
Water-Fat MRI

M219 Principles and Applications of MRI

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Learning Objectives

- Fat in MRI
 - chemical shift
- Fat Suppression
- Fat-Water-Separated MRI
 - multi-echo Dixon techniques
- Fat Quantification
 - liver fat quantification
- Free-Breathing Fat Quantification

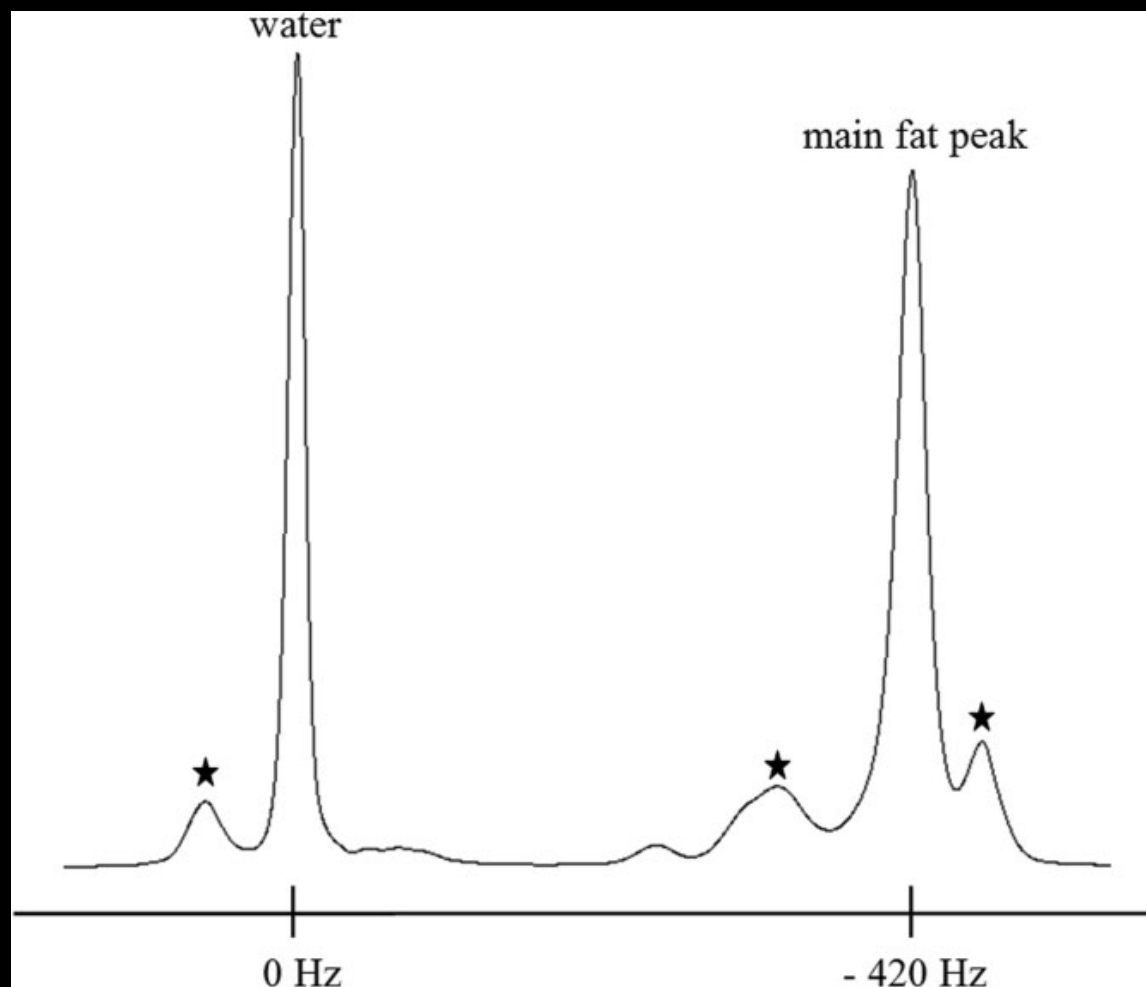
Fat in MRI

- ^1H MRI signal mainly from water & fat
- Bright fat signal
 - Short $T_1 \sim 300$ ms @ 1.5 T
 - can obscure structures of interest
 - can be mistaken for pathology
- Presence of fat
 - may indicate disease state:
liver, cardiac, breast, body, bone, muscle,
cancer, etc.

Chemical Shift of Fat

Triglycerides (fat) have a complex spectrum

main peak from methylene (-CH₂-) is at $\Delta\delta \approx -3.5$ ppm from water



$$\Delta f_{cs} [\text{Hz}] = \frac{\gamma}{2\pi} B_0 \cdot \Delta\delta [\text{ppm}] \cdot 10^{-6}$$

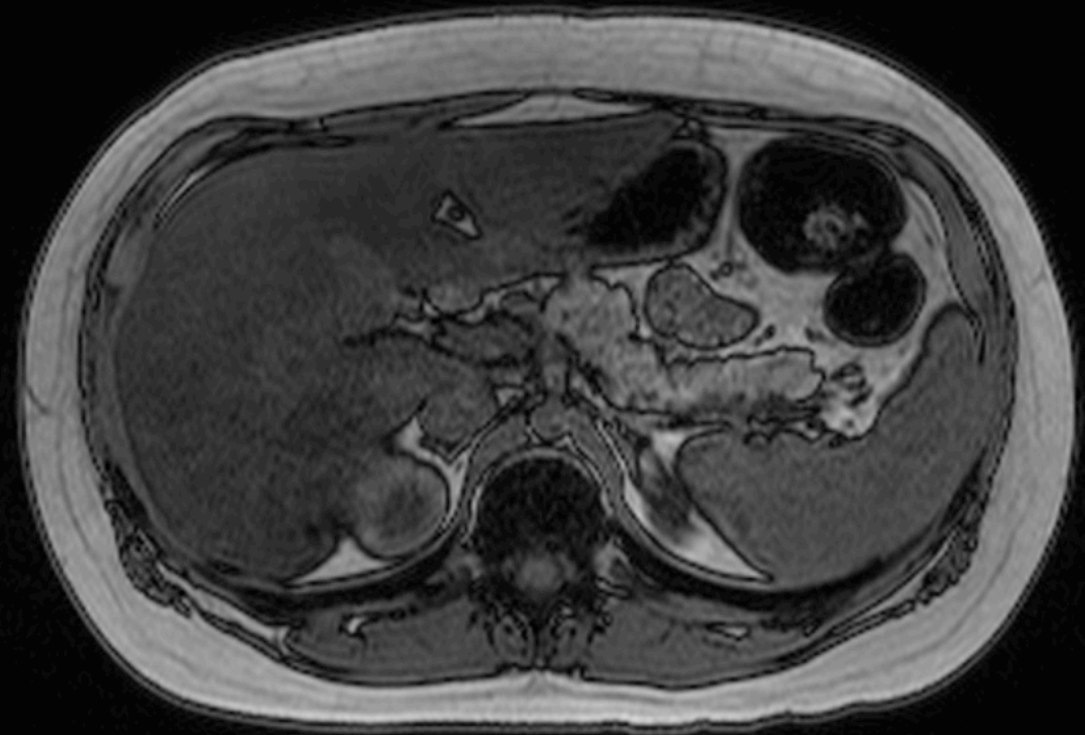
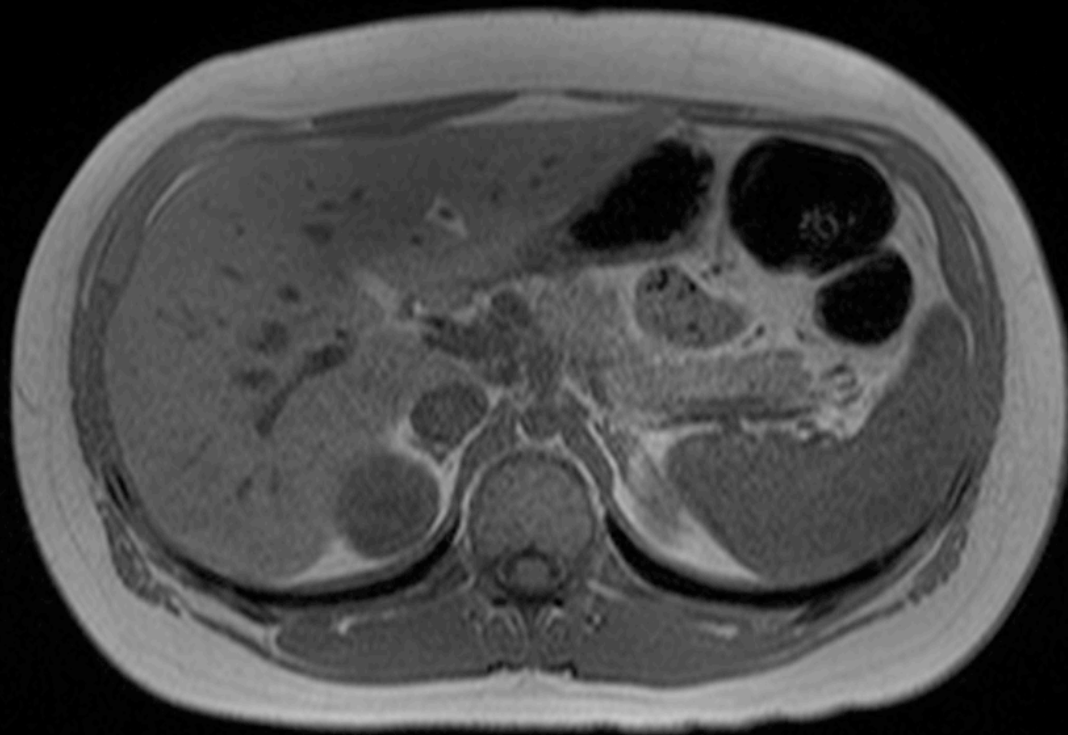
at $B_0 = 1.5$ T, $\Delta f_{cs} \approx -210$ Hz

