

Motion-resolved Quantitative MRI

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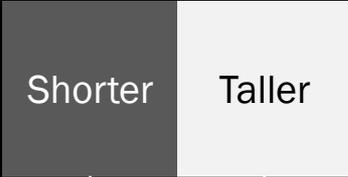
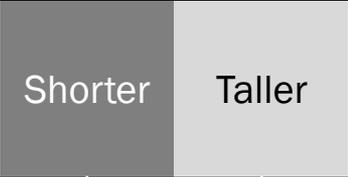
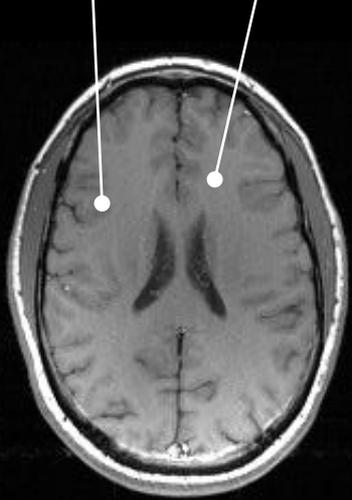
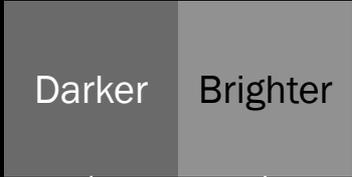
question: is jodie foster really short or is jennifer lawrence really tall?



8:31 PM - 4 Mar 2018

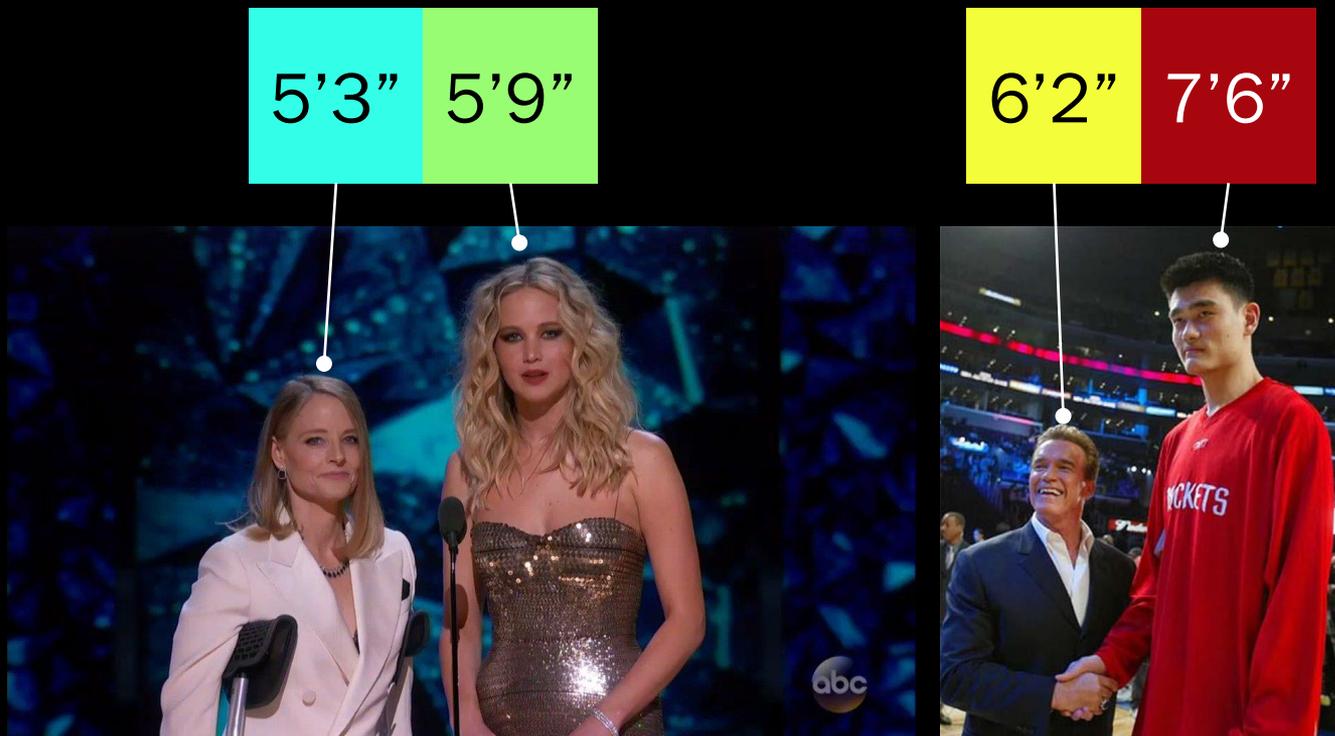
Qualitative imaging

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



Quantitative imaging

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



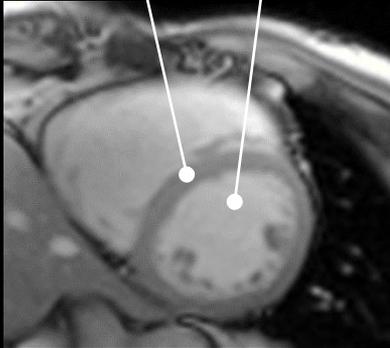
Quantitative imaging



Quantitative vs Qualitative imaging

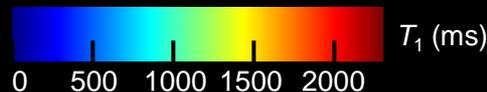
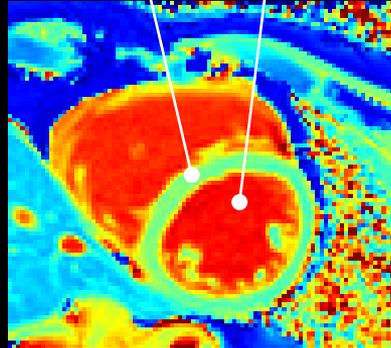
Qualitative

Unitless pixel values



Quantitative

Pixel values have units



More objective

- Measures absolute parameters associated with various (patho)-physiological tissue properties and disease states

More reproducible¹

- Direct comparison across subjects, sites, and times

More sensitive^{2,3}

- Detect mild or diffuse alteration of tissue properties

What can MRI quantify?

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

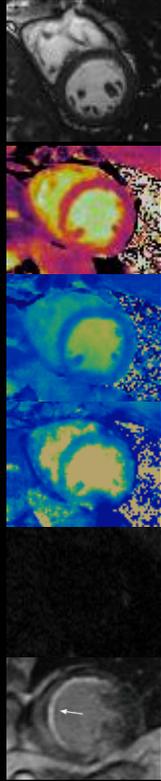
- Relaxation (T1, T2, T2*)
- Diffusion (ADC, helix angle, diffusion angle)
- Mechanical properties (stress, strain, stiffness)
- Flow (tissue perfusion or flow in larger vessels)
- Kinetics (K^{trans} /permeability)
- Tissue composition (water-fat, ECV, plasma volume)

Multi-parametric imaging:

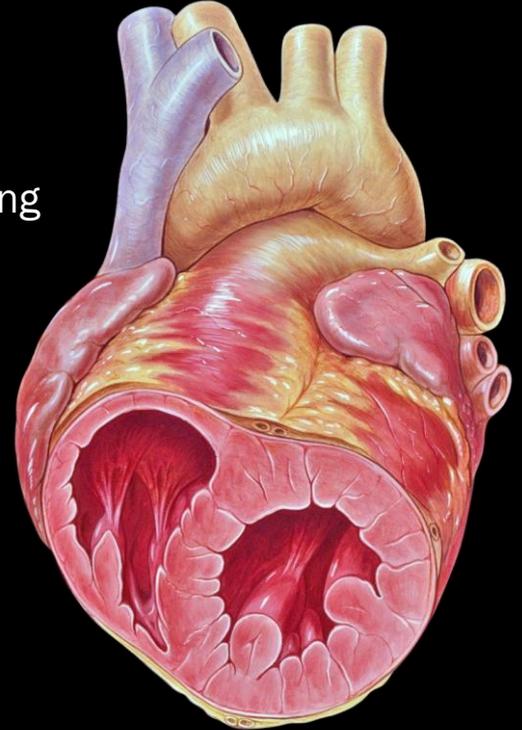
- Combines parameters for comprehensive assessment of tissue state and accurate diagnosis
 - e.g. chronic liver disease¹, prostate cancer², cardiovascular disease

	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	+	+	+		+	
	Cancer						
	Breast	+	+		+		
	Prostate	+	+		+	+	
	Liver	+	+	+	+	+	
	Liver fibrosis	+	+		+	+	
	Hepatic Carcinoma	+	+	+	+	+	
Hepatic/pancreatic steatosis						+	

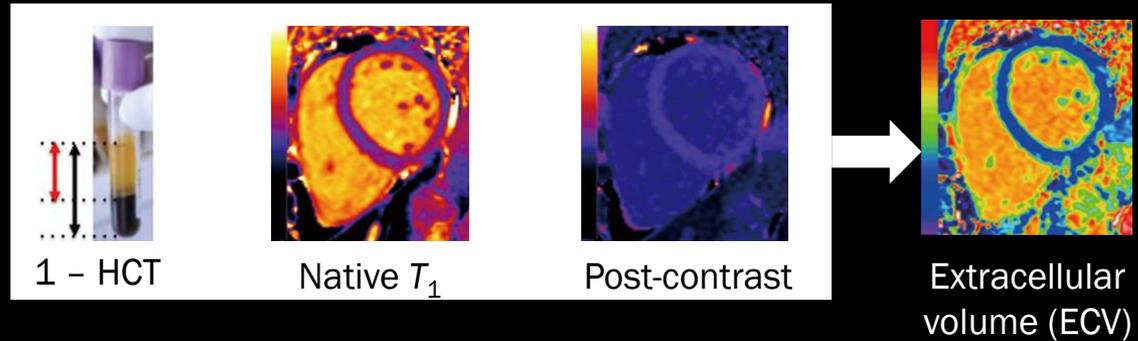
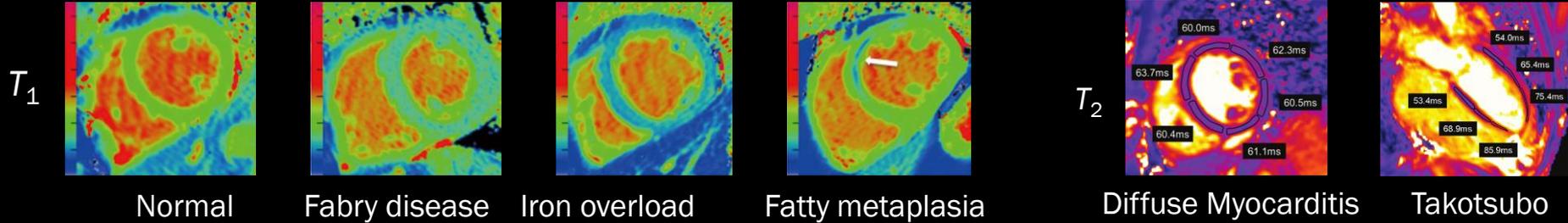
What can MRI tell us about the heart?



- Structure and function (cine)
- T1 mapping and extracellular volume fraction (ECV) mapping
- T2 mapping
- T2* mapping
- Perfusion
- Late gadolinium enhancement (LGE)

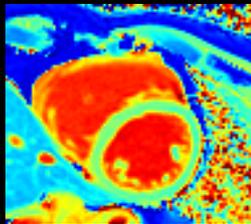
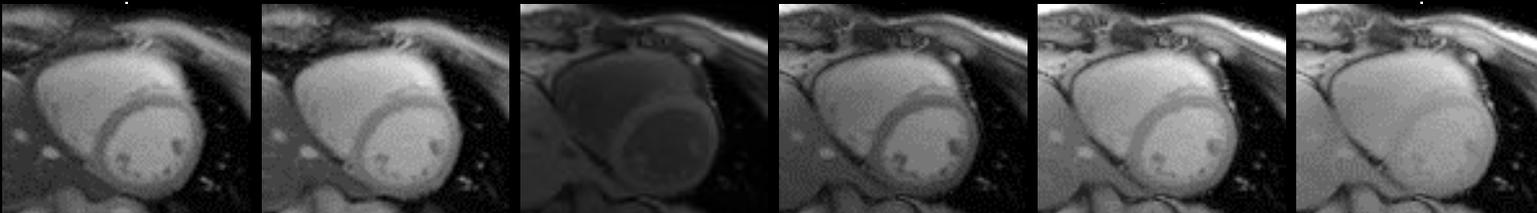
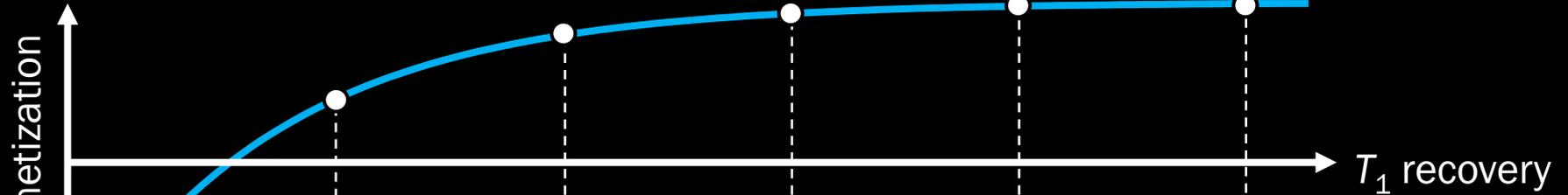


Quantitative cardiovascular MR (CMR)



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

Quantitative MRI = dynamic MRI

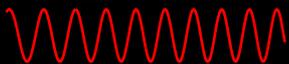
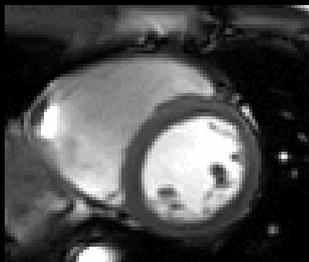


T_1 map

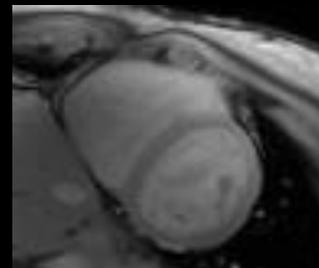
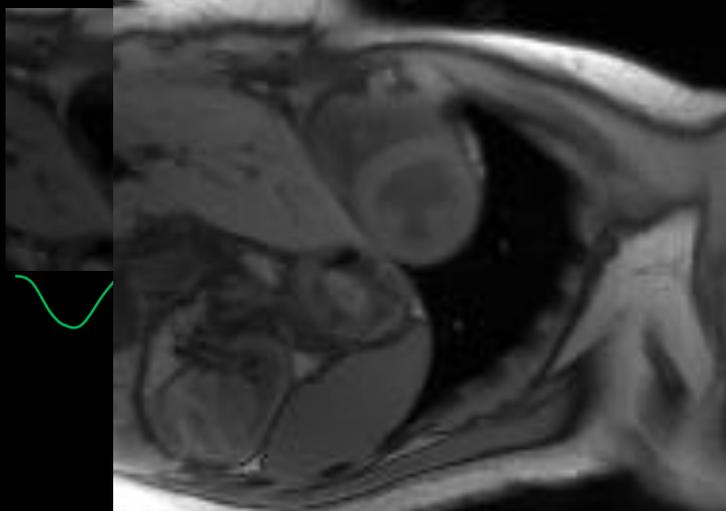
The challenge in the heart

Several dynamic processes overlap, e.g.:

Cardiac motion



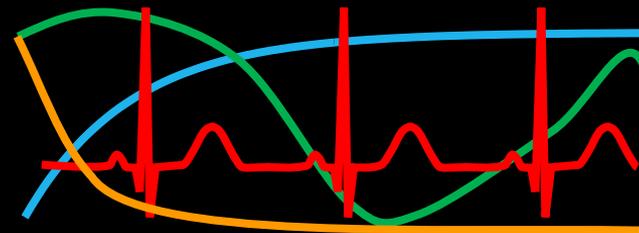
Respiration



Solutions

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:

MOLLI¹

T₂prep-SSFP⁵

Fingerprinting⁹

shMOLLI²

QALAS⁶

SASHA³

IR-T₂prep⁷

SAPPHIRE⁴

SR-T₂prep⁸

¹Messroghli DL et al., *MRM* 2004

²Piechnik SK et al., *JCMR* 2010

³Chow K, et al., *MRM* 2014

⁴Weingärtner S et al., *SCMR* 2013

⁵Giri S et al., *JCMR* 2009

⁶Kvernby S et al., *JCMR* 2014

⁷Blume U et al., *JMRI* 2010

⁸Akçakaya M et al., *MRM* 2015

⁹Hamilton JI et al., *MRM* 2016

Standard motion approach

Typically limits imaging to one dynamic at a time

	Cine	T_1 mapping	T_2 mapping
Cardiac motion	○	×	×
T_1 relaxation	×	○	×
T_2 relaxation	×	×	○
Respiration	×	×	×

Example current workflow: Serial

Long exams made from a disjointed sequence of scans, e.g.:



Each scan requires special setup by the technologist

Each scan uses ECG triggering or gating

Each scan uses a different breath hold (often one breath-hold per slice)

- Scans from different breath holds are not co-registered

Extended scan times and complex workflow limit the availability of cardiac MRI

Ideal workflow: All-in-one, free-running

Brief 20–30 min exam in one push-button scan:



No setup by the technologist

No ECG triggering or gating

No breath holds

- All maps and images are co-registered

All with 3D spatial coverage

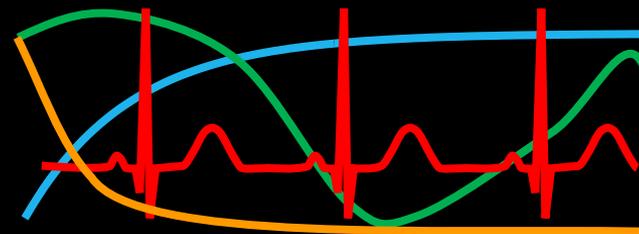
- **How can we get there?**
- **Where are we now?**

