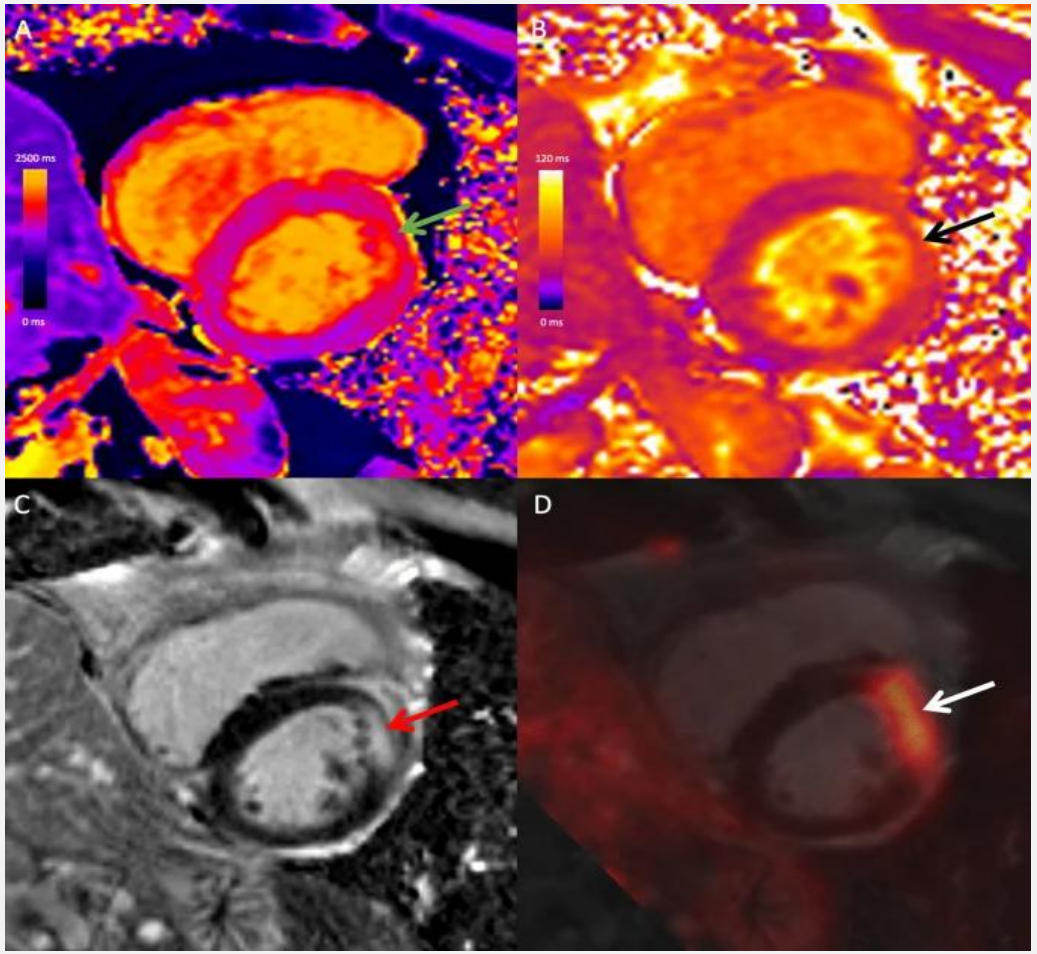
CARDIAC SARCOIDOSIS



Okasha JAHA 2019

SARCOIDOSIS

Mid-ventricular short-axis native T1 map



Native T2 map

LGE image

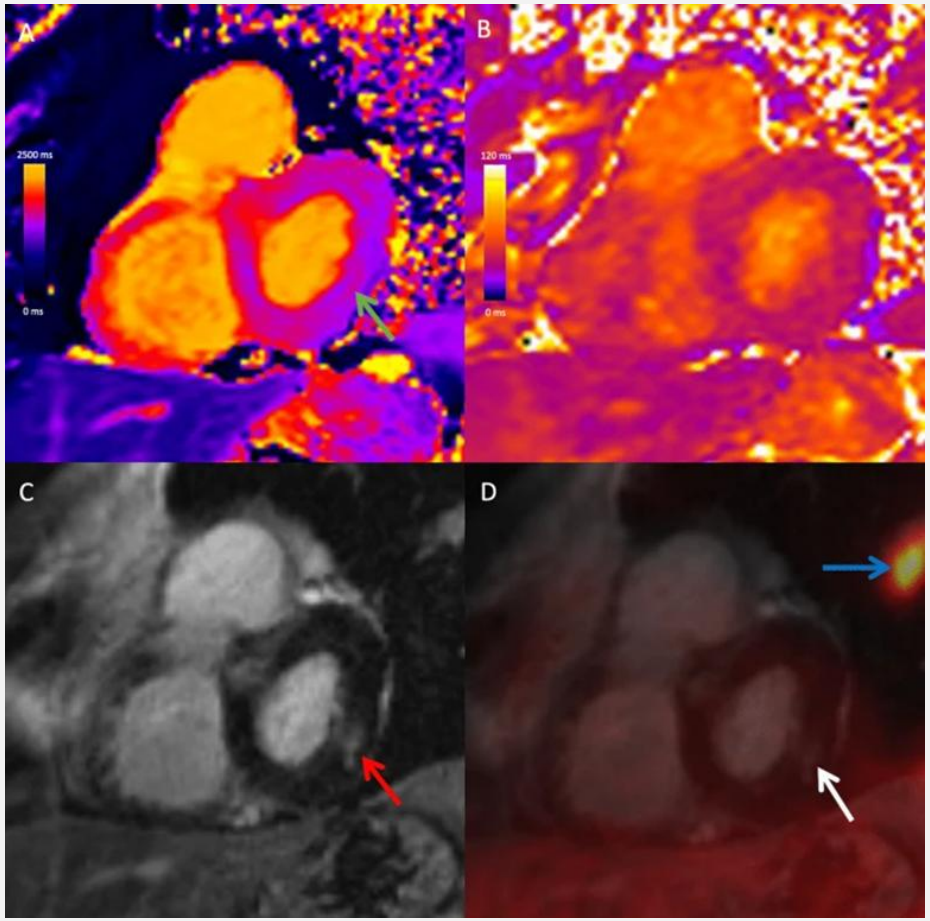
18F-FDG PET

cardiac sarcoidosis with active myocardial inflammation

Cheung et al, EJHI 2021

SARCOIDOSIS

Mid-ventricular short-axis native T1 map



