Cardiac Monitoring in Thalassemia

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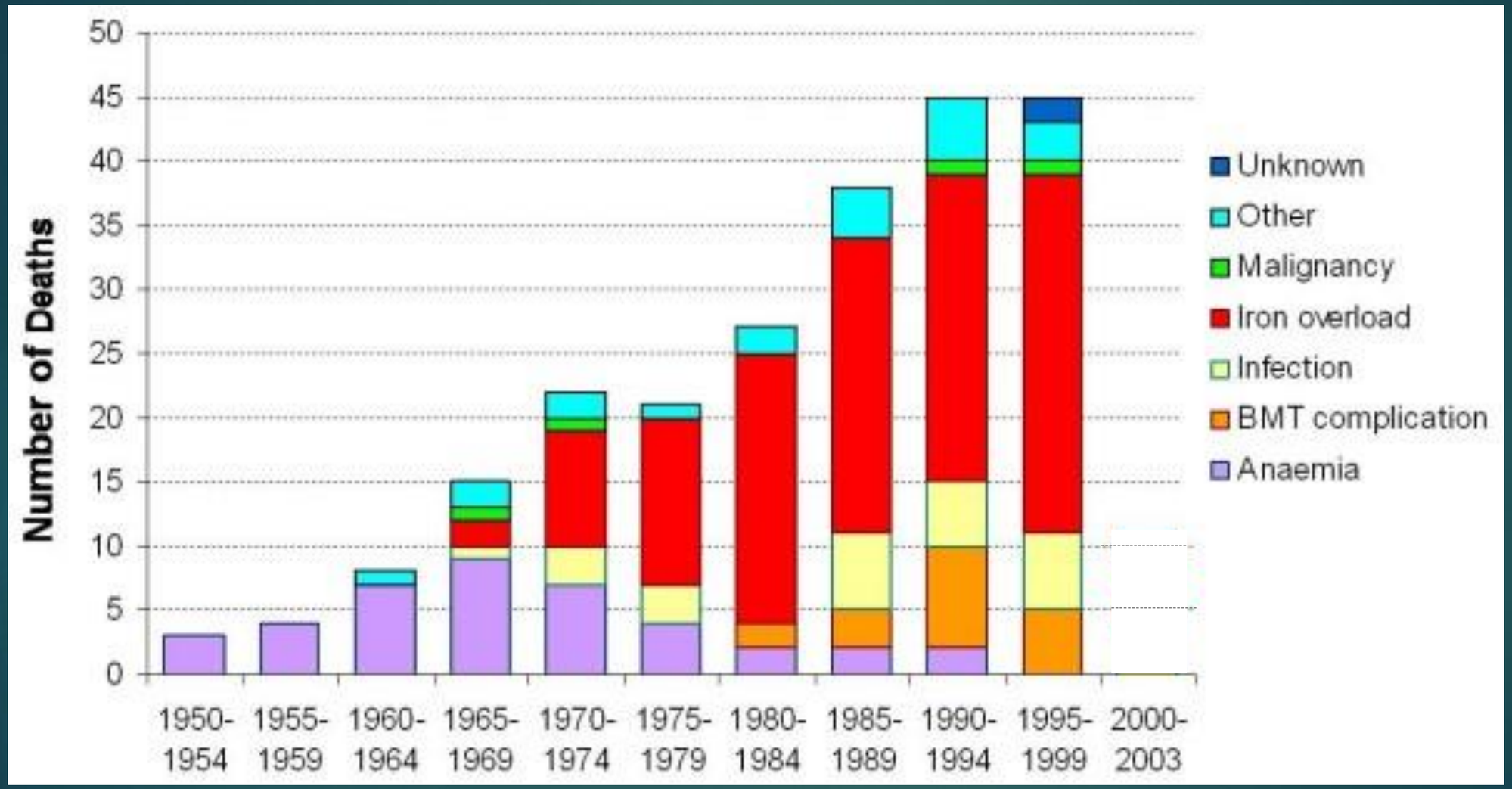
What is it about iron?

