



# Drépanocytose

## Transfusions et surcharge en fer

Nouveautés diagnostiques et  
thérapeutiques

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# Traitements

- Hydroxyurée
- Transplantation
- Transfusions

# Transfusions épisodiques indications

- Anémie brutale
  - Séquestration splénique
  - Erythroblastopénie transitoire
  - Hyperhémolyse aiguë (infection, ACS, malaria...)
- Douleurs et décompensation cardiaque (dyspnée, hypotension)
- Chirurgie majeure (Hb 10, HbS 60%)

# Transfusions chroniques/prophylactiques Indications

- Prévention AVC primaire/secondaire
- Douleurs chroniques débilantes
- Anémie avec insuffisance rénale chronique

# Indications controversées

Priapisme

Ulcères de jambe

Grossesse non compliquée

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## Contre indications

Anémie chronique stable

Infections

Petite chirurgie

Nécrose aseptique

# Transfusions

## Bénéfices

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Prévention primaire et  
secondaire des AVC

Diminution des épisodes  
douloureux et des  
syndromes thoraciques  
aigus

Action possible sur l'atteinte  
organique chronique

## Risques/soucis

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Réactions transfusionnelles  
aiguës

Infection

Alloimmunisation

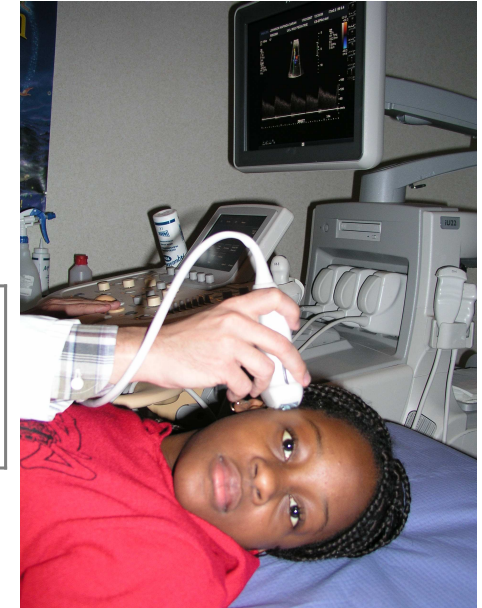
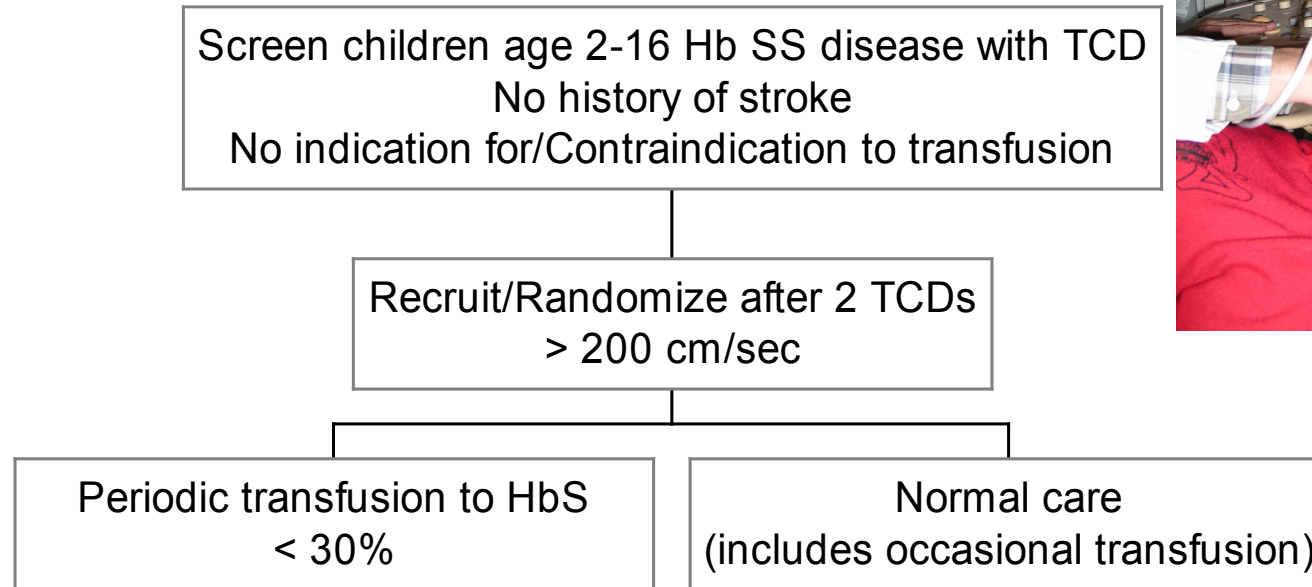
Surcharge en fer

