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Basics of Quantitative MRI

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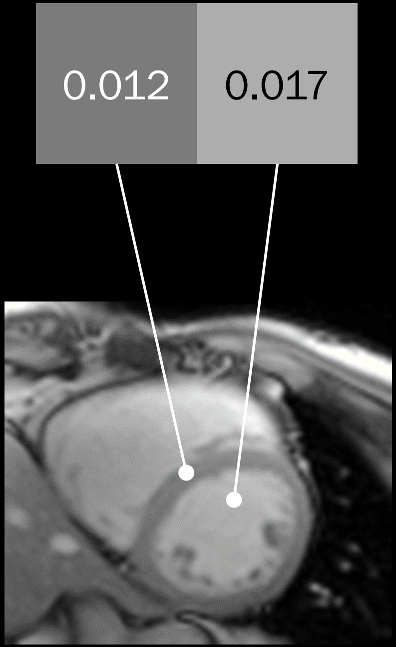
PBM M219
13 March 2024

Quantitative vs Qualitative Imaging

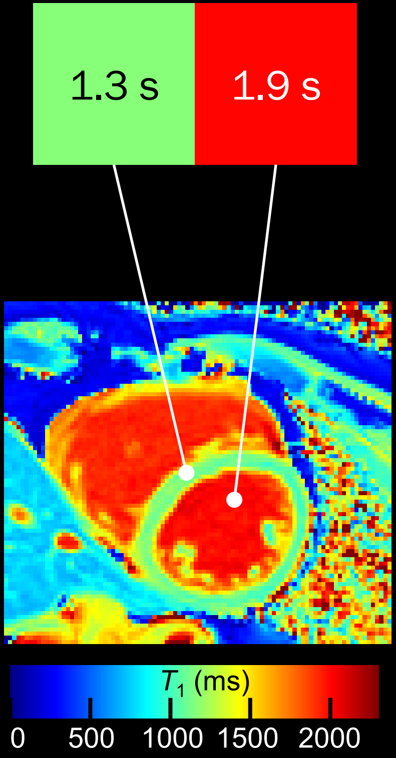
Qualitative

Unitless pixel values



Quantitative

Pixel values have units



More objective

- Measures absolute parameters associated with pathophysiological tissue properties and disease states

More reproducible[1]

- Directly compares subjects, sites, and times

More sensitive[2,3]

- Detects mild or diffuse alteration of tissue properties

[1]Metere R et al., PLoS One 2017
[2]Singh P et al., *Biomed Res Int* 2013
[3]h-Icí DO et al., *Eur Heart J CVI* 2014

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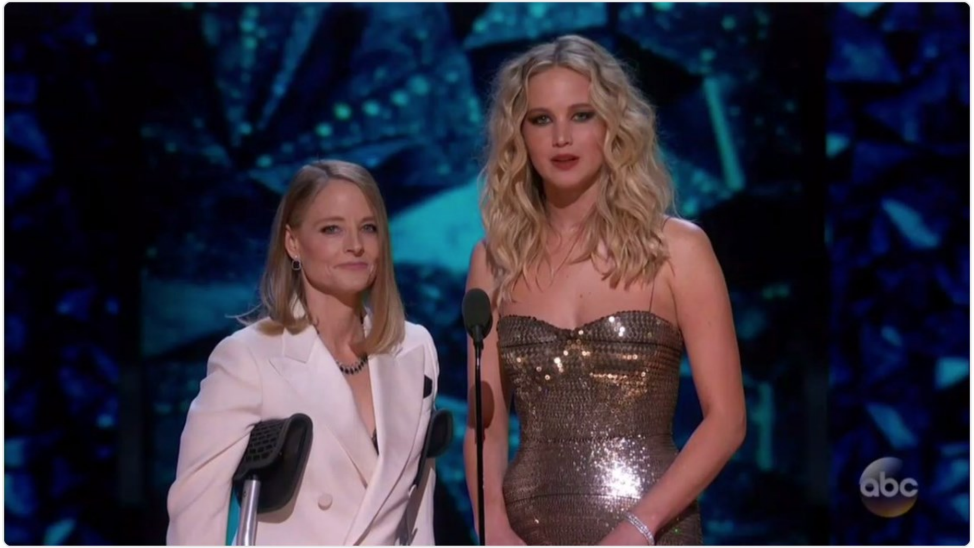
David Mack ✓
@davidmackau

Follow

question: is jodie foster really short or is jennifer lawrence really tall?

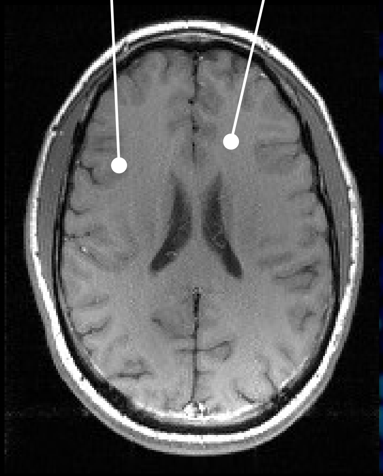


8:31 PM - 4 Mar 2018

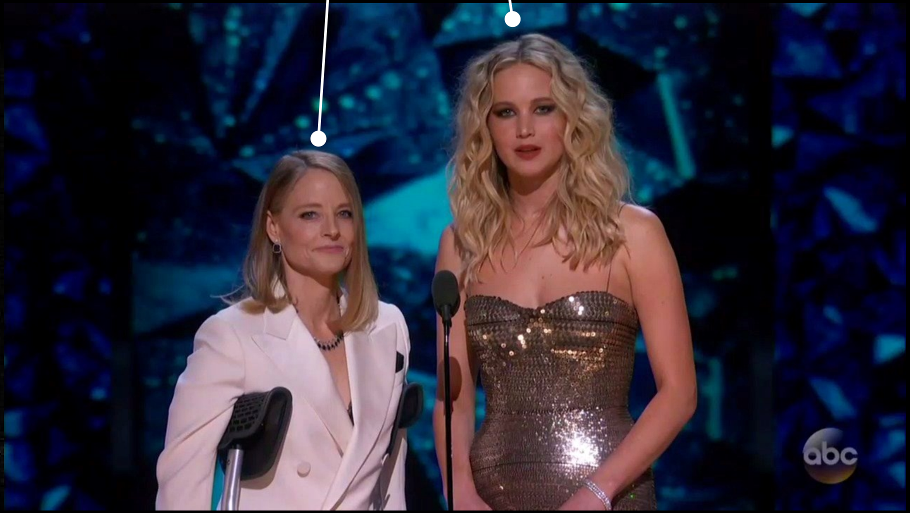
Qualitative imaging

Pixel brightness has no units. We can only make relative measurements.

Darker | Brighter



Shorter | Taller



Shorter | Taller

Qualitative imaging

Normal tissue must be present for comparison

- Not appropriate for diffuse disease

Cannot compare pixel values from:

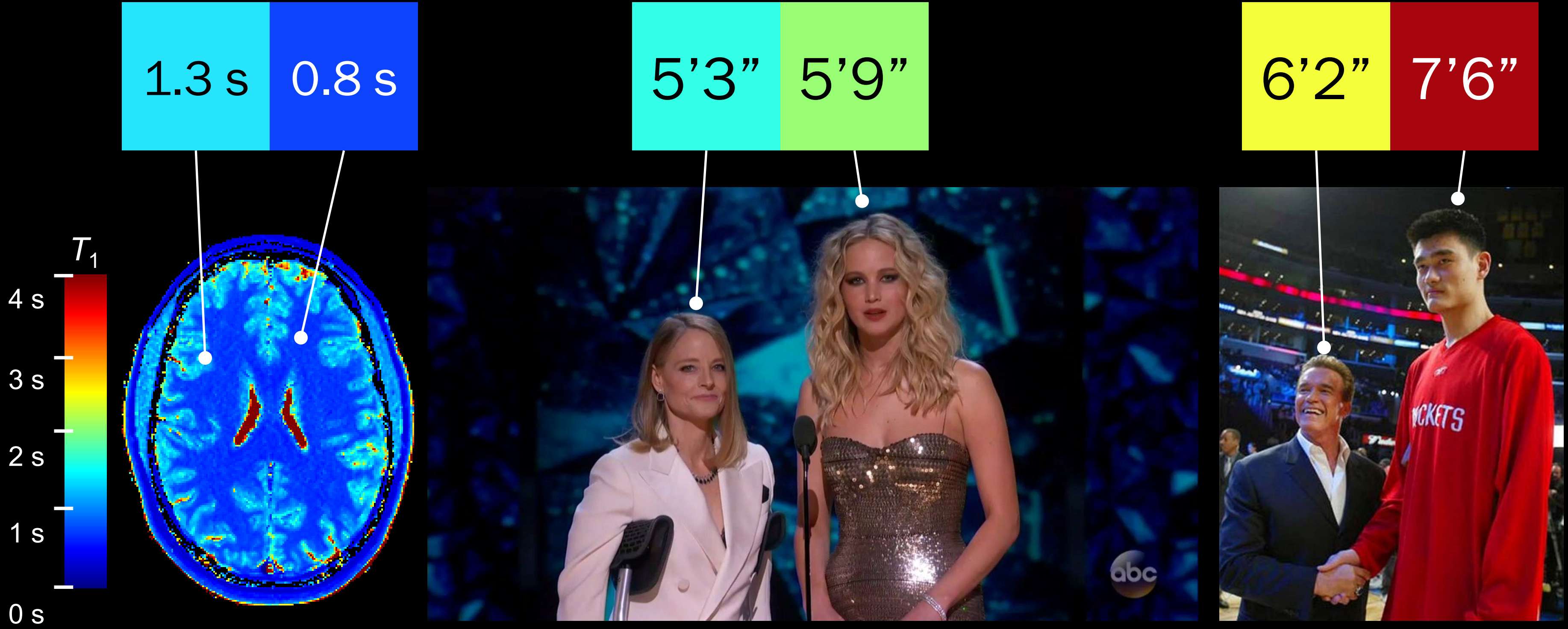
- different patients
- different scanners
- different times

Dependent on contrast weighting selection

- subtle changes may go undetected, e.g., during early stages of disease

Quantitative imaging: Measuring the actual property

Pixel value has a unit. We can make absolute measurements.



Quantitative imaging: Measuring the actual property

Qualitative vs. Quantitative imaging

Qualitative

Normal tissue must be present for comparison

Cannot compare pixel values from:

- different patients
- different scanners
- different times

Dependent on contrast weighting selection

- subtle changes may go undetected, e.g., during early stages of disease

Quantitative

No need for normal tissue: can detect diffuse disease

Can compare pixel values, allowing:

- patient comparisons
- scanner independence
- longitudinal monitoring

Incorporates multiple contrast weightings

- more sensitive to subtle changes, so promising for early detection

What tissue properties can we map?