Native T2 map

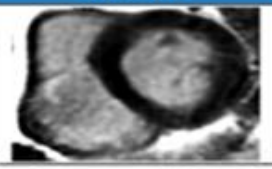
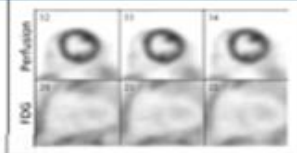
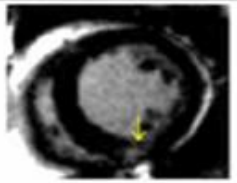
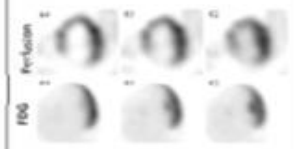
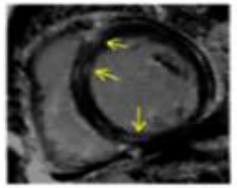
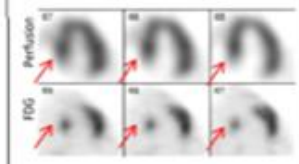
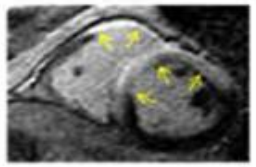
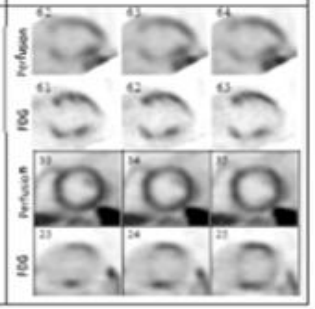
(LGE) image