Simple workflow and short scan time could make cardiac MRI far more accessible

Solutions

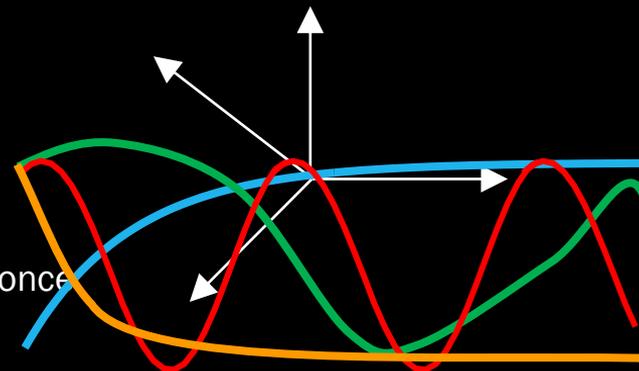
Standard approach: “freeze” the motion

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



Alternative paradigm: embrace the motion

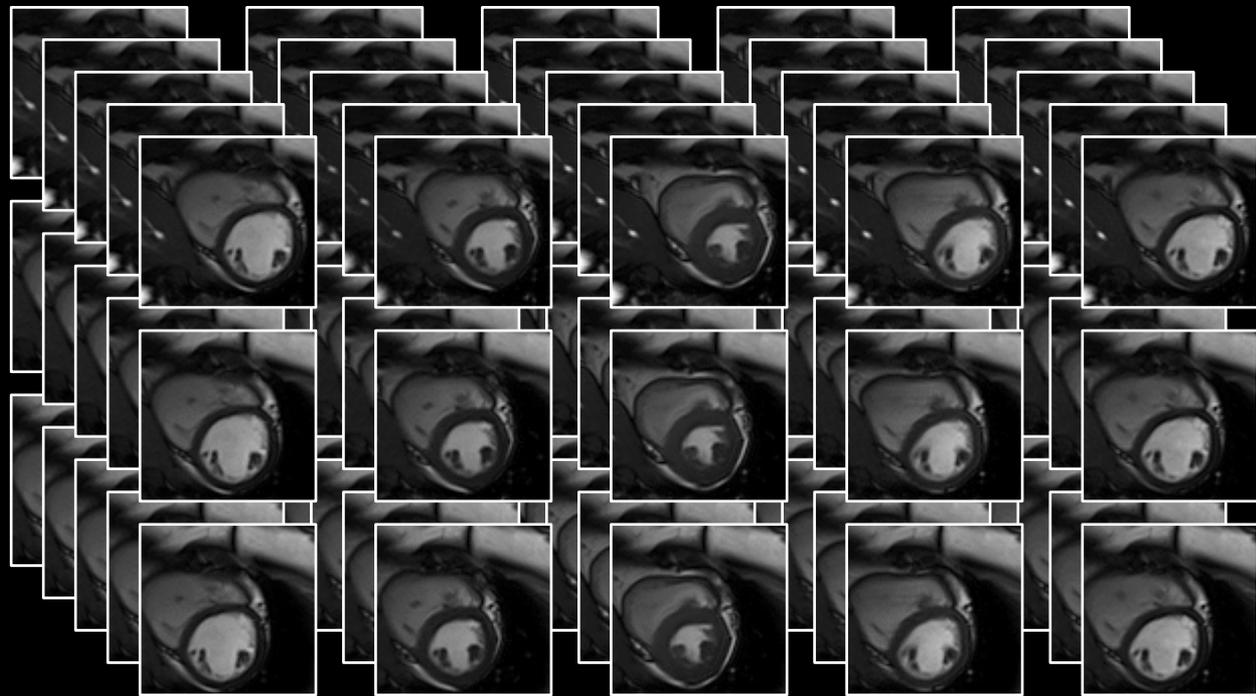
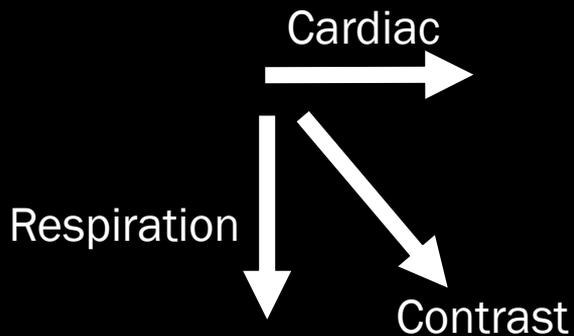
- Assign each dynamic its own time dimension
- No need for ECG
- Patient can breathe freely
- Resolve multiple overlapping processes, performing multiple tasks at once



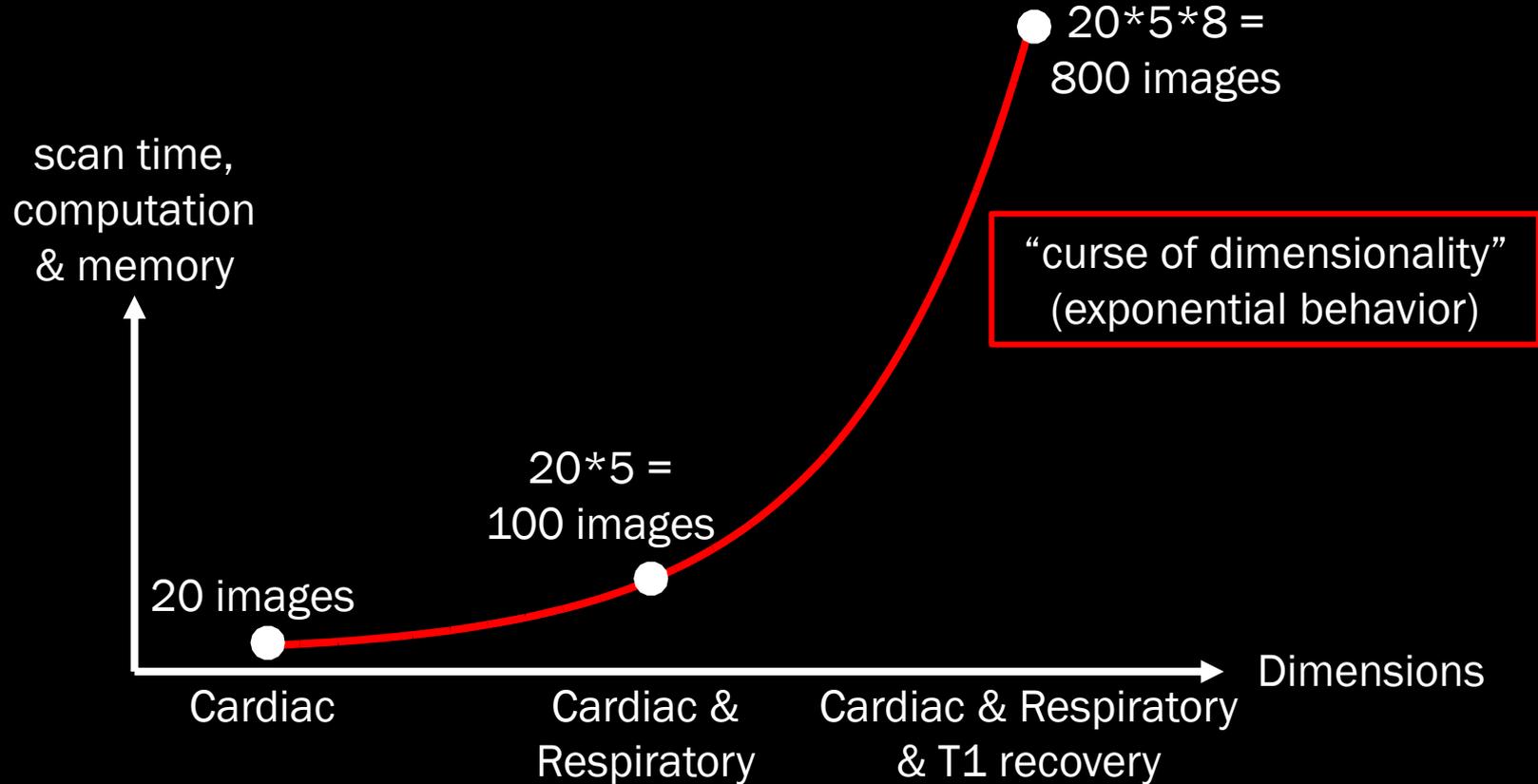
Alternative paradigm: Multidimensional imaging

Scan continuously, *capturing* (rather than freezing) overlapping dynamics

Organize data/images into array with multiple time dimensions



Multidimensional imaging: Challenge



Multidimensional imaging: Opportunity

Despite the “curse of dimensionality”, there is also an opportunity!

The “blessing of dimensionality”:

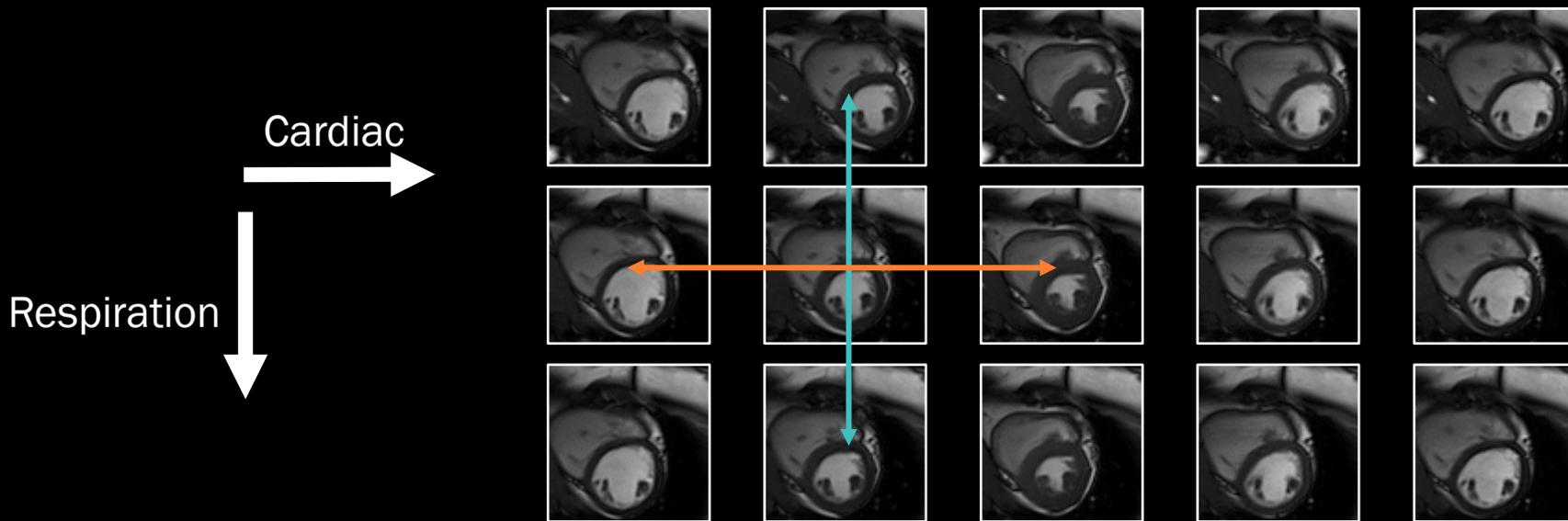
- High-dimensional spaces → sparse representations
- Organized structure → sparse representation along each individual dimension

Multidimensional image reconstruction approaches offer a way around the “curse”

- XD-GRASP: Compressed sensing Feng L et al., *Magn Reson Med* 2016
- XD flow: Compressed sensing Cheng JY et al., *Sci Rep* 2017
- Multitasking: Low-rank tensors Christodoulou AG et al., *Nature Biomed Eng* 2018
- HD-PROST: Low-rank tensors Bustin A et al., *Magn Reson Med* 2019
- LRTA: Low-rank tensors Yaman B et al., *IEEE Trans Comput Imaging* 2020

XD-GRASP: Multidimensional Compressed Sensing

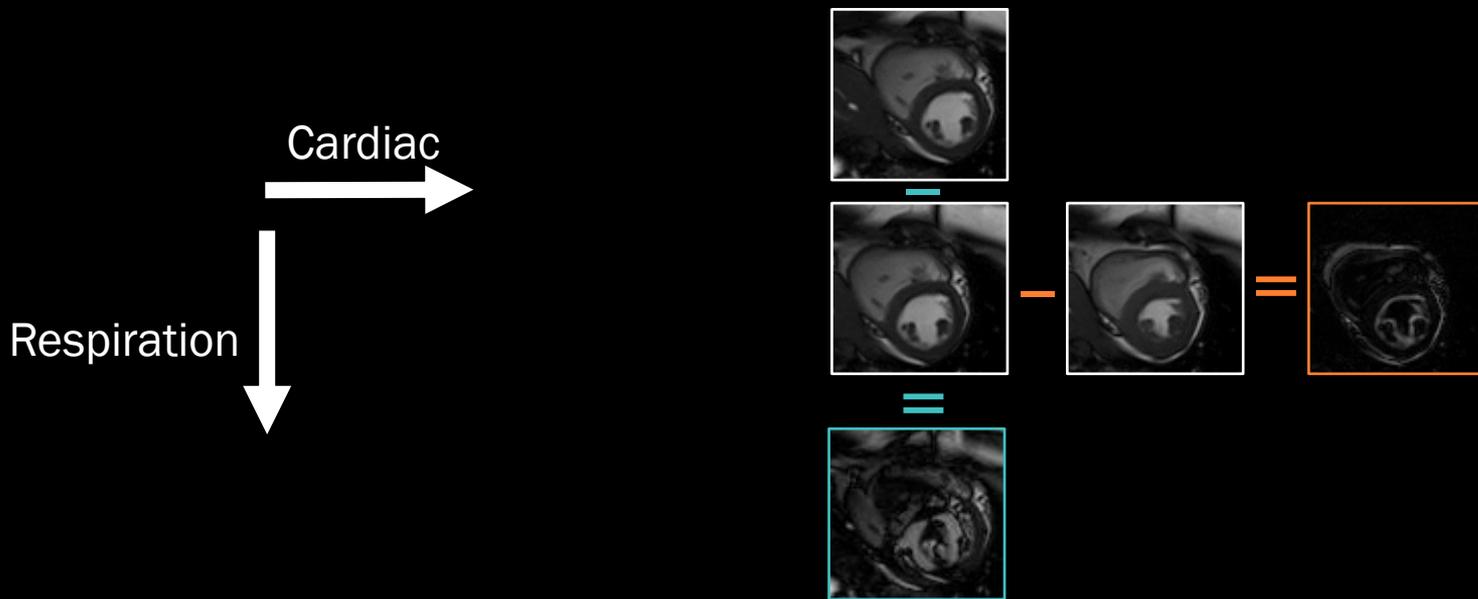
Treats cardiac motion/respiration as separate time dimensions,
then applies multidimensional compressed sensing.



Neighboring images in both directions
are very similar

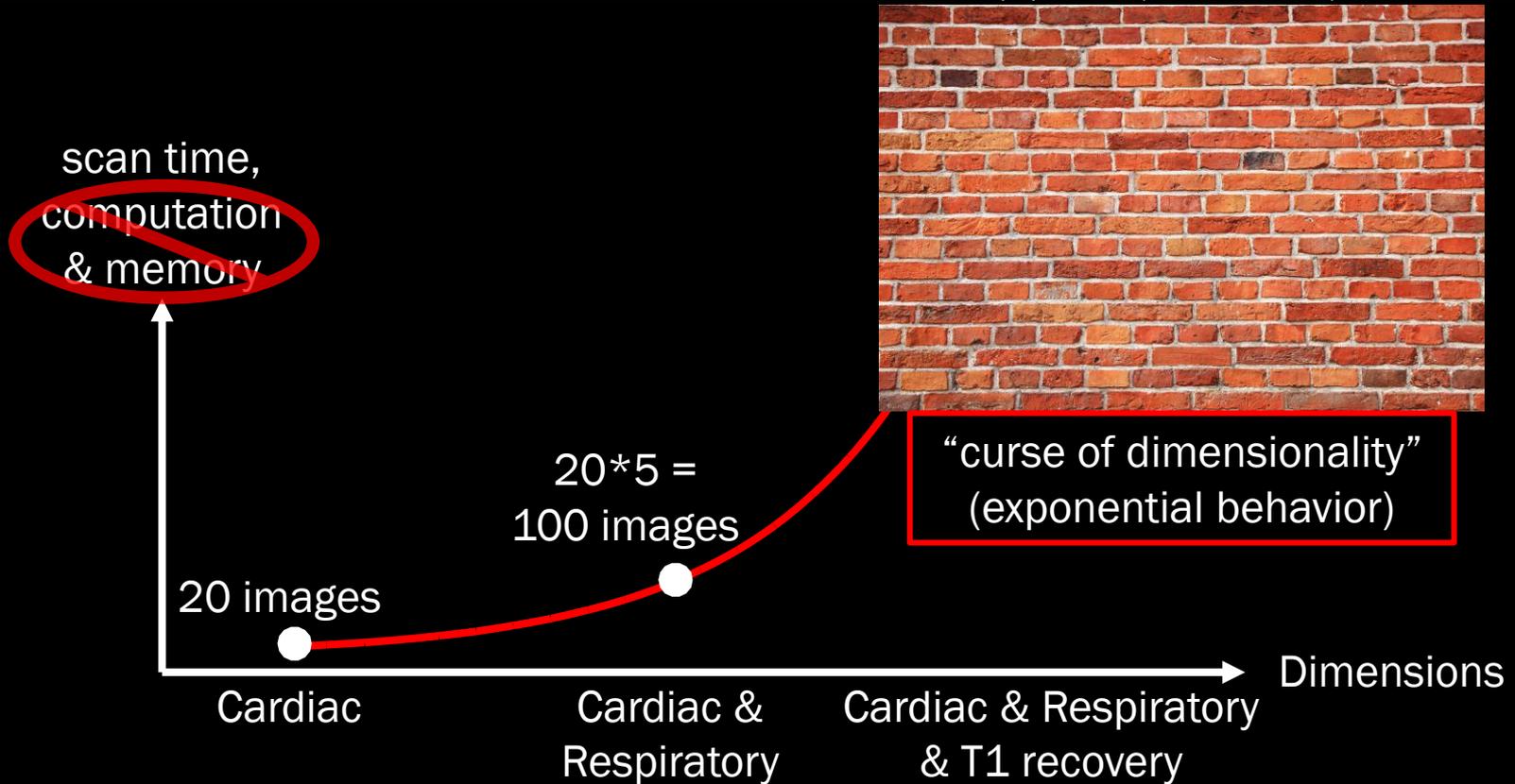
XD-GRASP: Multidimensional Compressed Sensing

Treats cardiac motion/respiration as separate time dimensions,
then applies multidimensional compressed sensing.