Abord IV

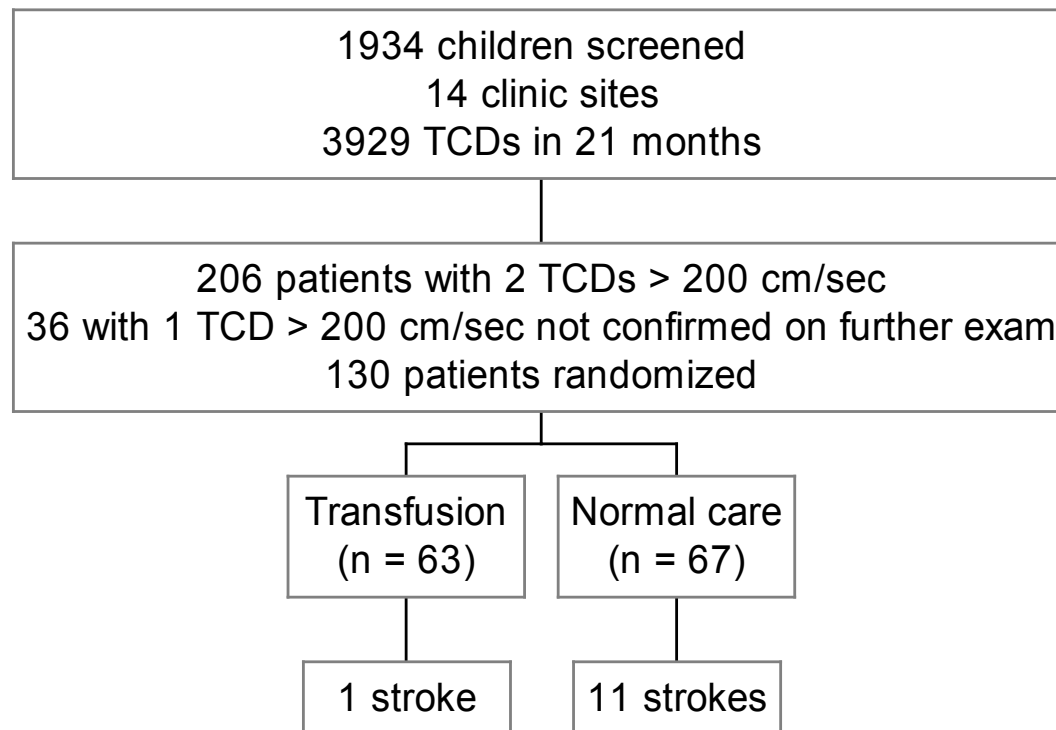
Disponibilité du sang

Coût

# Stroke: primary prevention STOP study



# STOP trial

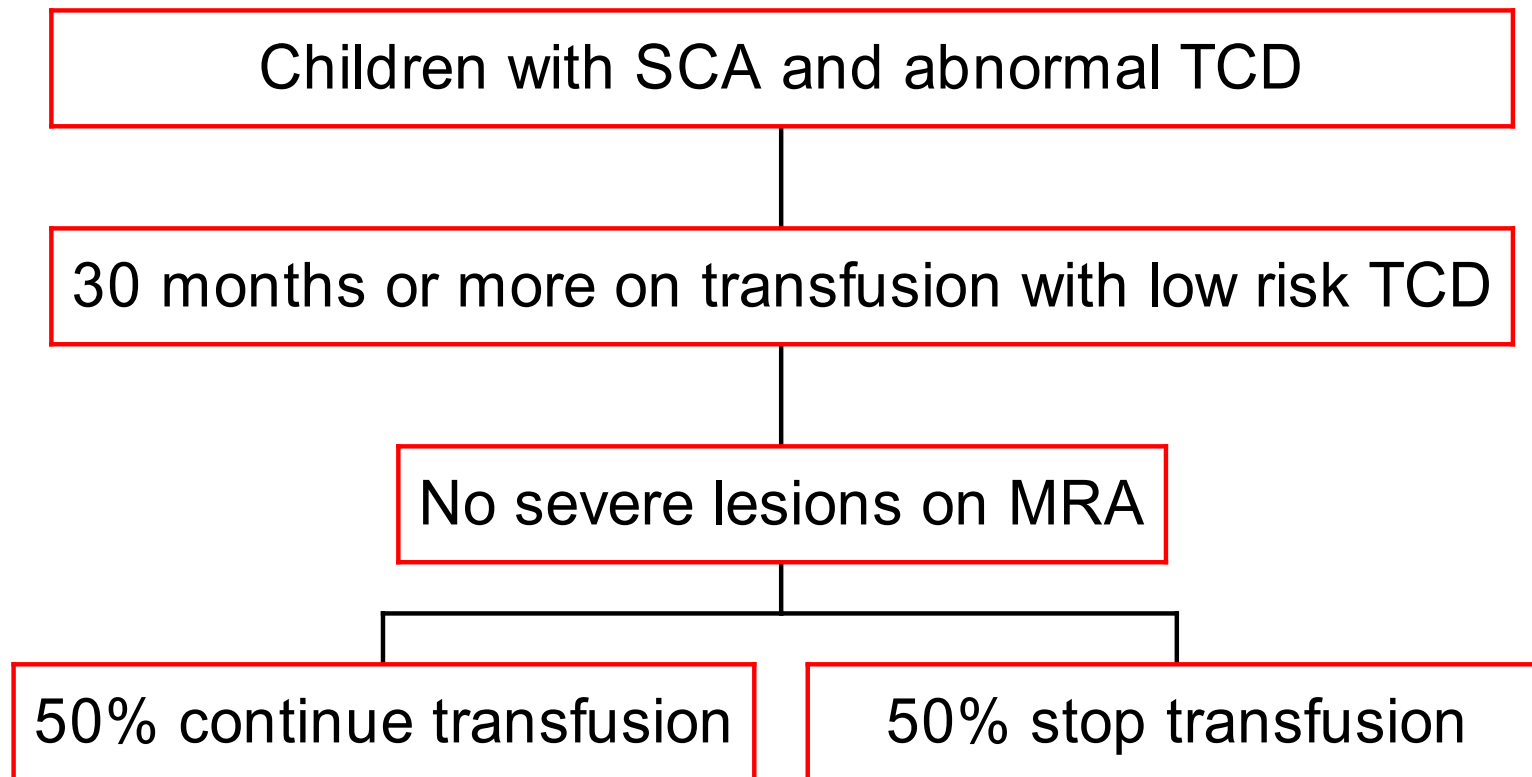


# STOP study conclusions

- TCD was able to predict stroke

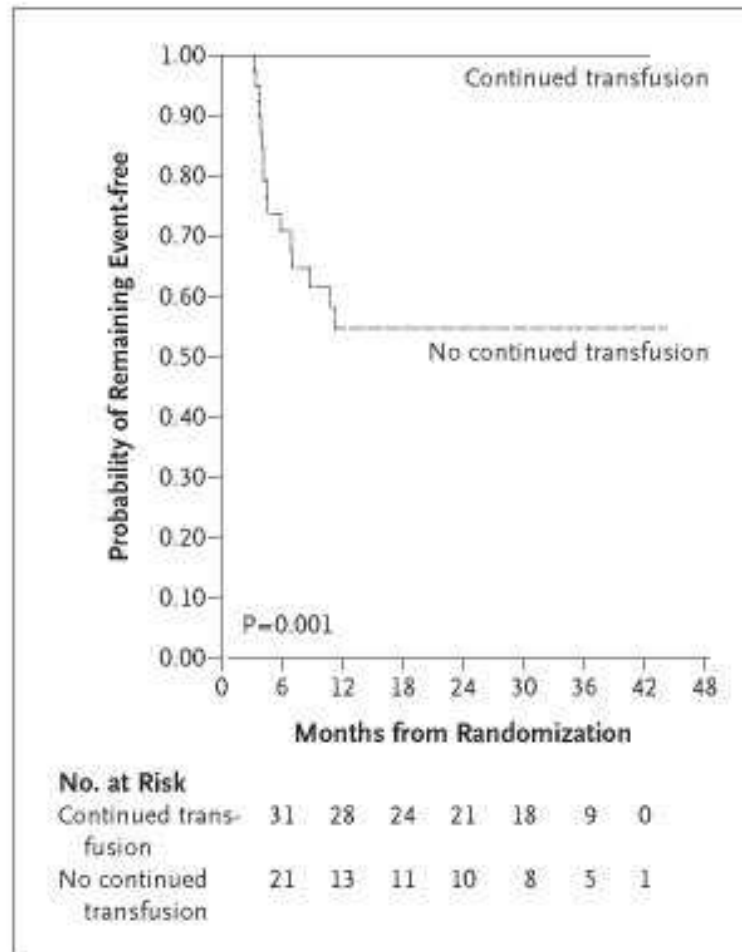
- 
- Transfusion was more effective than projected