- Human body has no mechanism to excrete iron
- Transfused red blood cells have decreased life span
- Transferrin becomes saturated resulting in increased free iron in blood stream
- Iron free radicals damage cellular components: DNA, proteins and cell membranes

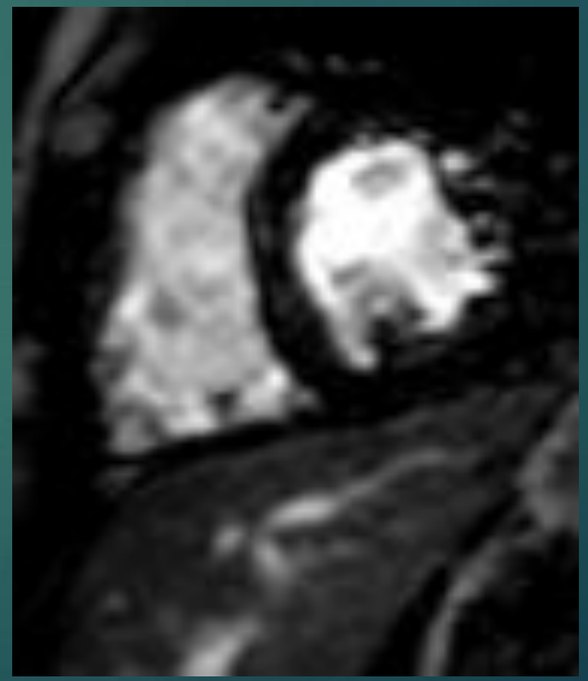
Why worry about the heart?

- Damage can include fibrous tissue formation (often microscopic)
- Diastolic dysfunction (stiffness impairs filling) can be seen early
- Can see abnormal thickening of muscle or enlargement of ventricles
- Systolic dysfunction (poor contraction) occurs late
- Likewise for rhythm abnormalities: delayed conduction or repolarization