18F-FDG PET

cardiac sarcoidosis with NO active myocardial inflammation

Cheung et al, EJHI 2021

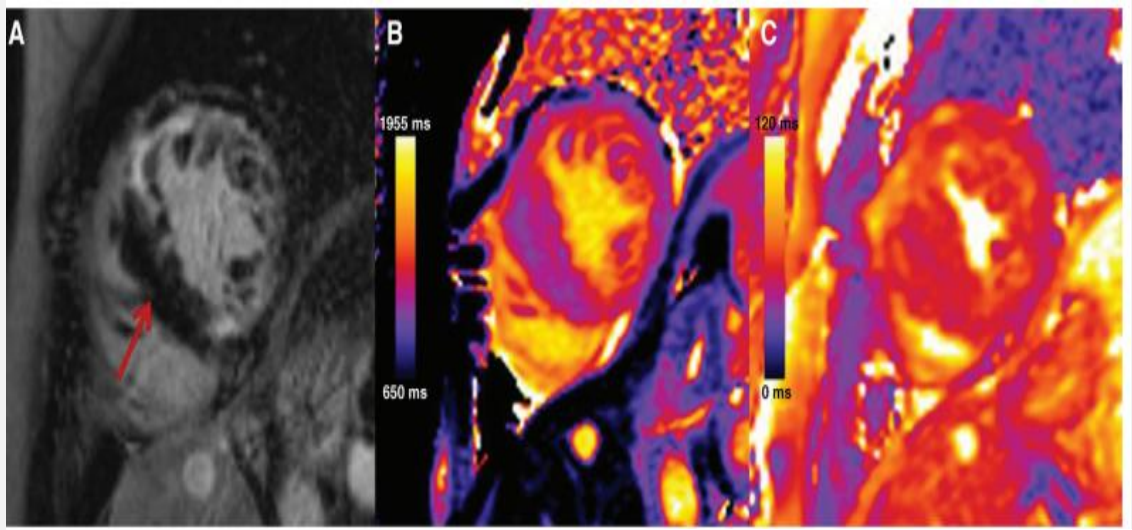
LIKELIHOOD OF CARDIAC SARCOIDOSIS BASED ON FINDINGS ON CARDIAC MRI AND PET ^{18}F-FDG SARCOIDOSIS IMAGING.

Likelihood probability	MRI likelihood	MRI example	MRI example illustrated	PET likelihood	PET example
No CS (<10%)	• No LGE • LGE present but clear alternative diagnosis (eg, ARVC)			• No FDG uptake and no perfusion defect	
Possible CS (50-90%)	• One focal areas of LGE but alternative diagnosis was more likely (eg, pulmonary hypertension)			• No FDG uptake but a small perfusion defect • Nonspecific FDG uptake and no perfusion defects*	
Probable CS (50-90%)	• Multifocal LGE in a pattern that is likely consistent with CS but cannot rule out other diagnosis (eg, myocarditis)			• Multiple noncontiguous areas of scar with no FDG uptake • Focal or focal on diffuse FDG uptake associated with resting perfusion defect	
Highly probable (>90%)	• Multifocal LGE in a pattern strongly consistent with CS with no alternative diagnosis • The following features were used to identify high likelihood: – Intense signal of LGE – Prominent involvement or insertion points with direct and contiguous extension across the septum into RAV ("hook sign")			• Multiple areas of focal FDG uptake and extra cardiac FDG • Multiple areas of both FDG uptake and perfusion defect	