# STOP 2 trial of halting transfusions



# Probability of remaining event-free

STOP-2 trial N Eng J Med 2005;353: 2769-2778



# Red cell exchange transfusion

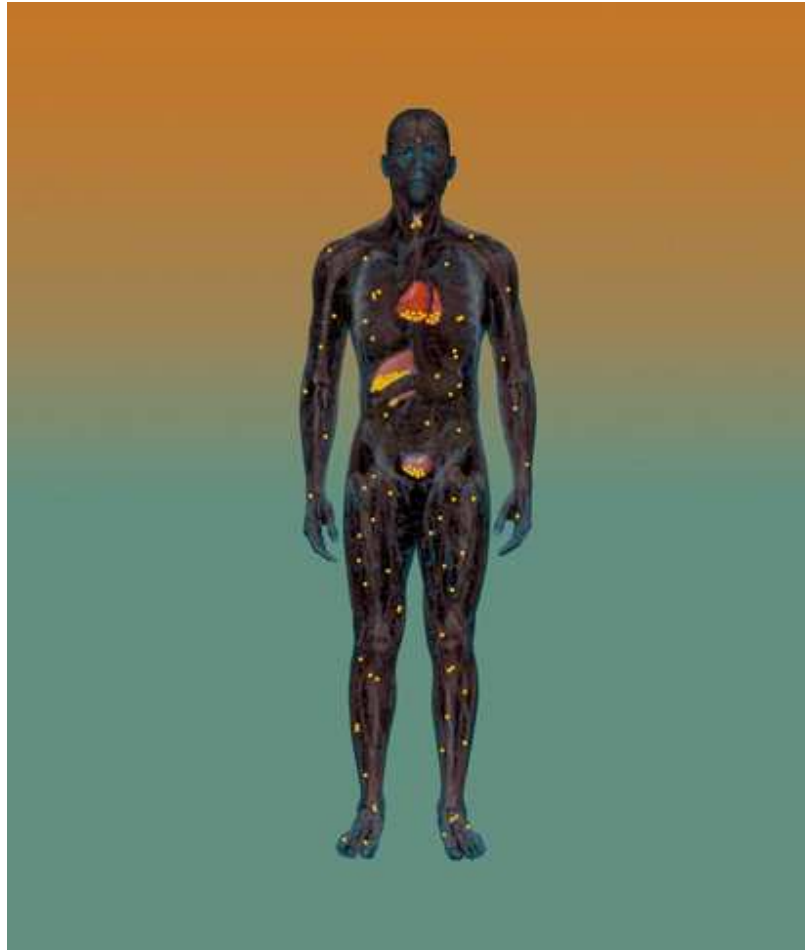
- Increased blood viscosity when Hb > 10 g/dl
- Acute red cell exchange is useful in
  - Acute infarctive stroke
  - Acute chest syndrome
  - Multi-organ failure syndromes
  - Priapism?
- Chronic red cell exchange (less iron overload)



**200–250 mg iron:  
Whole blood: 0.47 mg iron/mL  
'Pure' red cells: 1.16 mg iron/mL**

- **1 blood unit contains 200 mg iron**
- **A 60 kg thalassemia patient receiving 45 units of blood annually has transfusional iron intake of 9 g iron/year**
  - **0.4 mg iron/kg body wt/day**
- **In addition, up to 4 mg/day may be absorbed from the gut**
  - **Up to 1.5 g iron/year**