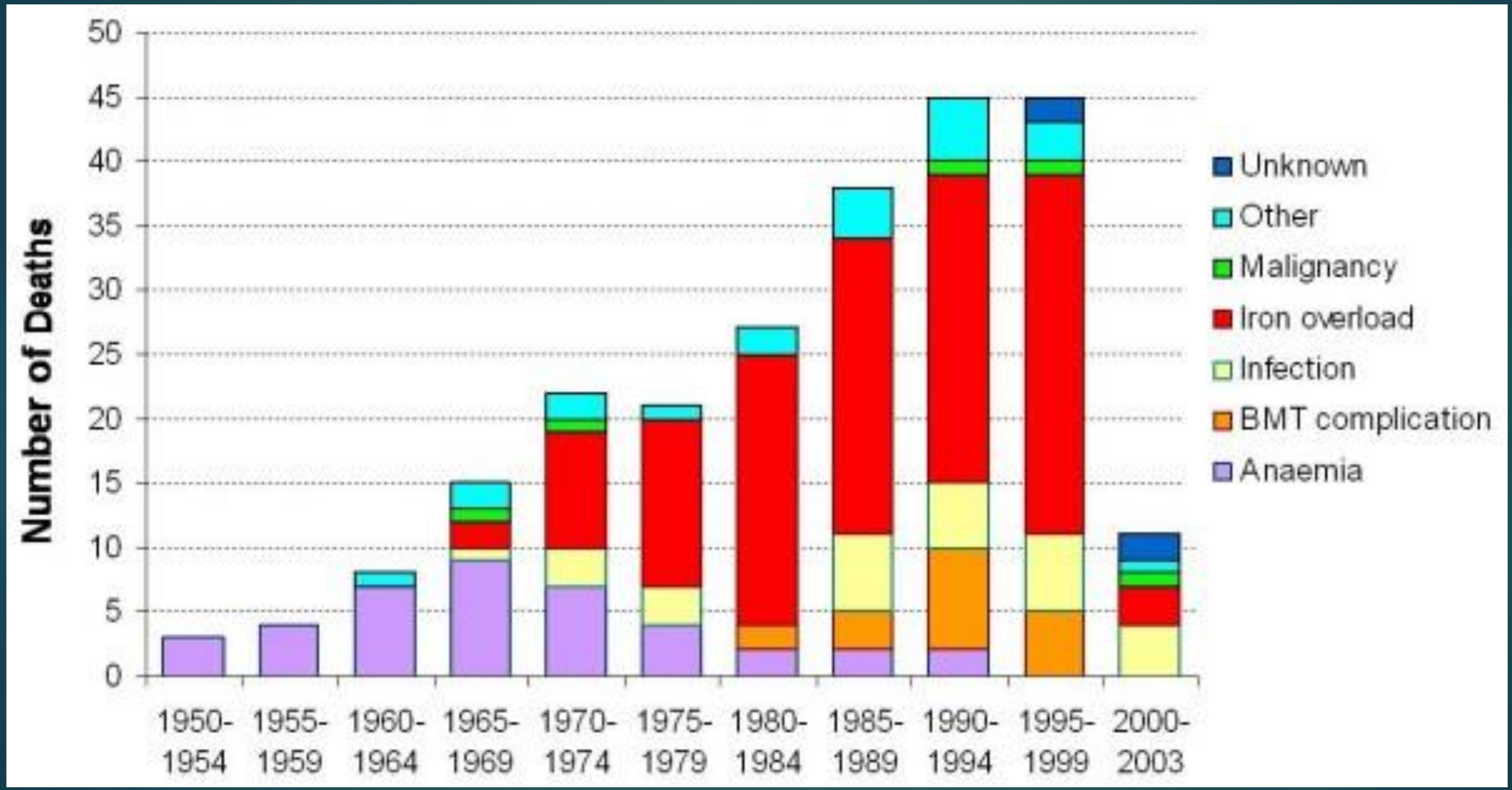

Number of Deaths
50
45
40
35
30
25
20
15
10
5
0
1950-1954
1955-1959
1960-1964
1965-1969
1970-1974
1975-1979
1980-1984
1985-1989
1990-1994
1995-1999
2000-2003
Unknown
Other
Malignancy
Iron overload
Infection
BMT complication
Anaemia

Liver vs. Cardiac Iron

- Little or no correlation…
  - Last in, last out…



Why measure cardiac iron?



Impact on Thalassemia