Various tissue processes and tissue parameters, e.g.:

- Relaxation (T1, T2, T2*)
- Diffusion (ADC, helix angle, diffusion angle)
- Mechanical properties (stress, strain, stiffness)
- Flow (tissue perfusion or flow in larger vessels)
- Kinetics (K^{trans}/permeability)
- Tissue composition (water-fat, ECV, plasma volume)
- (and more)

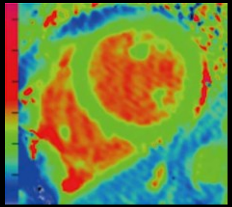
Multi-parametric imaging:

- Combines parameters for comprehensive assessment of tissue state and accurate diagnosis

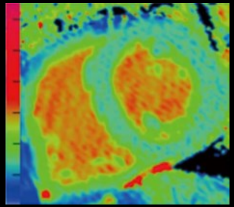
	Diseases	T1	T2	T2*	ADC	SWI/QSM	FF
Neuro	Stroke	+	+		+	+	
	Traumatic brain injury	+	+		+	+	
	Epilepticus	+	+		+	+	
	Multiple Sclerosis	+	+			+	
	Glioblastoma	+	+	+	+	+	
Cardiovascular	Iron overload cardiomyopathy	+	+	+			
	Myocarditis	+	+				
	Sarcoidosis		+				
	Intramyocardial Hemorrhage		+	+		+	
	Acute/chronic myocardial infarction	+	+		+		
	Dilated Cardiomyopathy	+	+				
	Hypertrophic Cardiomyopathy	+	+		+		
	Amyloidosis	+					
	Systemic lupus erythematosus	+			+		
	Diabetic cardiomyopathy /obesity/cardiac steatosis						+
	Cardiotoxicity	+					
Body	Liver iron overload	+	+	+		+	
	<u>Cancer</u>						
	Breast	+	+		+		
	Prostate	+	+		+	+	
	Liver	+	+	+	+	+	
	Liver fibrosis	+	+		+	+	
	Hepatic Carcinoma	+	+	+	+	+	
	Hepatic/pancreatic steatosis						+

Cardiac T1 and T2 examples

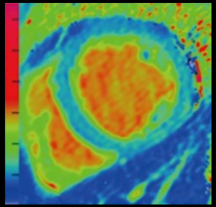
T_1



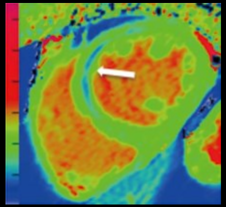
Normal



Fabry disease

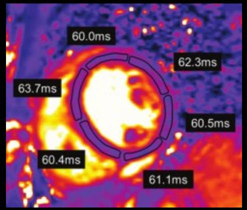


Iron overload

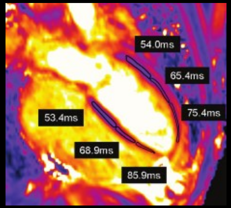


Fatty metaplasia

T_2



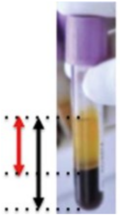
Diffuse Myocarditis



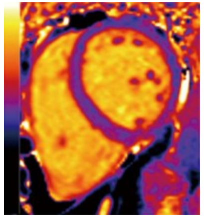
Takotsubo

T_1 w/Gd

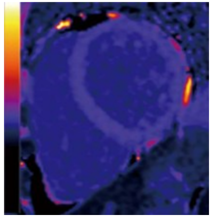
Perfusion/DCE



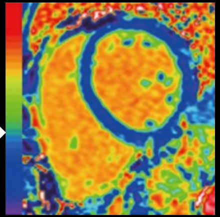
1 – HCT



Native T_1



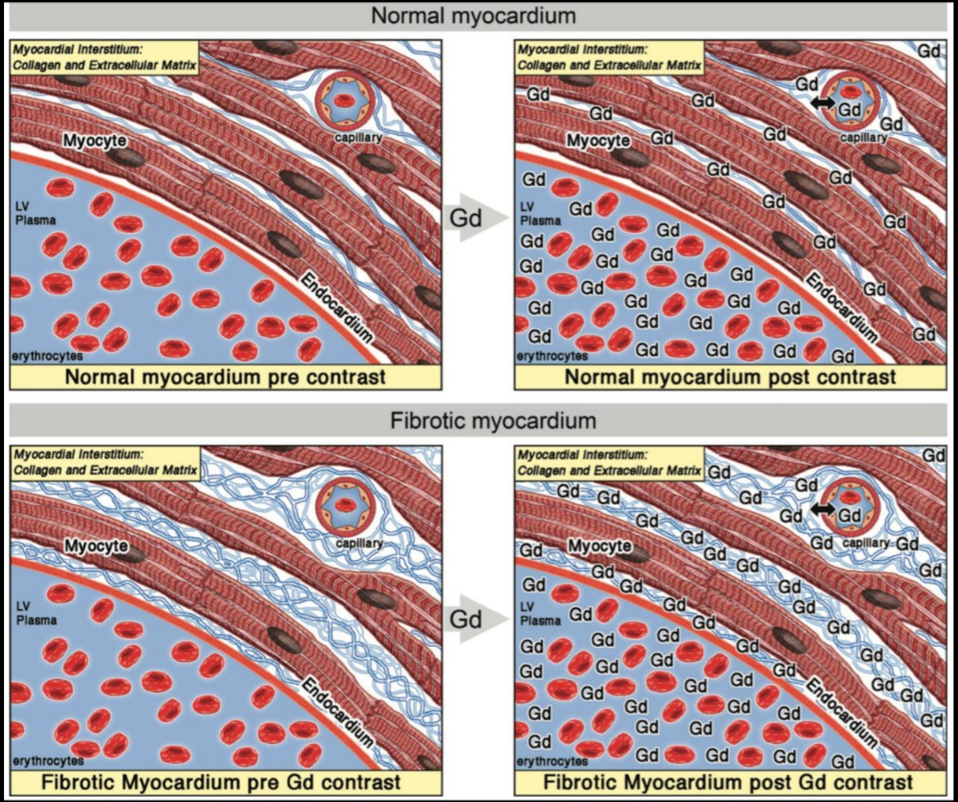
Post-contrast



Extracellular volume (ECV)

Bulluck H et al., *Circ J* 2015
Thavendiranathan P et al., *Circ Cardiovasc Imaging* 2012

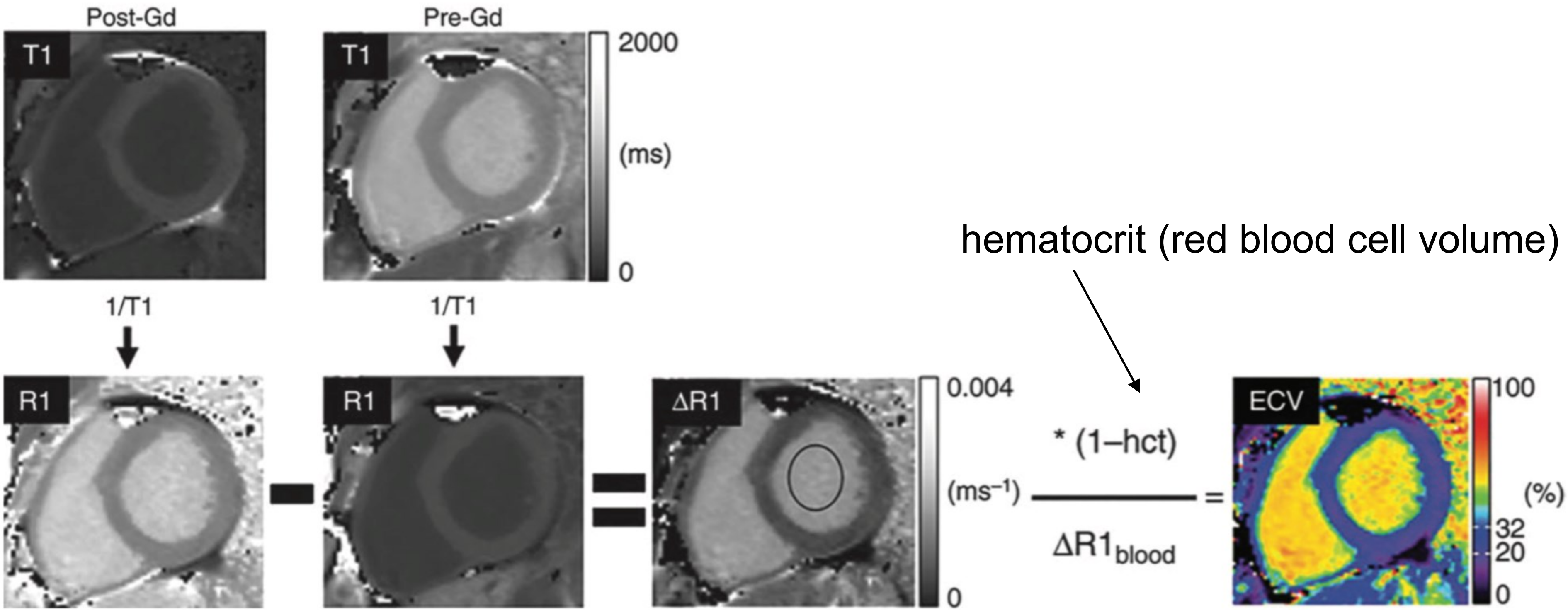
Myocardial fibrosis



$$\Delta R_1 \propto [Gd]$$

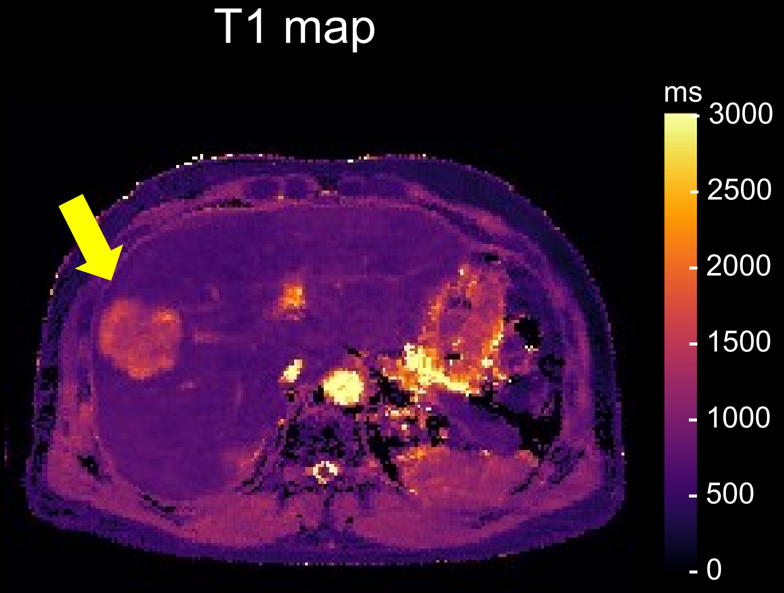
Schelbert EB, Messroghli DR, *Radiol* 2017