Neighboring images in both directions
have sparse differences

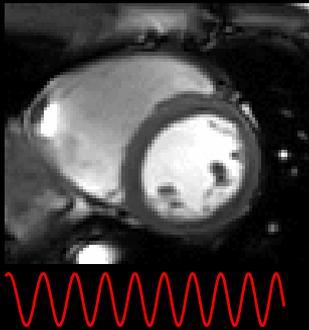
Multidimensional imaging: Challenge



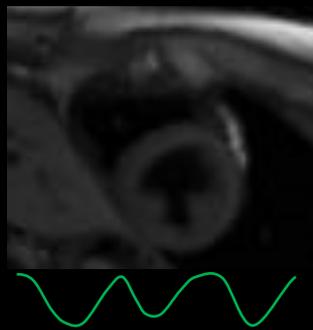
Multidimensional motion-resolved quantitative imaging: Challenge #1

Physiological motion dimensions AND physical process dimensions

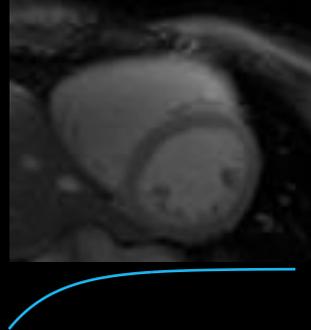
Cardiac motion



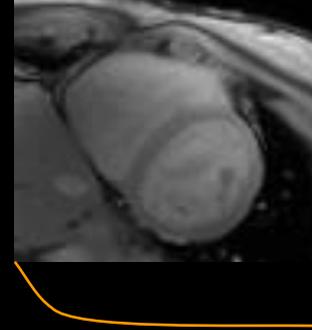
Respiratory motion



T_1 relaxation

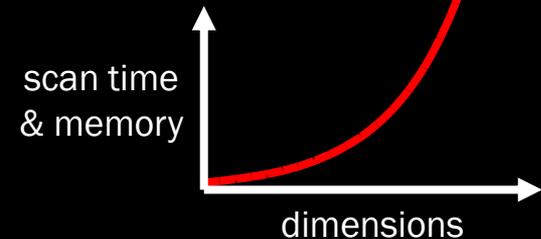


T_2 relaxation



Curse of dimensionality is especially relevant

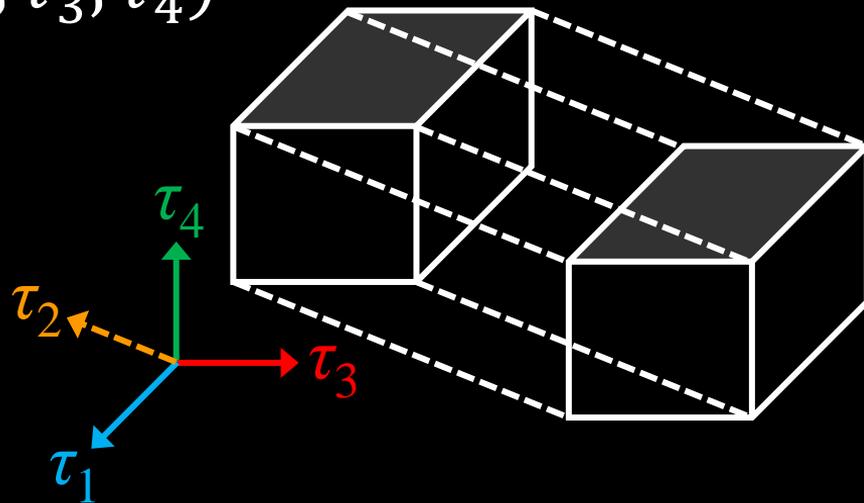
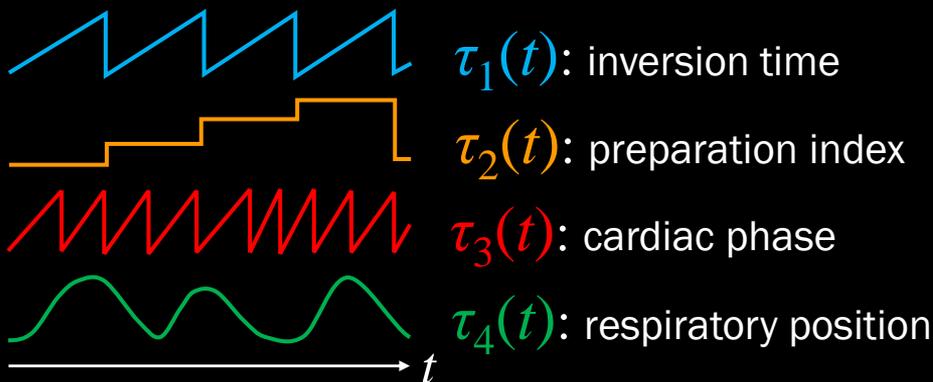
- Scan time and memory increase exponentially with # of dimensions



Multidimensional motion-resolved quantitative imaging: Challenge #2

Physiological motion dimensions are controlled by patient physiology

$$t \leftrightarrow (\tau_1, \tau_2, \tau_3, \tau_4)$$



Need to be robust to unpredictable $(\mathbf{k}, \tau_1, \tau_2, \tau_3, \tau_4)$ -space sampling

Magnetic resonance multitasking

Multidimensional imaging framework for quantitative imaging

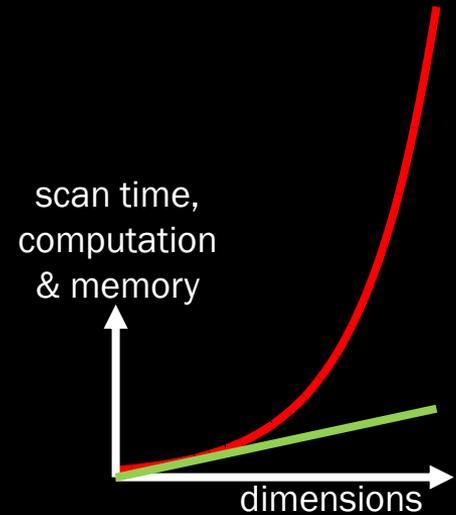
- Particularly focused on motion-resolved quantitative imaging

Challenge #1: Curse of dimensionality

- Solution: Low-rank tensor¹ (LRT) imaging to reduce scan time and memory
 - Directly addresses the curse of dimensionality
 - Scales well (\sim linearly), even ≥ 5 dimensions

Challenge #2: Unpredictable motion dimensions

- Solution: Hybrid implicit-explicit LRT reconstruction^{2,3} with flexible sampling requirements



Low-rank image model

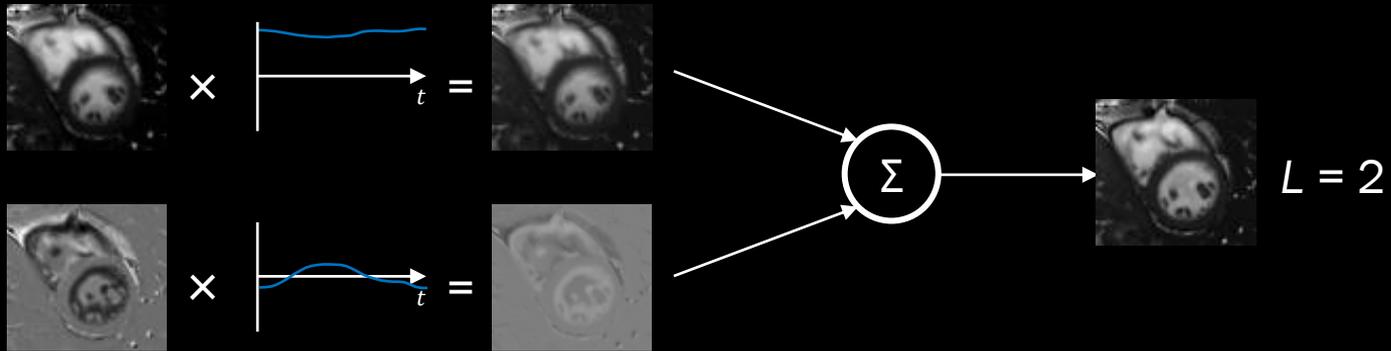
For one time dimension

Example: cardiac motion (cine imaging)

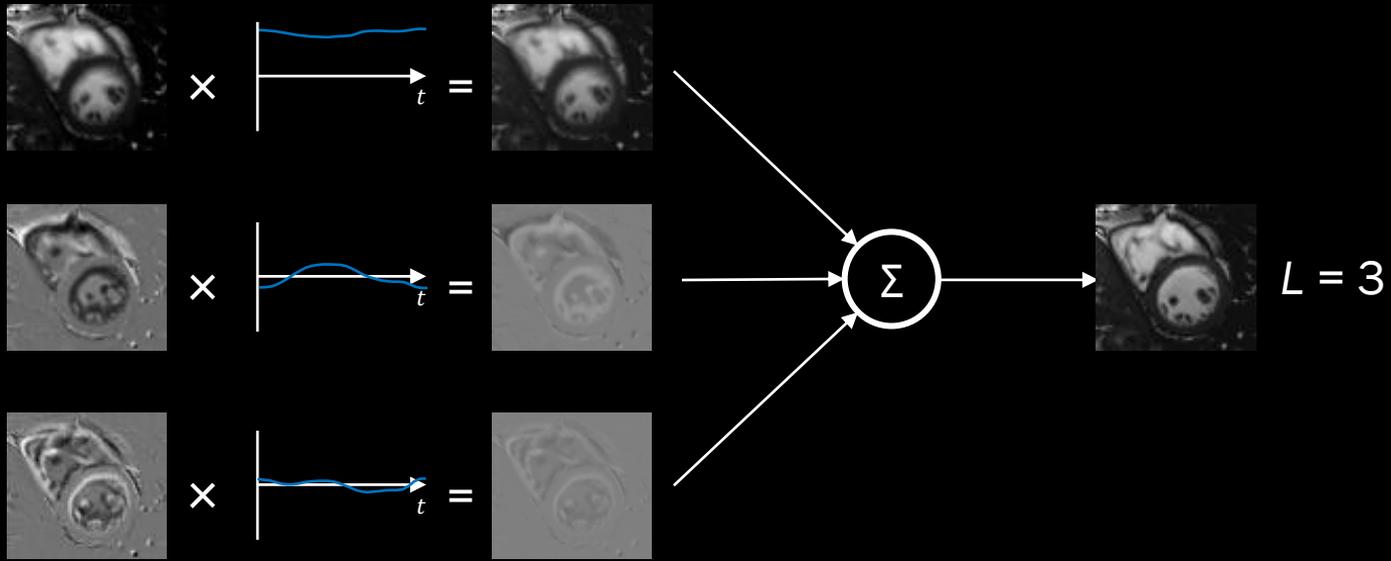


- 30 images (cardiac phases) in this sequence
- Images are so correlated as to be linearly dependent
 - Any image is a combination of L underlying basis images, $L < 30$
 - Any voxel time function is a combination of L temporal basis functions
- Image sequence is “low-rank” because rank $L < 30$

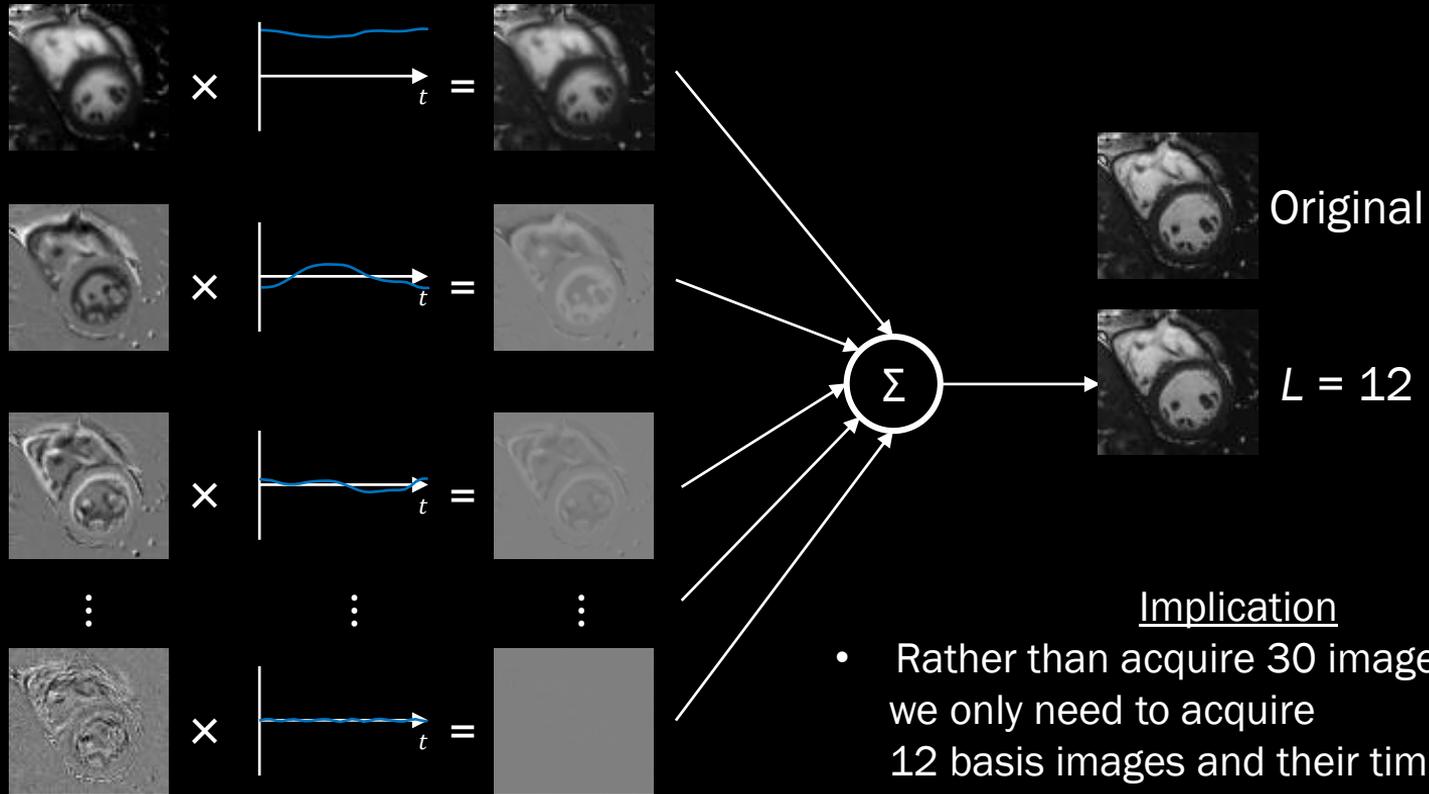
Low-rank image model



Low-rank image model



Low-rank image model



Low-rank image model

For one time dimension

Example: cardiac motion (cine imaging)



- Low-rank property established for many types of dynamics:
 - Dynamic contrast enhancement¹
 - Cardiac motion (cine)²
 - Free-breathing cine²
 - NMR relaxation³ (T1, T2)

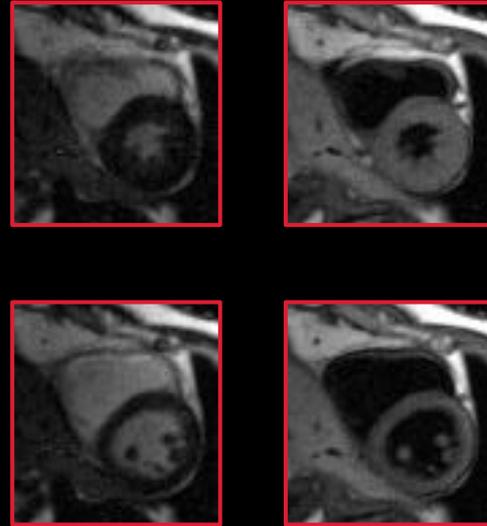
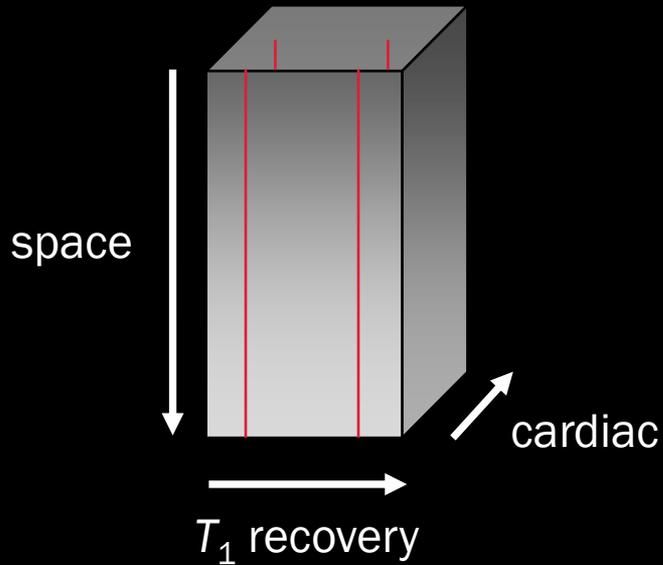
¹Liang Z-P, *IEEE-ISBI* 2007