# Iron overload



Pituitary → impaired growth

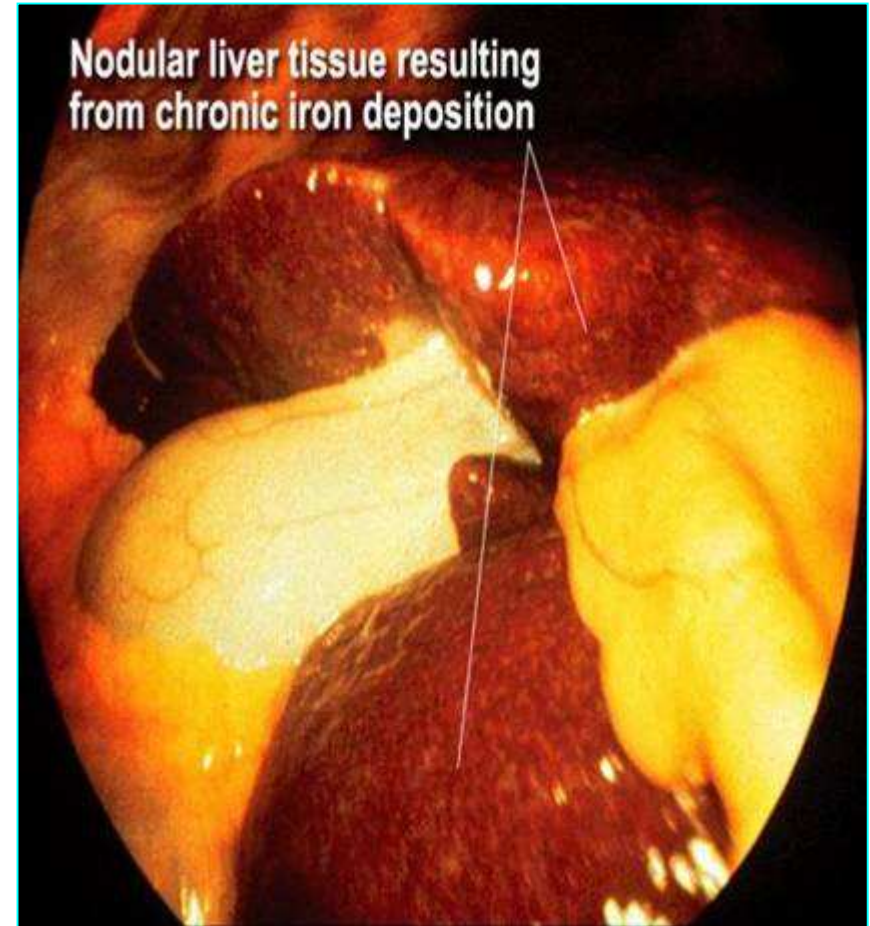
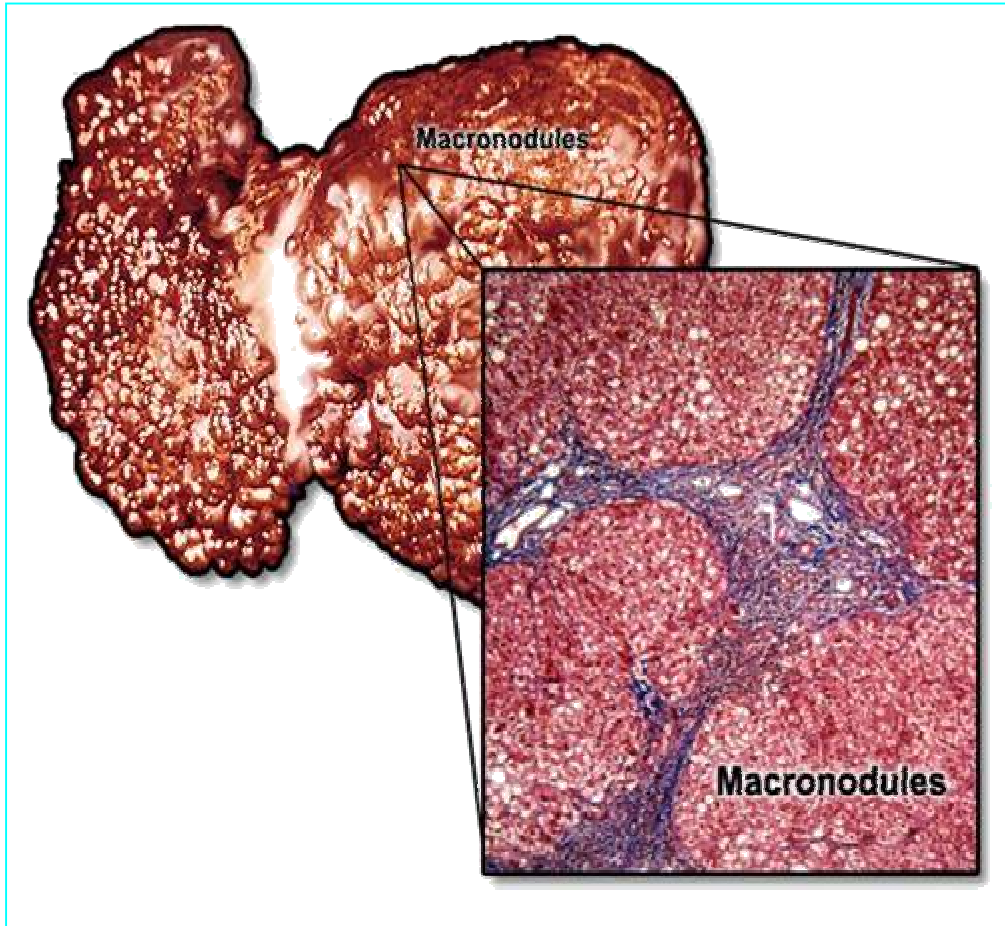
Heart → cardiomyopathy,  
cardiac failure