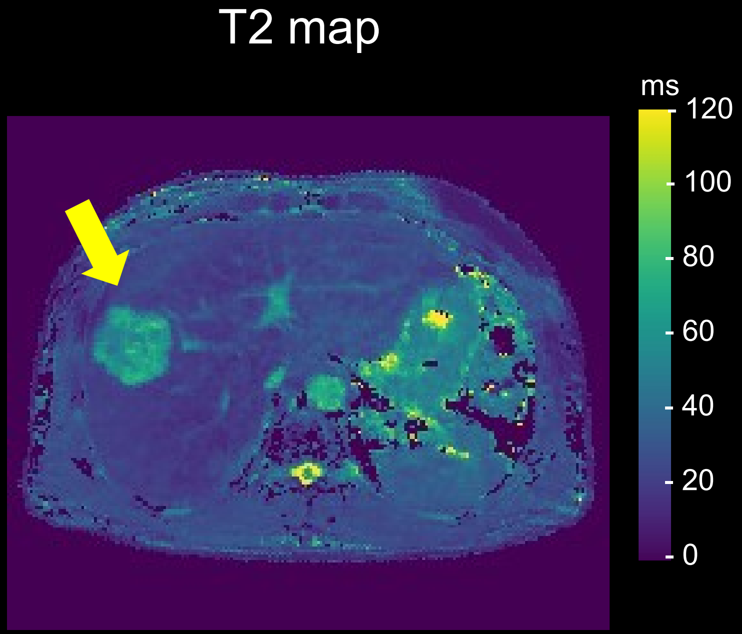
Extracellular volume fraction (ECV)



Schelbert EB, Messroghli DR, *Radiol* 2017

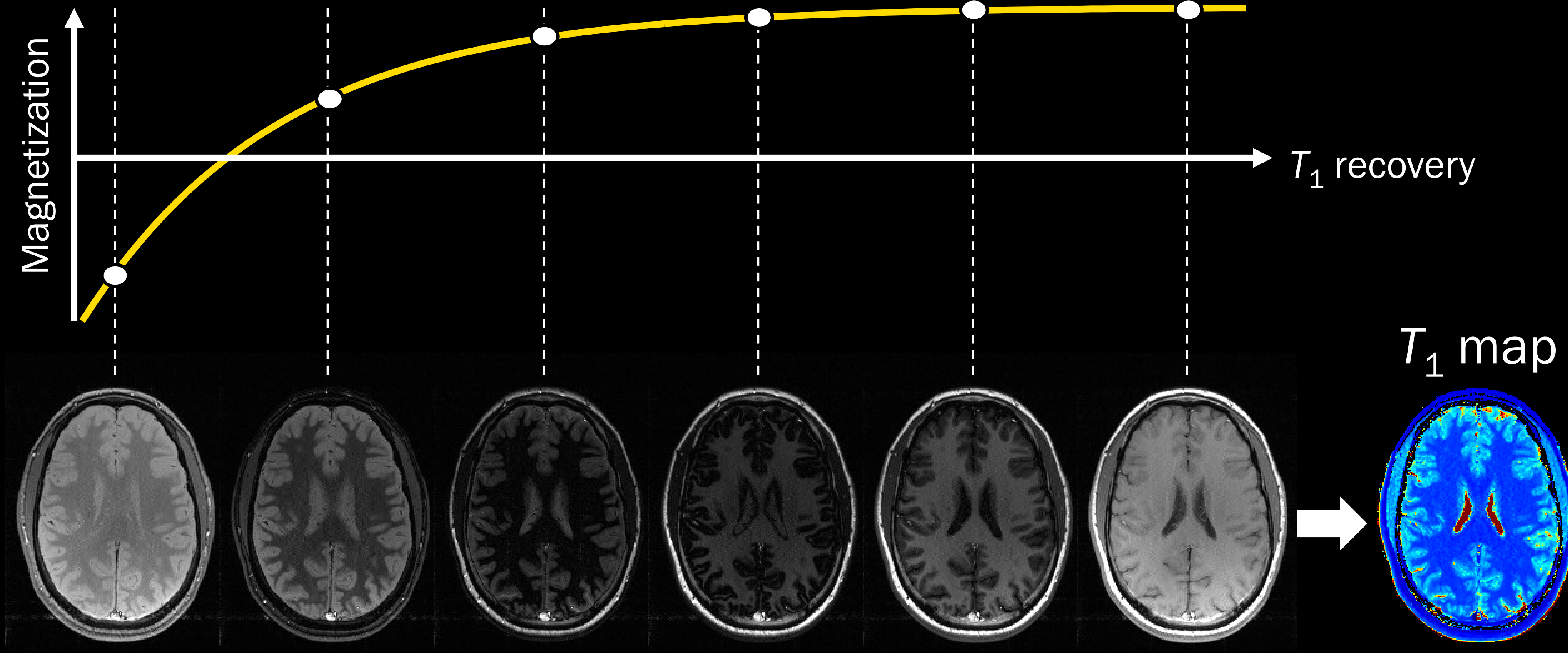
Liver cancer T1 and T2 examples





Fan Z, et al. *ISMRM* 2019 #698

To quantify MRI, we must collect multiple contrast weightings



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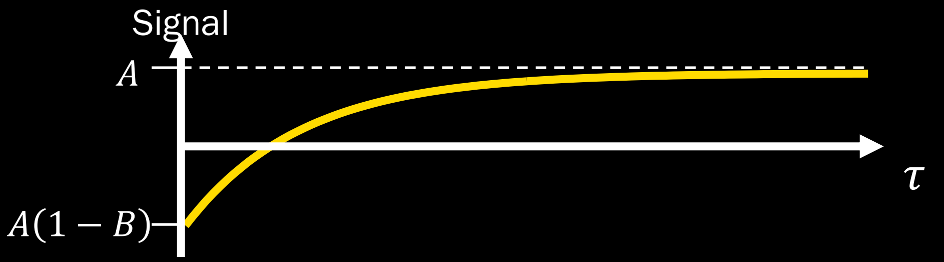
Scope of the lecture

- There are MANY pulse sequences available for mapping particular parameters
- We are <u>not</u> going to cover them all today (although we will see some variations at the end)
- We <u>will</u> cover important principles of mapping using T1, T2, and T2* as examples
    - Basic equation forms for "canonical sequences"
        - T1 mapping: Inversion-recovery spin echo (IR-SE)
        - T2 mapping: Spin echo (SE)
        - T2* mapping: Gradient echo (GE)
    - Types of error: accuracy/bias, precision, repeatability
    - How to choose the "best" images for quantification

T_1 mapping

Signal model:

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$

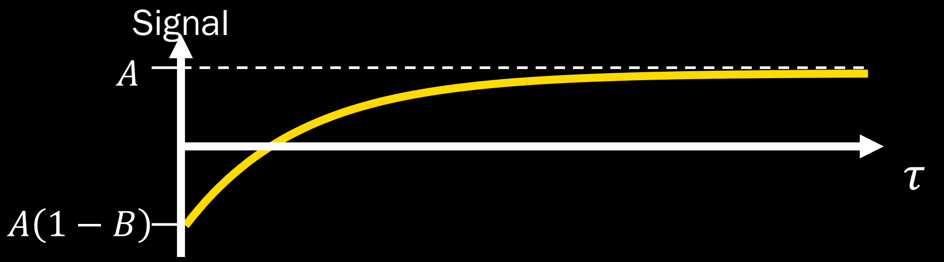


- Equation: What are these parameters?
  - Unknown A, B, T_1
  - Known/chosen τ's
- Acquisition: Which τ's should we choose?
- Analysis: Extracting A, B, T_1 by nonlinear optimization

T_1 mapping: Equation

Signal model:

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$



At steady state ($\tau \to \infty$): $S = A$.

- A combines proton density, T_2 or T_2* weighting, coil sensitivity, and $\sin(\alpha_{\text{exc}})$

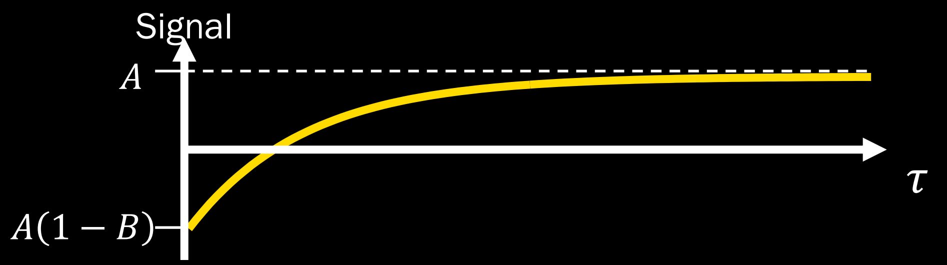
Immediately after preparation ($\tau = 0$): $S = A(1 - B)$.

- Assuming steady-state was reached: $B = 1 - \cos\left(\alpha_{\text{prep}}\right)$
  - For inversion recovery: $B = 1 - \cos(180°) = 1 - (-1) = 2$
  - For saturation recovery: $B = 1 - \cos(90°) = 1 - 0 = 1$

T_1 mapping: Acquisition

Signal model:

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$



How many τ's do we need to do mapping?