²Pedersen H et al., *MRM* 2009

³Petzchner FH et al., *MRM* 2011

Multitasking: Low-rank tensor imaging

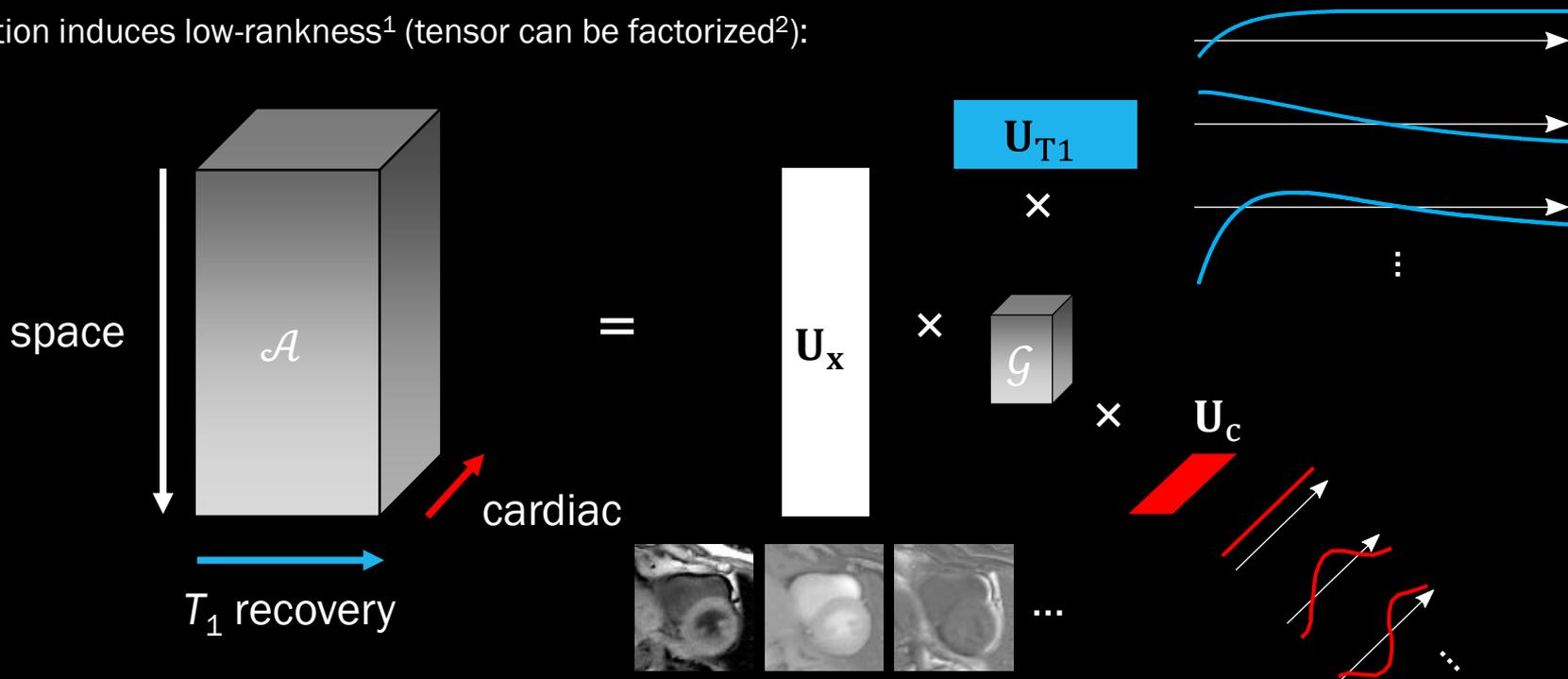
Represent images as tensor/array



Low-rank tensor model

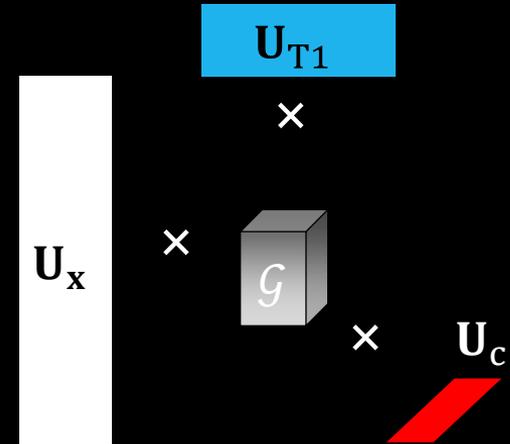
Represent images as tensor/array

Correlation induces low-rankness¹ (tensor can be factorized²):

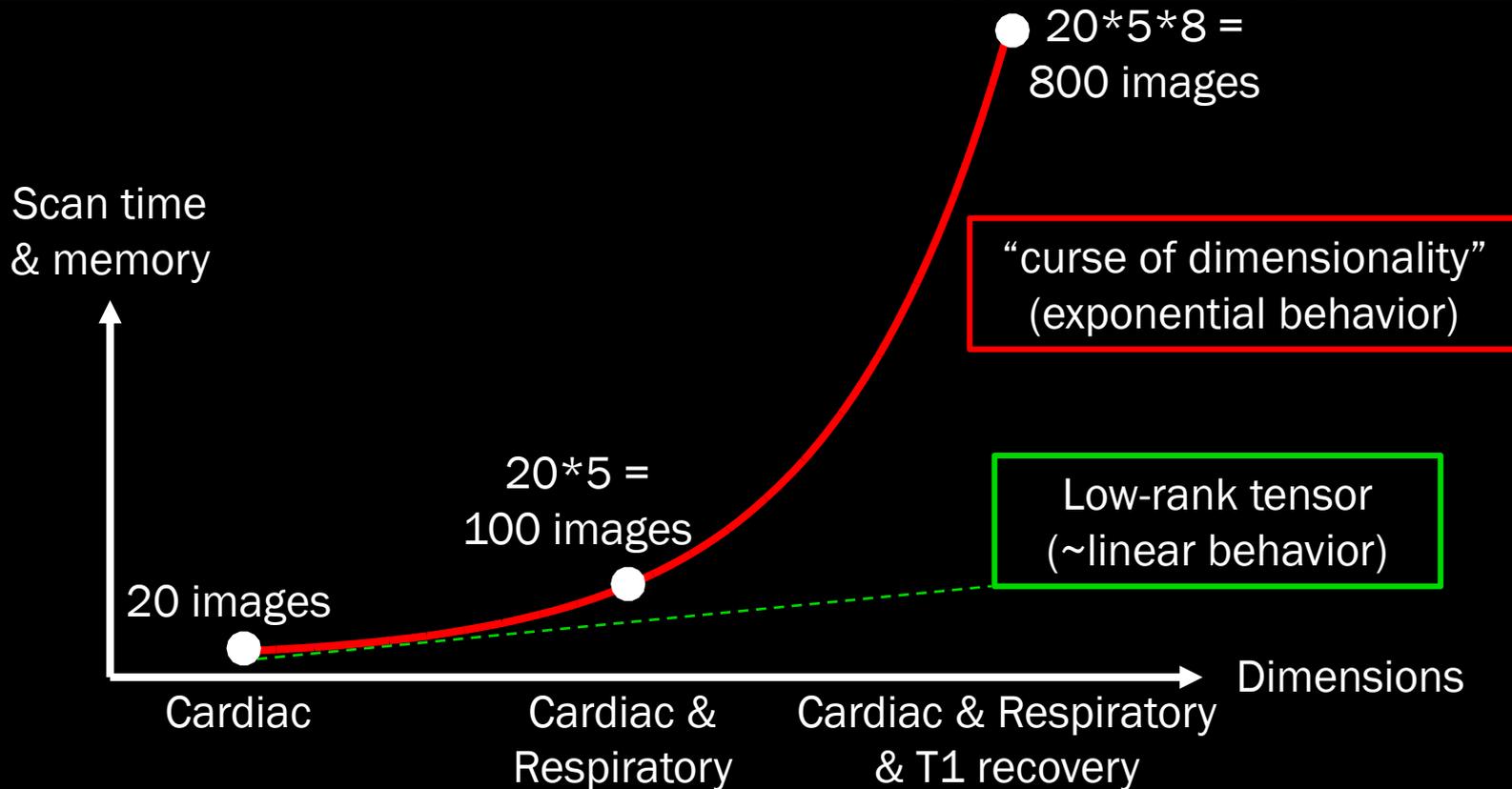


Low-rank tensor model: Implications

1. Factors are smaller than whole tensor
 - Short scan time, low memory
2. Exploits global correlation
 - Goes beyond image neighborhoods
3. Separates space from time
 - Will inform sampling/reconstruction
4. Each dimension has one factor matrix
 - # of dimensions = # of factor matrices



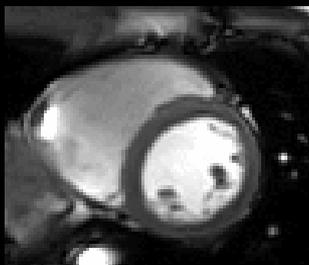
Multidimensional imaging: Challenge



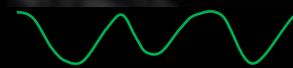
Multidimensional motion-resolved quantitative imaging: Challenge #1

Physiological motion dimensions AND physical process dimensions

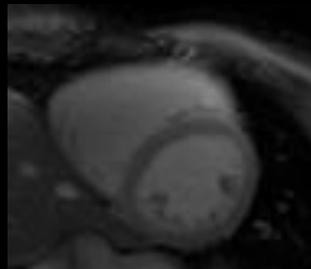
Cardiac motion



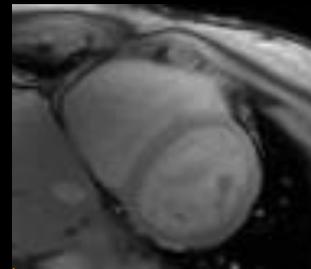
Respiratory motion



T_1 relaxation

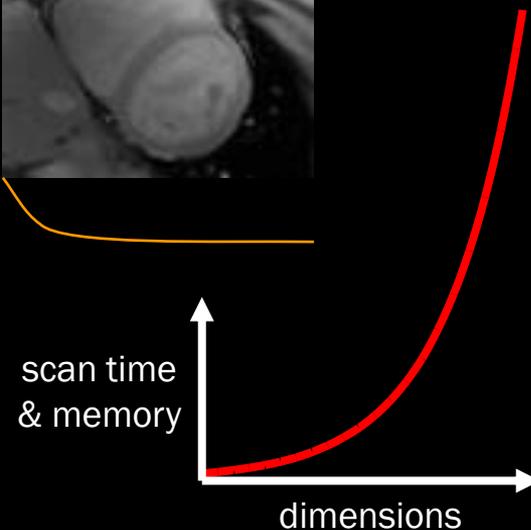


T_2 relaxation



Curse of dimensionality is especially relevant

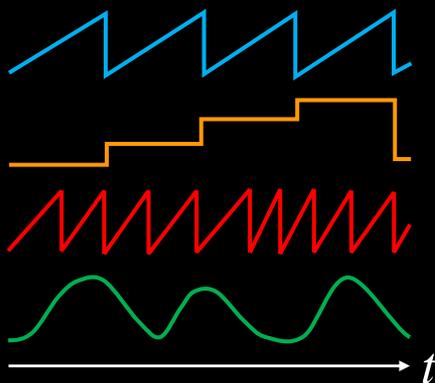
- Scan time and memory increase exponentially with # of dimensions



Multidimensional motion-resolved quantitative imaging: Challenge #2

Physiological motion dimensions are controlled by patient physiology

$$t \leftrightarrow (\tau_1, \tau_2, \tau_3, \tau_4)$$

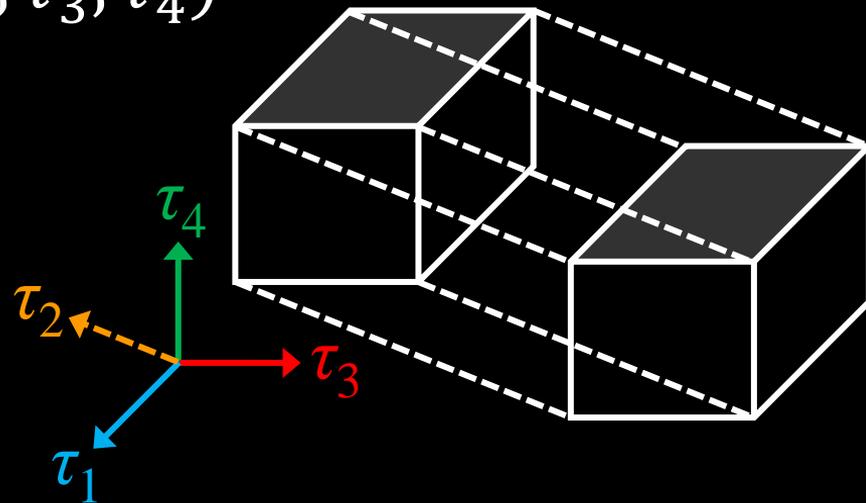


$\tau_1(t)$: inversion time

$\tau_2(t)$: preparation index

$\tau_3(t)$: cardiac phase

$\tau_4(t)$: respiratory position



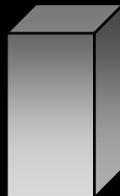
Need to be robust to unpredictable $(\mathbf{k}, \tau_1, \tau_2, \tau_3, \tau_4)$ -space sampling

LRT imaging strategies

Implicit strategy^{1,2}

$$\arg \min_{\mathcal{A}} \|\mathbf{d} - E(\mathcal{A})\|_2^2 + \lambda \sum_i \|\mathbf{A}^{(i)}\|_*$$

- Leaves tensor unfactored
- Tensor size still grows exponentially
 - E.g., 2 spatial + 4 time:
 - **210 GB per tensor**
- Flexible sampling patterns



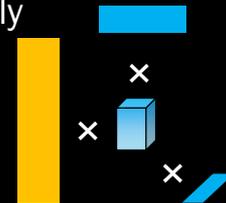
¹Trzasko JD et al., *ISMRM* 2013

²Yu Y et al., *PLoS One* 2014

Explicit strategy^{3,4}

1. Extract \mathcal{G} & temporal \mathbf{U} 's from SVDs of training data
2. $\arg \min_{\mathbf{U}_x} \|\mathbf{d} - E(\mathcal{G} \times_1 \mathbf{U}_x \times_2 \mathbf{U}_c \times_3 \cdots \times_5 \mathbf{U}_{T1})\|_2^2$

- Directly recovers tensor factors
- Storage of tensor factors grows ~linearly
 - E.g., 2 spatial + 4 time:
 - **67 MB per tensor**
- Uses specific training data sampling pattern



¹Christodoulou AG and Liang Z-P, *ISMRM* 2015

²He J et al., *IEEE-TMI* 2016

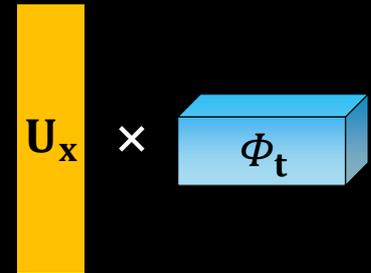
Multitasking strategy

Hybrid strategy

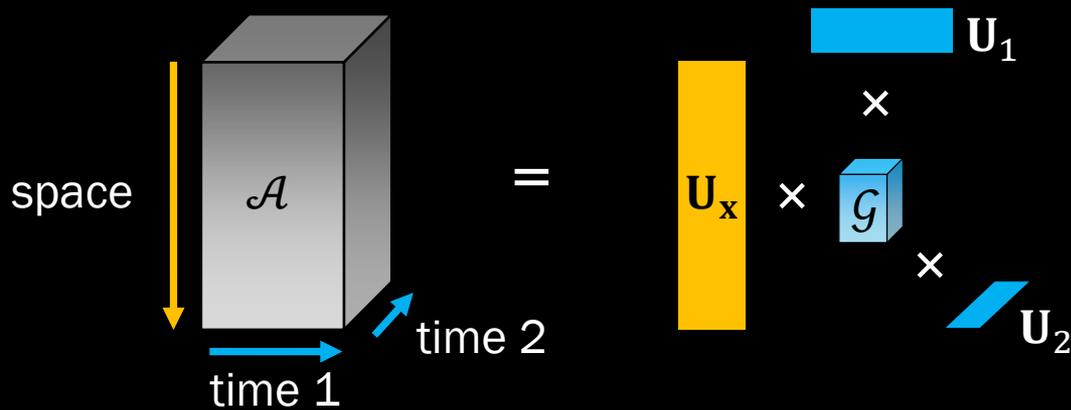
1. Implicit LRT recovery of missing training data
2. Extract Φ_t from HOSVD of completed training data

$$3. \arg \min_{\mathbf{U}_x} \|\mathbf{d} - E(\Phi_t \times_1 \mathbf{U}_x)\|_2^2$$

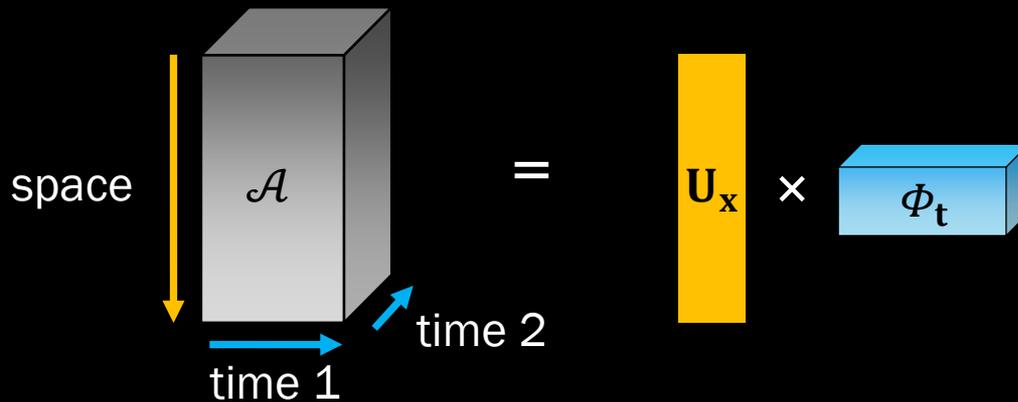
- Implicit recovery step only done for training subset of k-space
 - still only MBs/coil
- Training data used, but no specific pattern required
- Retains computational benefits of explicit strategy



Space is separated from time(s)



Space is separated from time(s)



Collect two interleaved sets of data:

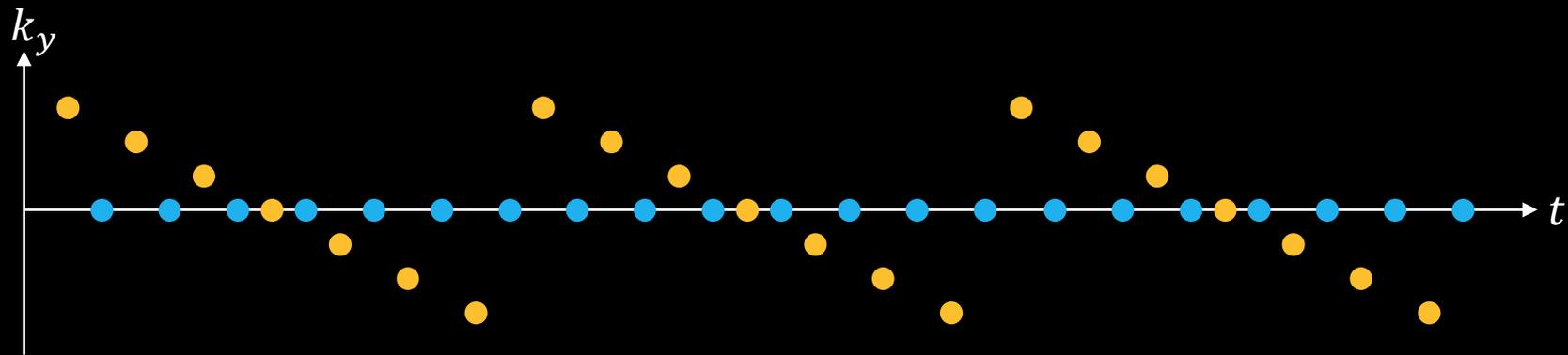
Imaging data

- Targets spatial factor U_x
- High spatial resolution
- Extensive k-space coverage