Liver → hepatic cirrhosis

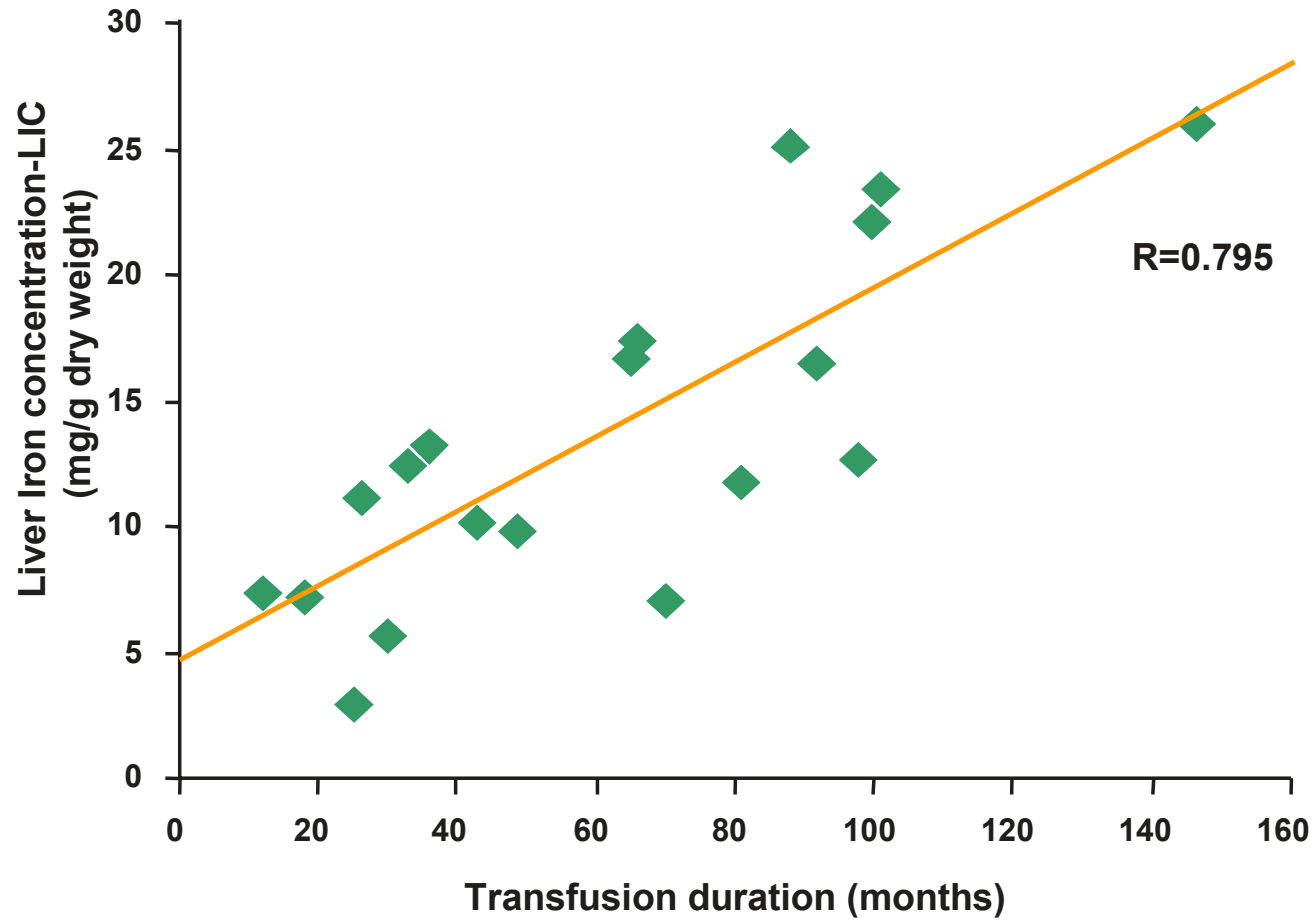
Pancreas → diabetes mellitus

Gonads → hypogonadism,  
infertility

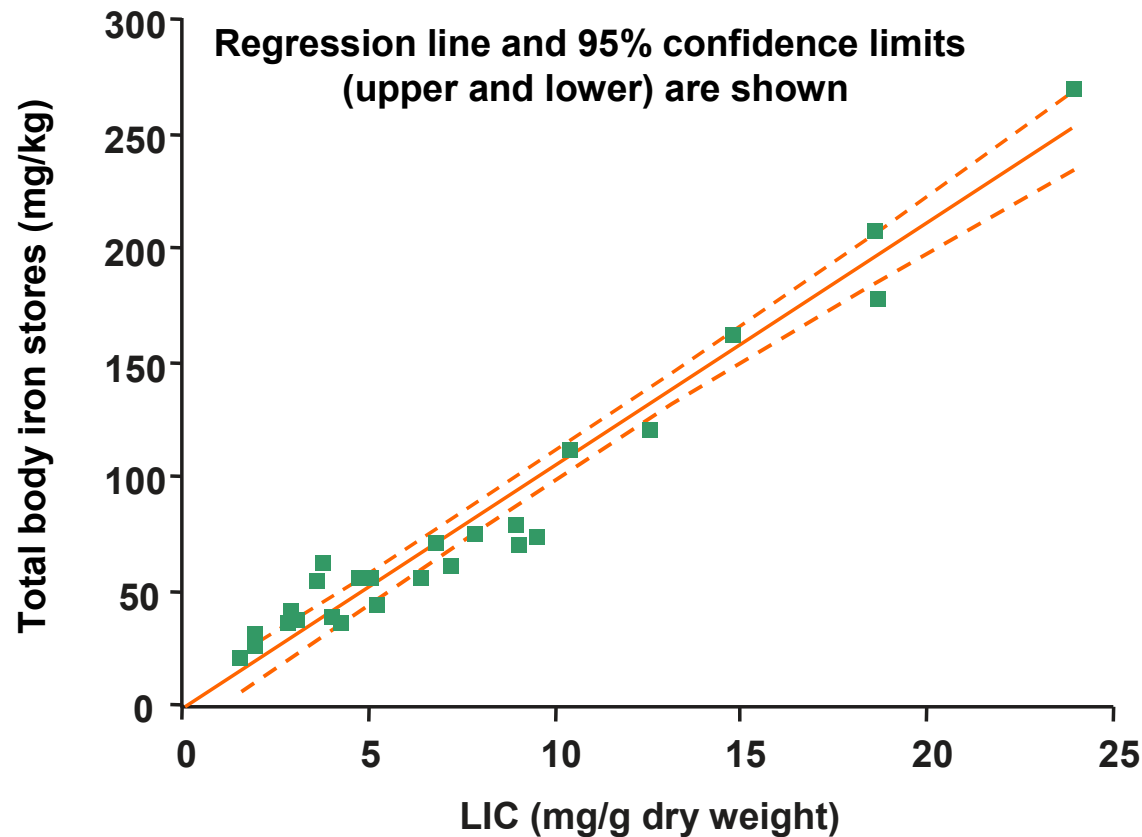
# Macro/microscopic aspect of iron overload in liver