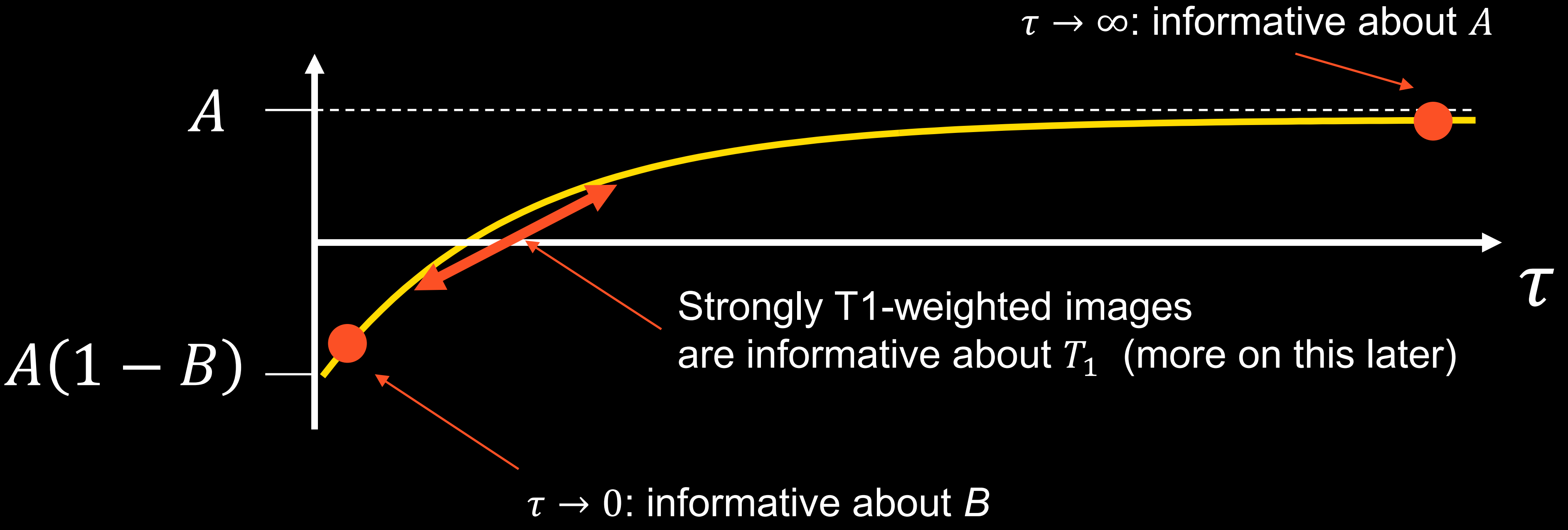
- Three unknowns: A, B, T_1
- Generally need at least as many τ's ($\geq$3 in this example)

Which τ's do we need?

- Intuition will only get us so far
- Optimal design/information theory can tell us how to maximize precision
  - e.g. Fisher information, Cramer-Rao analysis

T_1 mapping: Acquisition

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$



T_1 mapping: Analysis

Typically: voxelwise nonlinear least-squares fitting

$$S(\tau) = A\left(1 - Be^{-\tau/T_1}\right)$$

Two-point fitting:

Assume $B = 1 - \cos\left(\alpha_{\text{prep}}\right)$

$$\arg\min_{A,T_1} \sum_{\tau} \left| S(\tau) - A\left(1 - Be^{-\tau/T_1}\right) \right|^2$$

Three-point fitting:

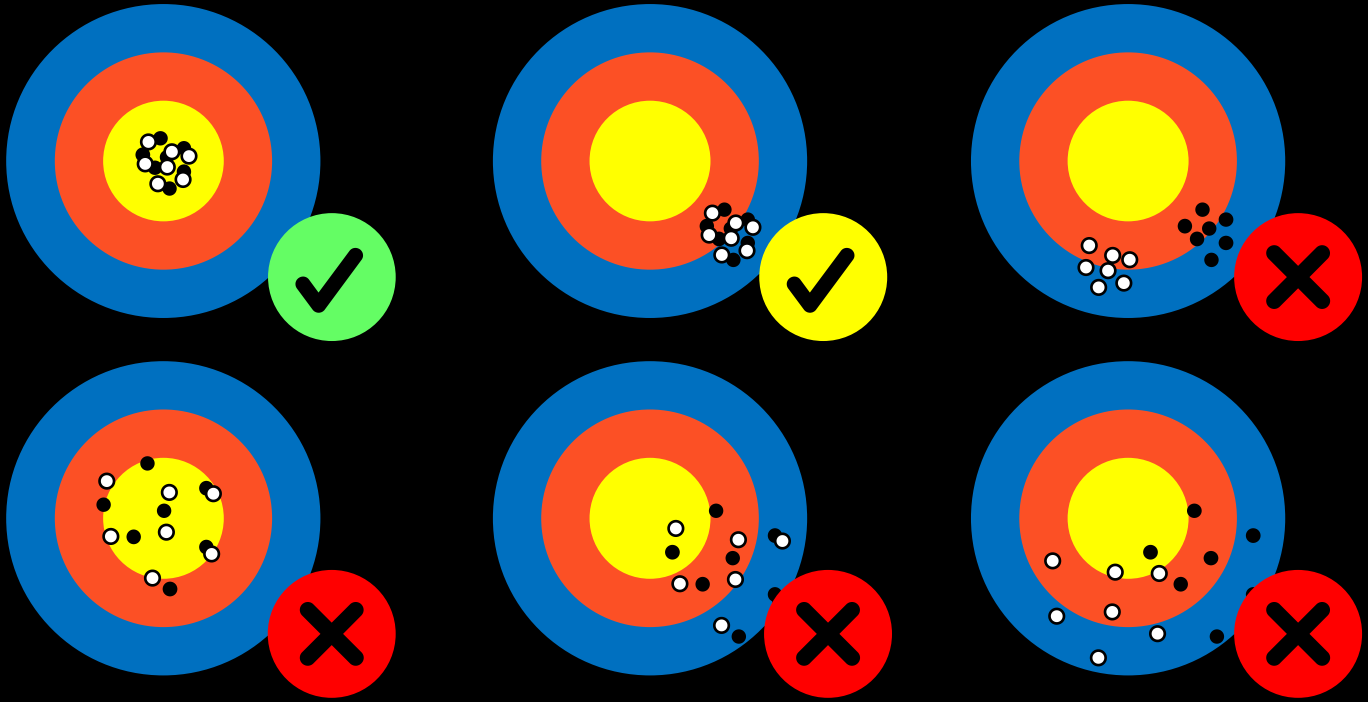
$$\arg\min_{A,B,T_1} \sum_{\tau} \left| S(\tau) - A\left(1 - Be^{-\tau/T_1}\right) \right|^2$$

Errors in quantitative mapping

Accurate (unbiased) | Systematic bias | Nonrepeatable bias

Precise

Imprecise



T_1 mapping: Analysis

Typically: voxelwise nonlinear least-squares fitting

$$S(\tau) = A\left(1 - Be^{-\tau/T_1}\right)$$

Two-point fitting:

Assume $B = 1 - \cos\left(\alpha_{\text{prep}}\right)$ ⟵ Potential nonrepeatable bias

$$\underset{A,T_1}{\arg\min} \sum_{\tau} \left| S(\tau) - A\left(1 - Be^{-\tau/T_1}\right) \right|^2$$

Three-point fitting:

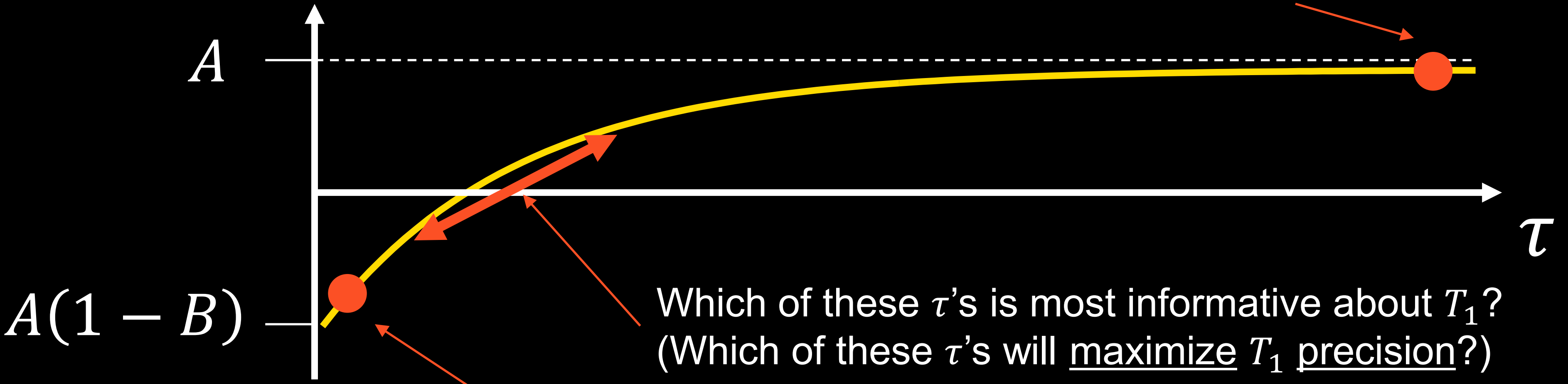
$$\underset{A,B,T_1}{\arg\min} \sum_{\tau} \left| S(\tau) - A\left(1 - Be^{-\tau/T_1}\right) \right|^2$$

More params. ~ less precision ⟶

T_1 mapping: Acquisition

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$

$\tau \to \infty$: informative about A



Which of these τ's is most informative about T_1?
(Which of these τ's will maximize T_1 precision?)

$\tau \to 0$: informative about *B*

Optimal design tool: Fisher information

How much information does $S = A\left(1 - Be^{-\tau/T_1}\right)$ carry about T1?

Under very narrow conditions*, Fisher information is

$$I(T_1) = \left|\frac{\partial S}{\partial T_1}\right|^2$$

In other words: how sensitive is S to T_1?

- We will want to choose the τ that maximizes sensitivity/information
  - This maximizes T_1 precision!
- $I(T_1)$ is common notation, but is not just a function of T_1, as we will see

*single parameter, single data point, Gaussian noise

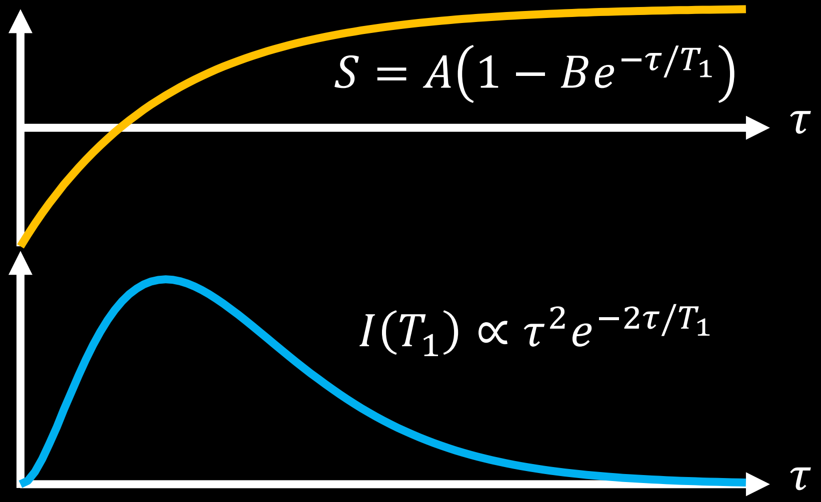
Optimal design tool: Fisher information

$$I(T_1) = \left|\frac{\partial S}{\partial T_1}\right|^2$$

$$\frac{\partial S}{\partial T_1} = \frac{\partial}{\partial T_1} A\left(1 - Be^{-\tau/T_1}\right)$$

$$= -\frac{AB}{T_1^2}\tau e^{-\tau/T_1}$$

$$I(T_1) = \frac{|A|^2 B^2}{T_1^4}\tau^2 e^{-2\tau/T_1}$$



Consistent with our intuition!