Training data

- Targets temporal factor Φ_t
- High speed
- One (or a few) k-space trajectories repeated

Space is separated from time(s)



Collect two interleaved sets of data:

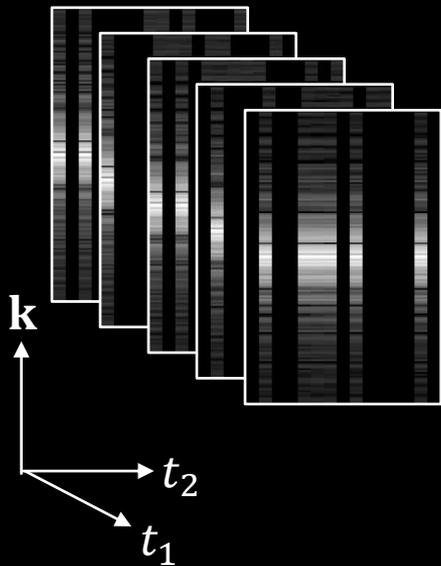
Imaging data

- Targets spatial factor U_x
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- High speed
- One (or a few) k-space trajectories repeated

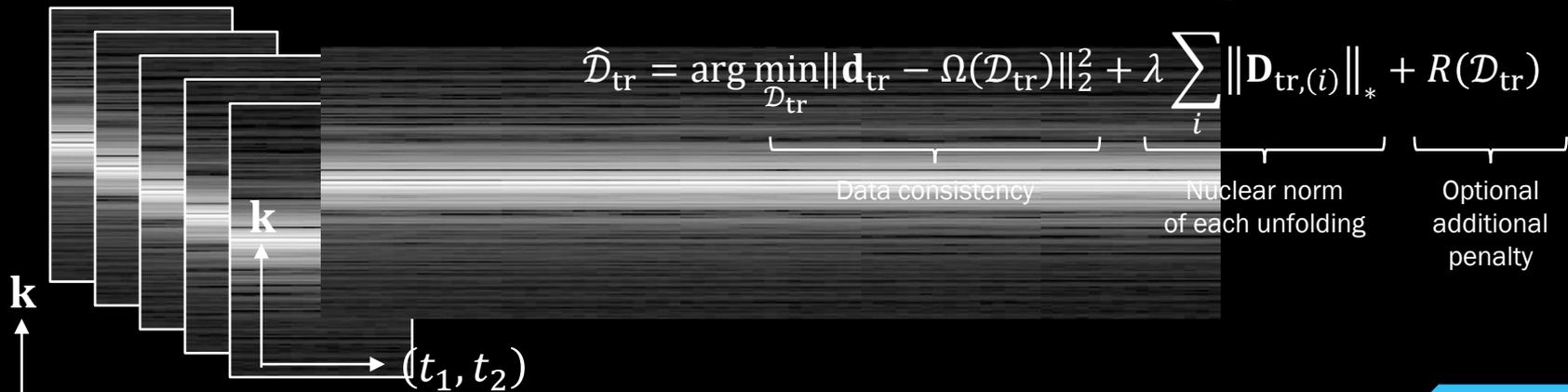
Image reconstruction



- For training data \mathcal{D}_{tr} , one (or a few) k-space trajectories are sampled very frequently
- This will cover many—but not necessarily all—time point combinations
- ”Missing” training data is recovered by unfactored low-rank tensor completion
 - Only one k-space trajectory \rightarrow still only MBs/coil

Image reconstruction

1. Complete low-rank training data tensor \mathcal{D}_{tr}



2. Extract Φ_t from SVD of unfolded $\hat{\mathbf{D}}_{tr,(1)}$ or HOSVD of $\hat{\mathcal{D}}_{tr}$



3. Recover spatial maps \mathbf{U}_x :

$$\hat{\mathbf{U}}_x = \arg \min_{\mathbf{U}_x} \underbrace{\|\mathbf{d} - \Omega(\Phi_t \times_1 [\mathbf{F}\mathbf{S}\mathbf{U}_x])\|_2^2}_{\text{Data consistency}} + \underbrace{R(\mathbf{U}_x)}_{\text{Optional additional penalty}}$$

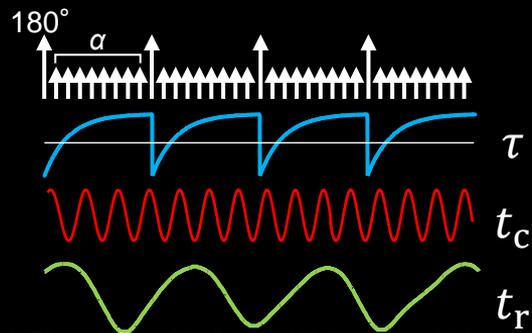


T_1 multitasking: Free-breathing, non-ECG T_1 mapping

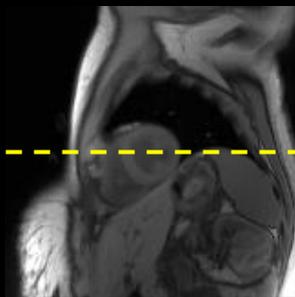
Continually acquire IR-FLASH

688 inversion times ($\Delta\tau = 3.56$ ms) up to 2.5 sec

- With LRT model, has similar scan time as far fewer inversion times (e.g., 8)
- Avoids binning radial spokes



3 overlapping timings



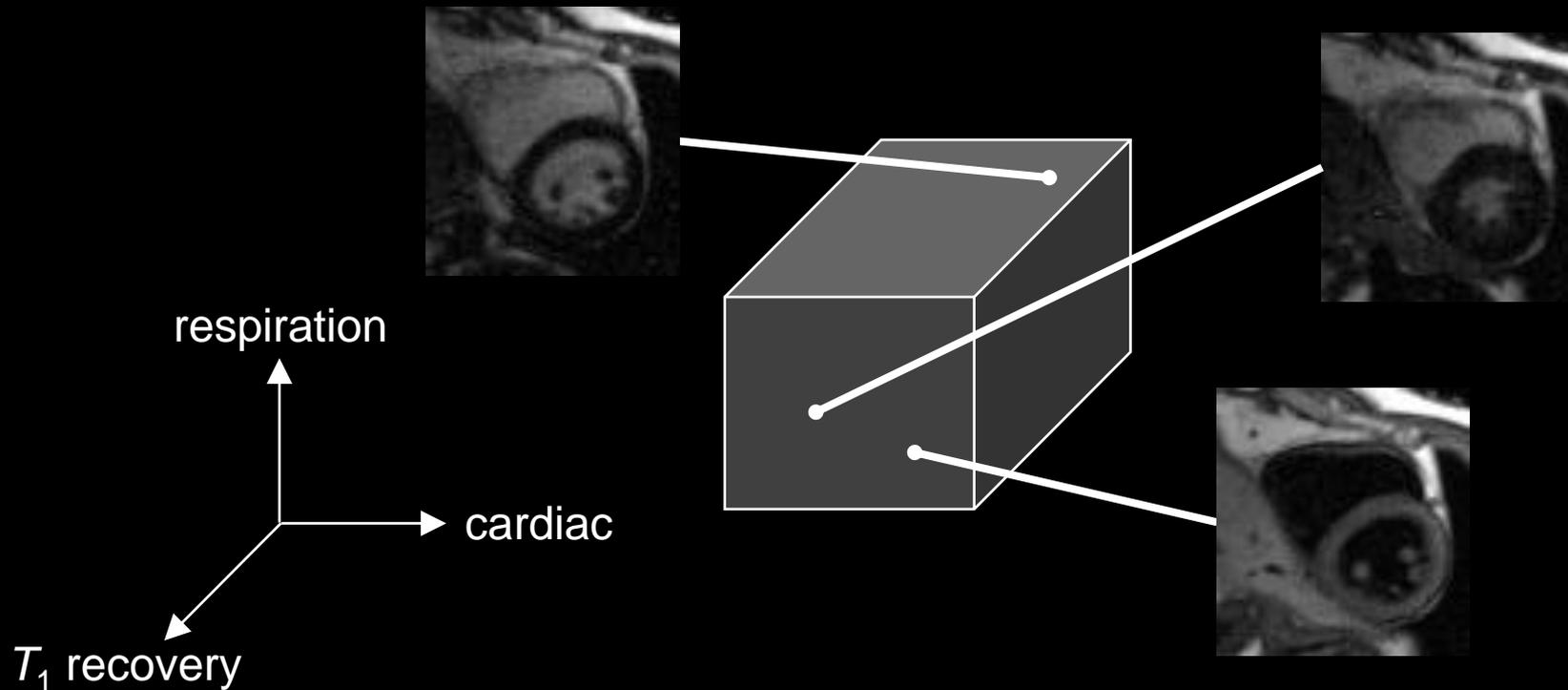
LV
Liver



Real-time evolution

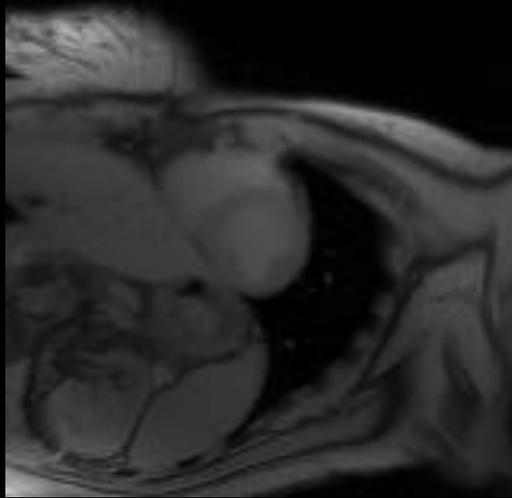
T_1 multitasking: Free-breathing, non-ECG T_1 mapping

3 time dimensions gives us a “cube” with an image at each point

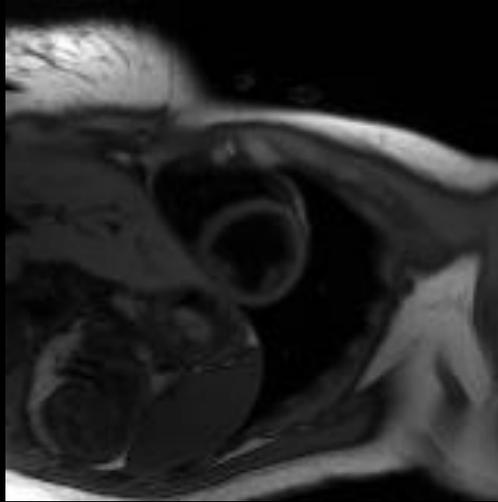


T_1 multitasking: Free-breathing, non-ECG T_1 mapping

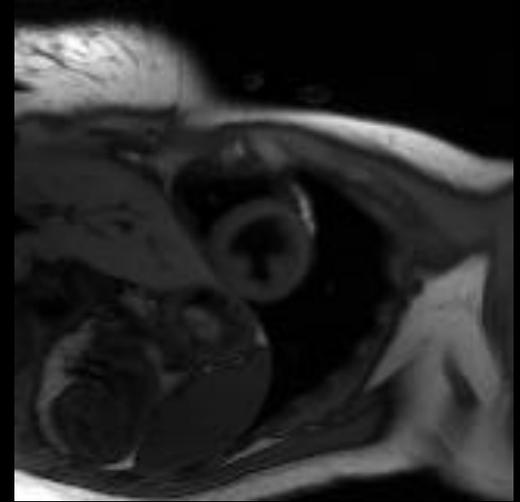
Can retrospectively isolate any of 3 time dimensions



T_1 recovery



Cardiac motion



Respiratory motion

T_1 multitasking: Free-breathing, non-ECG T_1 mapping

Provides multiple contrasts at every cardiac and respiratory phase



inversion time



cardiac phase



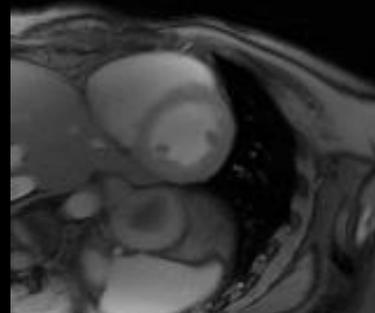
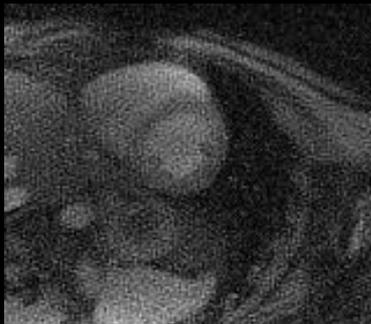
respiratory phase

T_1 multitasking: Acceleration demonstration

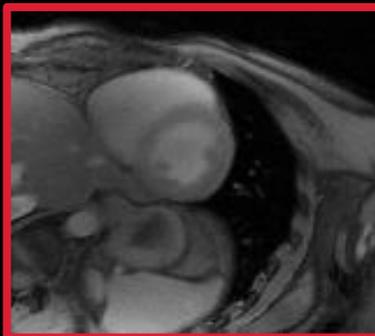
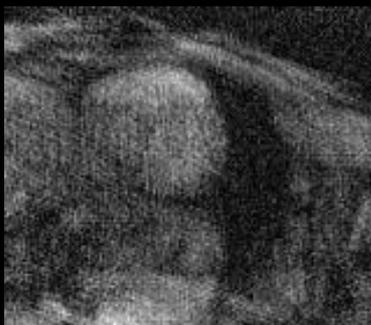
SENSE
(8 τ bins, $\Delta\tau=306$ ms)

Low-rank tensor
(344 τ bins, $\Delta\tau=7$ ms)

12 min scan



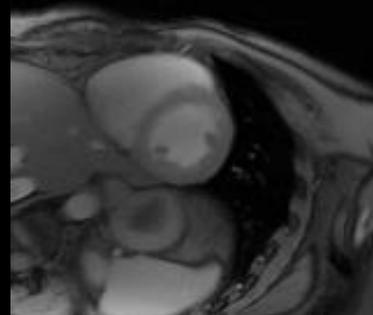
1 min scan



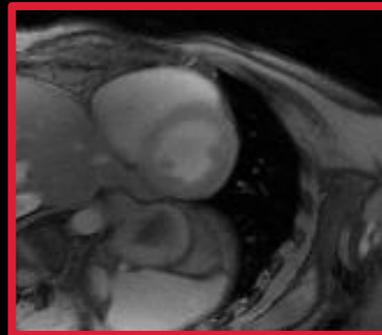
T_1 multitasking: Acceleration demonstration

Low-rank tensor

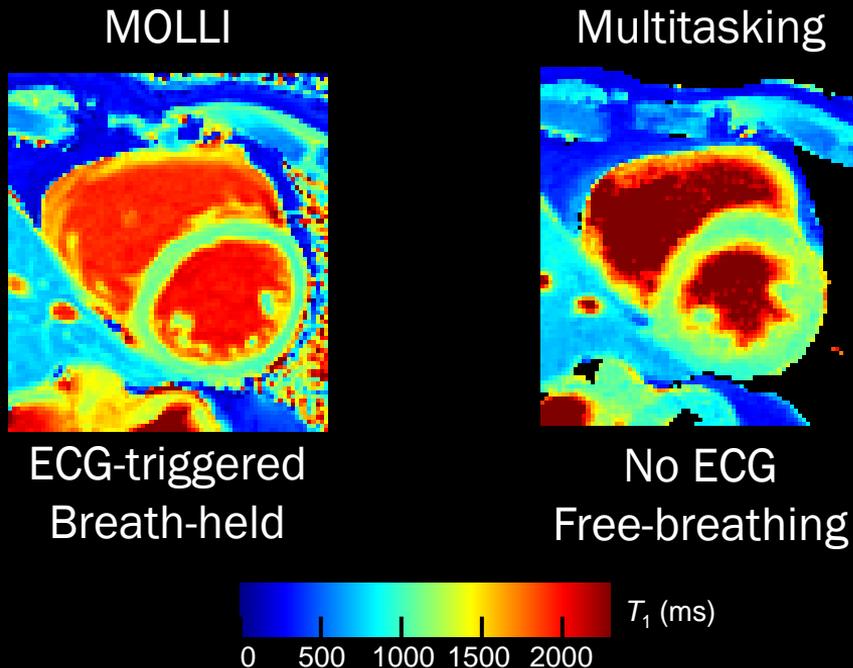
12 min scan



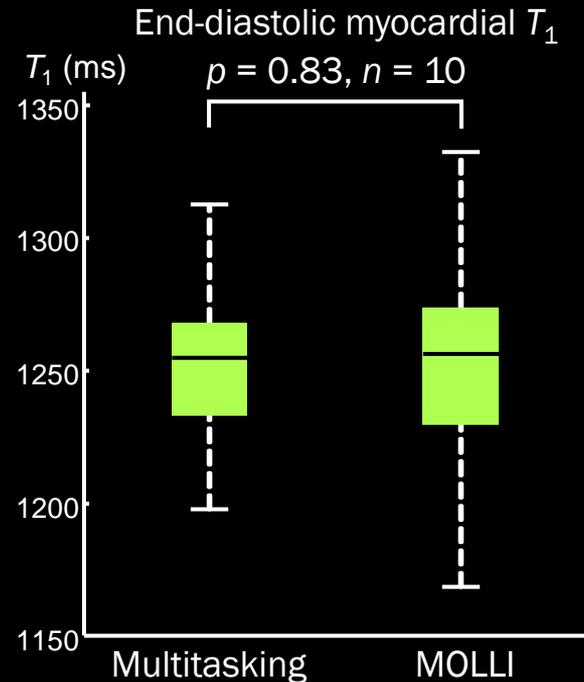
1 min scan



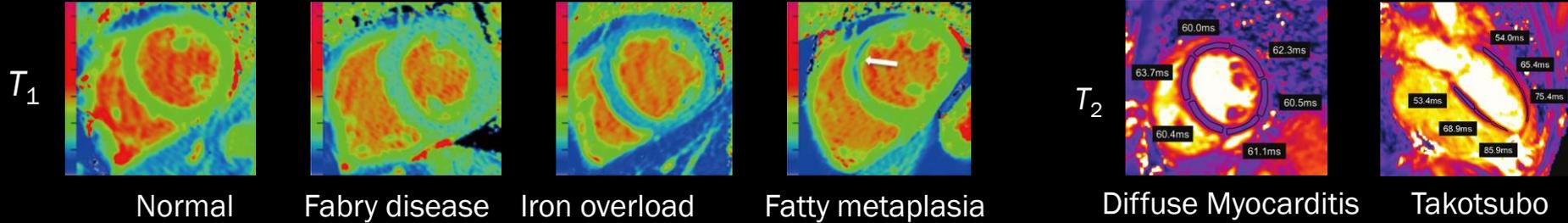
T_1 multitasking: Free-breathing, non-ECG T_1 mapping