Vita et al, 2018

Danon disease

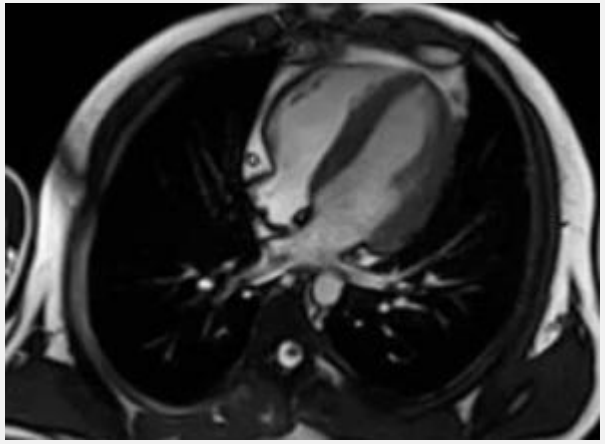
- Danon disease is an X-linked dominant genetic disorder caused by mutations in the gene encoding LAMP2 (lysosome-associated membrane protein-2) and resulting in glycogen accumulation in tissues including cardiac myocytes
- Men are more severely affected than women and typically present with cardiomyopathy, ventricular preexcitation, skeletal myopathy, and ocular disease with neurobehavioral problems
- LV wall thickening that is frequently misclassified as sarcomeric HCM.
- Extensive LGE resting
- Perfusion defects

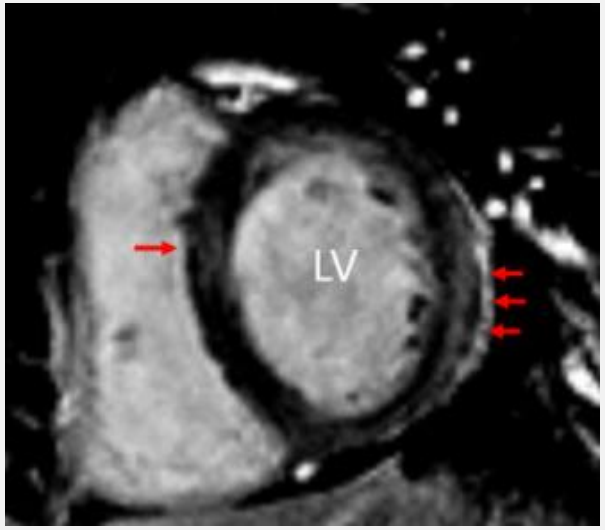


A, Midentricular short-axis LGE image demonstrates severe concentric wall thickening and extensive, midwall LGE that spares the septum (related to variations in the distribution of lysosomal accumulation and fibrosis within the myocardium (red arrow).
B, Midventricular short-axis native T1 map (1.5 T) demonstrates elevated global native T1 values (1205 ms), suggestive of fibrosis.
C, Midventricular short-axis T2 map (1.5 T) demonstrates elevated T2 values (53 ms), in keeping with edema. LGE indicates late gadolinium
enhancement

Friedreich ataxia

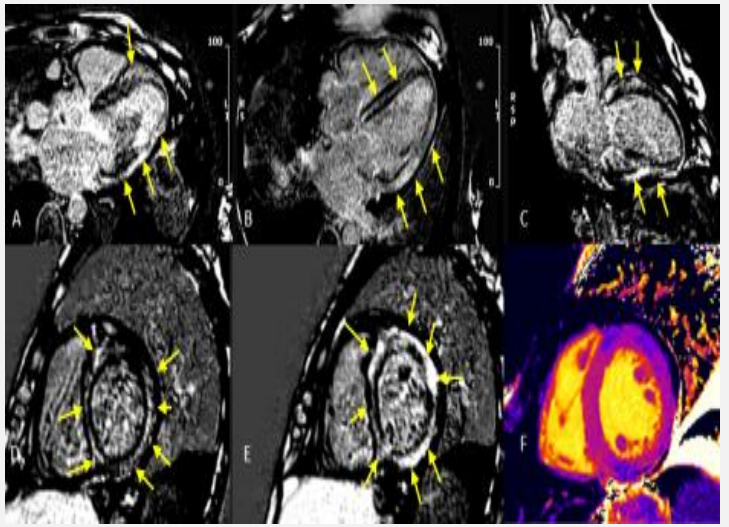
- Friedreich ataxia is a rare early-onset degenerative disease with an autosomal recessive inheritance pattern caused by mitochondrial iron accumulation
- presents with neurological and cardiovascular phenotypes
- cardiac myocyte hypertrophy and myocardial fibrosis
- progressive myocardial thickening and declining LV ejection fraction
- cardiac involvement is evident only late in the course of the disease
- CMR is useful in quantifying ventricular size, mass, and myocardial iron accumulation using T2* imaging