There is no information about T_1:

- at steady-state, when $S = A$
- right after prep, when $S = A(1 - B)$

But there is information in between!

Optimal design tool: Fisher information

$$I(T_1) = \left|\frac{\partial S}{\partial T_1}\right|^2$$

$$\frac{\partial S}{\partial T_1} = \frac{\partial}{\partial T_1} A\left(1 - Be^{-\tau/T_1}\right)$$

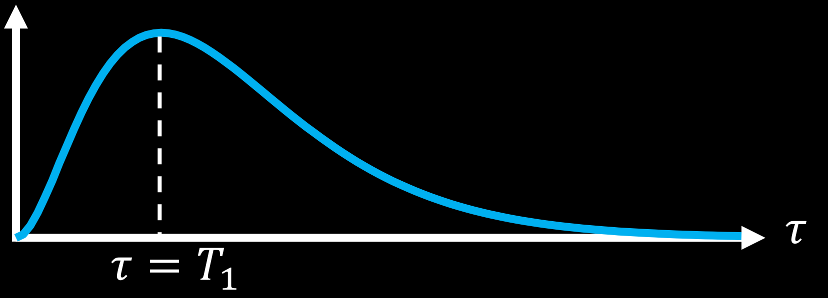
$$= -\frac{AB}{T_1^2}\tau e^{-\tau/T_1}$$

$$I(T_1) = \frac{|A|^2 B^2}{T_1^4}\tau^2 e^{-2\tau/T_1}$$

To maximize $I(T_1)$ over τ, we need to take another partial derivative over τ and set to 0:

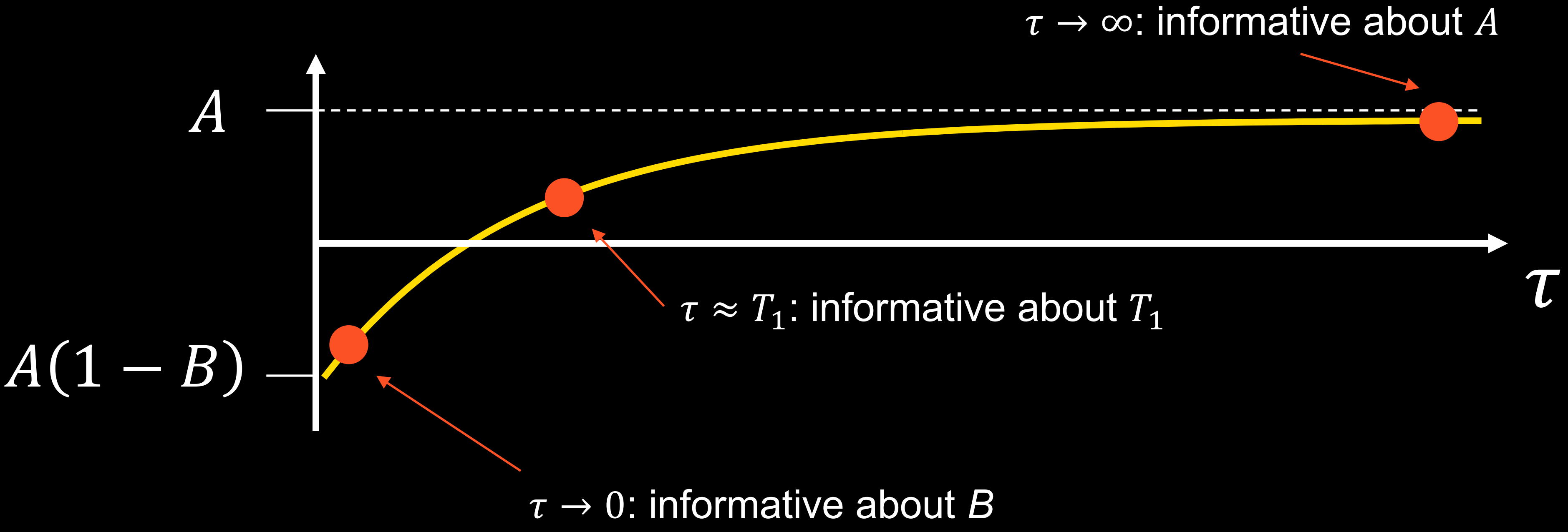
$$\frac{\partial}{\partial \tau}\tau^2 e^{-2\tau/T_1} = 0$$

$$\frac{2\tau e^{-2\tau/T_1}}{T_1}(T_1 - \tau) = 0$$



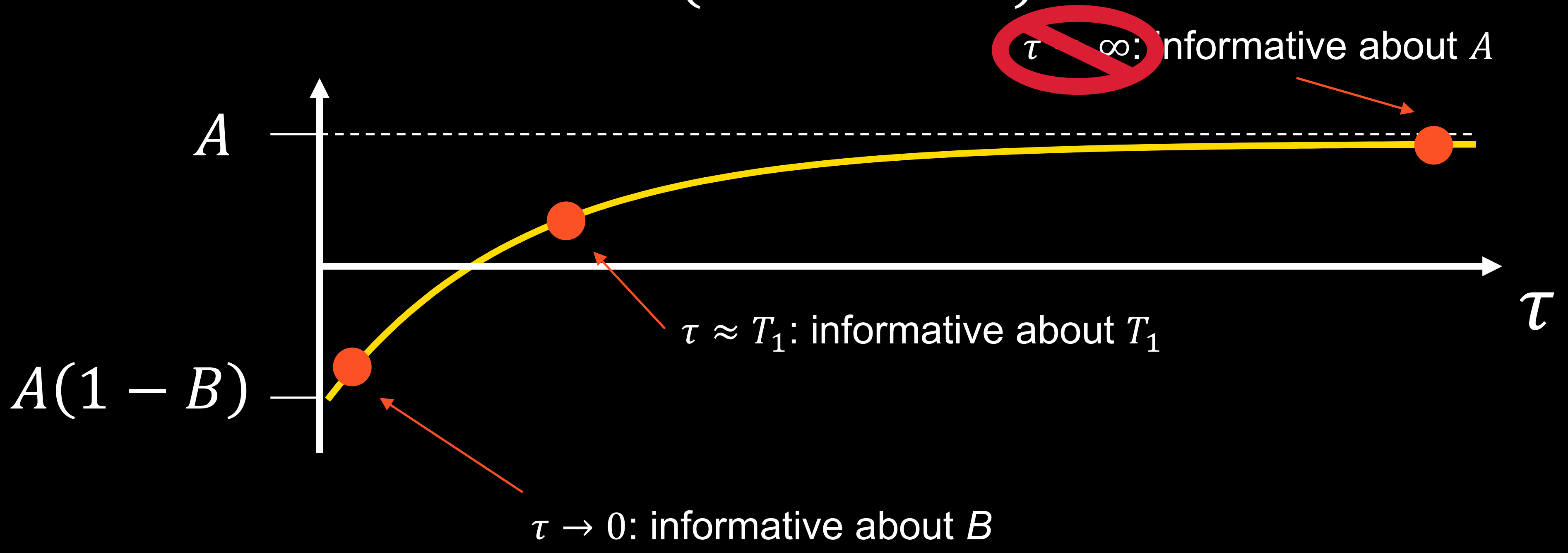
T_1 mapping: Theoretical optimal acquisition

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$



T_1 mapping: Practical optimal acquisition

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$



Optimal design tool: Cramér–Rao

We cannot wait forever, so what is most efficient?

SNR efficiency (SNRe):

$$SNRe = \frac{SNR}{\sqrt{T}} = \frac{\mu}{\sigma\sqrt{T}}$$

Scan time is included, because shorter scans can be repeated and averaged

What are the SNR and SNRe of our parameter maps?

- The Cramér–Rao bound ($\sigma^2 \geq I^{-1}$) is helpful here:

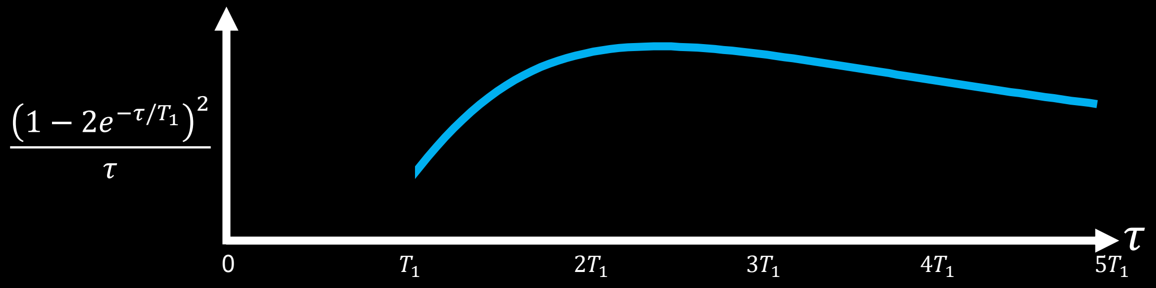
$\sigma^2 \geq I^{-1} \;\; \rightarrow \;\; SNRe \leq_{\propto} \sqrt{\frac{I}{T}}$, so we should maximize information "rate" I/T

Maximizing information rate on *A*

Assuming* scan time ∝ longest τ, let's maximize $\frac{I(A)}{\tau}$, the information rate on *A:*

$$S = A\left(1 - Be^{-\tau/T_1}\right)$$

$$\frac{I(A)}{\tau} = \frac{|\partial S/\partial A|^2}{\tau} = \frac{\left(1 - Be^{-\tau/T_1}\right)^2}{\tau}$$



Last inversion time should be 2–5x T1 for good SNR efficiency

*Ignores recovery time required after reading out

Preview: Full optimal design

Simplified version of Fisher information

- For one parameter at a time
  - e.g., information on T1 with known A, B
- For one τ at a time
  - Doesn't take entire set of timings into account
- Does not take into account which parameters we care about clinically
  - T1 more than A or B

Complete Fisher information/Cramér–Rao analysis:

$S(A, B, T_1; \boldsymbol{\tau})$ for sequence timings/params $\boldsymbol{\tau} = [\tau_1, \tau_2, \dots, \tau_N]^T$

$$I([A, B, T_1]^T) = \begin{bmatrix} \frac{\partial S^T}{\partial A} \\ \frac{\partial S^T}{\partial B} \\ \frac{\partial S^T}{\partial T_1} \end{bmatrix} \begin{bmatrix} \frac{\partial S}{\partial A} & \frac{\partial S}{\partial B} & \frac{\partial S}{\partial T_1} \end{bmatrix}$$

$$C = I([A, B, T_1]^T)^{-1} = \begin{bmatrix} \mathrm{Var}(A) & \mathrm{Cov}(A, B) & \mathrm{Cov}(A, T_1) \\ \mathrm{Cov}(B, A) & \mathrm{Var}(B) & \mathrm{Cov}(B, T_1) \\ \mathrm{Cov}(T_1, A) & \mathrm{Cov}(T_1, B) & \mathrm{Var}(T_1) \end{bmatrix}$$

$$\hat{\boldsymbol{\tau}} = \arg\min_{\boldsymbol{\tau}} \mathrm{Var}(T_1)$$

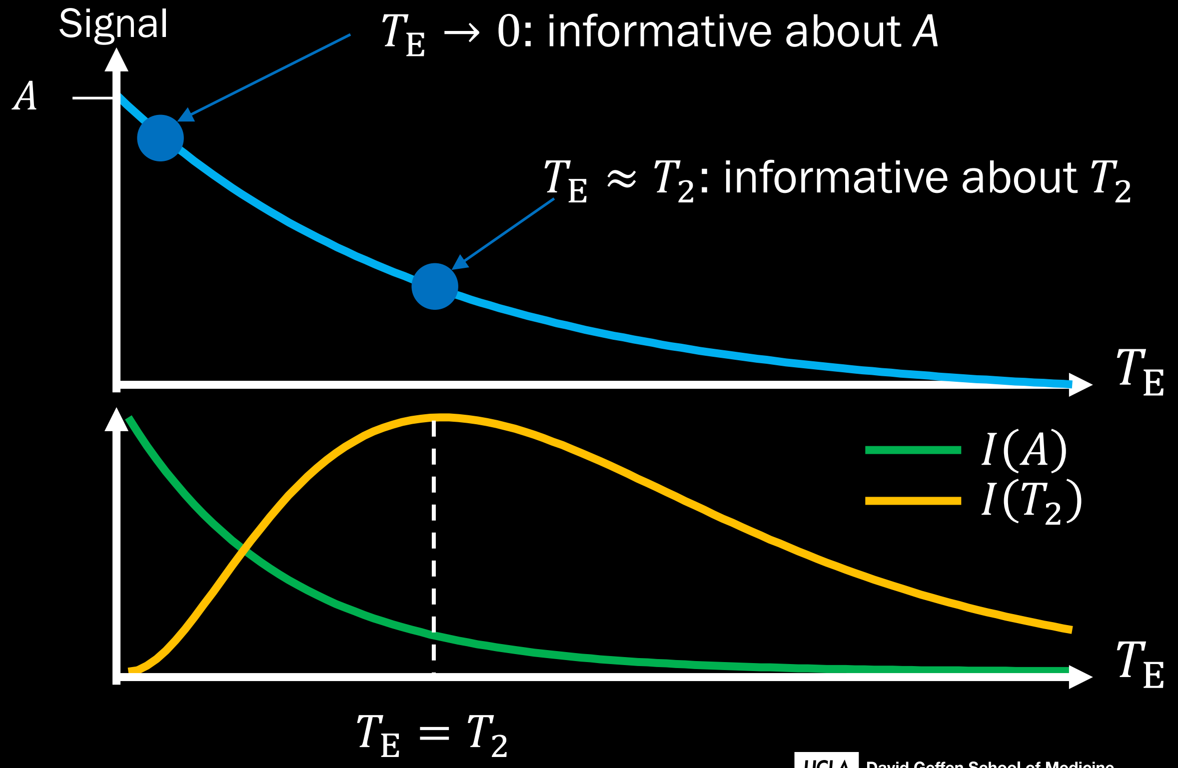
T_2 mapping

Basic form of equation for spin-echo sequences:

$$S = \underline{A}e^{-T_E/\underline{T_2}}$$

A combines:

- proton density
- coil sensitivity
- $\sin(\alpha_{exc})$



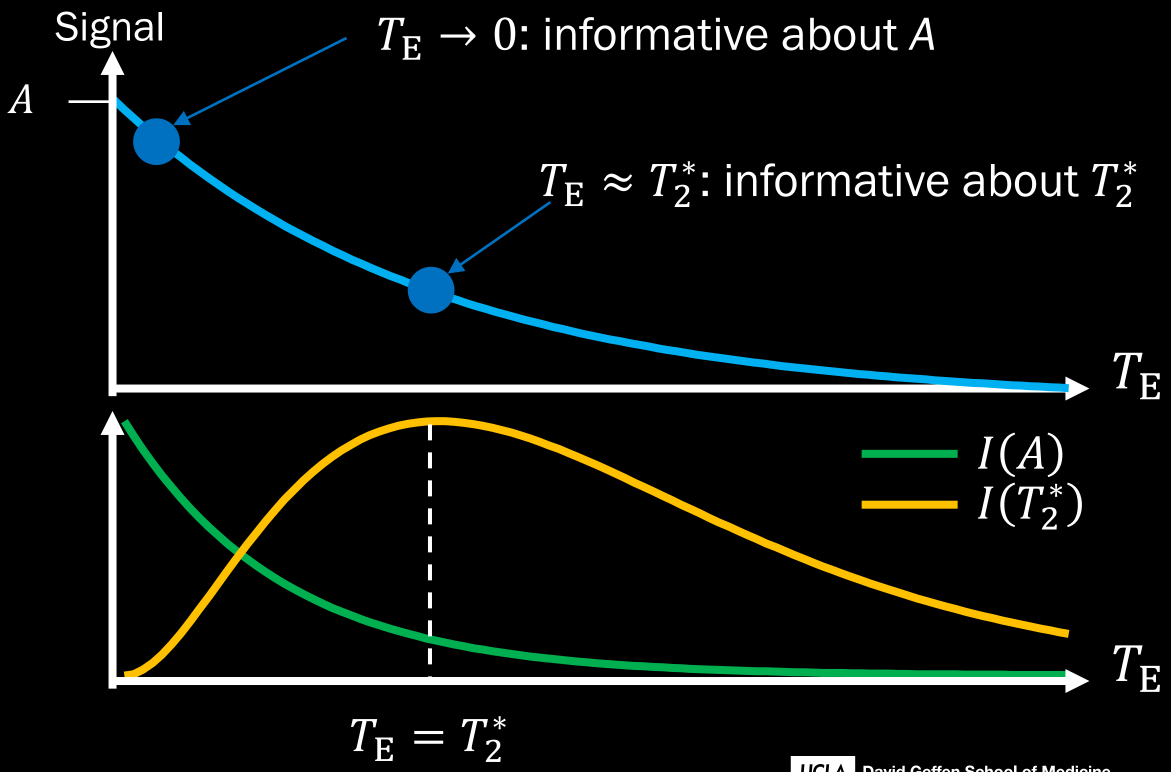
T_2^* mapping

The same as T2 mapping, but with a gradient-echo sequence:

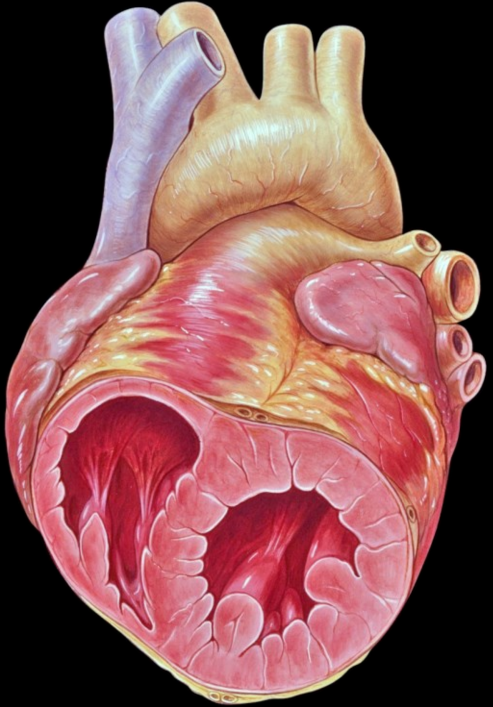
$$S = Ae^{-T_E/T_2^*}$$

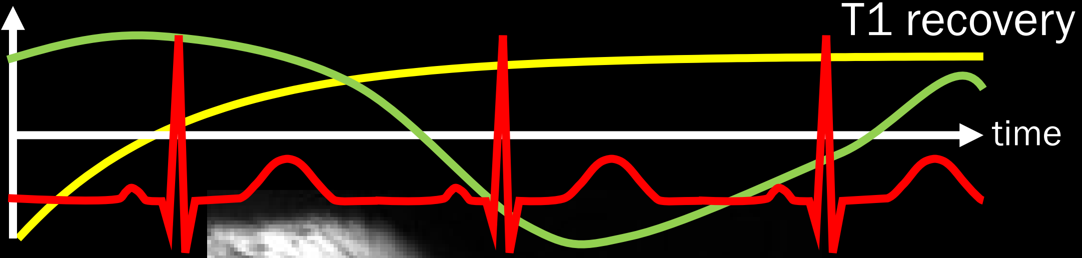
A combines:

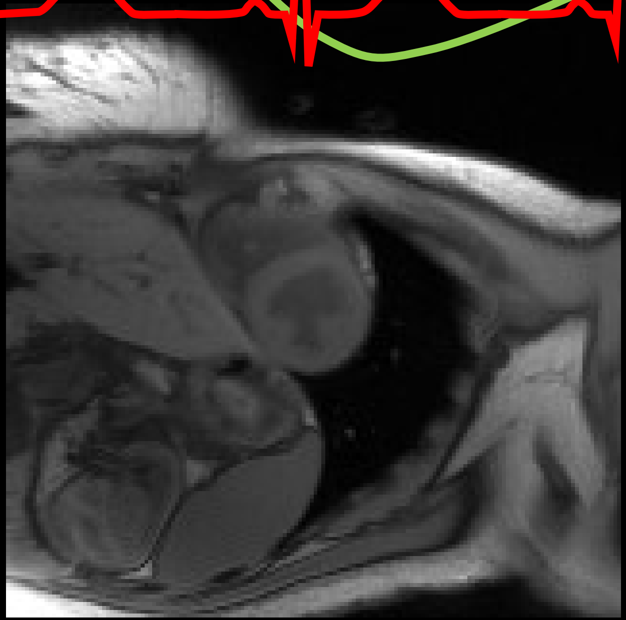
- proton density
- coil sensitivity
- $\sin(\alpha_{exc})$