ROI: myocardium



Quantitative cardiovascular MR (CMR)

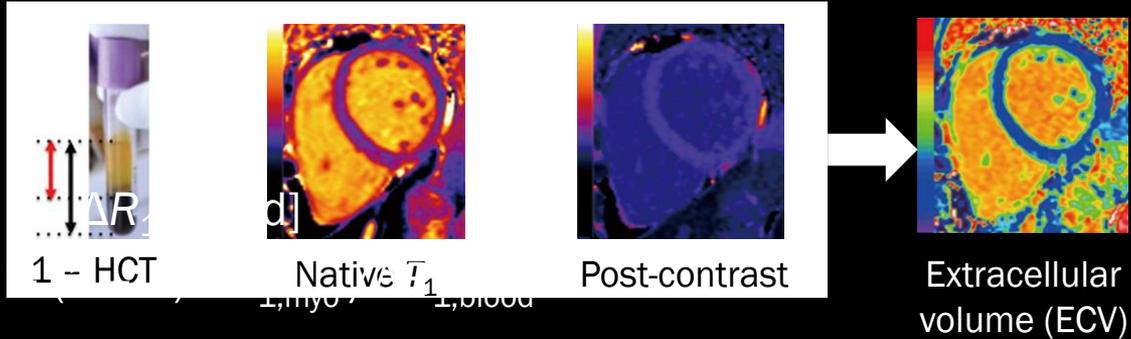


T_1 w/Gd



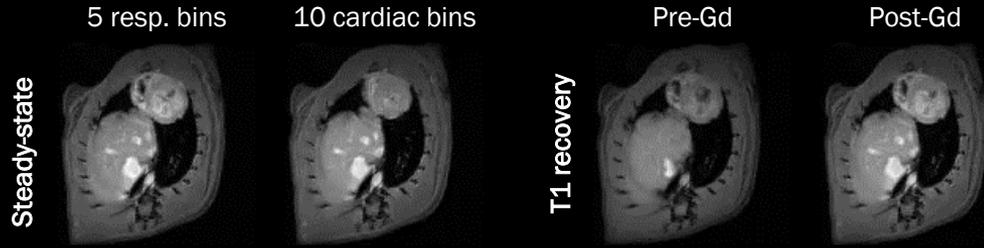
Perfusion

ECV

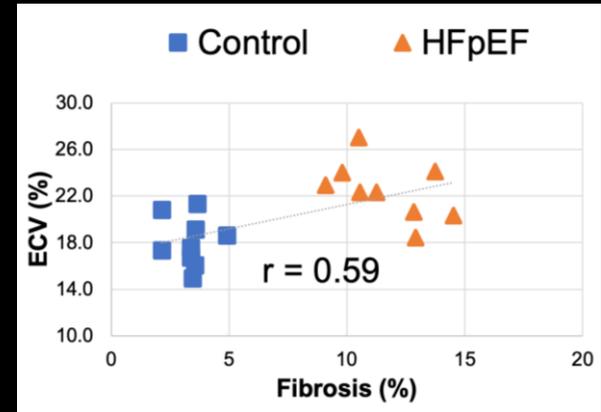
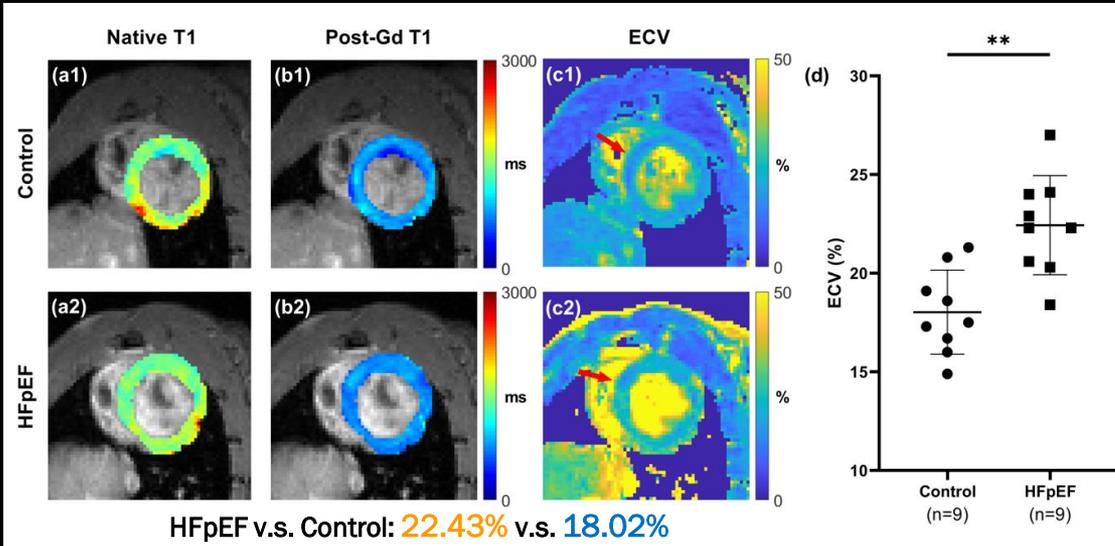
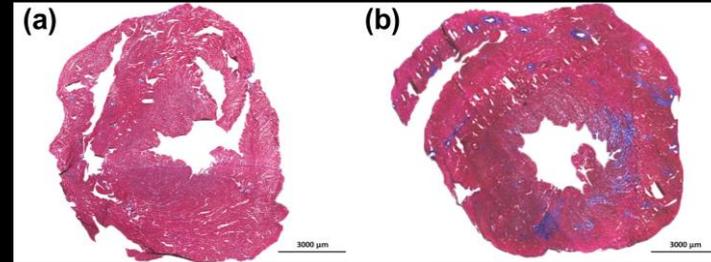


Bulluck H et al., *Circ J* 2015; Thavendiranathan P et al., *Circ Cardiovasc Imaging* 2012

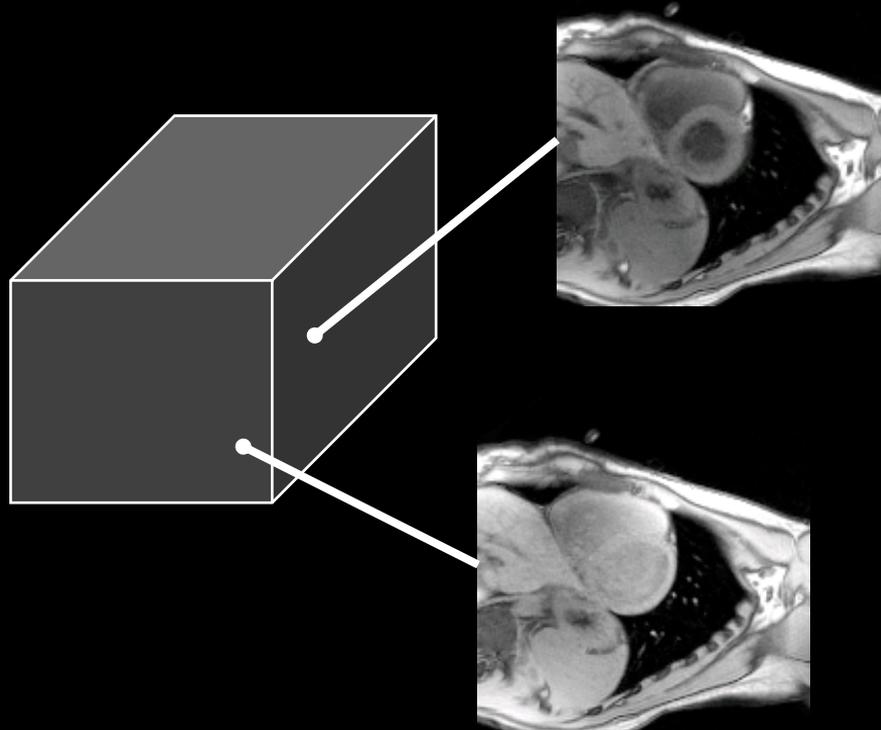
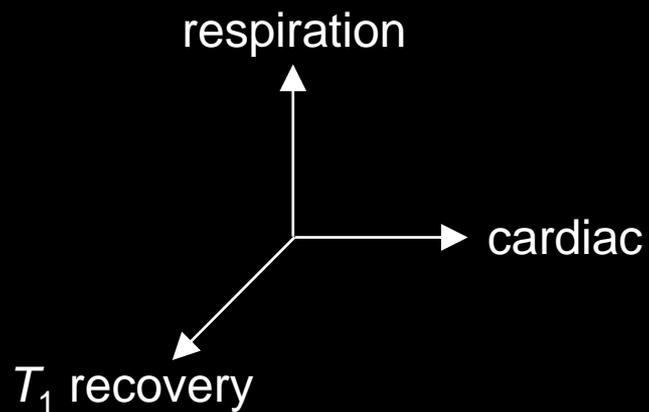
ECV Multitasking in small animals



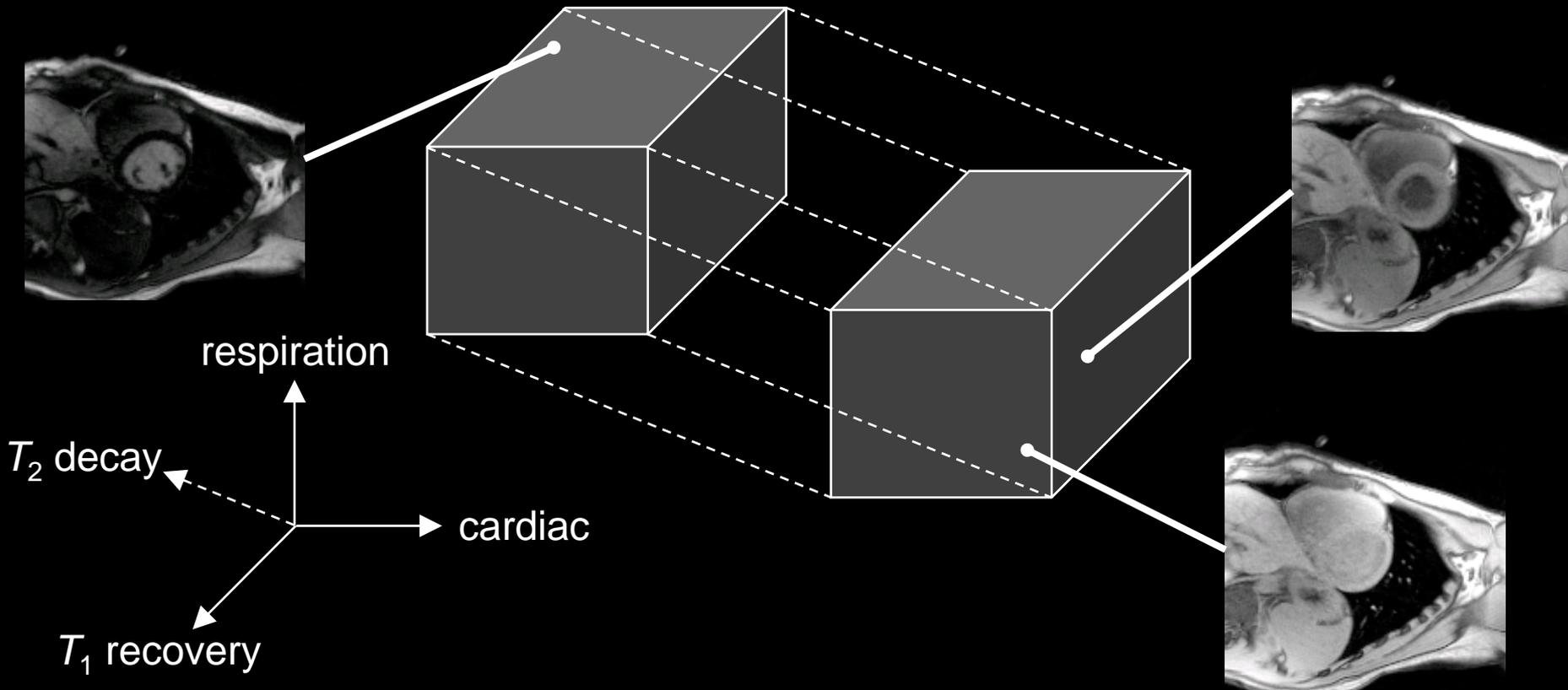
HFpEF animal model:
Dahl salt-sensitive (DSS) rats



Adding more time dimensions



Adding more time dimensions



T_1 - T_2 multitasking: Free-breathing, non-ECG T_1 - T_2 mapping

Adiabatic T2prep¹/inversion recovery² (T2IR)-prepared FLASH

¹Nezafat R et al., *MRM* 2006

²Brown R et al., *MRM* 2010

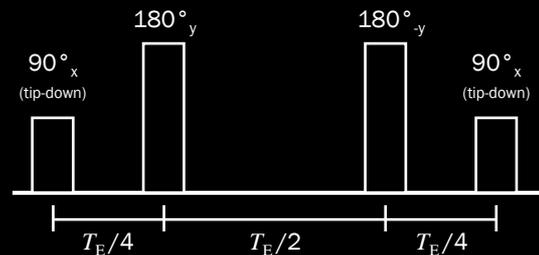


First 90° rotation tips magnetization into transverse plane

Refocusing pulses ensure T2 decay instead of T2*

Second 90° rotation interrupts T2 decay and stores T2-weighted magnetization along -z

T2-weighted “inversion”
(starting point of T1 recovery depends on T2)

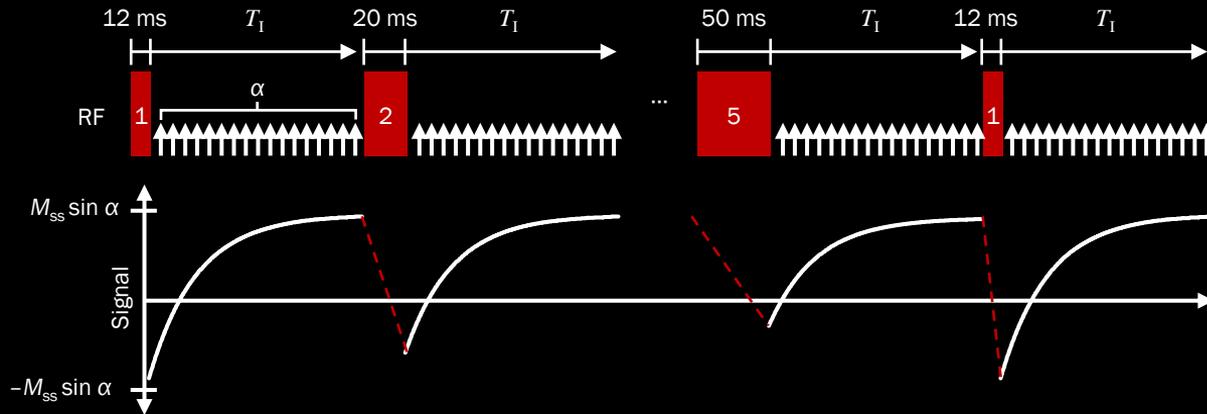


T_1 - T_2 multitasking: Free-breathing, non-ECG T_1 - T_2 mapping

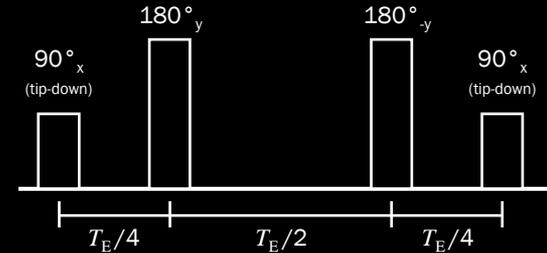
Adiabatic T2prep¹/inversion recovery² (T2IR)-prepared FLASH

¹Nezafat R et al., *MRM* 2006

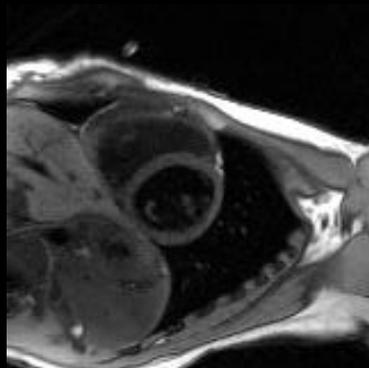
²Brown R et al., *MRM* 2010



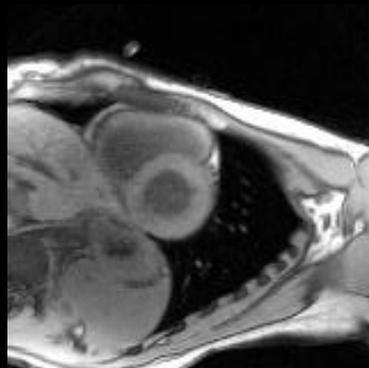
T2IR :



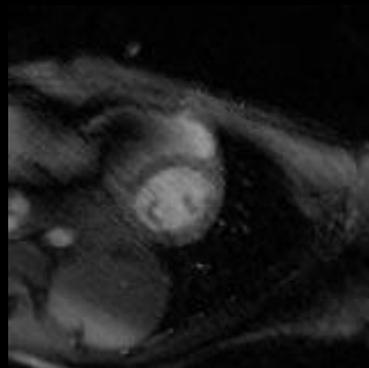
T_1 - T_2 multitasking: Free-breathing, non-ECG T_1 - T_2 mapping



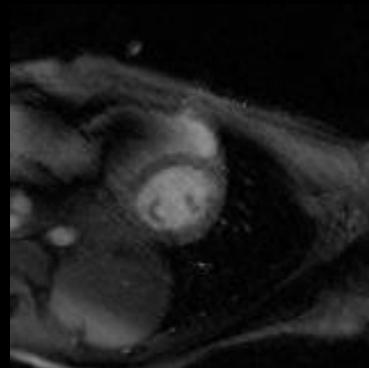
Cardiac motion



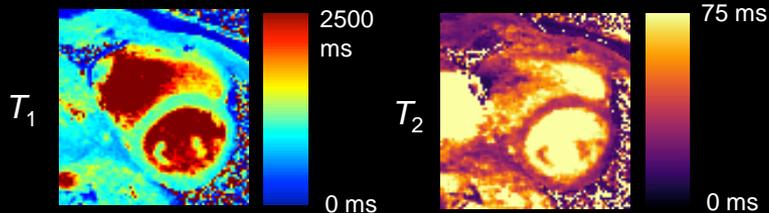
Respiration



T_1 recovery

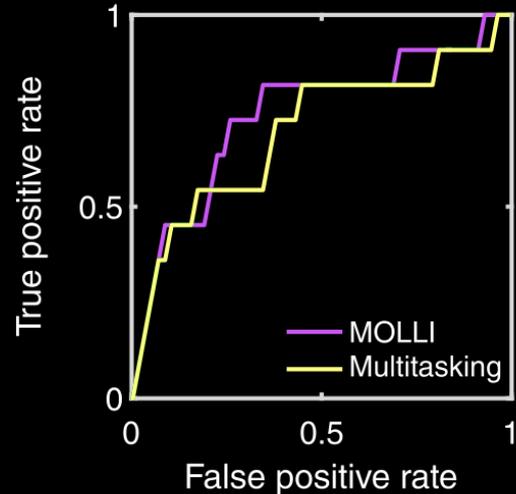


T_2 prep duration

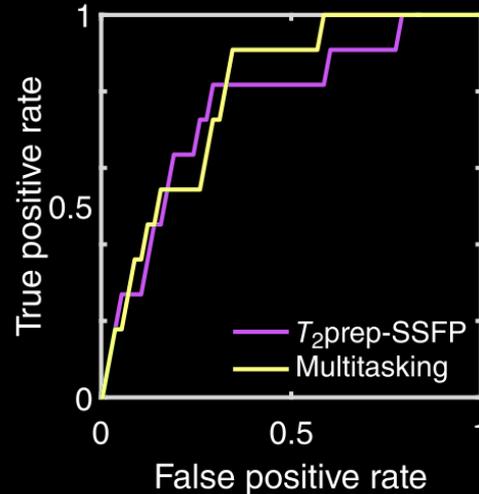


T_1 - T_2 multitasking: Can native T_1 - T_2 predict LGE in acute MI?