Myocardial oxalosis

- oxalic acid crystal deposition due to enzymatic deficiencies
- increased left ventricular mass and left atrial enlargement

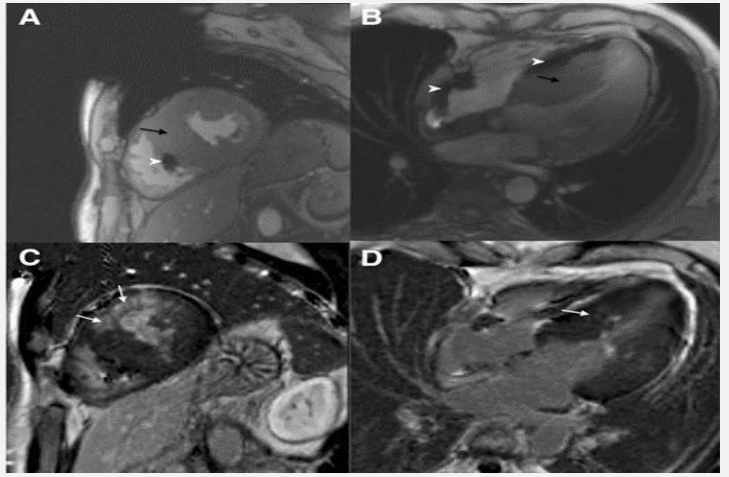


PRKAG2 deficiency

- increased glycogen storage due to increased cellular uptake

cardiac hypertrophy

Mucopolysaccharidoses



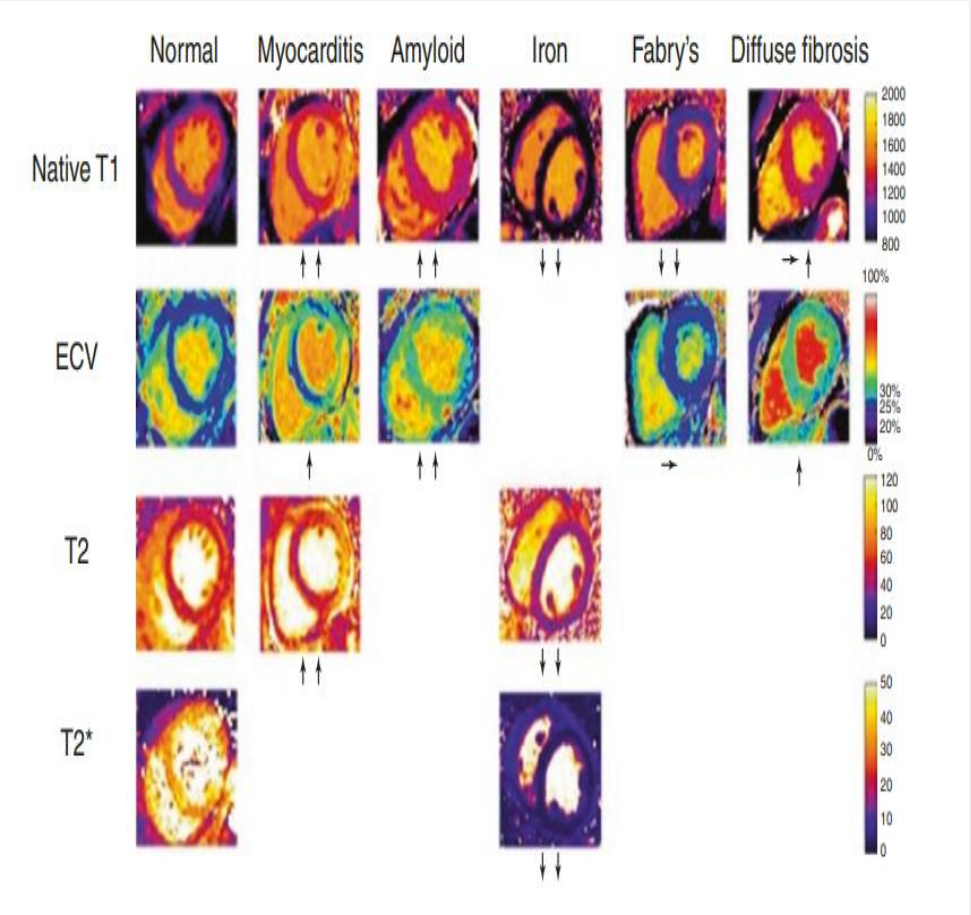
- accumulation of glycosaminoglycans
- cardiac wall thickening and valvular heart disease