- 2001: Introduction of cardiac MRI (CMR) for iron overload cardiomyopathy (IOC)
- 1990s: 46 deaths from IOC
- 2000-2003: 6 deaths (15 per 10 years)

  - Modell et al. JCMR. 2008

Detection of Myocardial Iron Overload

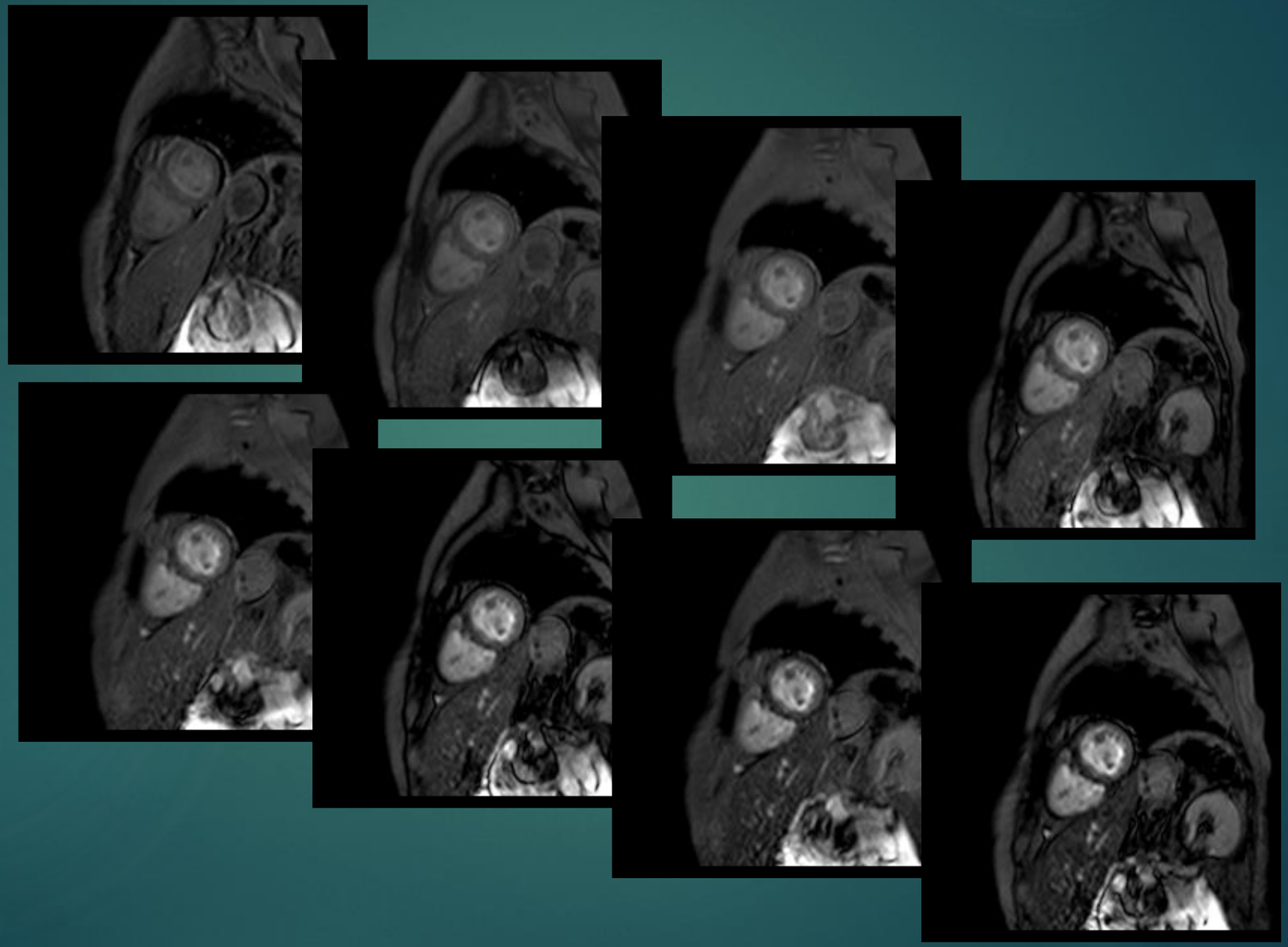
- Laboratory Markers:
  - Transferrin saturation: ethnic variability
  - Ferritin: lab differences, increased in many inflammatory diseases
  - Total body iron: not organ specific