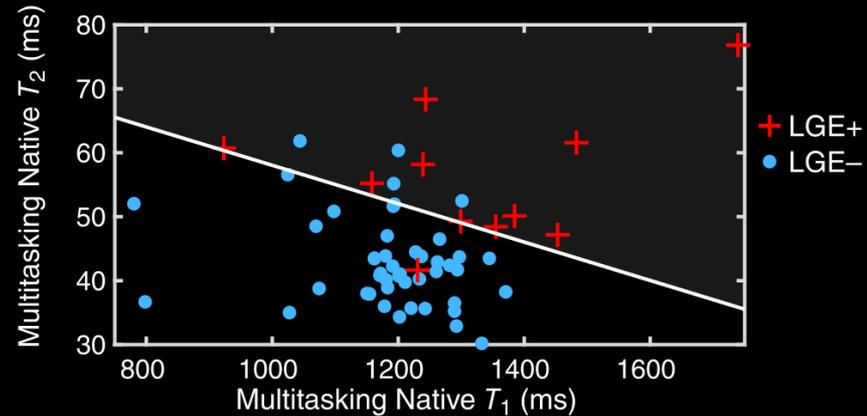
Pilot study in $n = 10$ acute MI patients



Method	AUC
MOLLI	0.74
Multitasking	0.70



Method	AUC
T_2 prep-SSFP	0.77
Multitasking	0.80



91% sensitivity, 91% specificity

Simultaneous Multi Slice (SMS) Multitasking

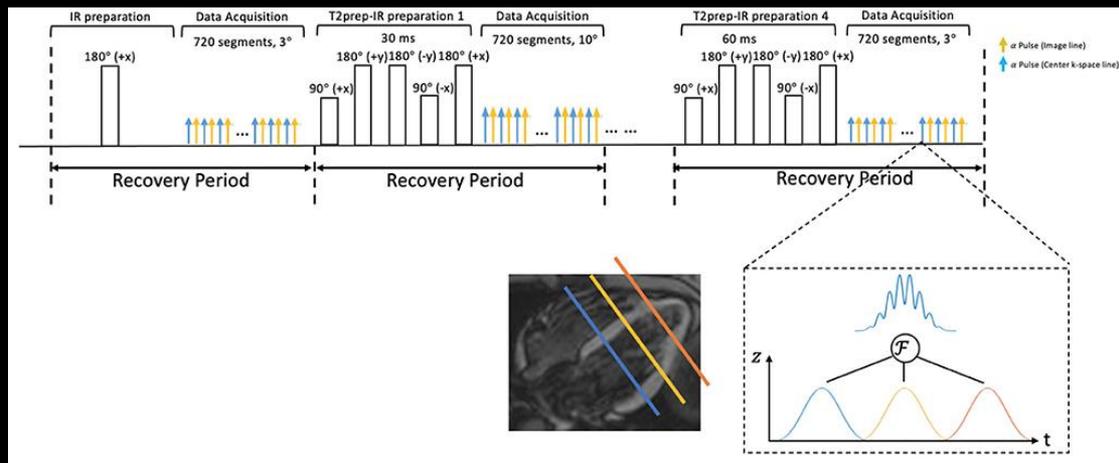
Radial SMS implementation of T1-T2 multitasking

3 slices with SMS Multitasking

- No ECG
- No breath-holds
- 3 min acquisition

3 slices with conventional mapping techniques

- ECG triggered
- 6 breath holds
- 4–7 min acquisition (with breath-hold recovery)



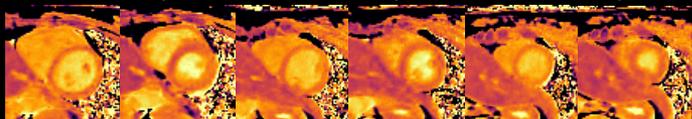
T1-T2 Simultaneous Multislice (SMS)

T1 Maps

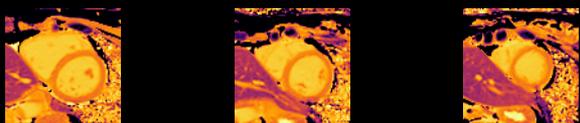
Base Mid Apex

Subject 1 Diastole Systole Diastole Systole Diastole Systole

Multitasking-T1



MOLLI-T1



3500

3000

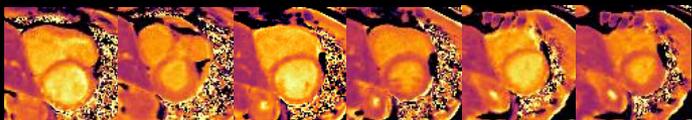
2000

1000

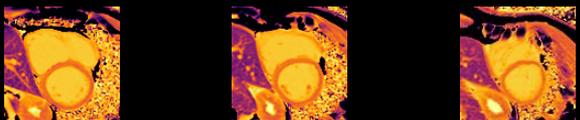
0 ms

Subject 2

Multitasking-T1



MOLLI-T1

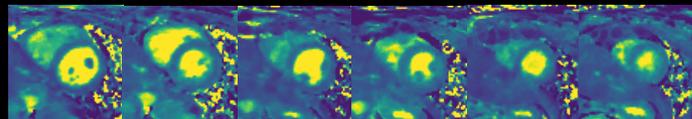


T2 Maps

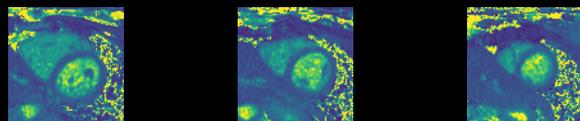
Base Mid Apex

Subject 1 Diastole Systole Diastole Systole Diastole Systole

Multitasking-T2



T2-prep FLASH



150

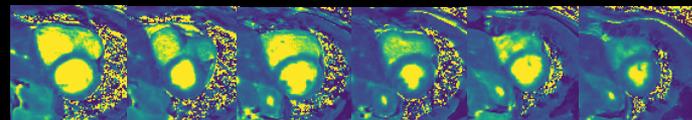
100

50

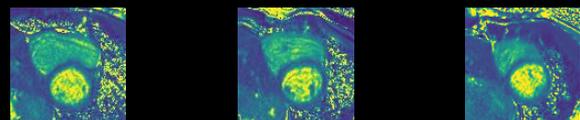
0 ms

Subject 2

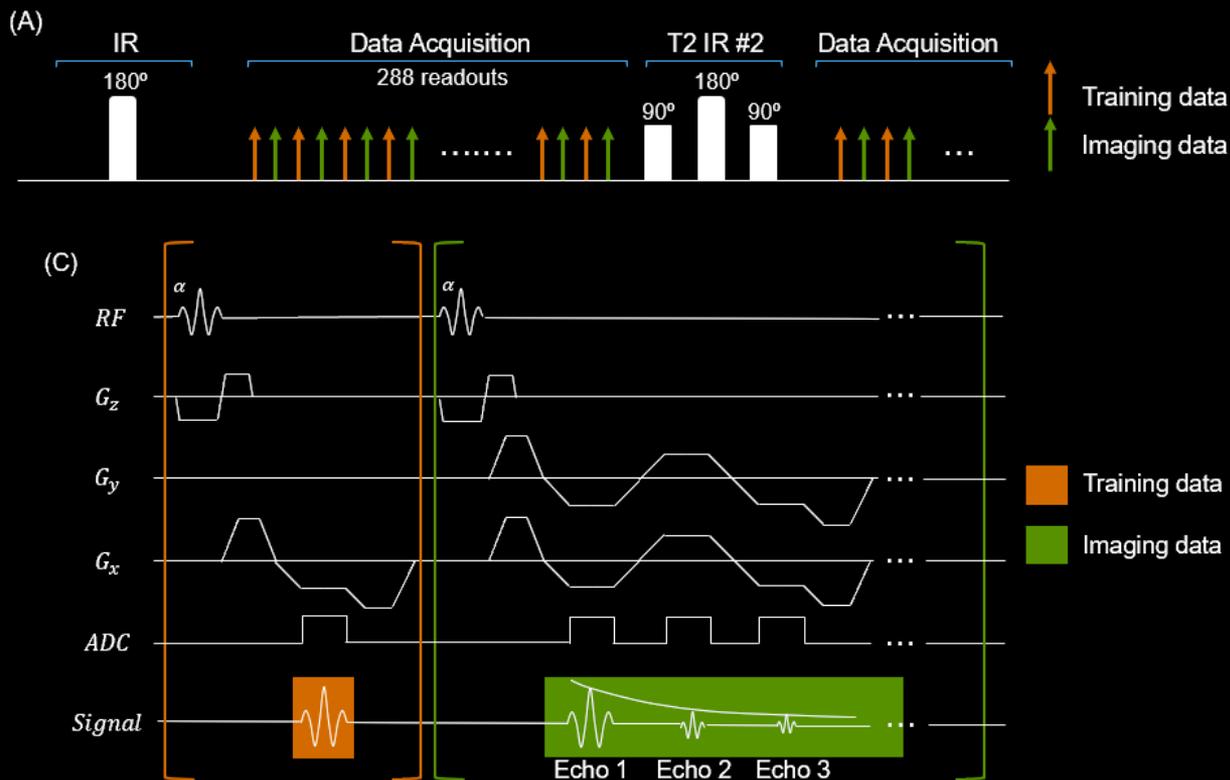
Multitasking-T2



T2-prep FLASH



Multiecho multitasking for T1-T2-T2*-fat fraction (FF)



MR Multitasking 2D T1-T2-T2*-fat fraction mapping

Healthy volunteer example

3-T scanner

1.7 x 1.7 x 8 mm resolution

Non-ECG, Free-breathing

2.5 min scan

T1

T2

T2*

Fat fraction

Reference

Multitasking

Reference

Multitasking

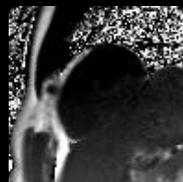
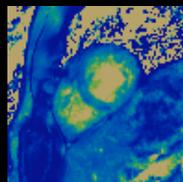
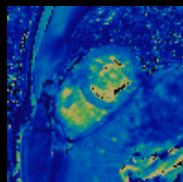
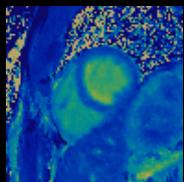
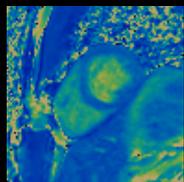
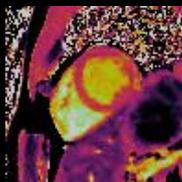
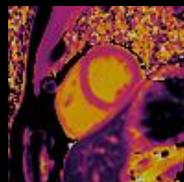
Reference

Multitasking

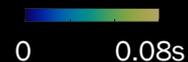
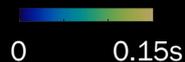
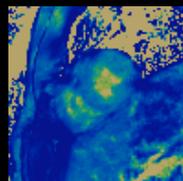
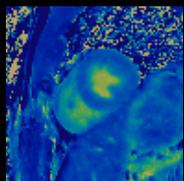
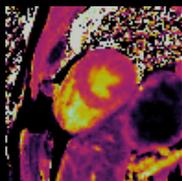
Reference

Multitasking

Diastolic

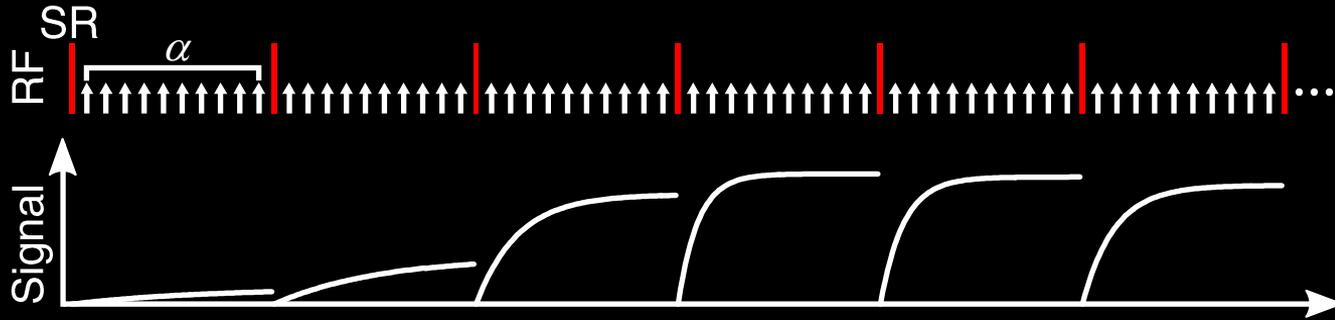


Cardiac-resolved



Myocardial perfusion multitasking

Continuous-acquisition saturation recovery (SR)-prepared FLASH



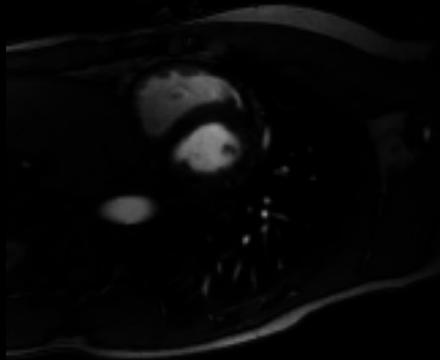
Real-time evolution

3 time dimensions representing:

- 1) Cardiac motion
- 2) Saturation recovery
- 3) Gd dynamics

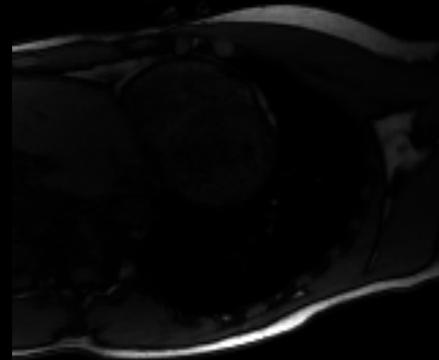
Myocardial perfusion multitasking

Retrospective time dimension/“task” selection



Task: Cine

$\tau = 160$ ms
18th cardiac cycle



Task: Perfusion

$\tau = 280$ ms
End-diastole

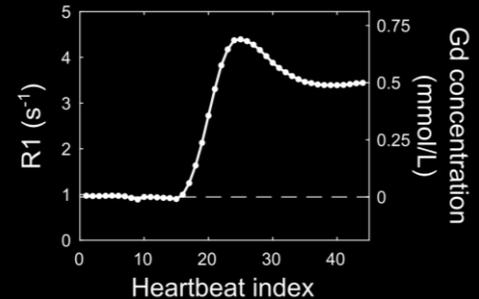
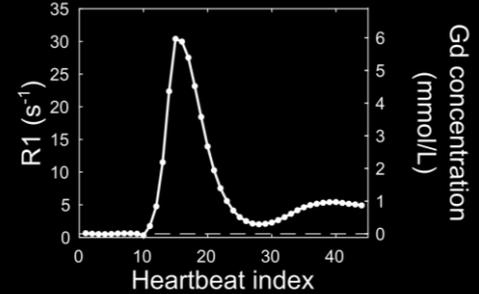
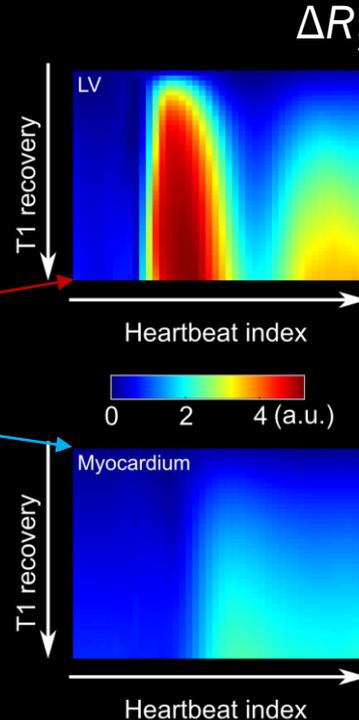
Myocardial perfusion multitasking