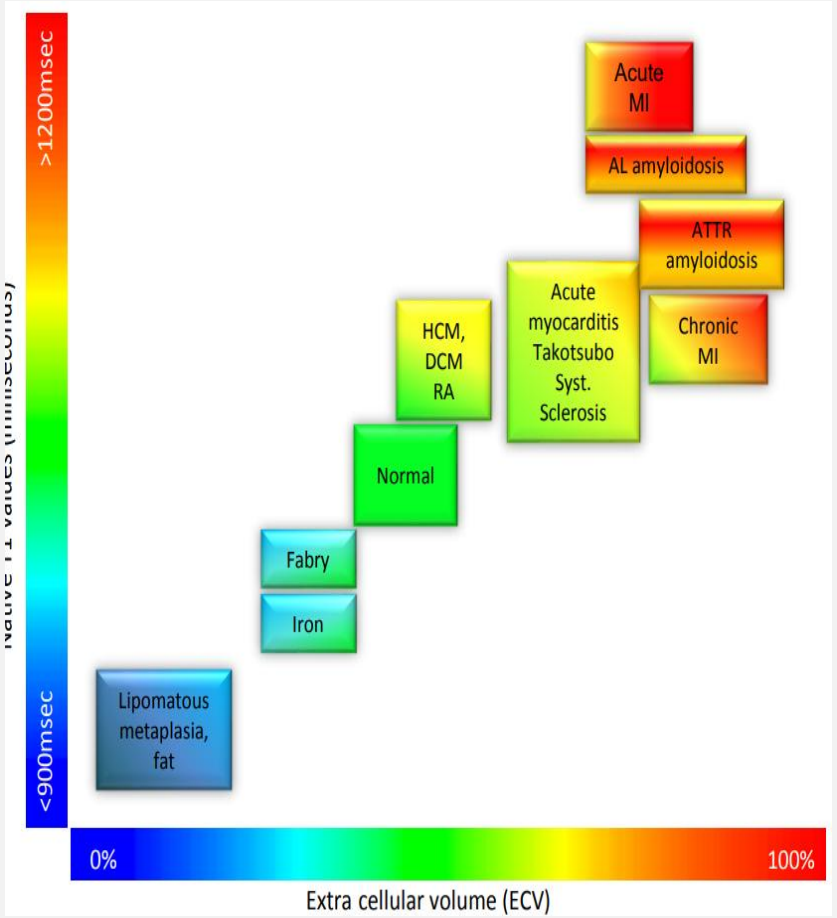
Pompe disease

- inherited lysosomal storage disorder characterized by abnormal glycogen accumulation within lysosomes
- cardiac wall thickening