at $B_0 = 3.0$ T, $\Delta f_{cs} \approx -420$ Hz

Chemical Shift of Fat

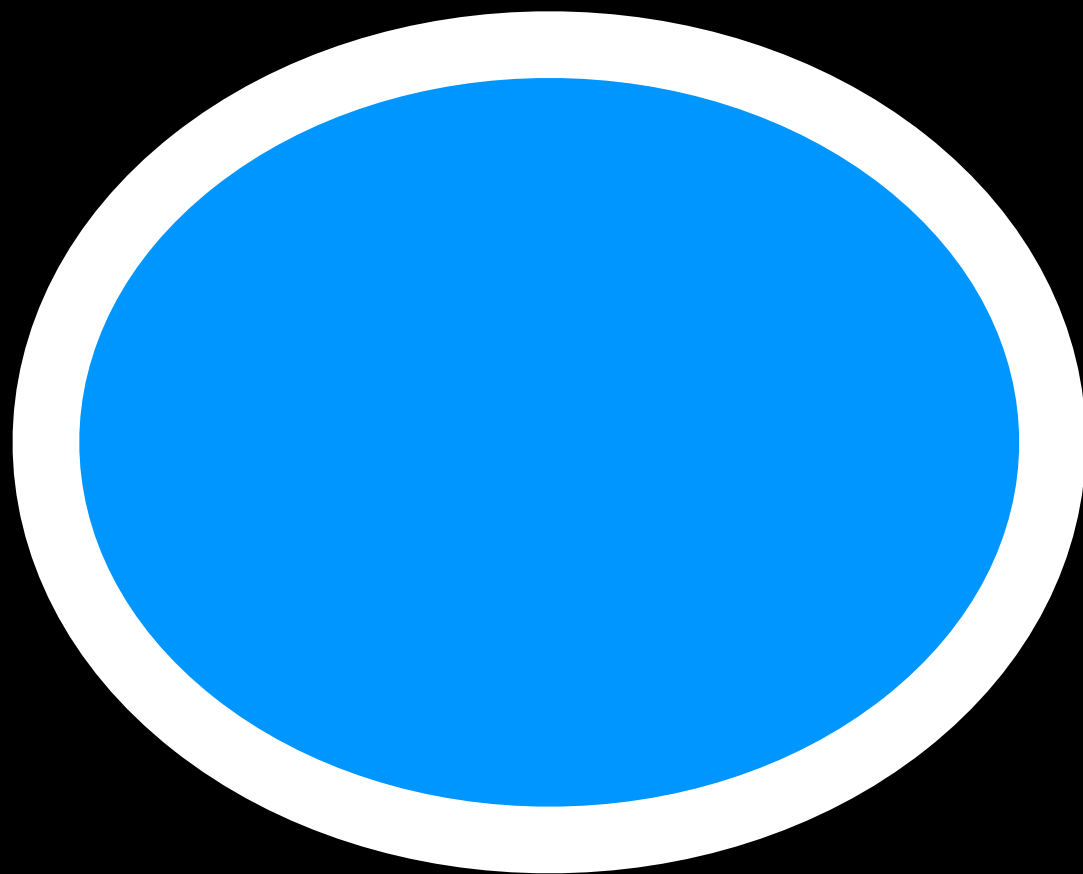
- Dark line artifacts
 - GRE
 - bSSFP

Example: 3D GRE at 3 T

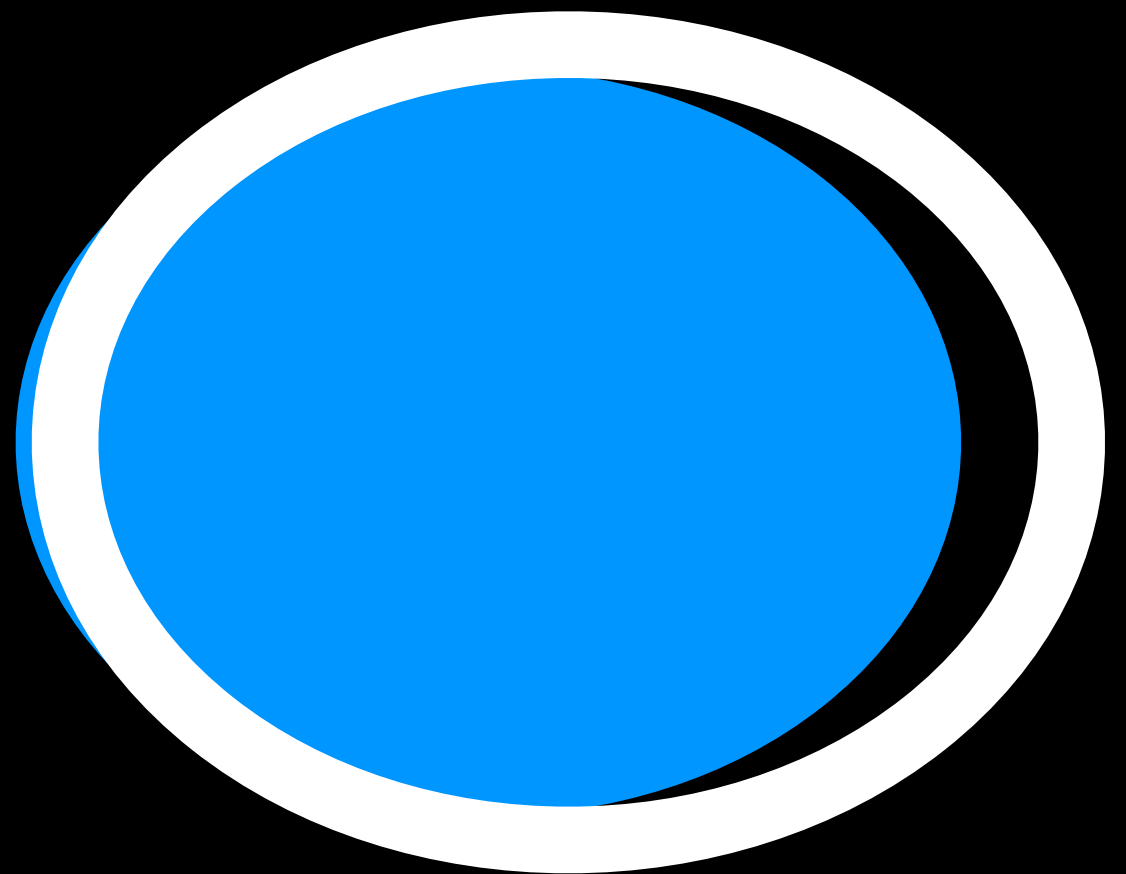


Chemical Shift of Fat

- Chemical shift artifacts
 - Cartesian



readout direction →

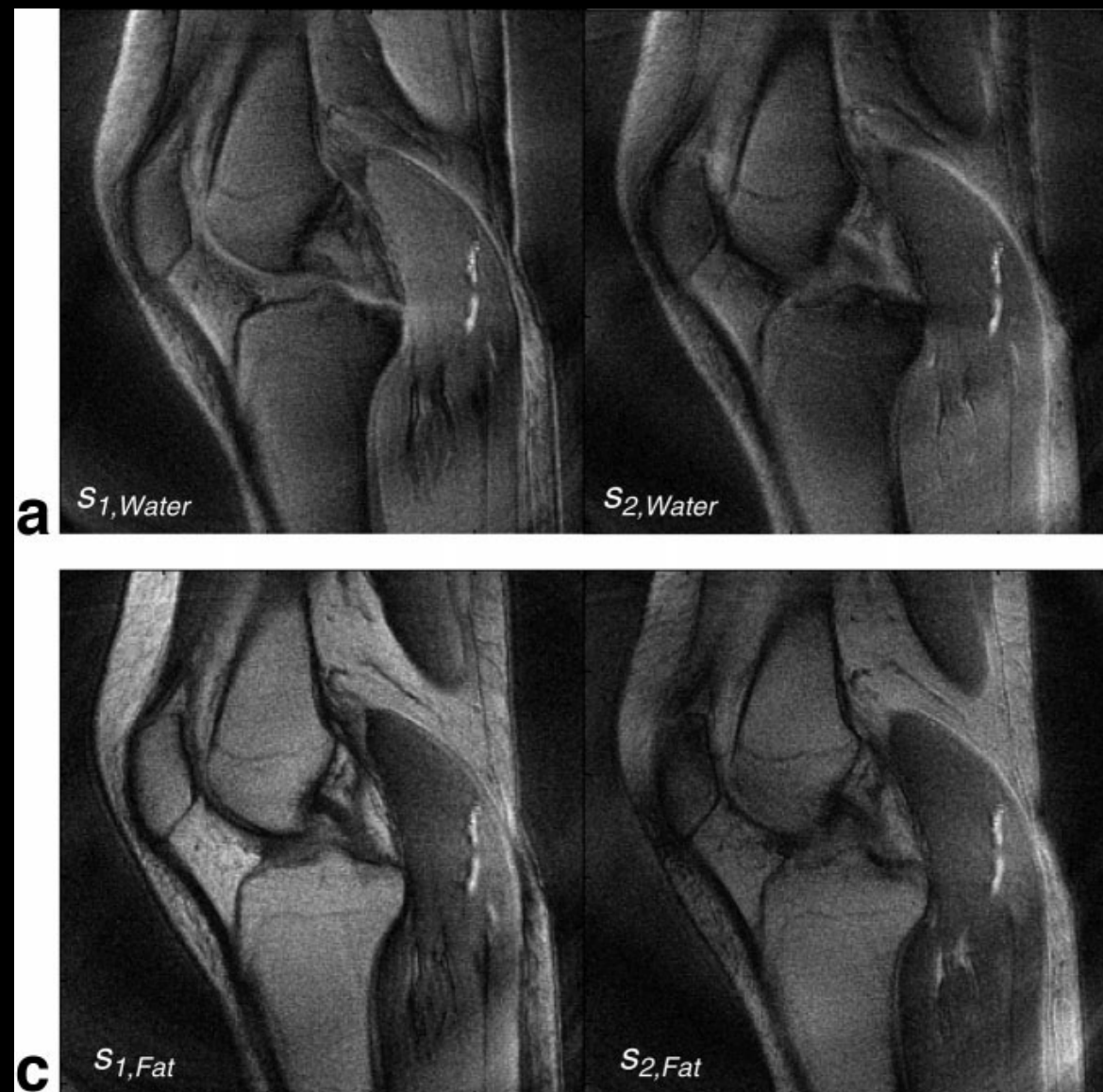
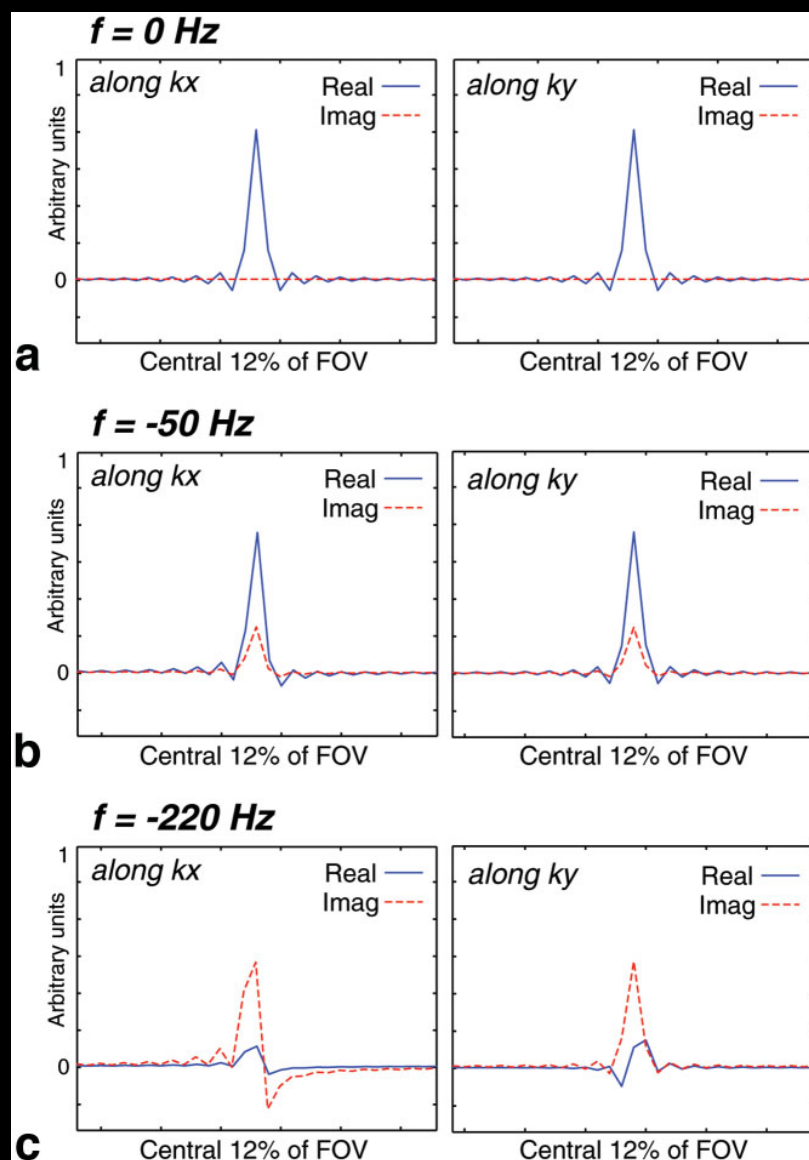


readout direction →

Chemical Shift of Fat

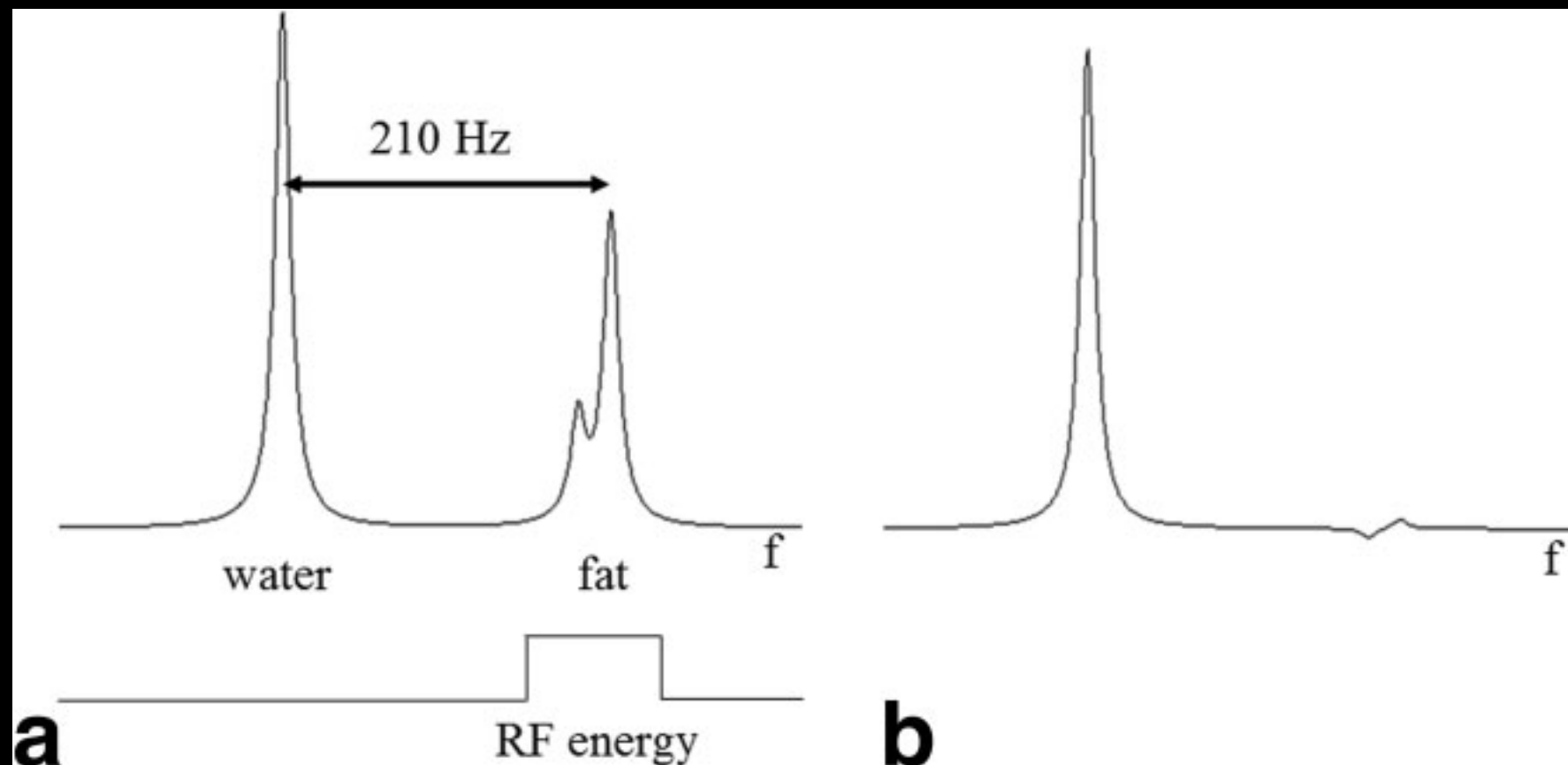
- Blurring artifacts
 - EPI, non-Cartesian

Example: Concentric Rings (Wu et al., MRM 2009)