- Electrocardiogram:
  - Premature ventricular complexes
  - Lengthening of QTc
  - Atrioventricular block
  - Usually late findings: conduction system infiltrated

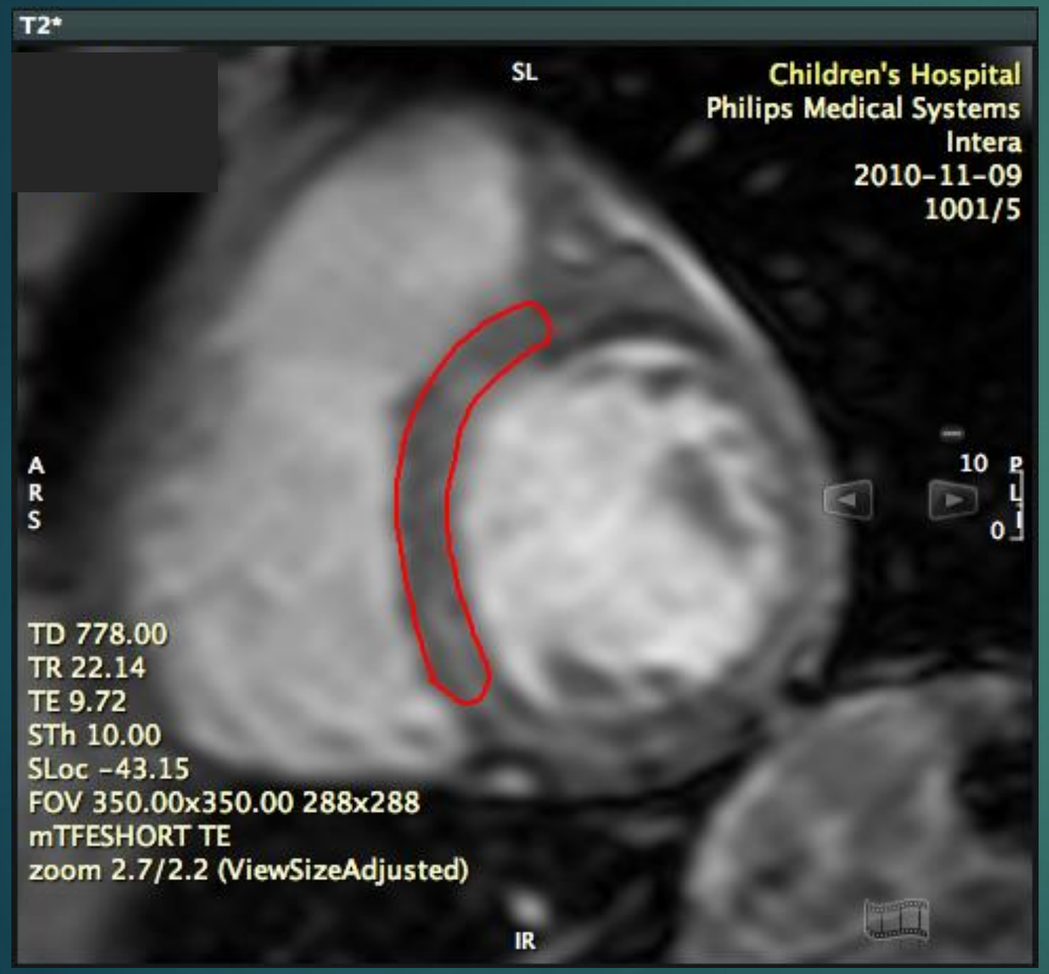
Detection of Myocardial Iron Overload

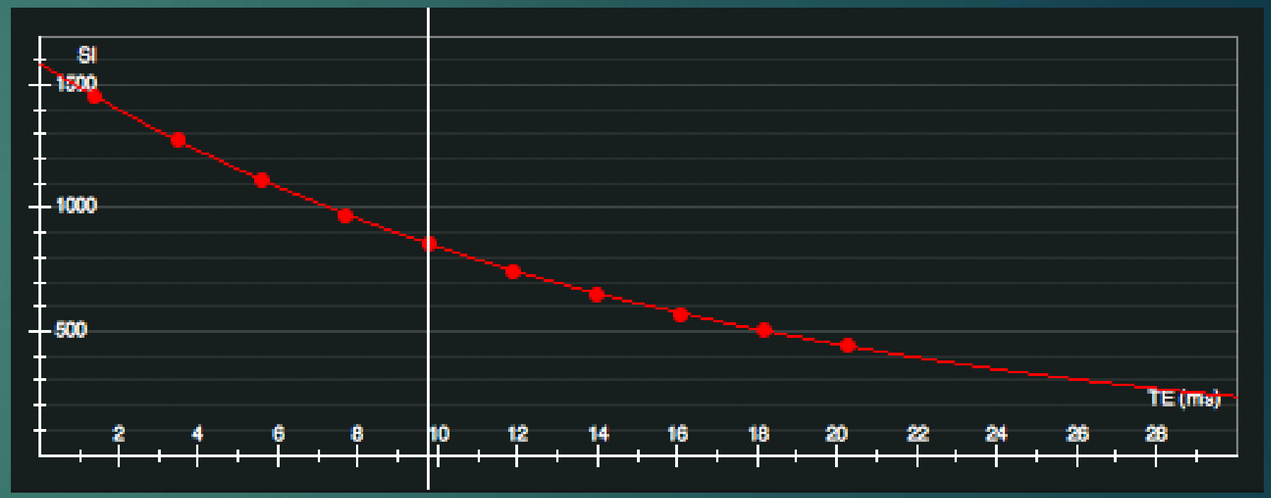
- Echocardiogram
  - Poor contraction, enlarged ventricle are late findings
  - Impaired filling is difficult to determine by echo
- Transcatheter biopsy:
  - Iron deposits are usually patchy
  - Invasive procedure