Single-bolus perfusion quantification from time-resolved T_1 maps

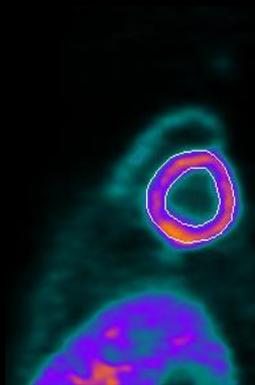
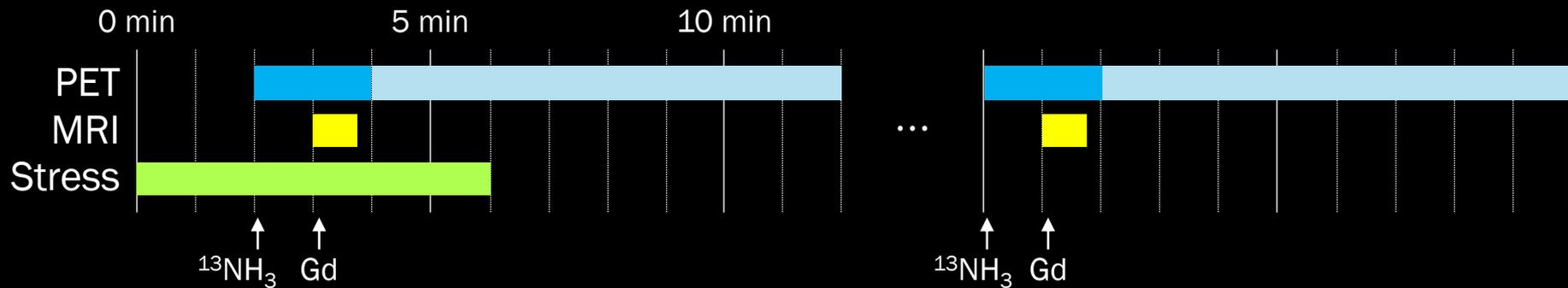
Multiple SR times available

$\tau = 64$ ms

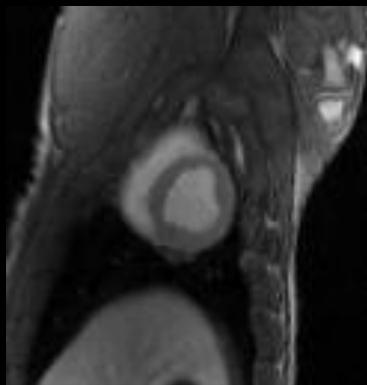
$\tau = 264$ ms



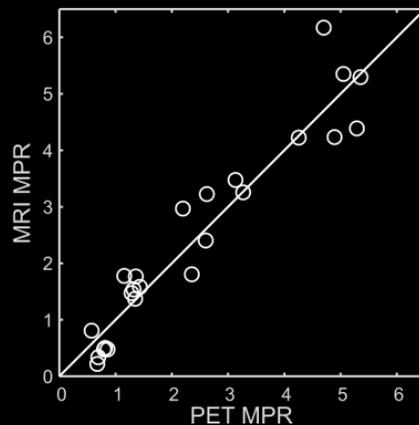
Myocardial perfusion multitasking: Simultaneous PET-MR



^{13}N -ammonia PET



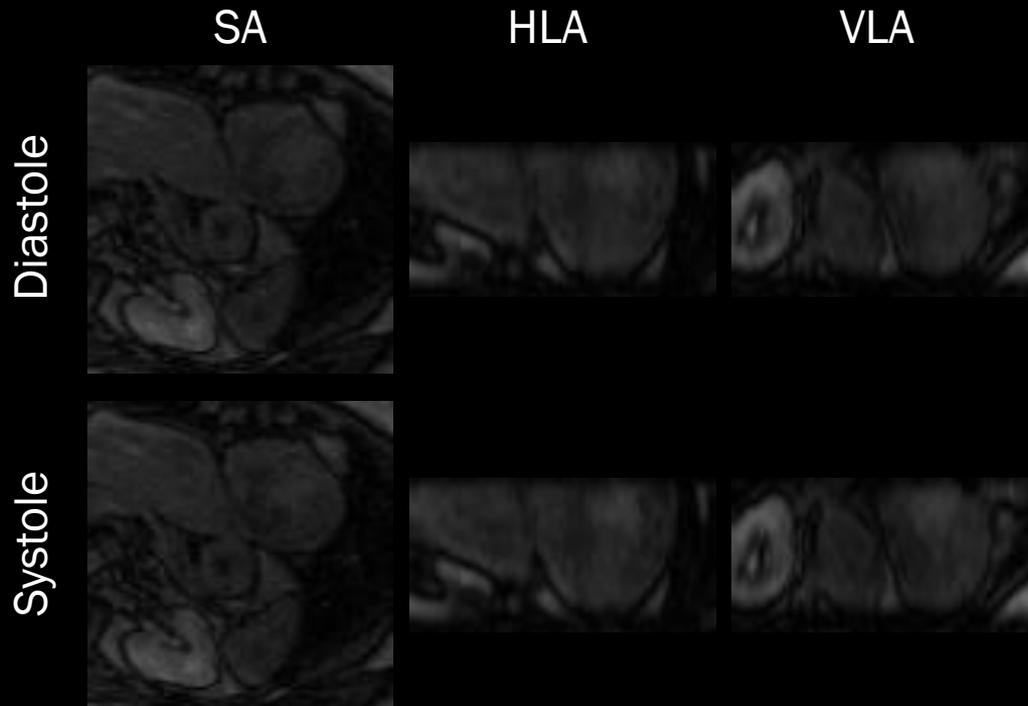
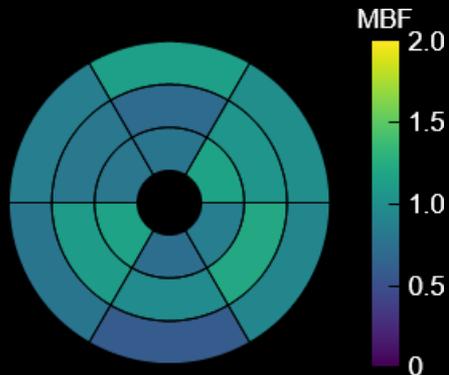
MR Multitasking



ICC = 0.95

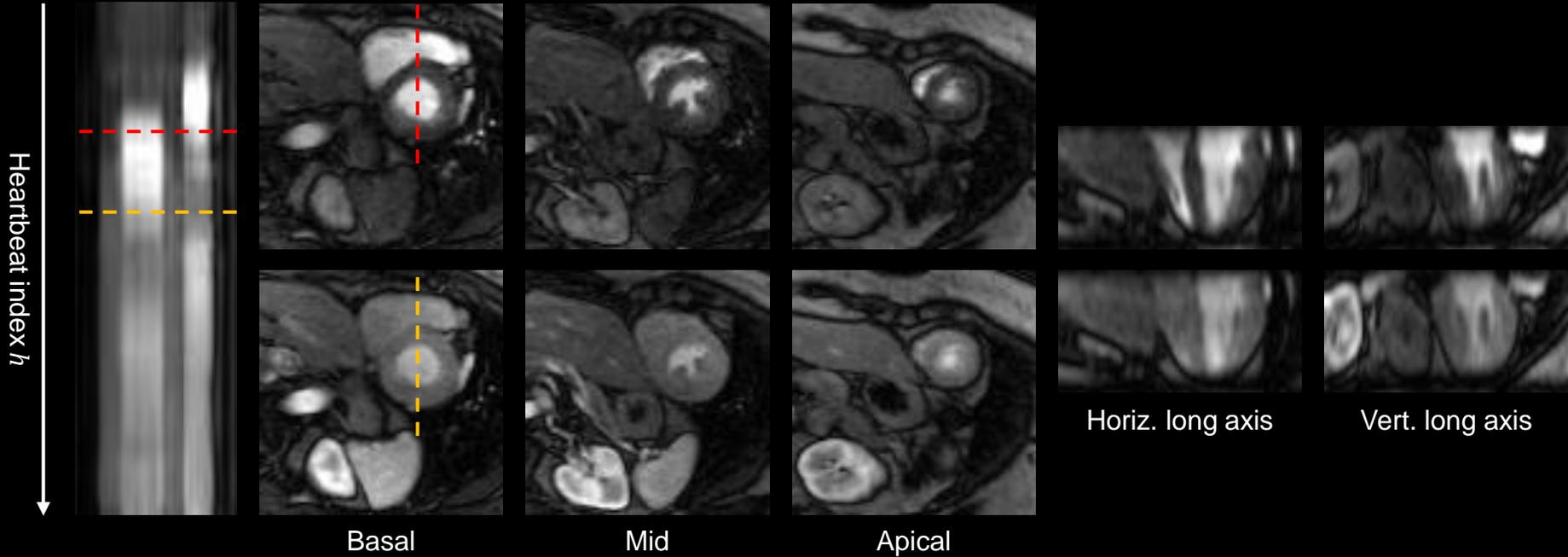
New developments: 3D perfusion

- 3D spatial coverage
 - 2 x 2 x 8 mm
 - 12 slices
- Free-breathing, non-ECG
- 20 cardiac phases
- Single-bolus quantification



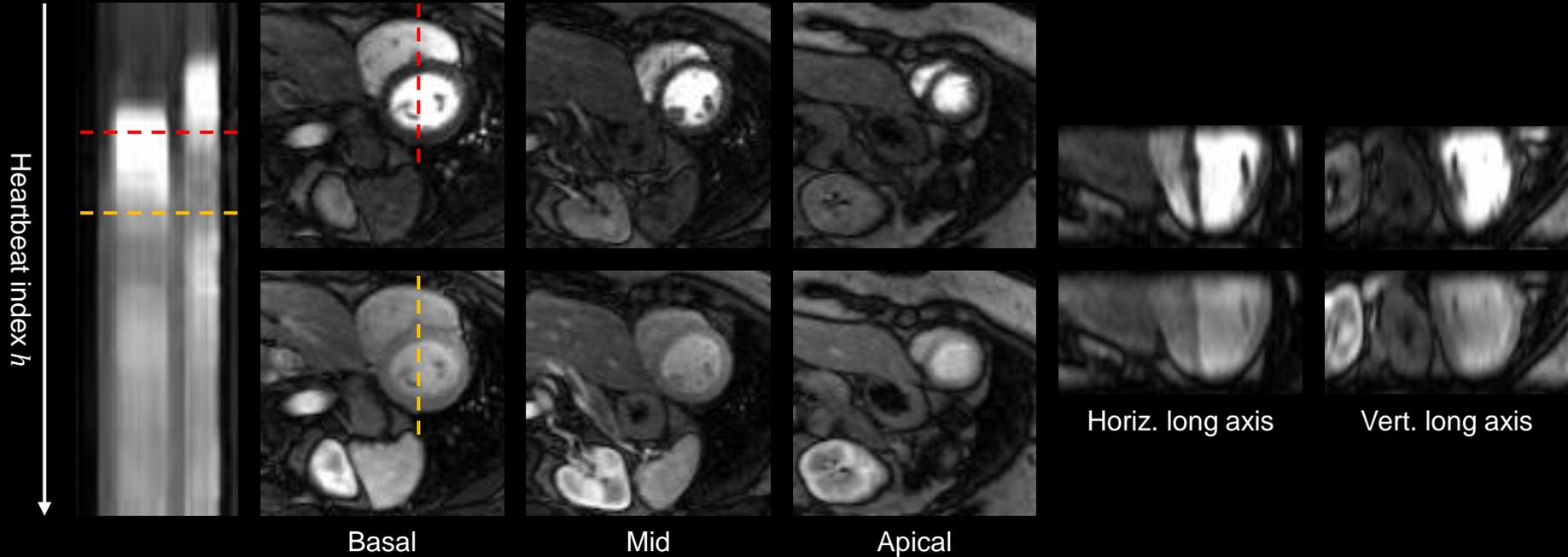
Myocardial perfusion multitasking: 3D free-breathing

Systole



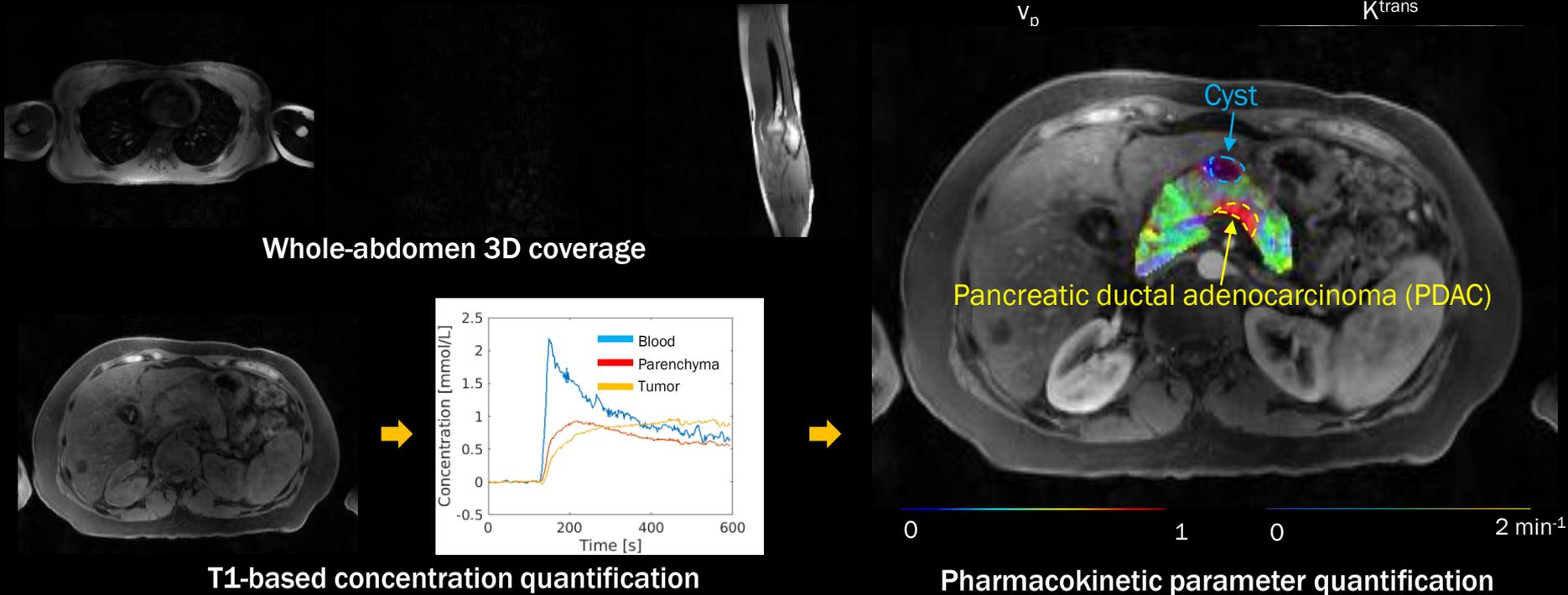
Myocardial perfusion multitasking: 3D free-breathing

Diastole



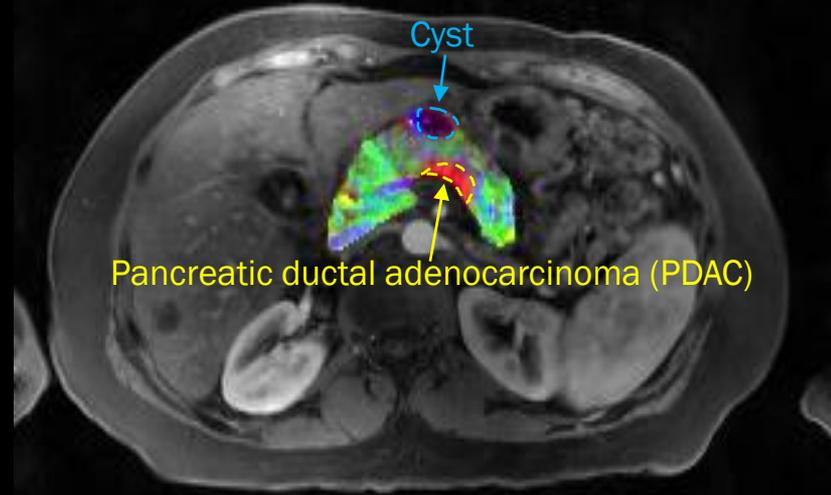
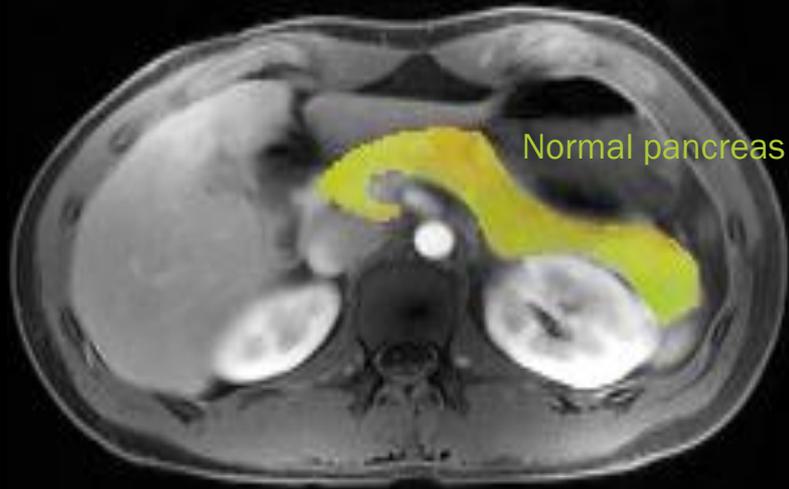
MR Multitasking for free-breathing quantitative DCE

6-D imaging: 3 spatial dimensions \times respiration $\times T_1$ recovery \times DCE



MR Multitasking for free-breathing quantitative DCE

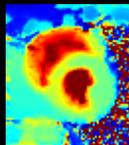
6-D imaging: 3 spatial dimensions \times respiration $\times T_1$ recovery \times DCE



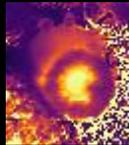
MR Multitasking: Outlook

Potential implications

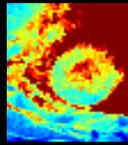
- No need for ECG or breath holds
- Shorter and simpler exams
- Retrospective imaging decisions
- Reduced financial and training demands
- Replacement of serial clinical protocols with a single, quantitative "push-button" scan



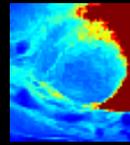
Native
T1



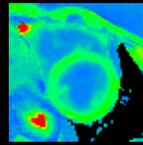
T2



Stress
Perfusion
T1



Rest
Perfusion
T1



Post-Gd
T1/ECV

Future directions

Translate

- Validate extensively
- Integrate into PACS
- Develop high-dimensional display tools

Improve

- Explore new, more powerful image models
- Incorporate additional biomarkers and dimensions
- Investigate time-resolved parameter maps

Analyze

- Develop multiparameter analysis for diagnosis, risk prediction, therapy monitoring, and more

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MR Multitasking throughout the body