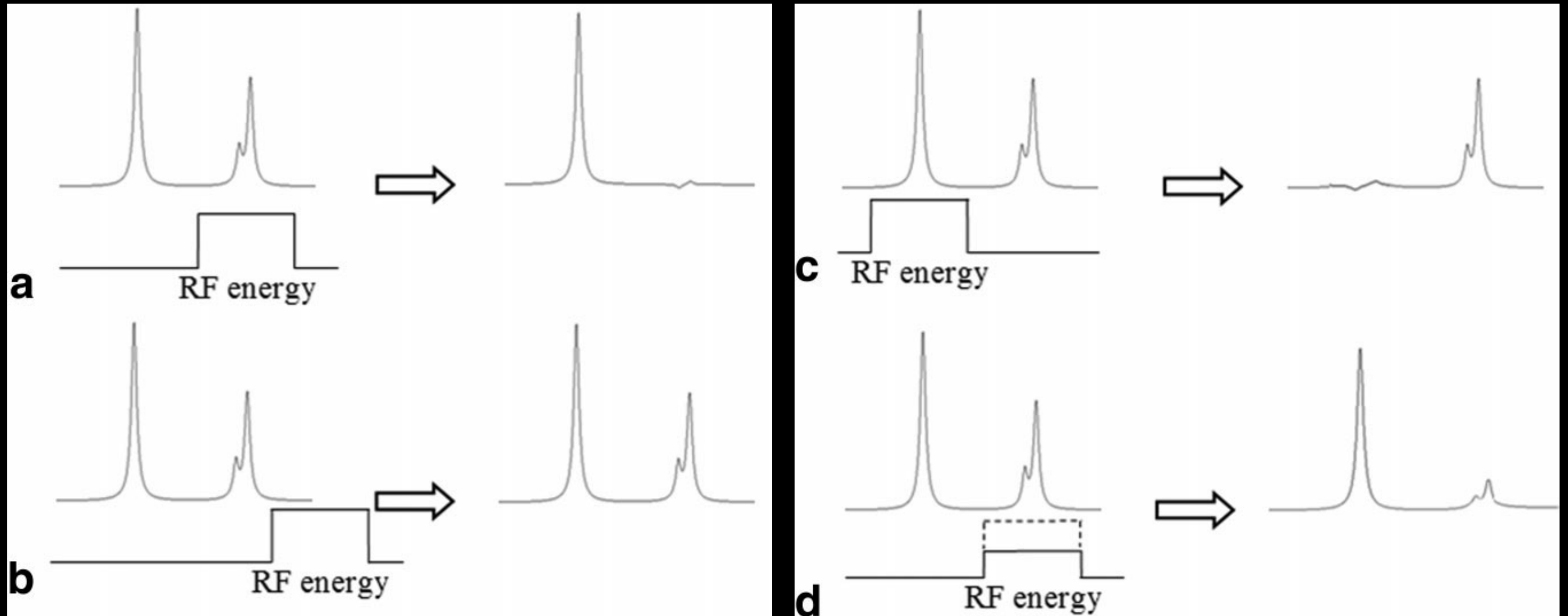
Fat Suppression

- Fat saturation
 - chemical shift selective (CHESS) saturation



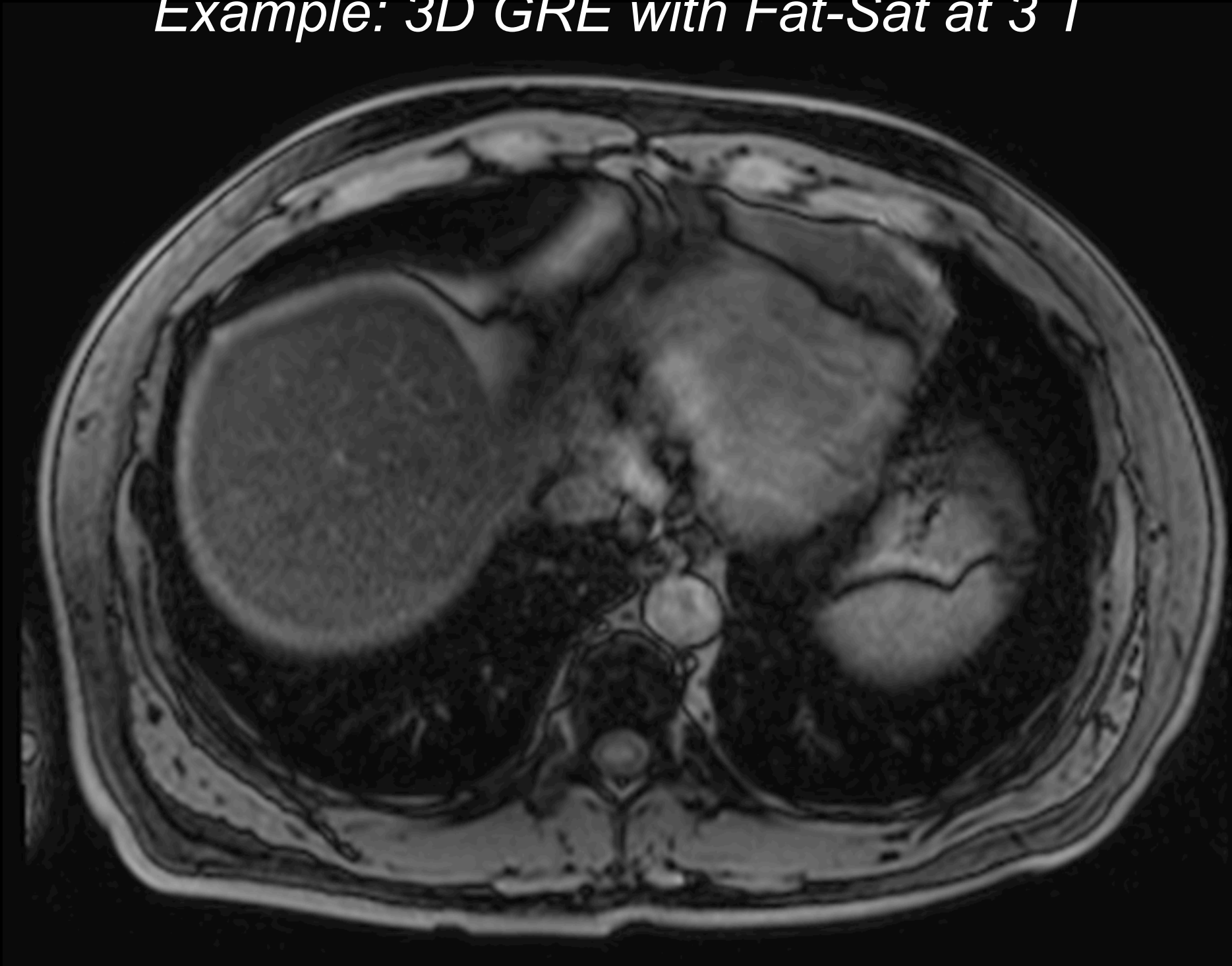
Fat Suppression

- Fat saturation
 - sensitive to B_0 and B_1 variations



Fat Suppression

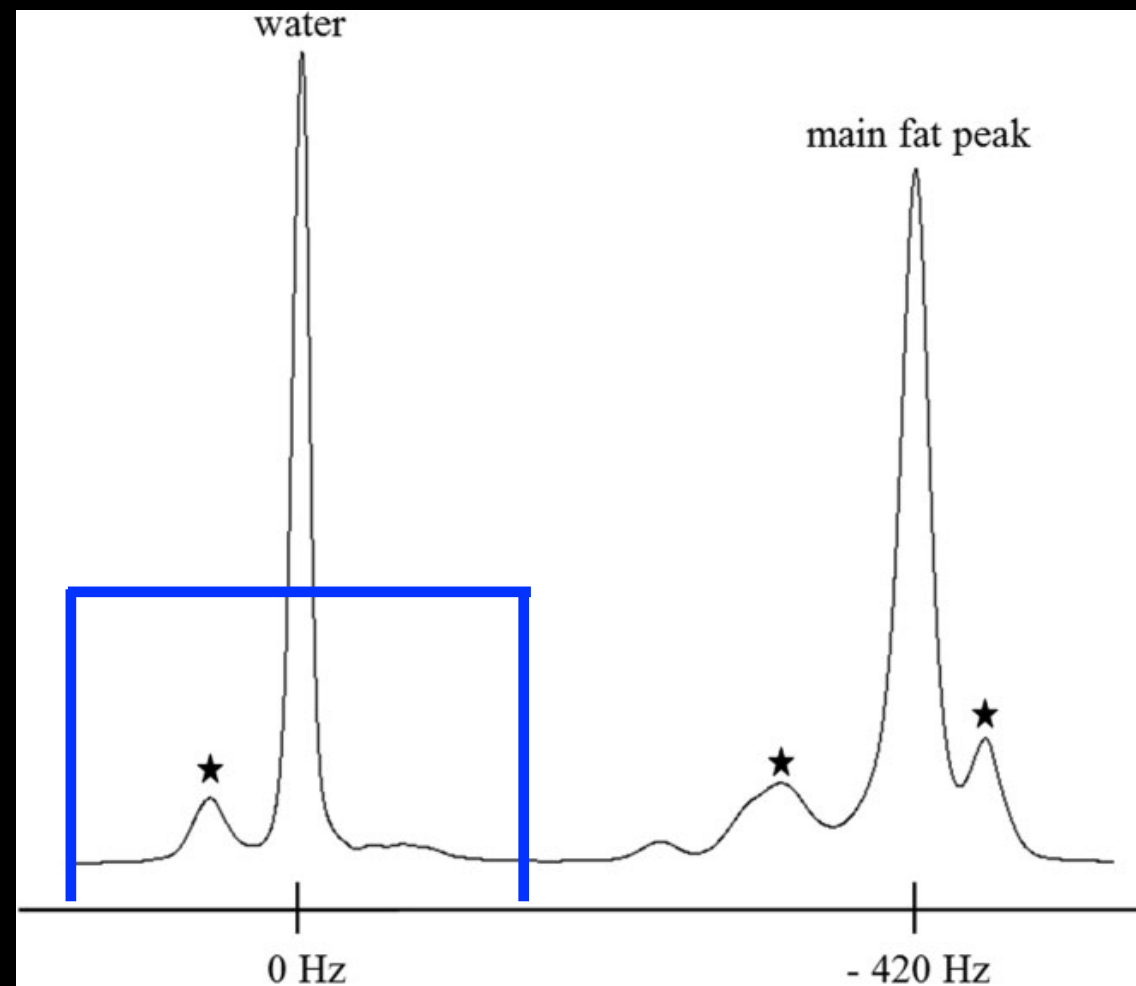
Example: 3D GRE with Fat-Sat at 3 T



Note that B_0 and B_1 variations are greater at 3.0 T

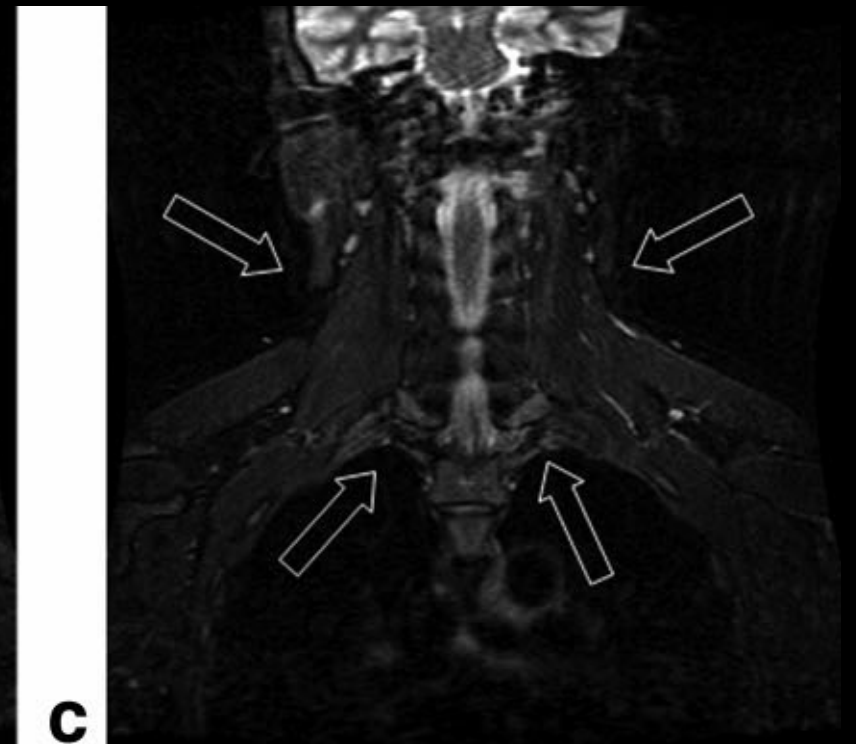
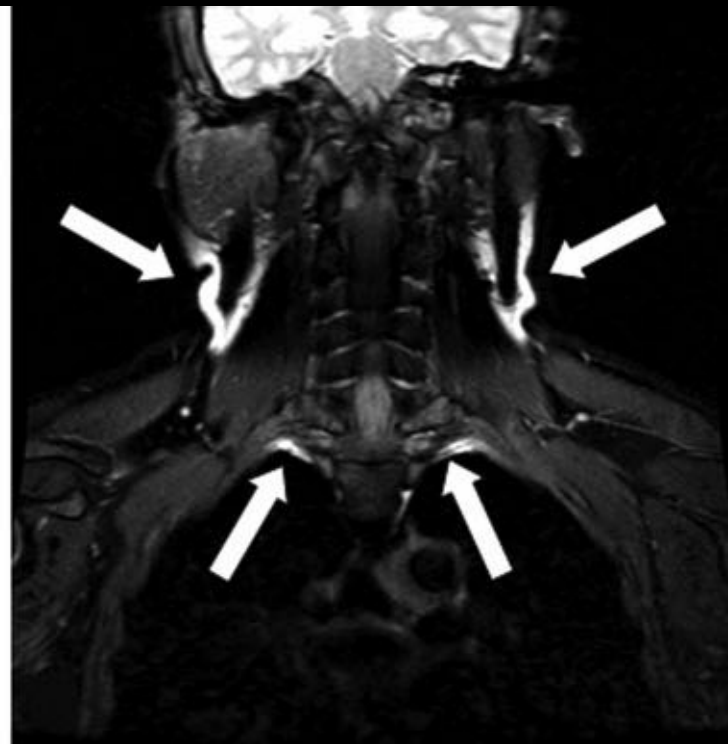
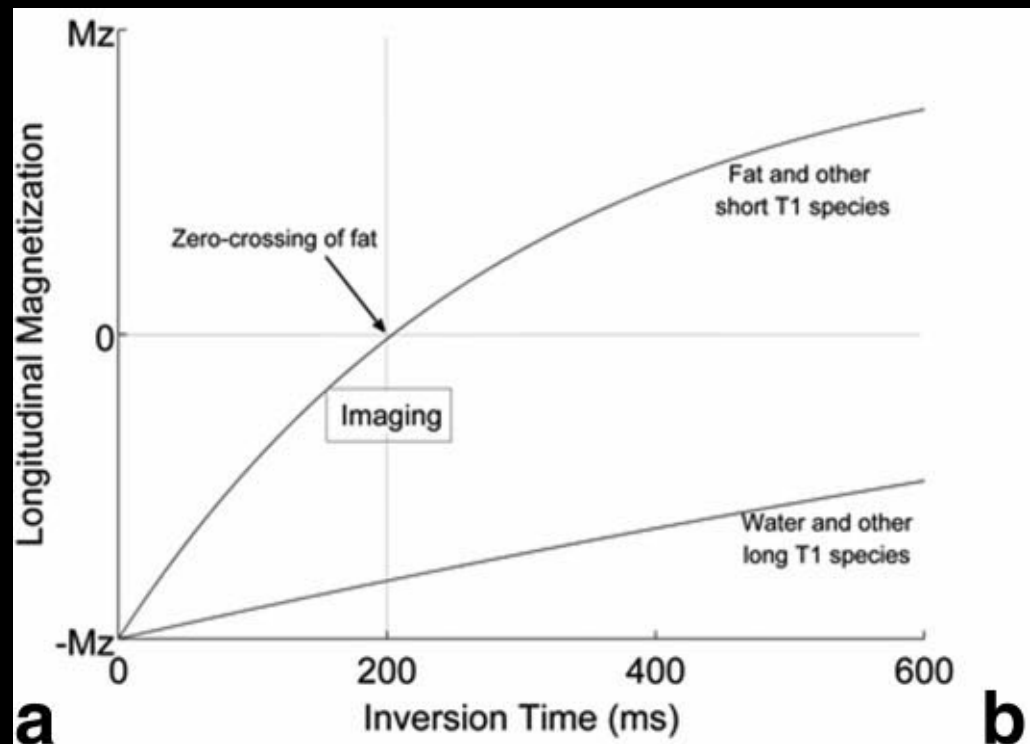
Fat Suppression

- Water-only excitation
 - relatively insensitive to B_1 variations
 - sensitive to B_0 variations



Fat Suppression

- Short-TI inversion recovery (STIR)
 - can be insensitive to B_0 variations
 - sensitive to B_1 variations
 - limits image contrast