TAKE HOME MESSAGES

- Accurate and highly reproducible
- Comprehensive tissue characterization
- Diagnosis
- Phenotype
- Risk stratification & prognosis
- Follow up and response to treatment



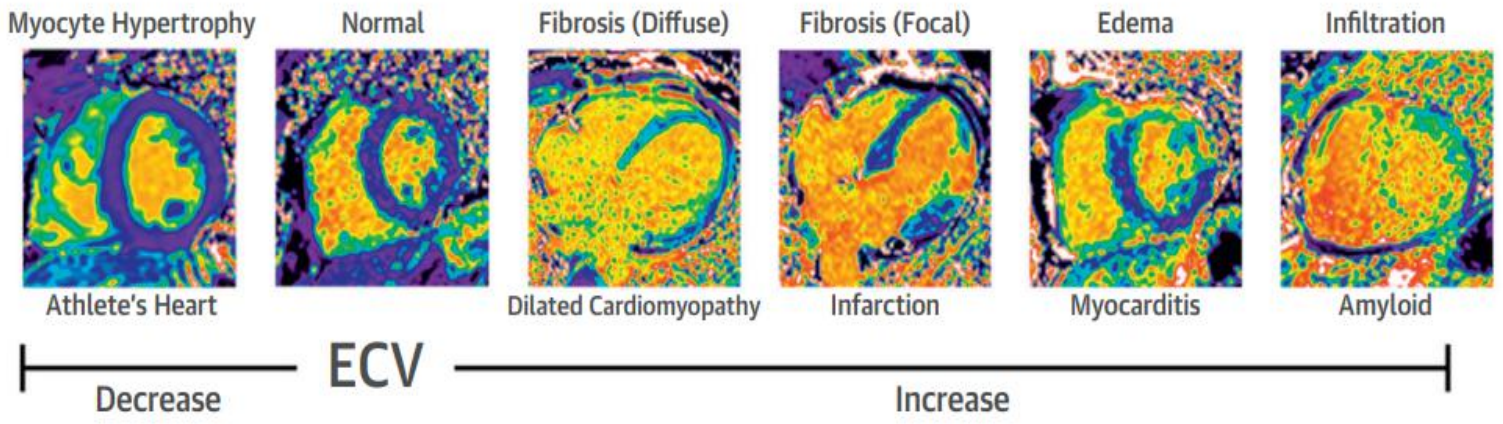


MAPPING TECHNIQUES

- T2 mapping
- T1 mapping
- ECV

Native T_1 ↑	Native T_1 ↓
• *Oedema* e.g. tissue water↑ in acute MI, inflammation, pericardial effusion	• *Fat/Lipid overload* e.g. lipomatous metaplasia in chronic MI, Anderson-Fabry, lipoma
• *Increase of interstitial space* *e.g.* (replacement) fibrosis, scar, cardiomyopathy, amyloid deposition	• *Iron overload*

T_2 ↑	T_2 ↓
• *Oedema* e.g. tissue water↑ in acute MI, inflammation, pericardial effusion (T_2 more sensitive than native T_1 for oedema detection)	• *Fat/Lipid overload* • *Iron overload* (T_2*↓)



Robinson, A.A. et al. J Am Coll Cardiol Img. 2019;12(11):2332-44.

- Although fibrosis is certainly a cause of increased ECV, it is not the only cause
- Expansion of the interstitial space may also occur from diffuse protein deposition (as in amyloid) or edema
- Changes in vascular volume can affect ECV estimates as well
- ECV is a volume fraction, so that it can be changed indirectly via changes in size of the intracellular volume

Endomyocardial Fibrosis

- eosinophilic inflammatory infiltration of the ventricular endocardium. The inflammatory process eventually leads to local necrosis and endomyocardial fibrosis
- apical obliteration associated with enlargement of the respective atrium restrictive physiology with shrunken ventricles due to fibrosis
- subendocardial enhancement, not restricted to any coronary territory involving the ventricular apex , overlying thrombus at the ventricular apex
- EGE: allow detection of apical thrombi.