Parameter mapping in moving organs







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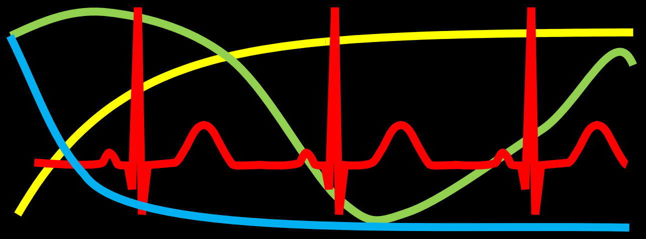
Parameter mapping in moving organs

Standard approach: “freeze” the motion

- Synchronize imaging with ECG
- Ask the patient to hold their breath
- Often: capture as few processes as possible



Incomplete list of options:

MOLLI[1] **shMOLLI**[2] **SASHA**[3] **SAPPHIRE**[4]

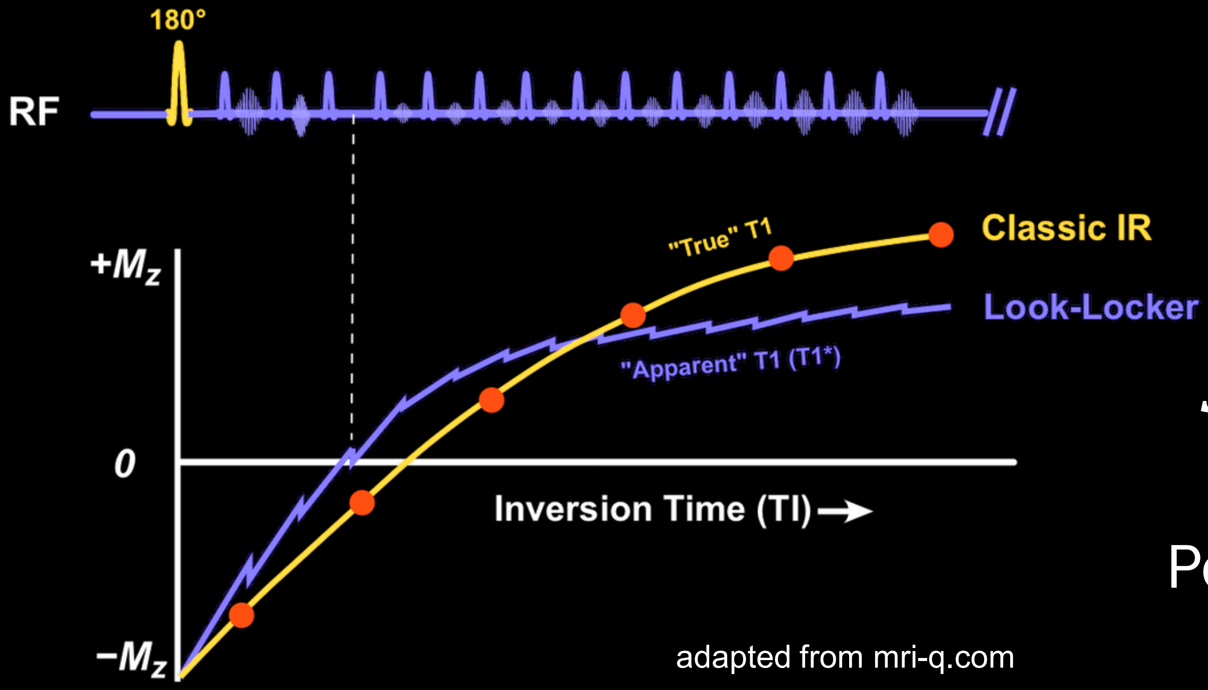
T_2prep-SSFP[5] **QALAS**[6] **IR-T_2prep**[7] **SR-T_2prep**[8]

Fingerprinting[9]

[1]Messroghli DL et al., *MRM* 2004 [2]Piechnik SK et al., *JCMR* 2010 [3]Chow K, et al., *MRM* 2014 [4]Weingärtner S et al., *SCMR* 2013
[5]Giri S et al., *JCMR* 2009 [6]Kvernby S et al., *JCMR* 2014 [7]Blume U et al., *JMRI* 2010 [8]Akçakaya M et al., *MRM* 2015
[9]Hamilton JI et al., *MRM* 2016

T_1 mapping: Look–Locker effect

What if we take a shortcut, collecting images throughout the same recovery period?



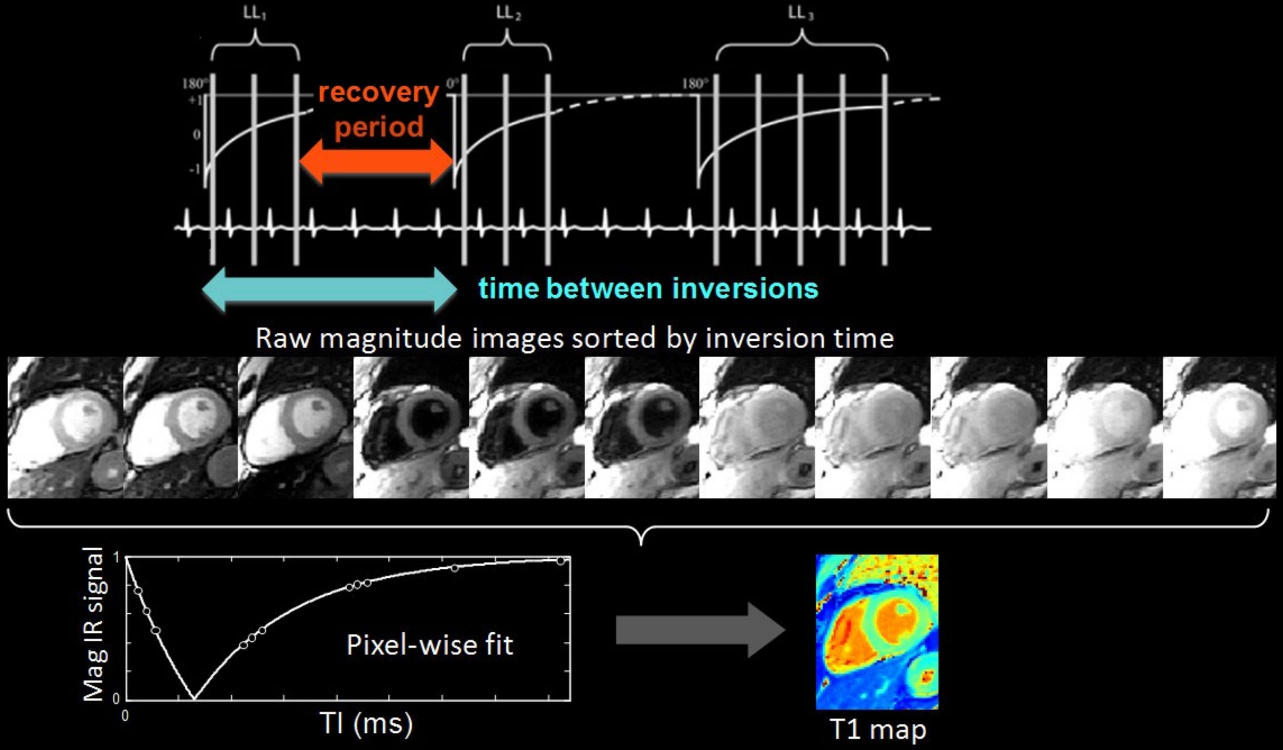
$$S = A\left(1 - B e^{-\tau/T_1^*}\right)$$

Post-fitting conversion:

$$T_1 \approx (B/A - 1)T_1^*$$

T1 mapping example: MOLLI

Breath-hold, ECG-triggered T1 maps in 11–17 heart beats



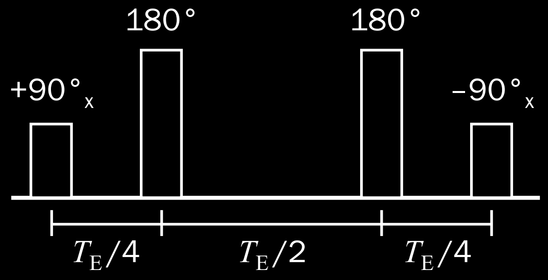
Messroghli DR et al. *Magn Reson Med* 2004
Kellman P, et al. *J Cardiovasc Magn Reson* 2014

UCLA David Geffen School of Medicine

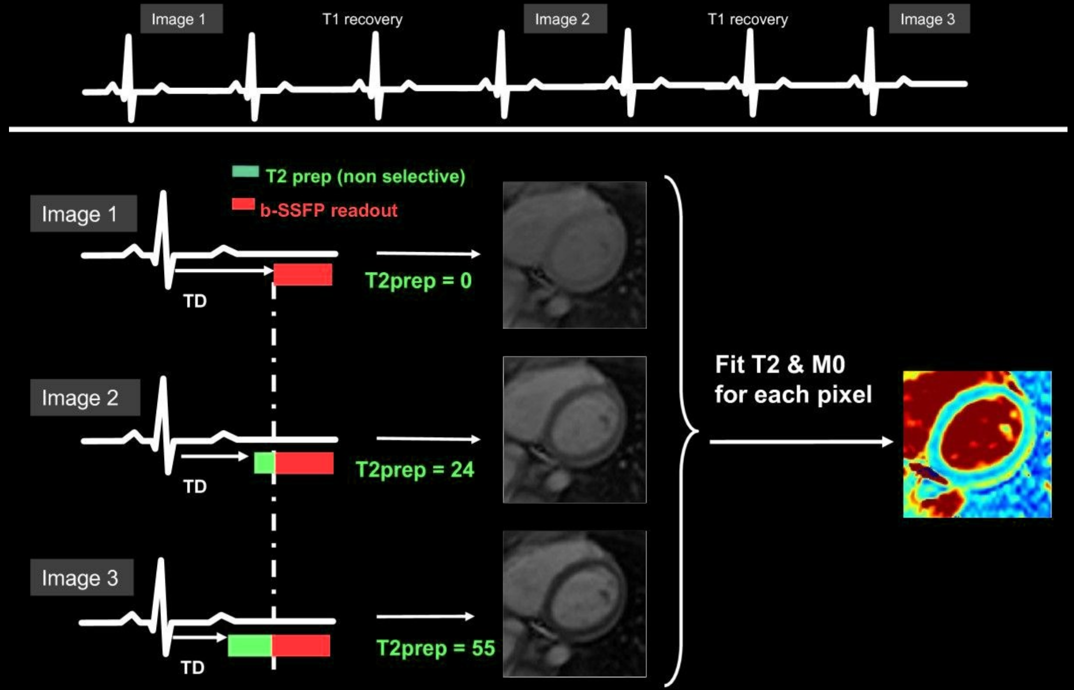
T2 mapping example: T2prep-SSFP

Breath-hold, ECG-triggered T2 maps in 7 heart beats

T2 prep :