Fat Suppression

Table 1
Most Commonly Used Techniques for Fat Suppression and Fat-Water Imaging

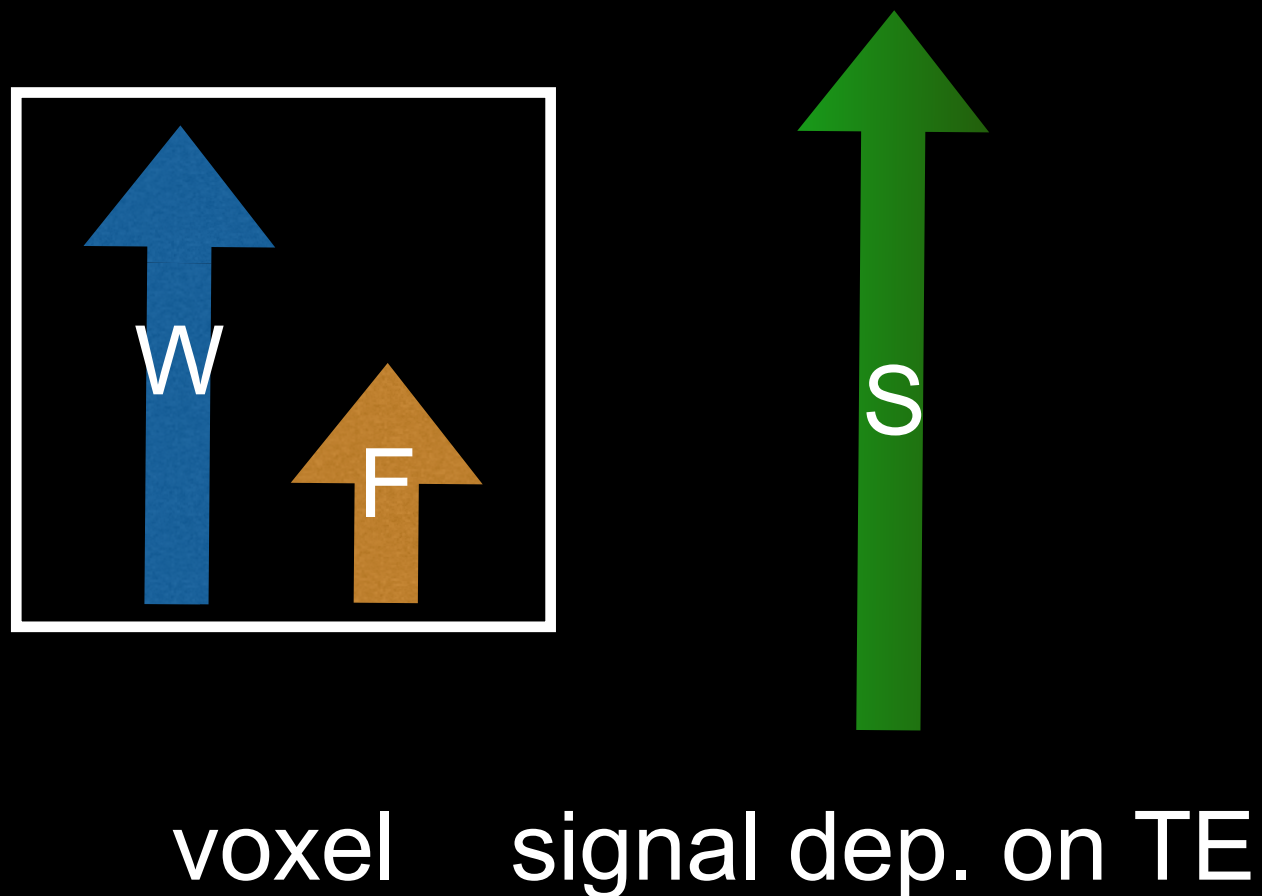
Method	Advantages	Disadvantages	Suggested applications
Chemically selective fat suppression	<ul style="list-style-type: none"> ● Versatile ● Relatively fast ● Applicable to most pulse sequences 	<ul style="list-style-type: none"> ● Sensitive to B_0 and B_1 inhomogeneities ● Low sequence efficiency 	<ul style="list-style-type: none"> ● Most applications except: ● Head and neck ● Mediastinum ● Extremities with metal implants
Spatial-spectral pulses, water excitation	<ul style="list-style-type: none"> ● Insensitive to B_1 inhomogeneities ● Versatile ● Relatively fast ● Practical to most pulse sequences except FSE 	<ul style="list-style-type: none"> ● Sensitive to B_0 inhomogeneities ● Low sequence efficiency ● Longer excitation pulses 	<ul style="list-style-type: none"> ● 3D imaging of cartilage in knee ● Most applications except: ● Head and neck ● Mediastinum ● Extremities
STIR	<ul style="list-style-type: none"> ● Robust to B_0 and B_1 inhomogeneities ● Reliable fat suppression 	<ul style="list-style-type: none"> ● Mixed contrast ● Inherent T_1 weighting ● Only works with PD and T_2W ● Low SNR efficiency ● Suppresses short T_1 species and enhancing tissue after contrast 	<ul style="list-style-type: none"> ● Head and neck ● Chest ● Abdomen ● Extremities ● Large field of view ● Inhomogeneous B_0 ● T_2/PD applications

Fat-Water-Separated MRI

- Separate fat from water
 - based on chemical shift freq differences
- Robust fat suppression
 - improve image contrast, esp. at 3.0 T
- Accurate fat quantification
 - tissue characterization: distribution and composition

Fat-Water-Separated MRI

Fat and water exhibit different MR frequencies
i.e., fat is slightly out-of-sync with water signal

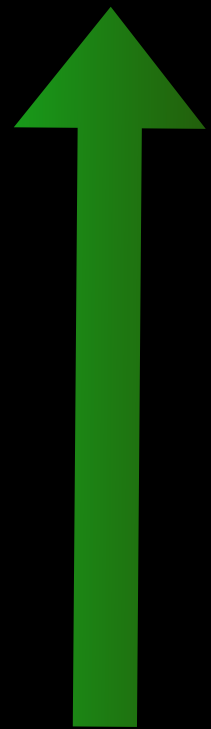


Fat-Water-Separated MRI

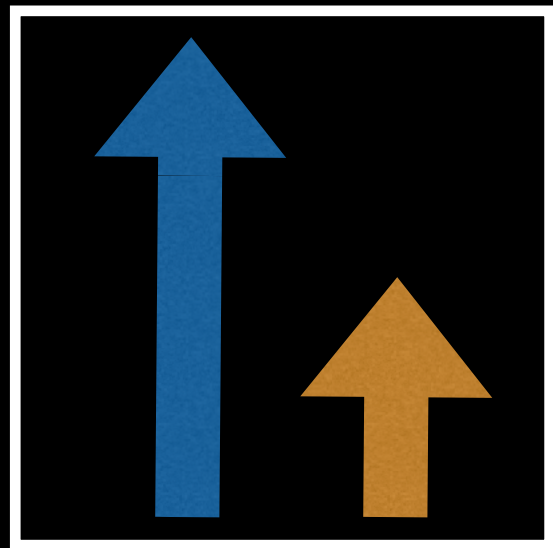
Acquire multiple images with different fat/water sync

in phase

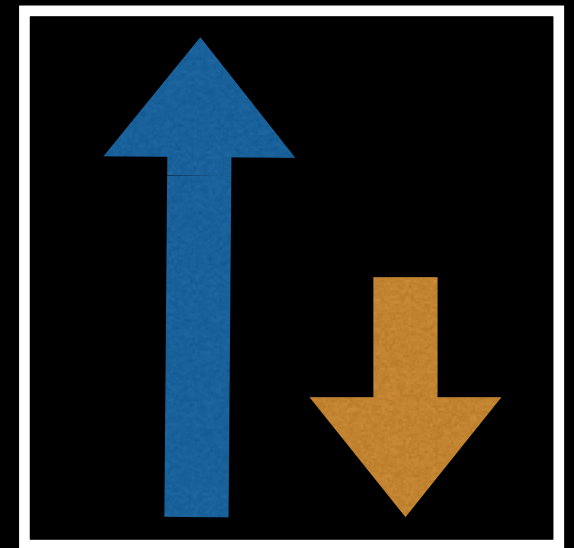
out of phase



S₁

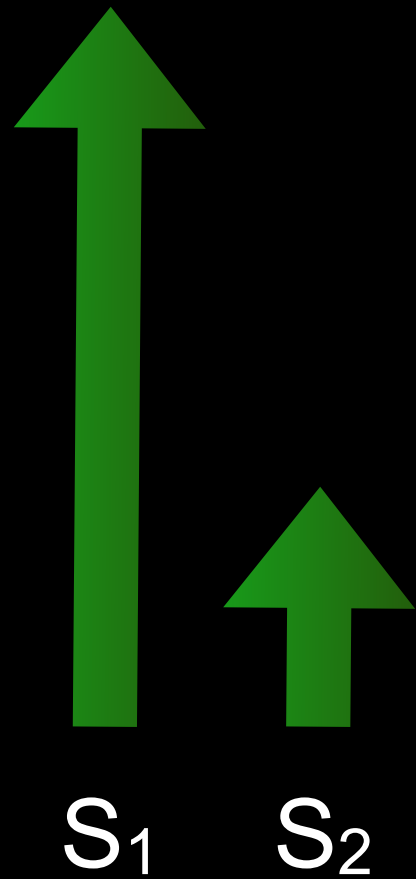


S₂

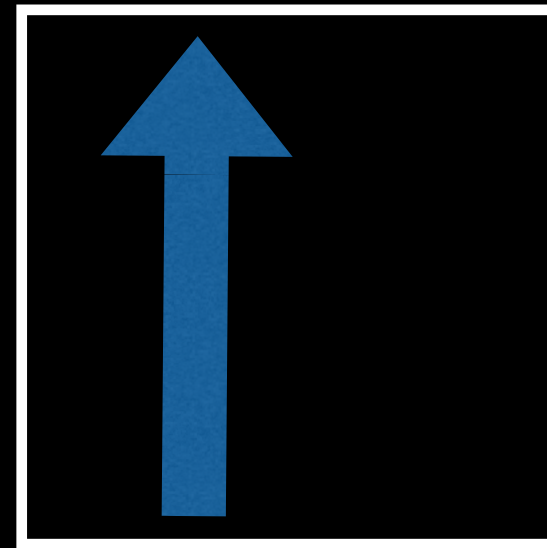


Fat-Water-Separated MRI

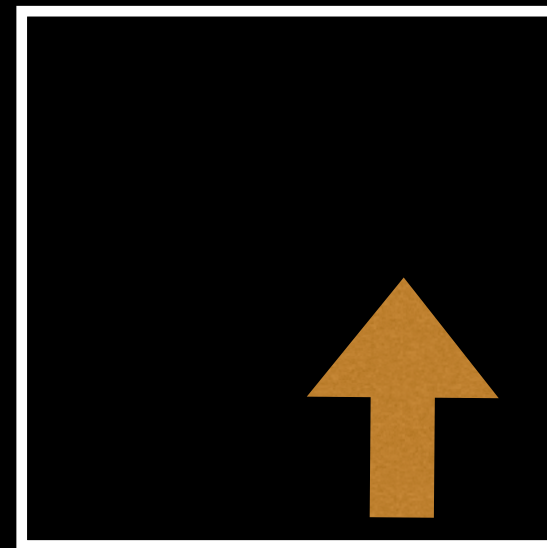
Estimate the water and fat component in each voxel



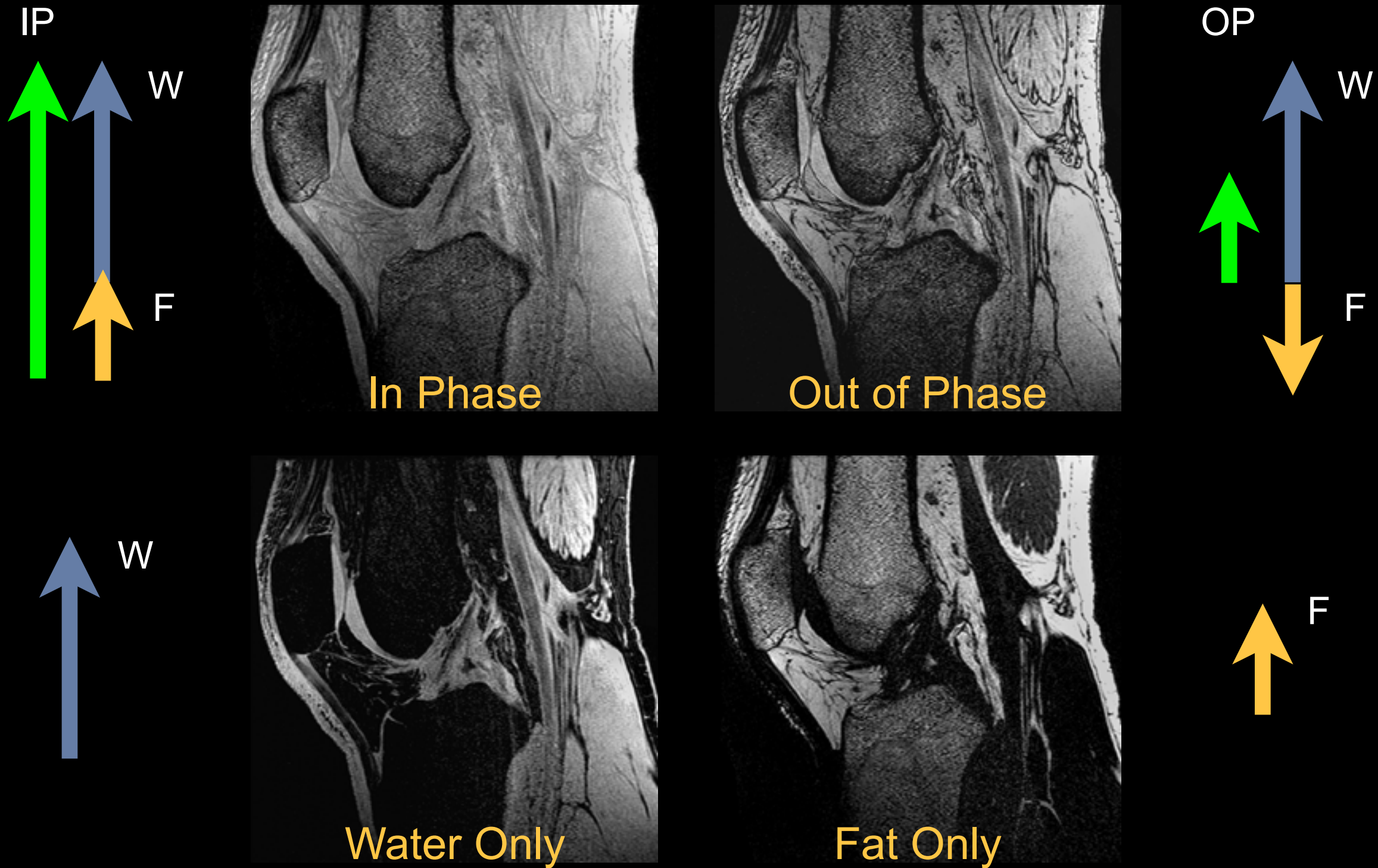
$$(S_1 + S_2) / 2 = W$$



$$(S_1 - S_2) / 2 = F$$



Fat-Water-Separated MRI



Fat-Water-Separated MRI

- In practice
 - other factors affect MR frequency
 - fat contains multiple subcomponents
 - need more than 2 measurements pts
 - need robust fat/water estimation algorithm
 - extra steps for quantitative fat fraction

2-Point Dixon

$$s(\mathbf{r}; \text{TE}_n) = s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}$$

$$s_0 = s(\mathbf{r}; \text{TE}_0) = s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_0} = s_W + s_F$$

$$2\pi\Delta f_{cs}\text{TE}_0 = 2n \cdot \pi \quad \text{“in-phase” (IP) TE}_0$$

$$s_1 = s(\mathbf{r}; \text{TE}_1) = s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_1} = s_W - s_F$$

$$2\pi\Delta f_{cs}\text{TE}_1 = (2n + 1)\pi \quad \text{“out-of-phase” (OP) TE}_1$$

2-Point Dixon

$$s_0 = s_W + s_F \quad \text{“in-phase” TE}_0 \quad (0, \pi) \text{ acquisition}$$

$$s_1 = s_W - s_F \quad \text{“out-of-phase” TE}_1$$

$$s_W = \frac{1}{2}(s_0 + s_1)$$

$$s_F = \frac{1}{2}(s_0 - s_1)$$

	in-phase TE (ms)	out-of-phase TE (ms)
1.5 T	0, 4.6, 9.2, 13.8, ...	2.3, 6.9, 11.5, ...
3.0 T	0, 2.3, 4.6, 6.9, ...	1.2, 3.5, 5.8, ...

not so simple in practice ...