White Blood Short Echo Time



Method of Analysis

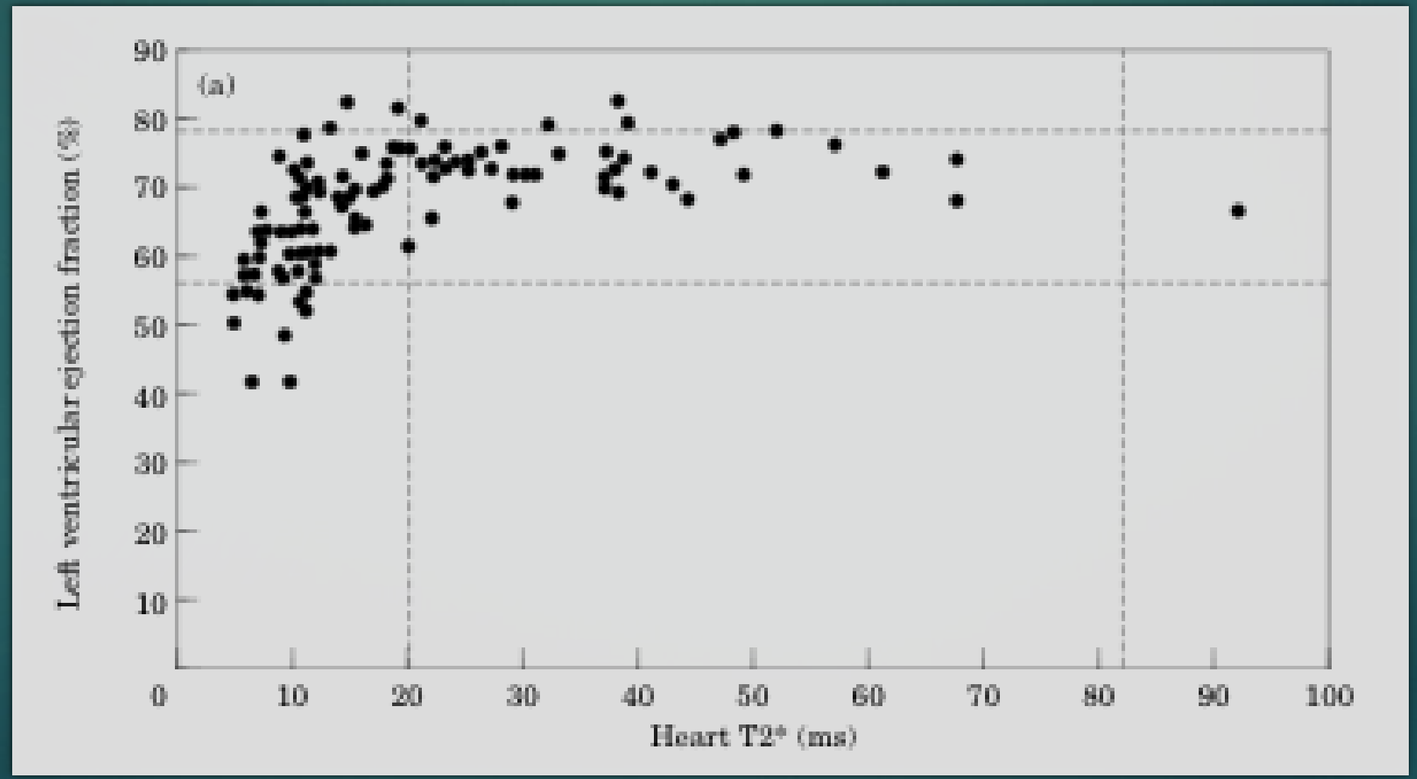




T2* = 15.1ms
SD = 0.11ms

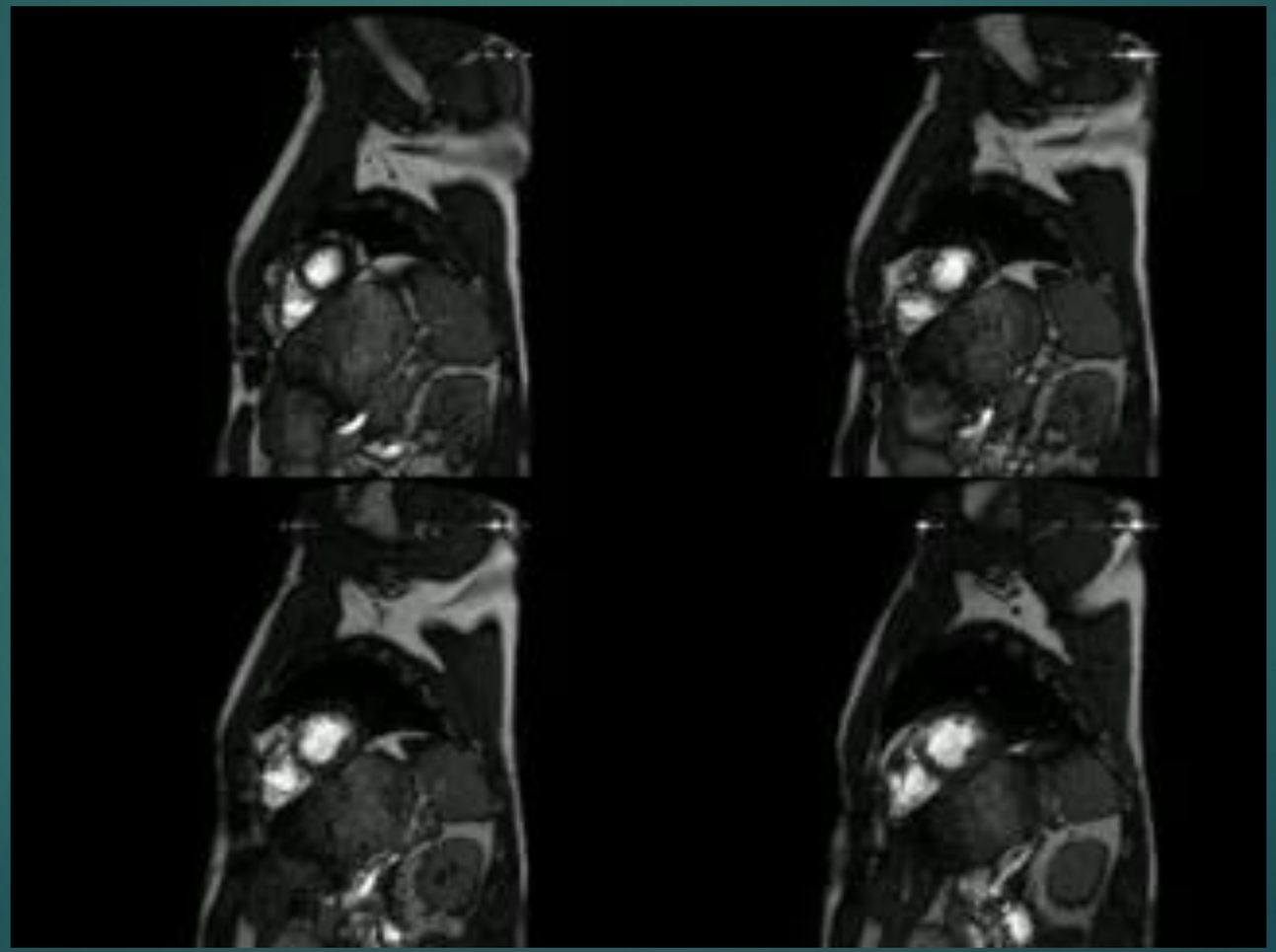
What Can We Learn from Cardiac T2*

- Abnormal < 20ms
- Anderson 2001:
  - Declining LVEF
  - Increasing LV end-systolic volume and indexed wall mass



Ventricular Systolic Function

Ventricular Systolic Function



Current Cardiac Care Protocol

- ECG
- Echocardiogram
- Cardiac MRI
  - Left ventricular volume: diastole and systole
  - Left ventricular end-diastolic mass
  - T2*: black blood and white blood – short echo time
- Yearly
- Out-of-towners
- Study protocols

Diastolic Function by MRI?

Peak Filling Rates Assessed by CMR Imaging Indicate Diastolic Dysfunction From Myocardial Iron Toxicity

Bjoern P. Schoennagel, Roland Fischer, Regine Grosse, Christoph Berliner, Mahmoud Wehbe, Gregory Kurio, Gunnar Lund, Zhiyue J. Wang, Joachim Graessner, Gerhard Adam and Jin Yamamura