# Transfusions and iron overload

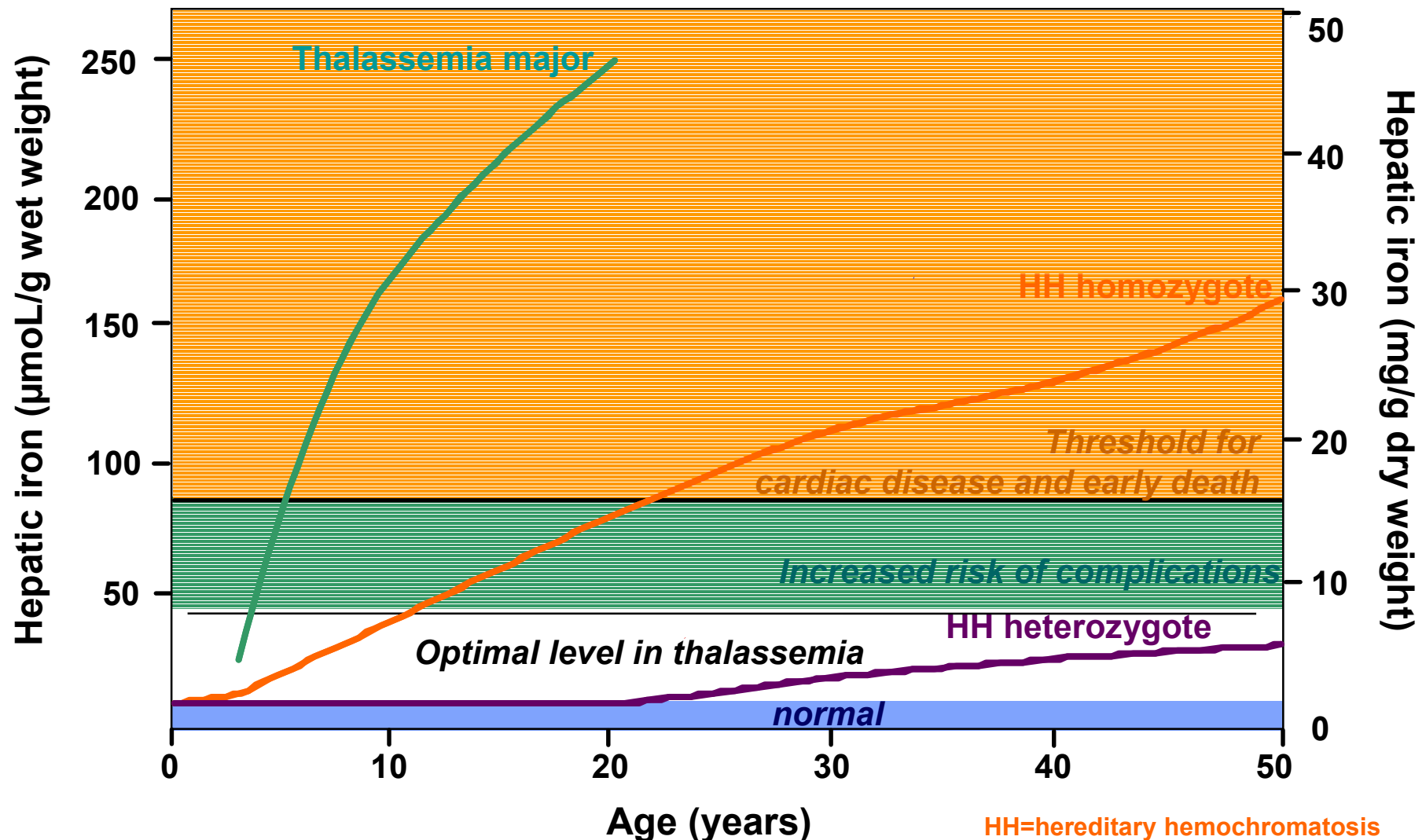


# LIC (liver iron concentration) as indicator of iron overload



**Total iron body stores = 10.6 x (LIC)**

# Liver iron and risk from iron overload



# How do we characterize iron stores ?

- Iron Input
  - Transfusion burden
- Serum markers
  - Ferritin
  - Iron, iron binding capacity & transferrin saturation
  - Nontransferrin bound iron
- Liver iron
  - Biopsy
  - SQUID
  - CT
  - MRI



# Summary of serum markers

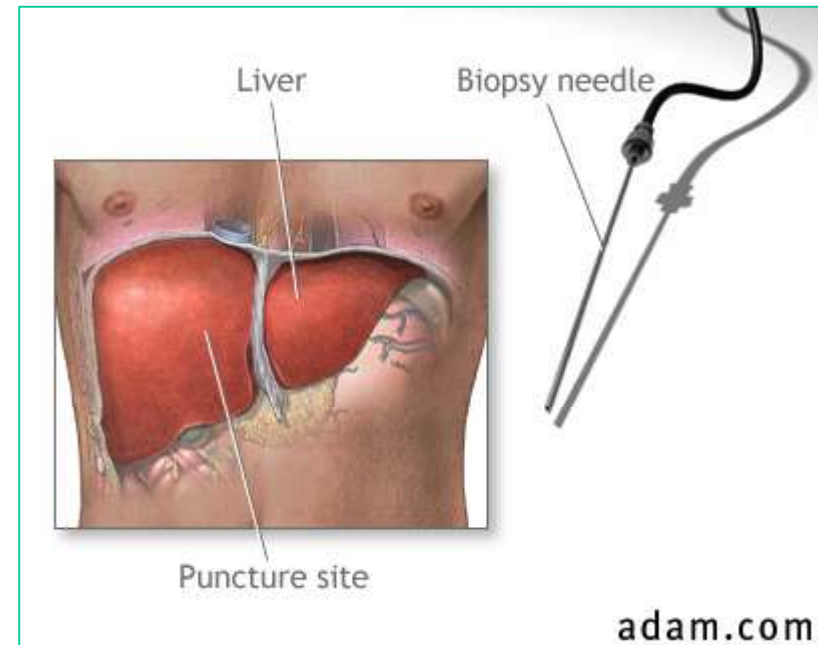
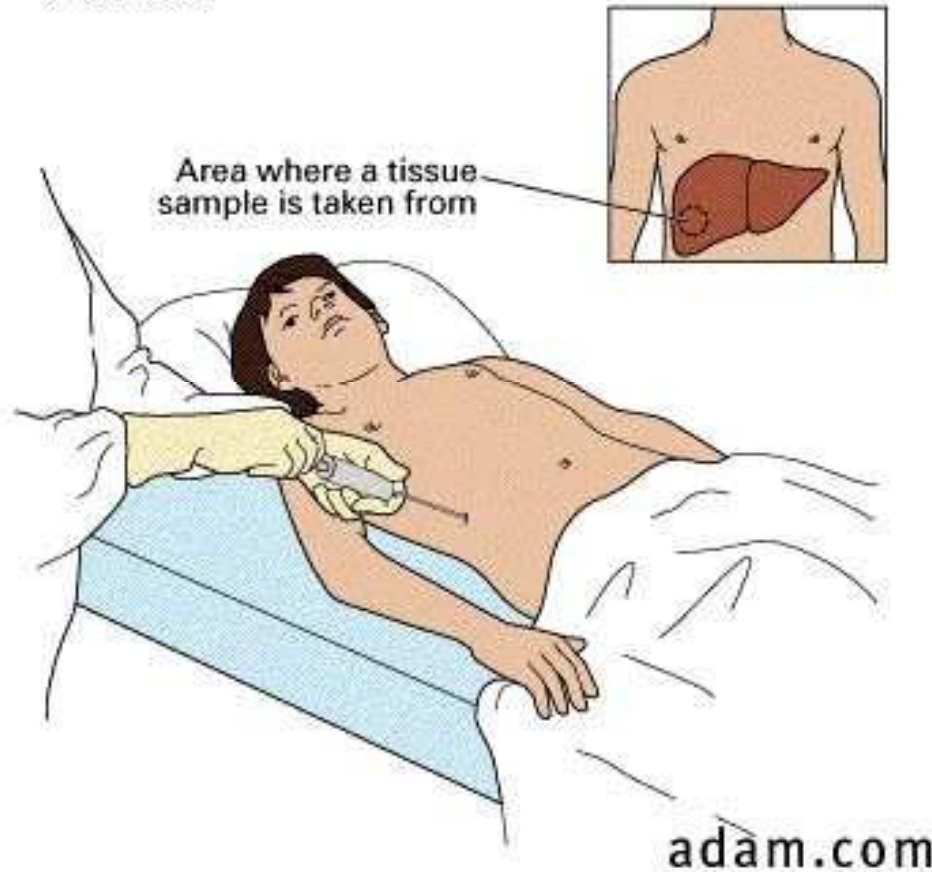
	Ferritin	Serum Iron	NTBI
Availability	+++++	+++	+
Cost	low	moderate	variable
Reliability	++	++	variable
Clinical Validation	+++	+	+
Greatest Weakness	Inflammation False negative	Nonlinear Method dep.	No standard. Unproven.