2-Point Dixon: Limitations

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i\phi_0} \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s_0 = (s_W + s_F)e^{-i\phi_0} \quad \Delta\text{TE} = \text{TE}_1 - \text{TE}_0$$

$$s_1 = (s_W - s_F)e^{-i(\phi_0 + \phi)} \quad \phi = 2\pi\psi(\mathbf{r})\Delta\text{TE}$$

$$\begin{aligned} \hat{s}_W &= \frac{1}{2}(s_0 + s_1) \\ &= \frac{1}{2}e^{-i\phi_0} [s_W(1 + e^{-i\phi}) + s_F(1 - e^{-i\phi})] \end{aligned}$$

signal loss **crosstalk**

field map ψ causing a problem ...

3-Point Dixon

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i\varphi_0} \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s_{-1} = (s_W - s_F)e^{i\phi} \quad (-\pi, 0, \pi) \text{ acquisition} \quad \text{e.g., by SE}$$

$$s_0 = (s_W + s_F) \quad \phi = 2\pi\psi(\mathbf{r})\Delta\text{TE}$$

$$s_1 = (s_W - s_F)e^{-i\phi} \quad \text{note: } \phi_0 \text{ removed}$$

$$2\hat{\phi} = \angle(s_{-1}^* s_1) \quad \text{estimate and remove field map}$$

calculate s_W and s_F

3-Point Dixon

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i\varphi_0} \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s_0 = (s_W + s_F) \quad (0, \pi, 2\pi) \text{ acquisition} \quad \text{works better!}$$

$$s_1 = (s_W - s_F)e^{-i\phi} \quad \phi = 2\pi\psi(\mathbf{r})\Delta\text{TE}$$

$$s_2 = (s_W + s_F)e^{-i2\phi} \quad \text{note: } \phi_0 \text{ removed}$$

$$2\hat{\phi} = \angle(s_0^* s_2) \quad \text{estimate and remove field map}$$

$$\hat{s}_W = \frac{1}{2}[s_0 + s_1 e^{i\hat{\phi}}] \quad \hat{s}_F = \frac{1}{2}[s_0 - s_1 e^{i\hat{\phi}}]$$

$$\hat{s}_W = \frac{1}{4}[s_0 + s_2 e^{i2\hat{\phi}}] + \frac{1}{2}s_1 e^{i\hat{\phi}} \quad \text{better SNR}$$

3-Point Dixon: Limitations

Field map estimation

$$2\hat{\phi} = \angle(s_0^* s_2)$$

$2\hat{\phi}$ wraps at $[-\pi, \pi]$: $\hat{\phi}$ wraps at $[-\pi/2, \pi/2]$

if $\phi - \hat{\phi} = \pi$ water/fat swap!

phase unwrapping problem ... not solved yet

improve with polynomial fitting, region growing

Also have T_2 (T_2^*) decay as TE increases

Extended 2-Point Dixon

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i\phi_0} \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s_0 = (s_W + s_F)e^{-i\phi_0} \quad \Delta\text{TE} = \text{TE}_1 - \text{TE}_0$$

$$s_1 = (s_W - s_F)e^{-i(\phi_0 + \phi)} \quad \phi = 2\pi\psi(\mathbf{r})\Delta\text{TE}$$

extract ϕ_0 from phase of s_0 and remove from s_1

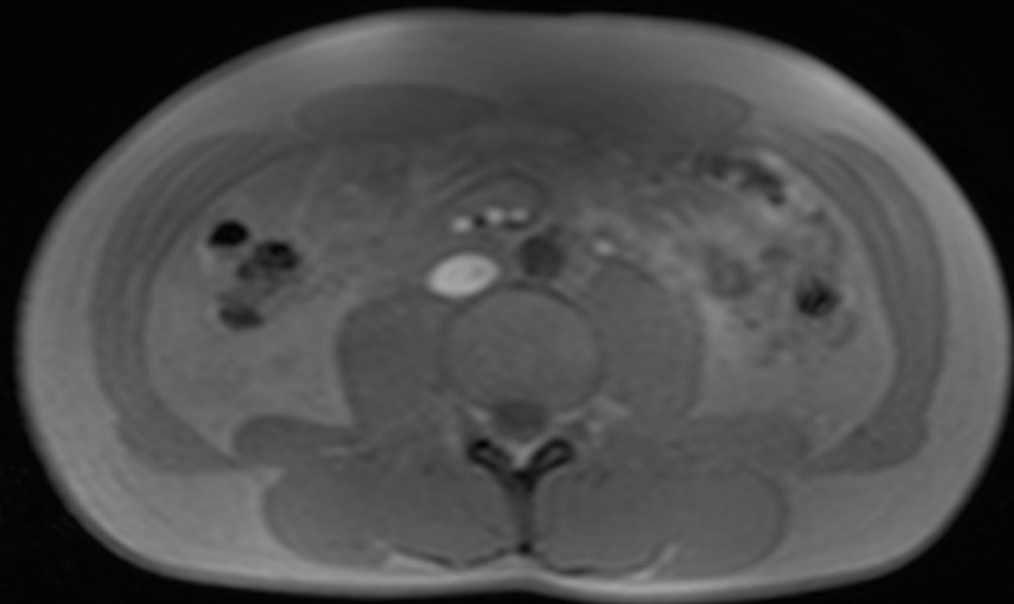
$$s'_1 = (s_W - s_F)e^{-i\phi} \quad (s'_1)^2 = |s_W - s_F|^2 e^{-i2\phi}$$

estimate 2ϕ from phase of $(s'_1)^2$ and remove ϕ

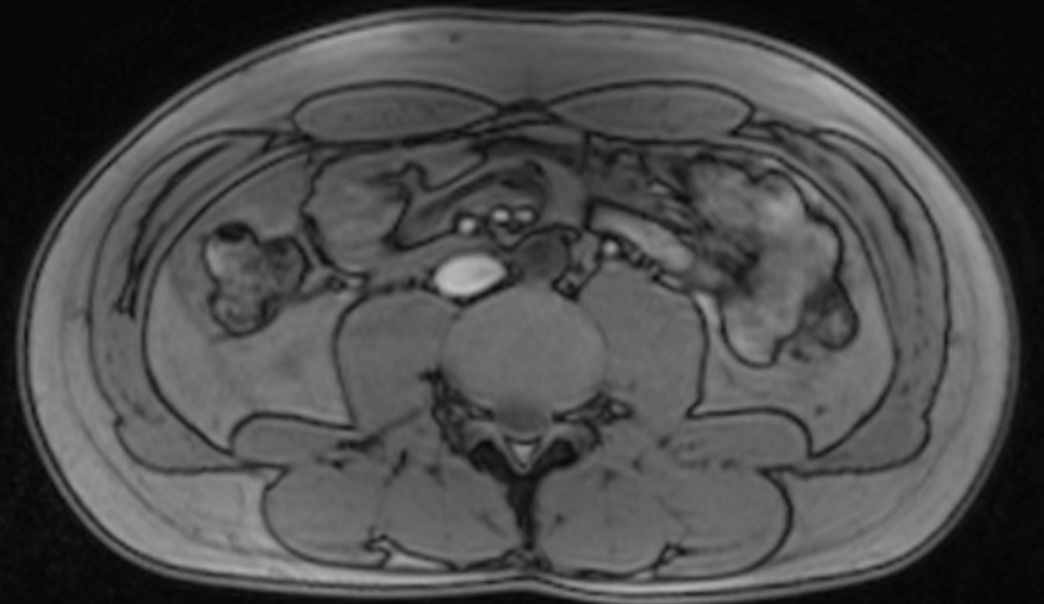
phase unwrapping problem... esp. challenging when $s_W \approx s_F$