Stores T2 weighting in longitudinal magnetization



Giri S et al., *J Cardiovasc Magn Reson* 2009

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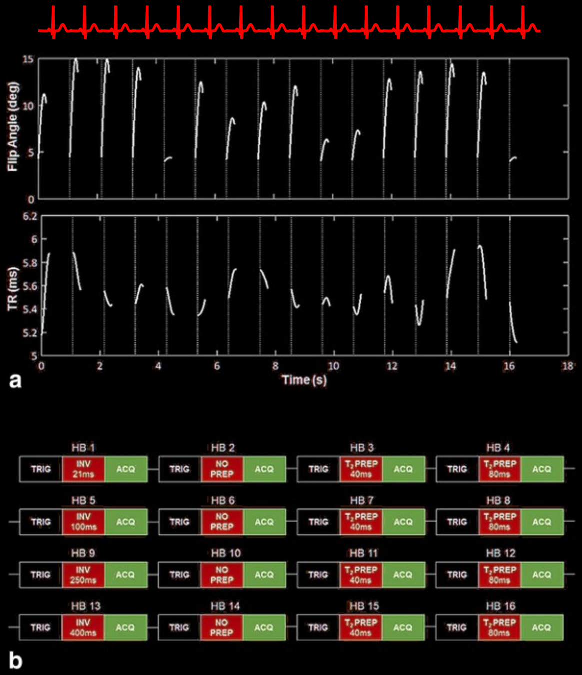
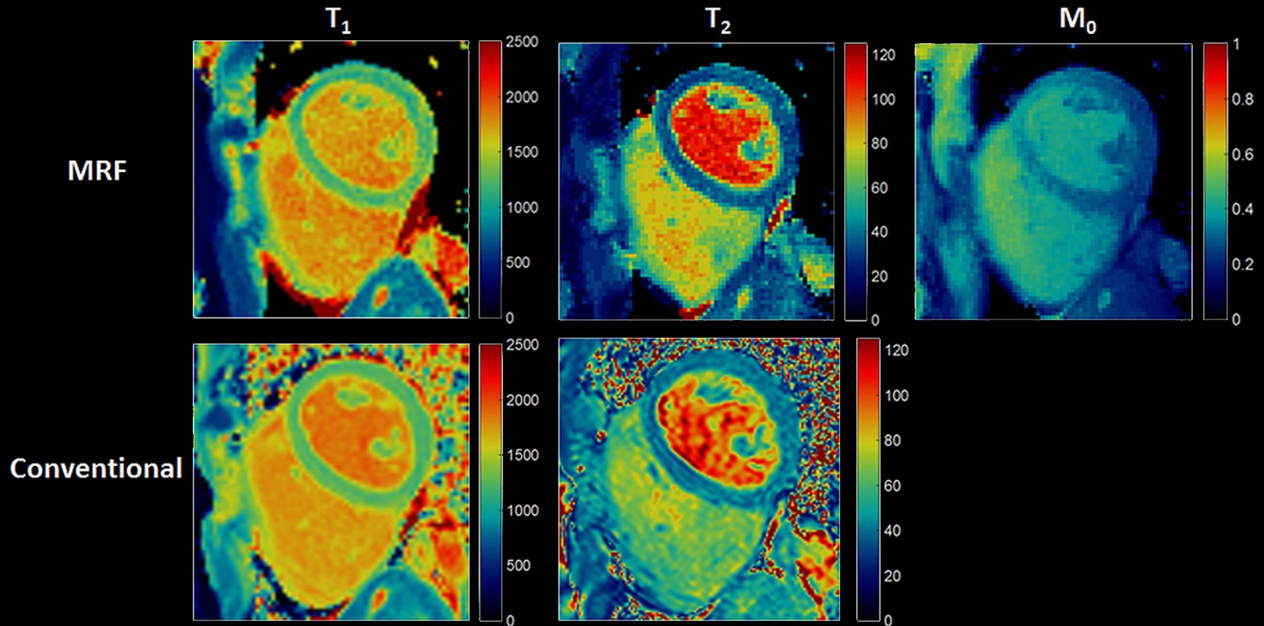
Multiparameter mapping example: Fingerprinting

Breath-hold, ECG-triggered T1-T2 maps in 16 heart beats



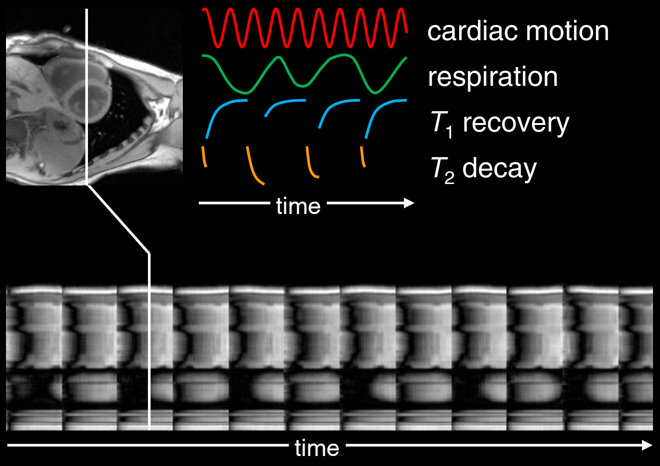


Hamilton JI et al., *Magn Reson Med* 2017

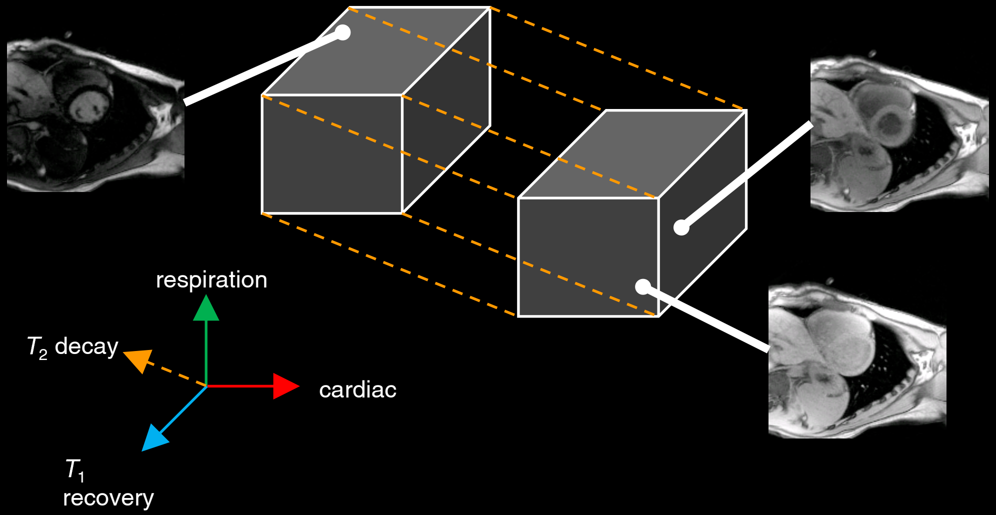
Multiparameter mapping example: Multitasking

Multidimensional framework for motion-resolved quantitative imaging

- e.g., free-breathing, non-ECG myocardial T_1-T_2 mapping



Multiple overlapping dynamics…



…reorganized as multiple time dimensions ("tasks")

Christodoulou AG et al., *Nature BME* 2018

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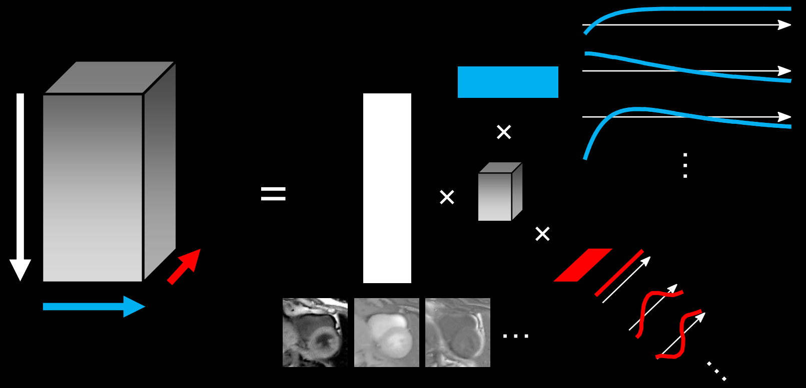
Multiparameter mapping example: Multitasking

6-D imaging example:

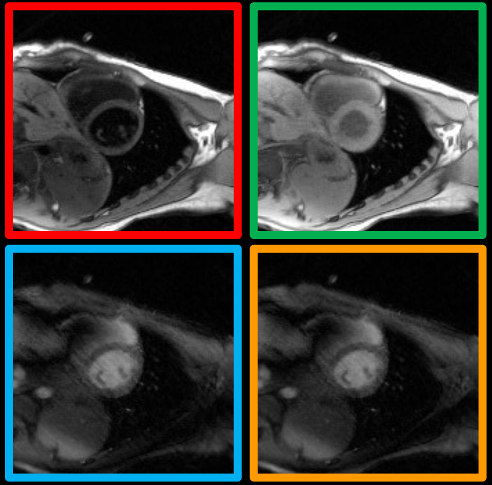
2 spatial dimensions + cardiac motion + respiration + T_1 recovery + T_2prep duration

Image tensor

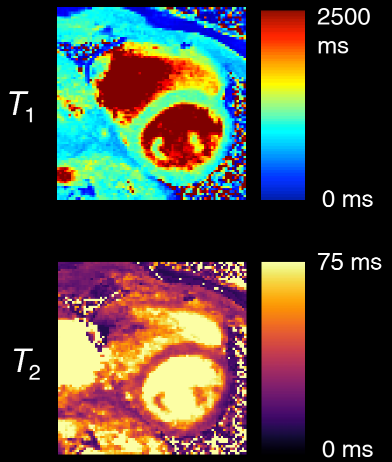
Factored basis function representation



Reconstructs a low-rank/factorizable image tensor (grows ~linearly, not exponentially)



Processes can be isolated after image reconstruction



Produces co-registered, synchronized cine maps

Christodoulou AG et al., *Nature BME* 2018