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# Liver biopsy

## Liver Biopsy

A tiny incision is made between the ribs and a needle is inserted in order to reach the area of the liver where a tissue sample is taken. The procedure requires a local anesthesia.



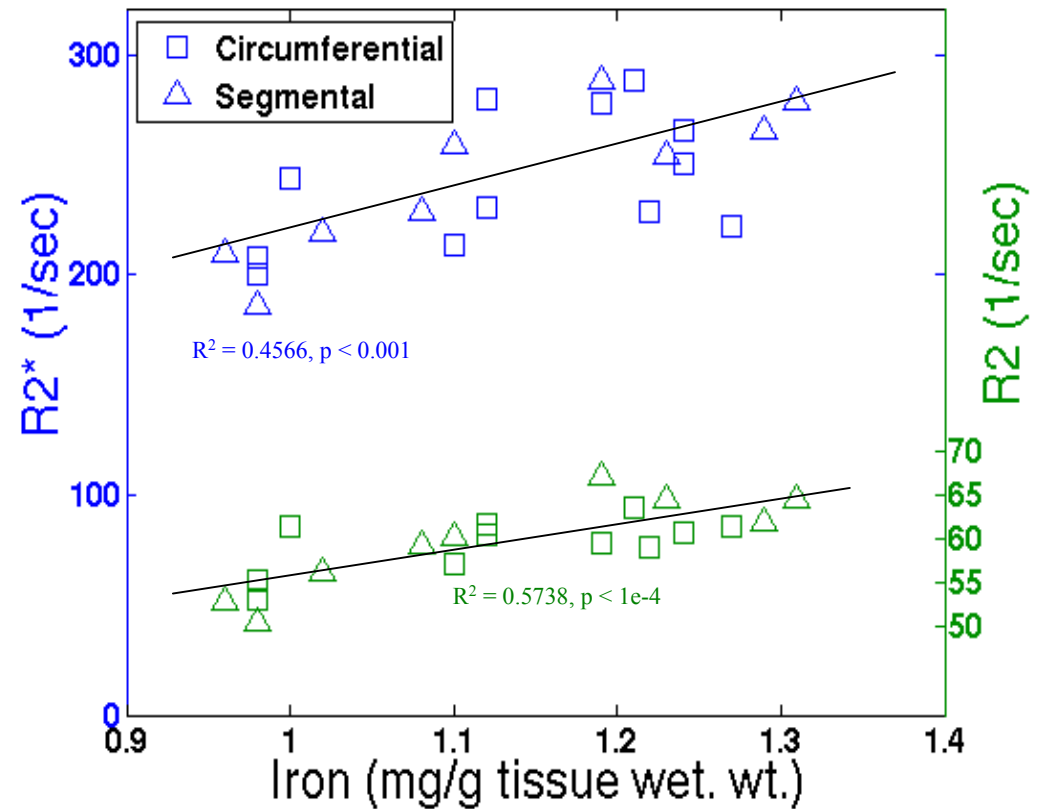
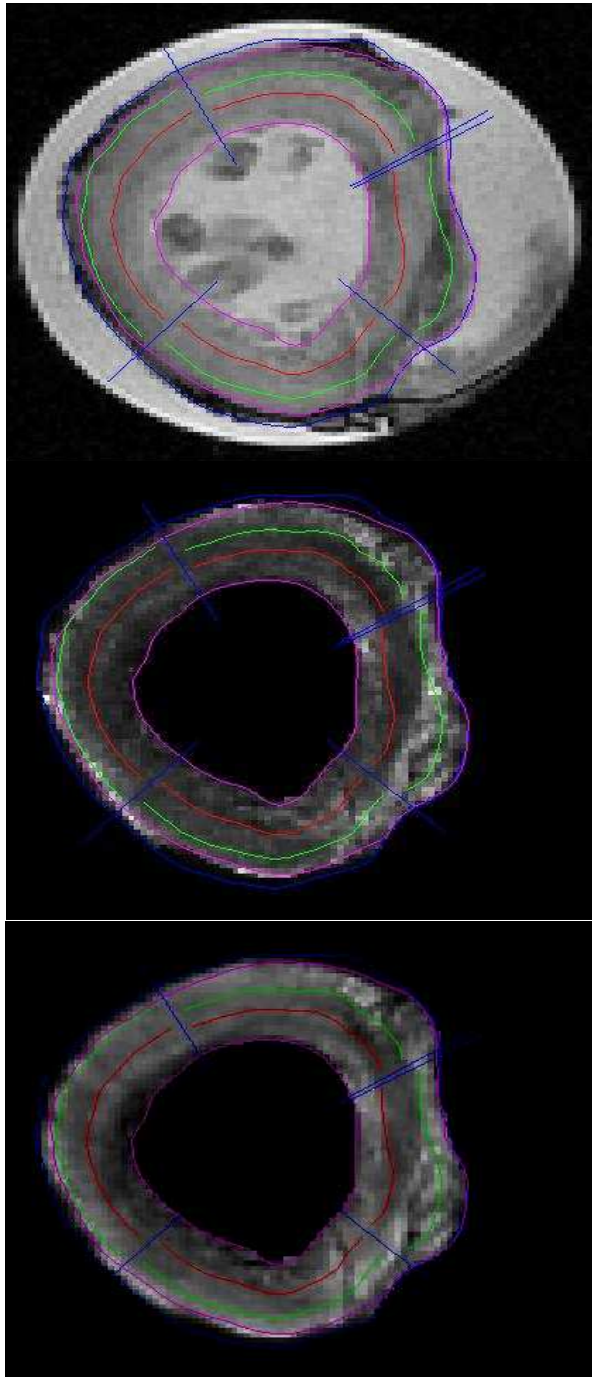
Slide Courtesy of Tim St. Pierre