Extended 2-Point Dixon

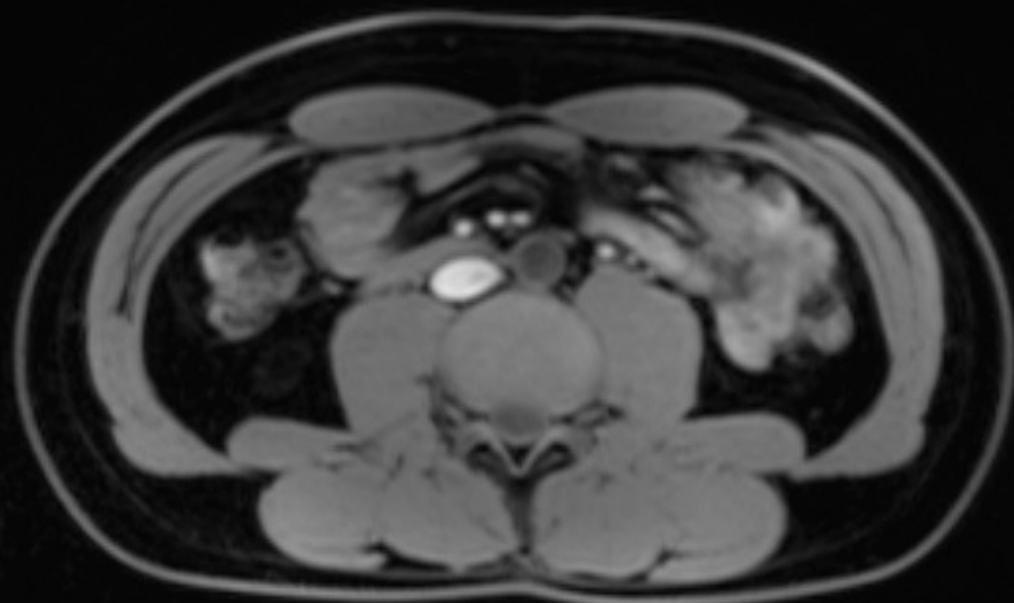
Example: 3 T abdominal scan



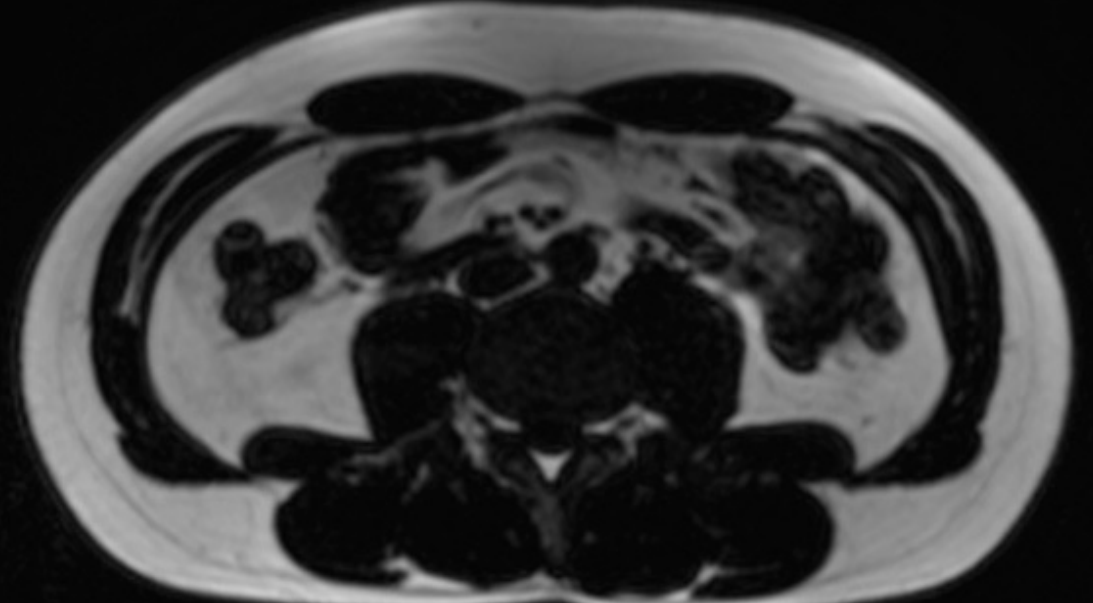
In-phase (3 T), TE = 2.6 ms



Out-of-phase (3 T), TE = 1.3 ms



Water



Fat

F/W MRI Sequence Design

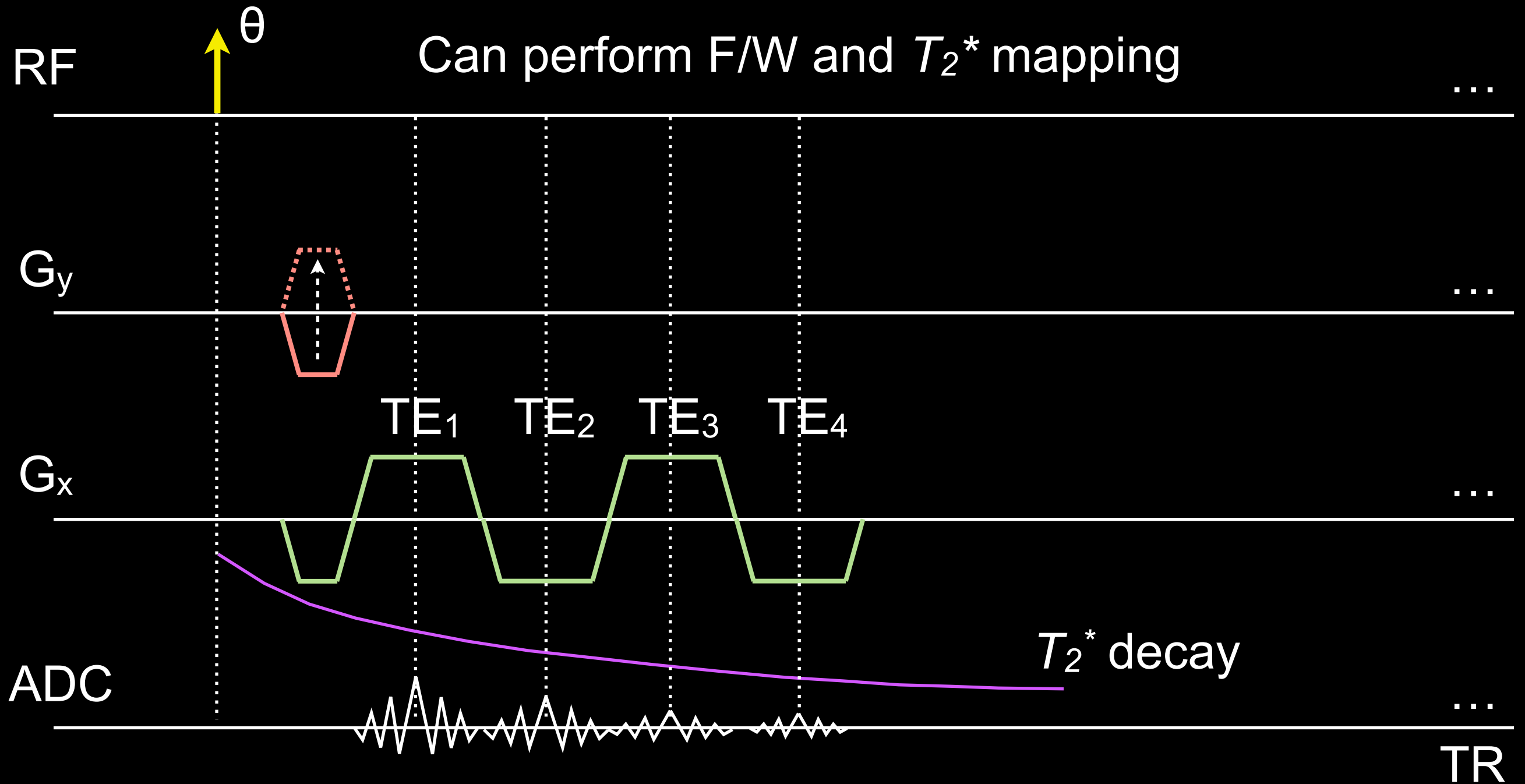
- Can be GRE, bSSFP, SE, FSE, etc.
 - can achieve negative F/W phase angles with SE-type sequences
- Need multiple TE_n 's ($n = 1 \dots N$)
 - repeat scans with different TEs
 - acquire multiple TEs each TR

F/W MRI Sequence Design

Multi-echo Gradient Echo (bipolar)

ΔTE can be non-uniform

Can perform F/W and T_2^* mapping

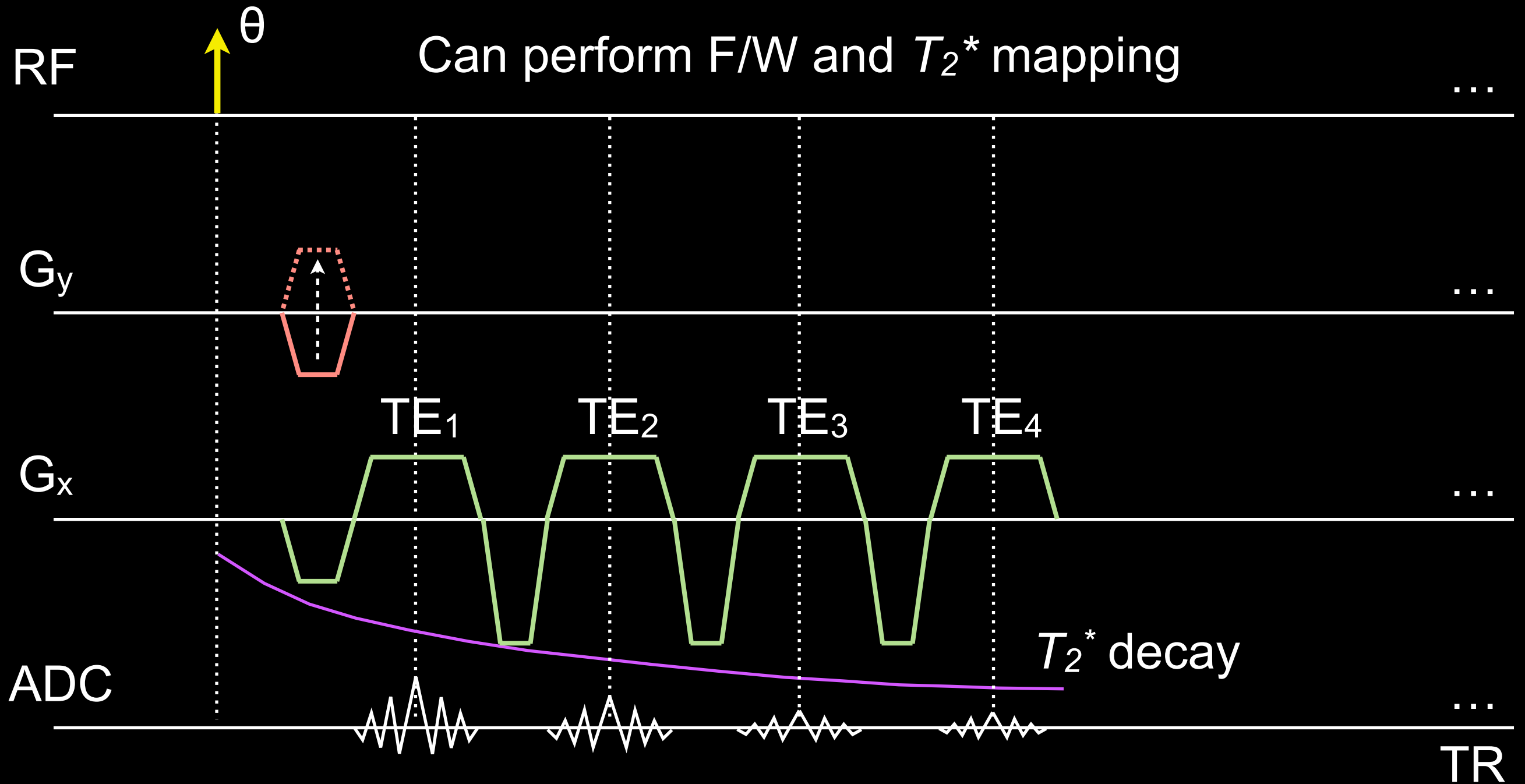


F/W MRI Sequence Design

Multi-echo Gradient Echo (unipolar)

ΔTE can be non-uniform

Can perform F/W and T_2^* mapping



F/W MRI Sequence Design

- ΔTE depends on
 - number of readout points (resolution)
 - readout bandwidth
 - image FOV
 - gradient and slew rate constraints
 - *same as EPI echo spacing*
- Number of TEs (N) depends on
 - initial TE
 - ΔTE
 - T_2^* decay
 - TR

Fat-Water-Separated MRI

Signal Equation

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

- $s(\mathbf{r}; \text{TE}_n)$: acquired images at TE_n
- known: $\Delta f_{cs} = -3.5$ ppm (-210 Hz @ 1.5 T)
- unknown: water s_W , fat s_F , and field map ψ
- non-linear equation due to ψ
- 2PD and 3PD look at special choices of TE_n

To be more flexible ... arbitrary choices of TE_n ?

Fat-Water-Separated MRI

Signal Equation Revisited

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})e^{-i2\pi\Delta f_{cs}\text{TE}_n}] \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

- known: Δf_{cs} and TE_n
- unknown: complex s_W , complex s_F , and scalar ψ
- measured: complex s_n ($n = 1 \dots N$)
- 5 unknowns, need $N = 3$ complex measurements
- solve **non-linear equation**

Fat-Water-Separated MRI

- Advanced algorithms
 - Single-point Dixon ($\pi/2$ acquisition)
 $s = (s_W + i s_F)$
 - Direct phase encoding ($\theta_0, \theta_0 + \theta, \theta_0 + 2\theta$)
 - 2PD with flexible TEs
 - Iterative least squares (e.g., IDEAL)
 - Graph cut
 - Magnitude-based F/W separation
 - *and more!*
- many are available in the ISMRM Toolbox

F/W MRI using IDEAL

PDw FSE, 1.5 T, TE shifts of (-1, 0, 1) ms



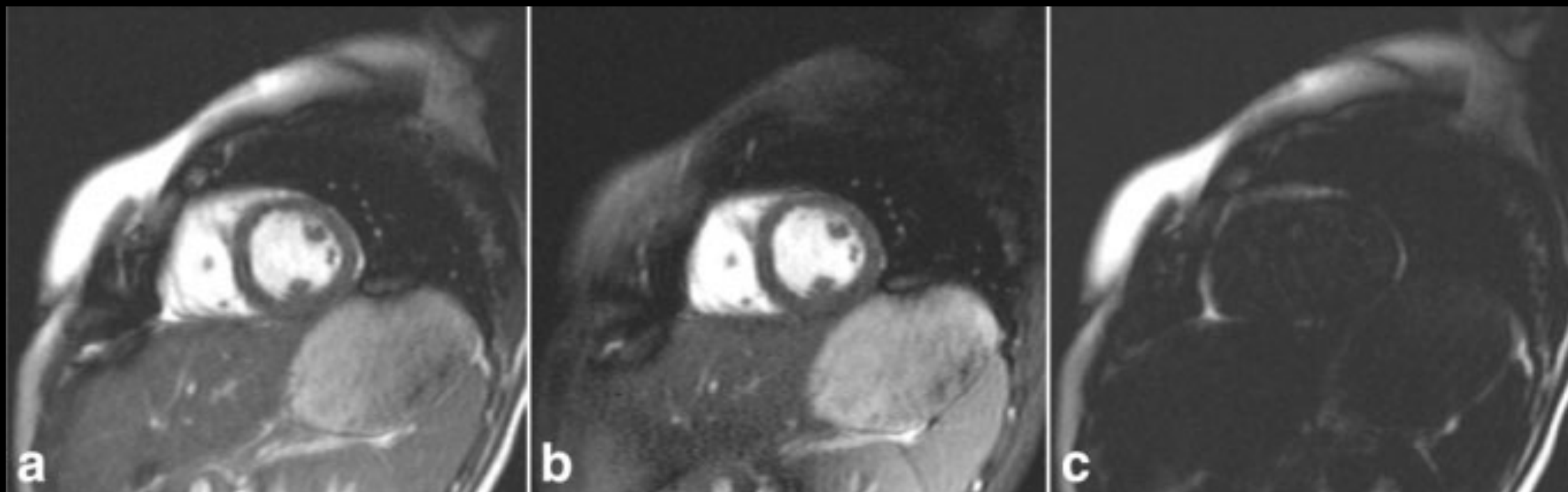
source

water

fat

F/W MRI using IDEAL

bSSFP, 1.5 T, TE/TR = (0.9, 1.9, 2.9)/5.2 ms



source

water

fat

F/W MRI: SNR Performance

Multiple TEs requires longer scan ...

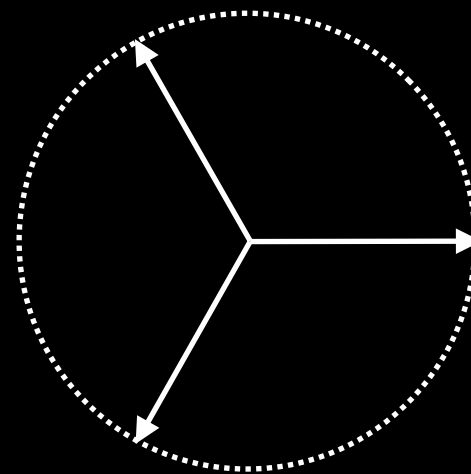
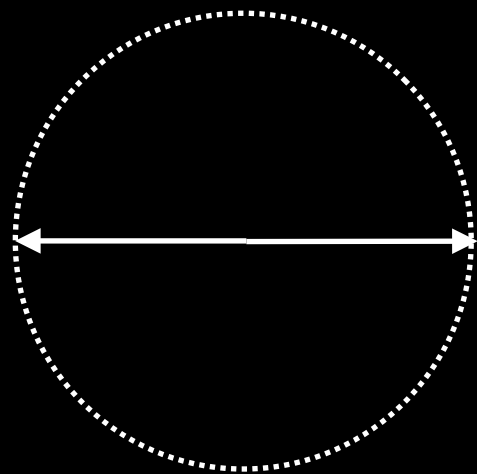
F/W calculation needs to be SNR efficient!