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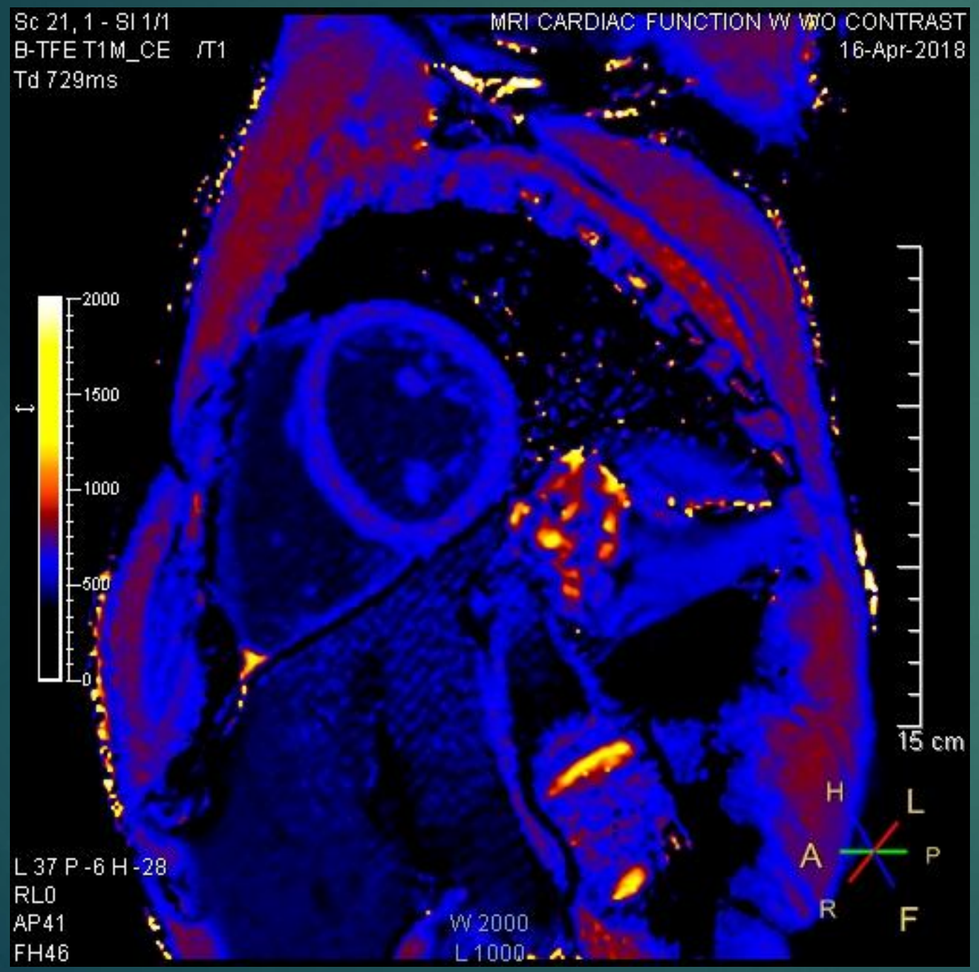
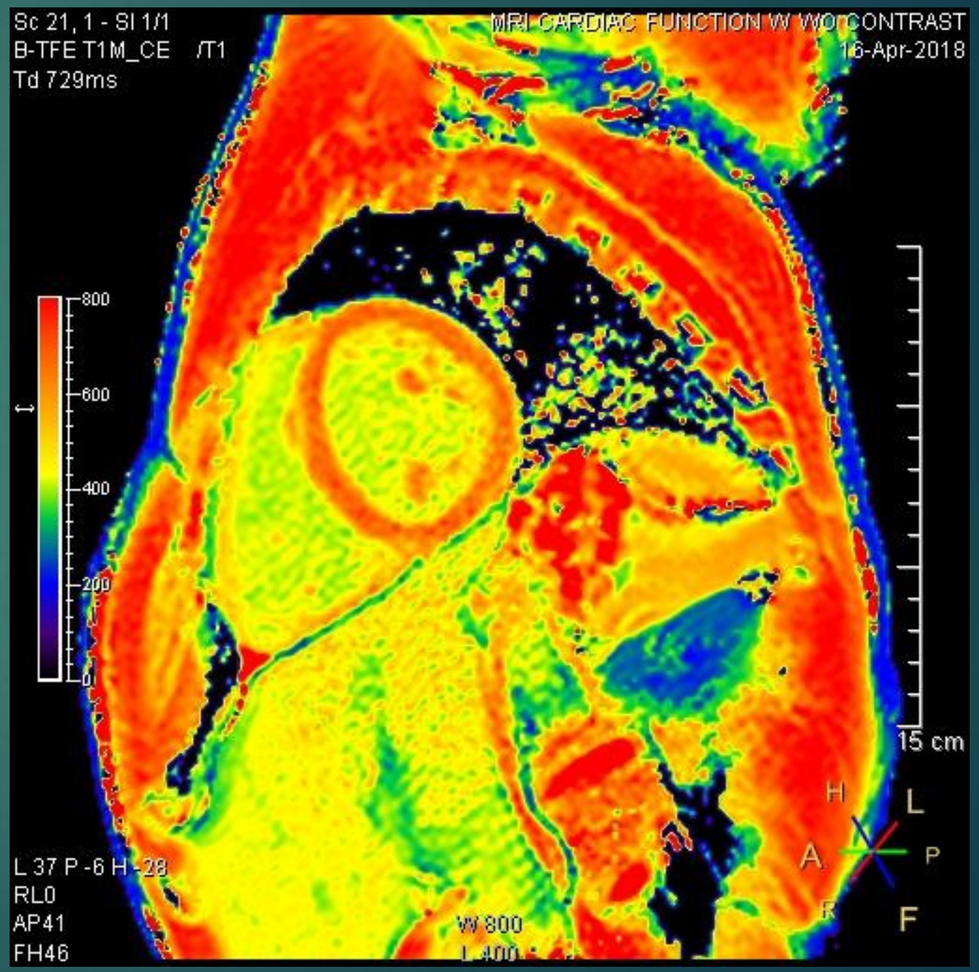
Extracellular Volume





Future Cardiac Care Protocol

- ECG
- Echocardiogram
- Cardiac MRI
  - Left ventricular volume: diastole and systole
  - Left ventricular end-diastolic mass
  - T2*: black blood and white blood – short echo time
  - Diastolic function: Atrial volumetrics
  - Extracellular volume: microfibrosis

Thank you for your attention

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