# Comparison of other methods

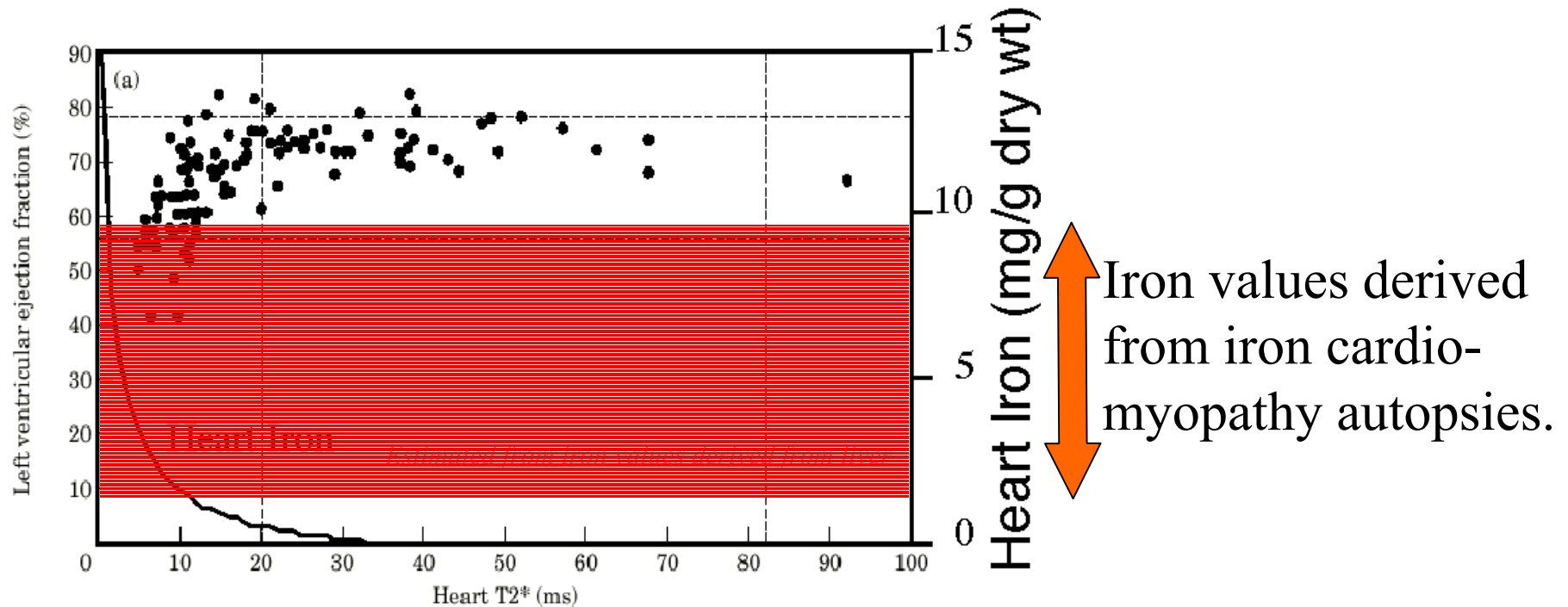
	SQUID	CT	MRI
Availability	+	+ (++++)	++ (++++)
Cost	\$\$\$\$	\$\$ (~\$300)	\$\$\$ (\$750)
Comfort	++++	++++	+++
Validation	++	+	++++
Organs	Liver, spleen	All	All
Limitations	Limited scope, availability	Unvalidated	Standardization, Dedicated pers.

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# Human cardiac R2 and R2\* versus Iron



# Extrapolation of human T2\*-iron relationships to heart



# Summary

- Blood transfusion burden is an important metric of iron burden.
- Ferritin remains an inexpensive and widely available tool for monitoring chelation therapy.
- Labile iron metrics show promise for predicting endocrine and cardiac iron toxicity but require further refinements and validation.
- Liver iron concentration (by any technique) is a good metric of total iron balance.

# Summary (cont'd)

- MRI is the most accurate and widely available noninvasive tool to assess liver iron.
- Comprehensive MRI assessment of liver/cardiac iron and cardiac function will become the standard of care as barriers to broad implementation are overcome.

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# Iron chelation

	Deferoxamine Desferal ®	Deferiprone Ferriprox ®	Deferasirox Exjade ®
Characteristics	SQ or IV Half life 20'	PO 2-3 hours	PO 8-16 hours
Monitoring	Ferritin Ears and eyes Liver, heart	Ferritin CBC, ALT Liver, heart	Ferritin Creat, ALT Liver, heart
Advantages	Experience Effective  Comb DFP	Orally Enhanced removal of heart iron Comb DFO	Orally Once daily Effective at 20- 30mg/kg
Disadvantages	Parenteral Ear, eye, bone toxicity	Agranulocytosis Weekly CBC	Limited long term data Monitor creat

# Deferasirox is effective across a range of transfusion-dependent anemias

■  $\beta$ -thalassemia (n=83) ■ Other anemias, eg DBA, MDS (n=80)