Effective Number of Signal Averages (NSA)

2PD $(0, \pi)$: NSA = 2

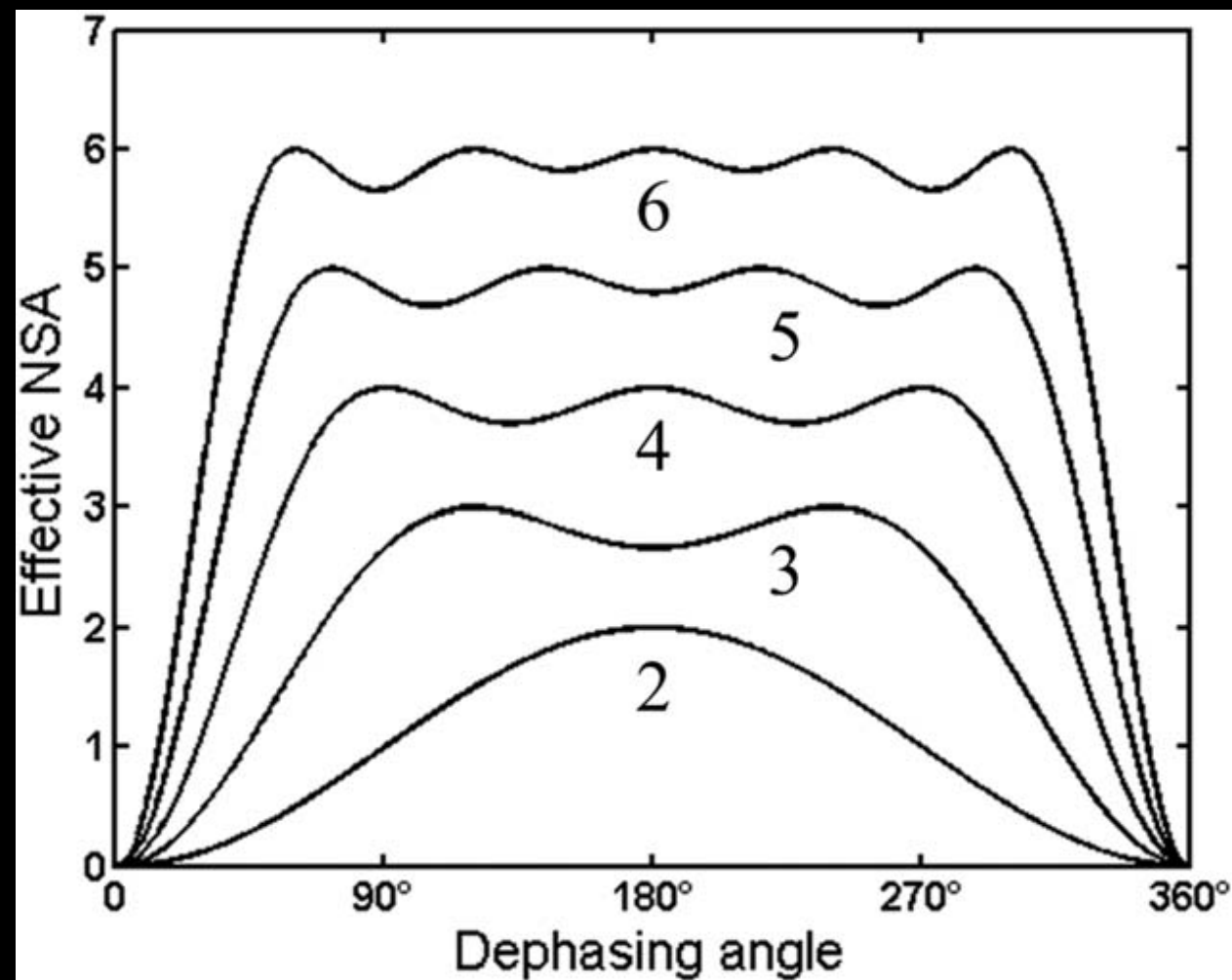
3PD $(0, \pi, 2\pi)$: NSA = 2.67

$(0, 2\pi/3, 4\pi/3)$: NSA = 3



F/W MRI: SNR Performance

In general, want phase angles evenly distributed over 2π
less critical as number of TEs increases



F/W MRI: SNR Performance

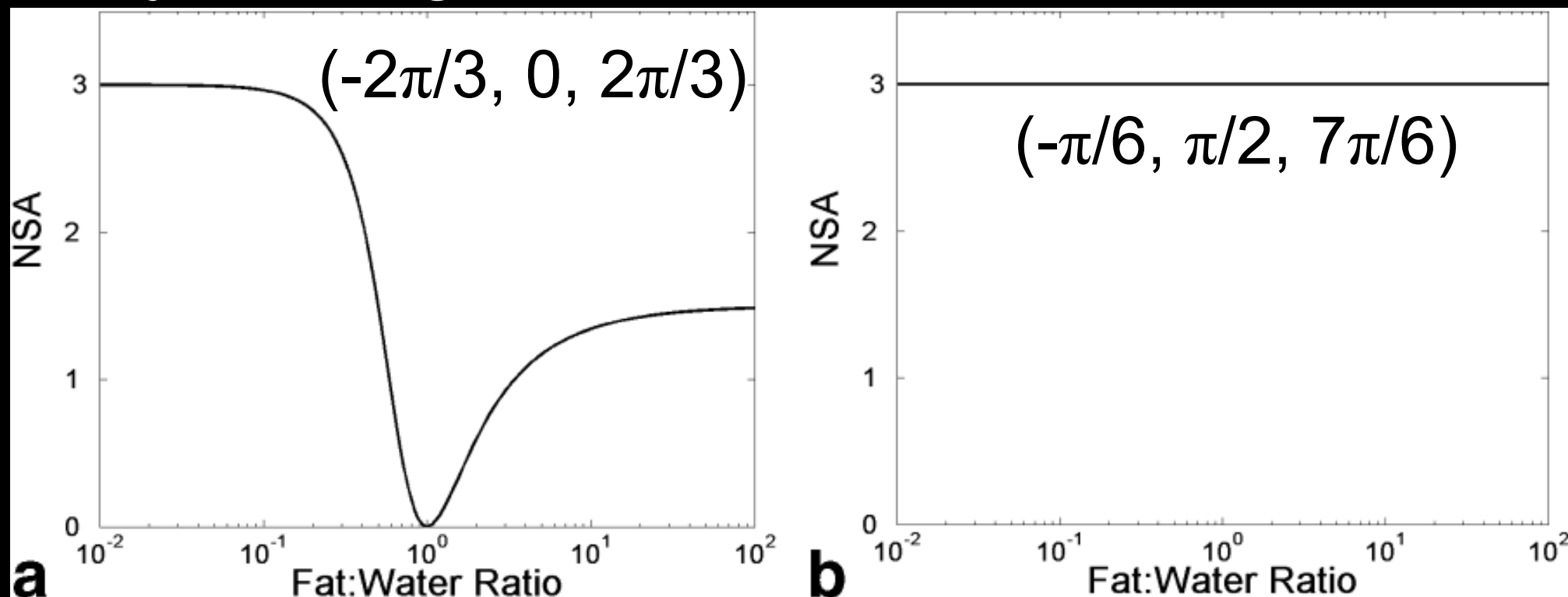
NSA depends on

ΔTE

actual TEs

fat/water ratio in each voxel

Can analyze using Cramer-Rao Bounds, Monte-Carlo sim



Reeder SB et al., MRM, 2005; 54: 636-644

Pineda AR et al., MRM 2005; 54: 625-635

Fat-Water-Separated MRI

Signal Equation (augmented)

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r})e^{-\text{TE}_n/T_{2,W}^*(\mathbf{r})} + \sum_{j=1}^M s_{F,j}(\mathbf{r})e^{-i2\pi\Delta f_{cs,j}\text{TE}_n} e^{-\text{TE}_n/T_{2,Fj}^*(\mathbf{r})}] \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r})e^{-\text{TE}_n/T_{2,W}^*(\mathbf{r})} + s_F(\mathbf{r})\sum_{j=1}^M \alpha_j e^{-i2\pi\Delta f_{cs,j}\text{TE}_n} e^{-\text{TE}_n/T_{2,Fj}^*(\mathbf{r})}] \cdot e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

$$s(\mathbf{r}; \text{TE}_n) = [s_W(\mathbf{r}) + s_F(\mathbf{r})\sum_{j=1}^M \alpha_j e^{-i2\pi\Delta f_{cs,j}\text{TE}_n}] \cdot e^{-\text{TE}_n/T_{2,W}^*(\mathbf{r})} e^{-i2\pi\psi(\mathbf{r})\text{TE}_n}$$

- $T_{2,W}^*$ decay as TE_n increases
- fat spectrum has multiple components (peaks)
- can assume single $T_{2,W}^*$ and reference fat spectrum
- solve for water s_W , fat s_F , $T_{2,W}^*$, and field map ψ
- need more measurements ($N \geq 4$)

Fat Quantification

- Qualitative F/W MRI
 - separate fat from water signal
 - $N = 2$ or 3 TEs is common
- Quantitative F/W MRI
 - distribution / volume of fat
 - composition of fat (fat/water ratio):
multi-peak and T_2^* modeling
 $N = 6+$ TEs is recommended

Fat Quantification

Signal Fat Fraction

$$\text{sFF}(\mathbf{r}) = \frac{|s_F(\mathbf{r})|}{|s_W(\mathbf{r})| + |s_F(\mathbf{r})|}$$

- easy to calculate
- amount of fat “signal” in each voxel
- not necessarily amount of “fat”
- hard to reproduce with different scan parameters

Fat Quantification

Signal Equation (RF-spoiled GRE)

$$s_X(T_1, TR, \theta) = \rho_X \cdot \frac{(1 - e^{-TR/T_1}) \sin \theta}{1 - e^{-TR/T_1} \cos \theta}$$

- s depends on T_1 , TR, θ
- T_1 bias for sFF calculations
minimize with low θ and long TR
- different equations for SE, bSSFP, etc.

Fat Quantification

Proton Density Fat Fraction

$$\text{PDFF}(\mathbf{r}) = \frac{\rho_F(\mathbf{r})}{\rho_W(\mathbf{r}) + \rho_F(\mathbf{r})}$$

- need to correct for T_1 , θ , noise effects
- potential role as an imaging biomarker

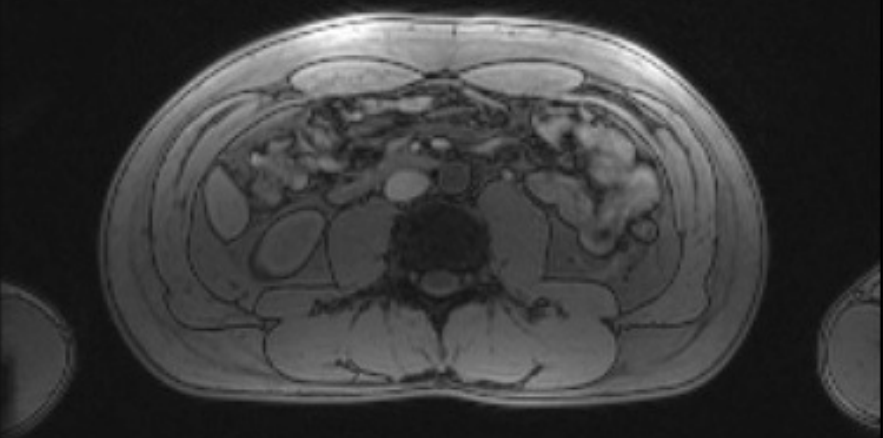
Liver Fat Quantification

- Non-alcoholic fatty liver disease (NAFLD) is the leading cause of chronic liver disease
- Current gold standard is biopsy
- MRI fat quantification is becoming the new gold standard

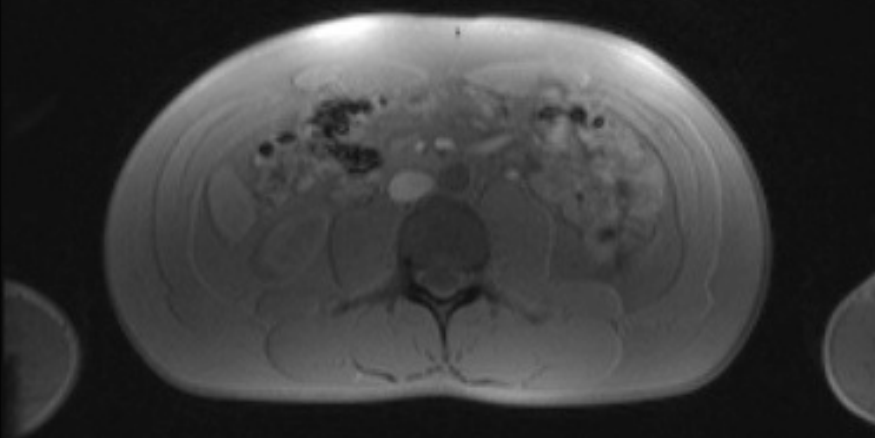
Liver Fat Quantification

Example: Multi-echo GRE in liver at 3 T

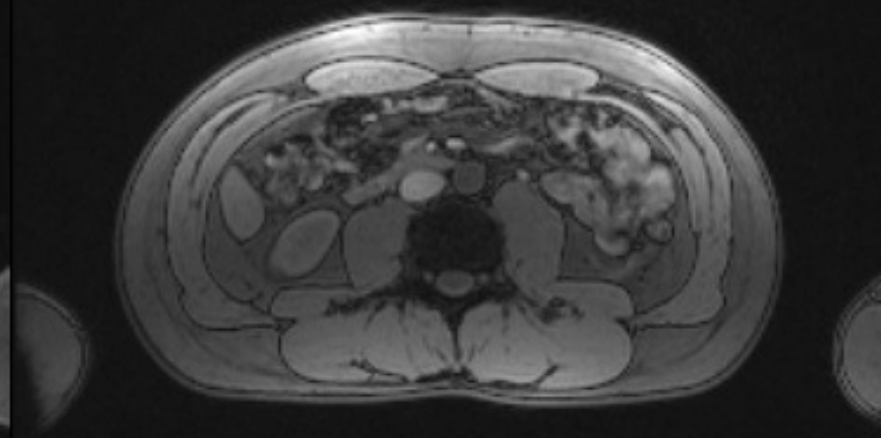
TE = 1.2 ms



TE = 2.5 ms

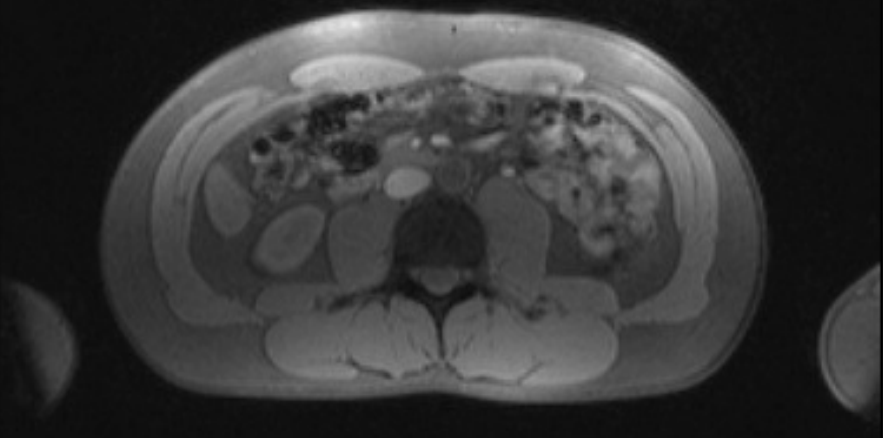


TE = 3.7 ms

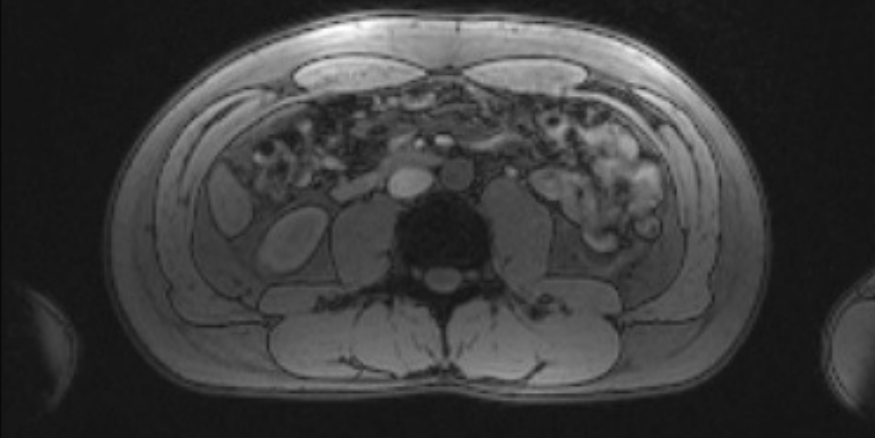


TR = 9.2 ms, $\theta = 4^\circ$, 22 sec BH scan

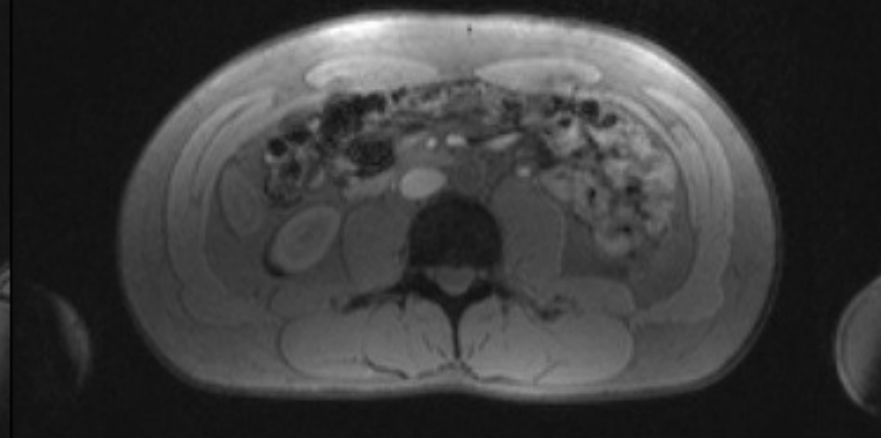
TE = 4.9 ms



TE = 6.2 ms



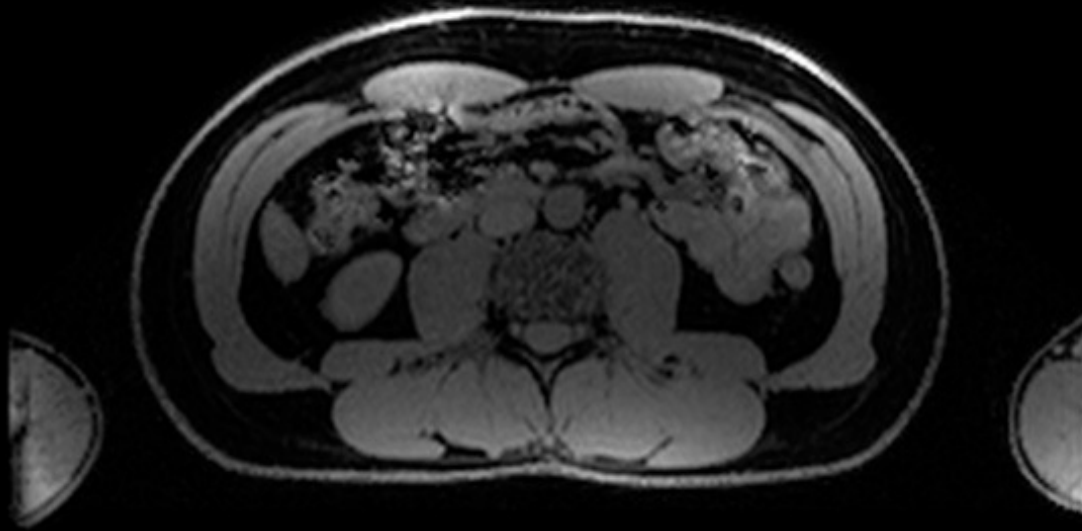
TE = 7.4 ms



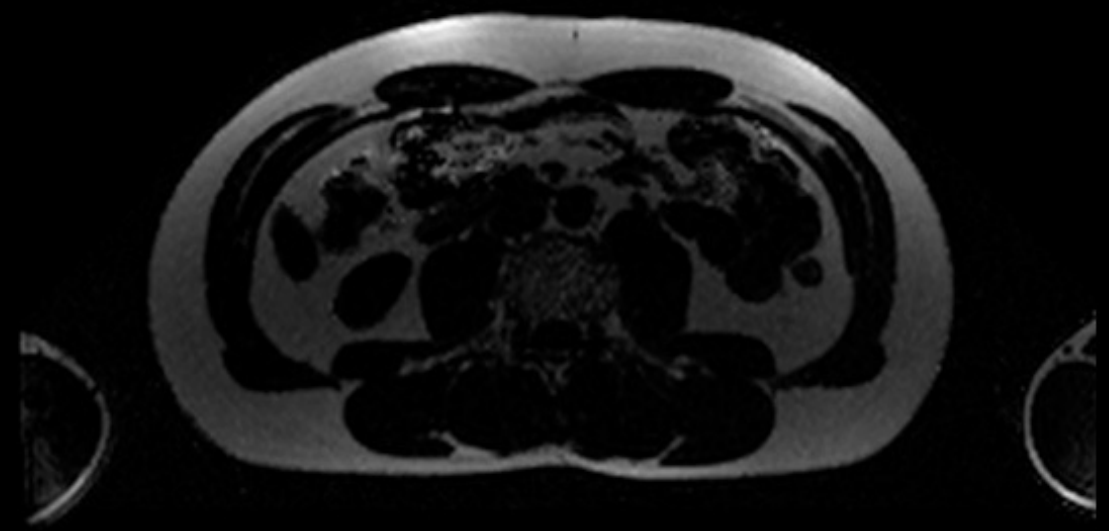
Liver Fat Quantification

Example: Multi-echo GRE in liver at 3 T

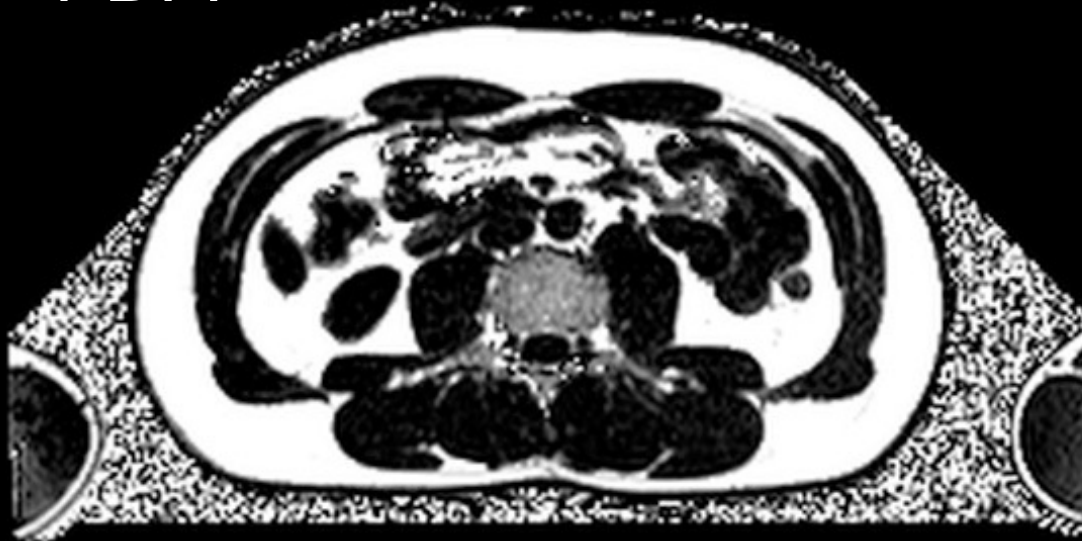
Water



Fat



PDFF



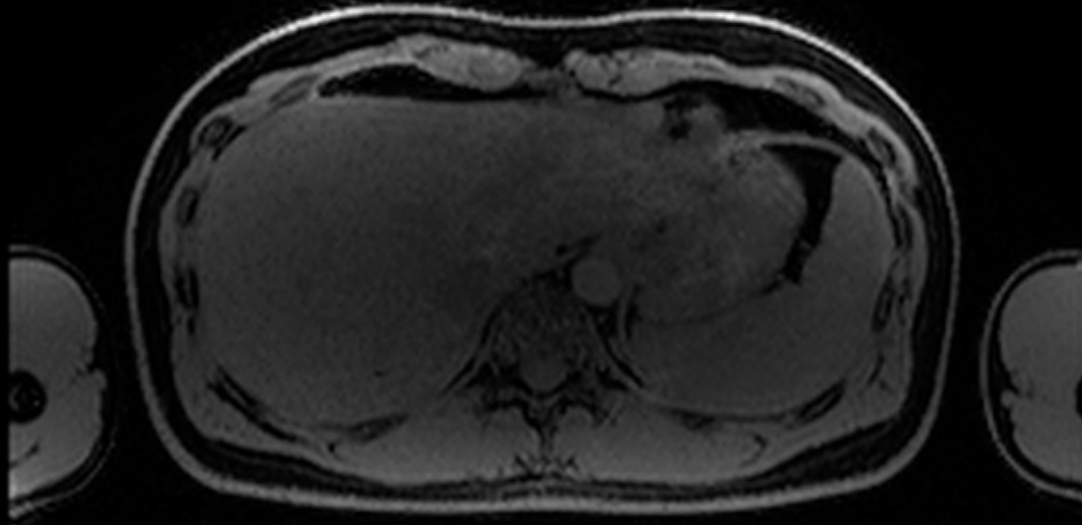
R_2^*



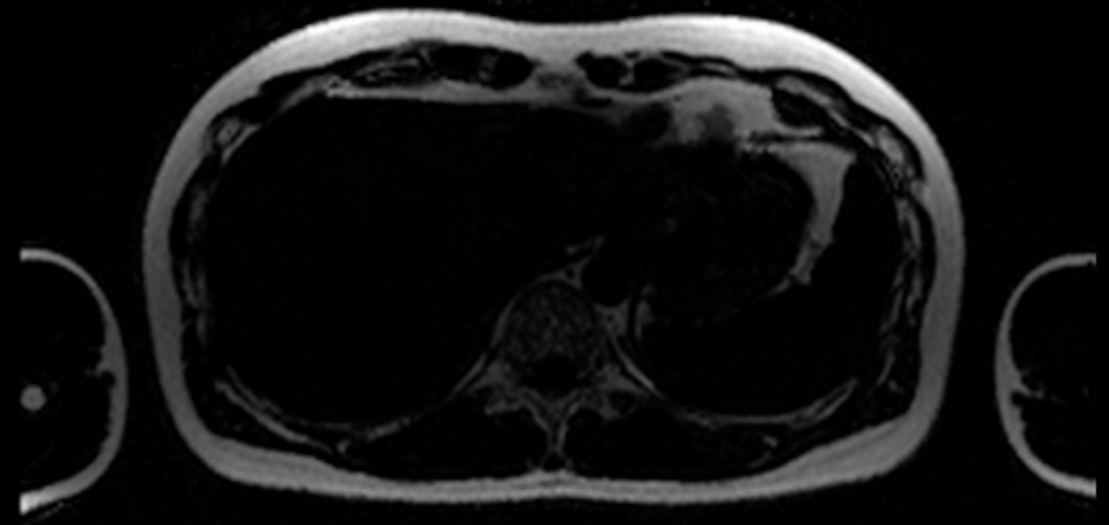
Liver Fat Quantification

Example: Multi-echo GRE in liver at 3 T

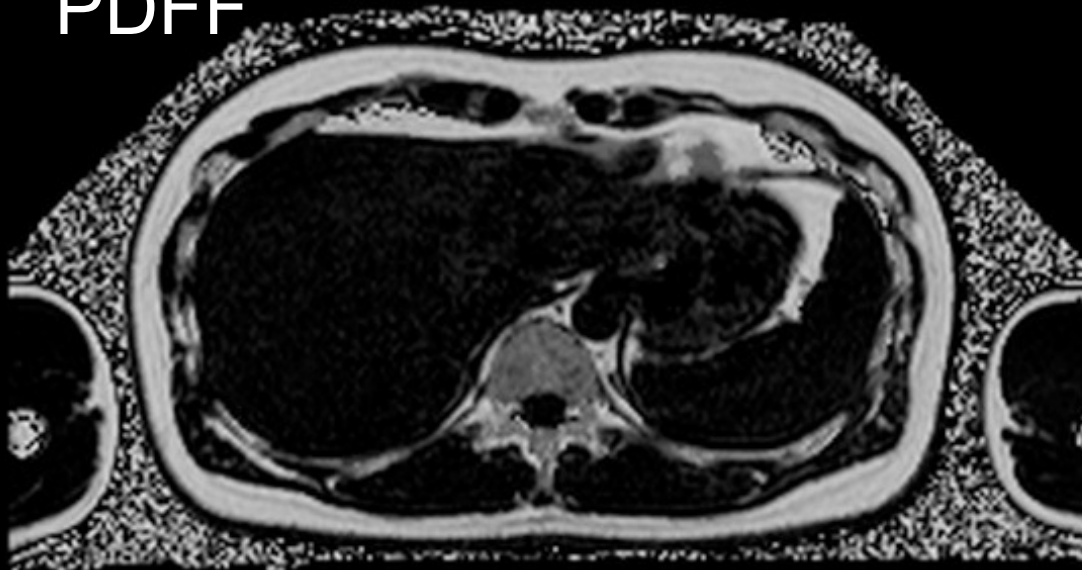
Water



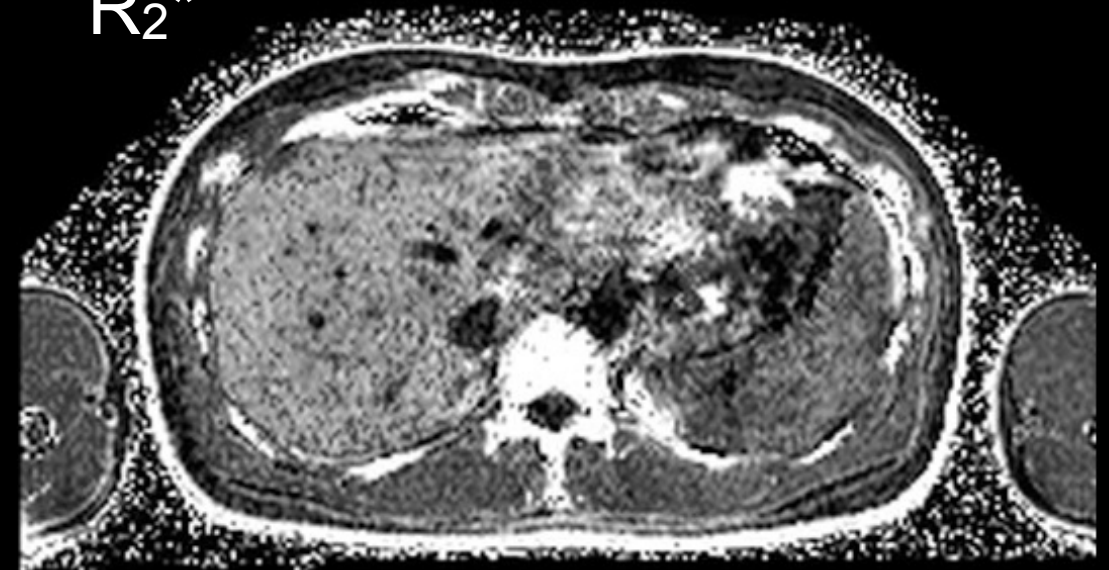
Fat



PDFF

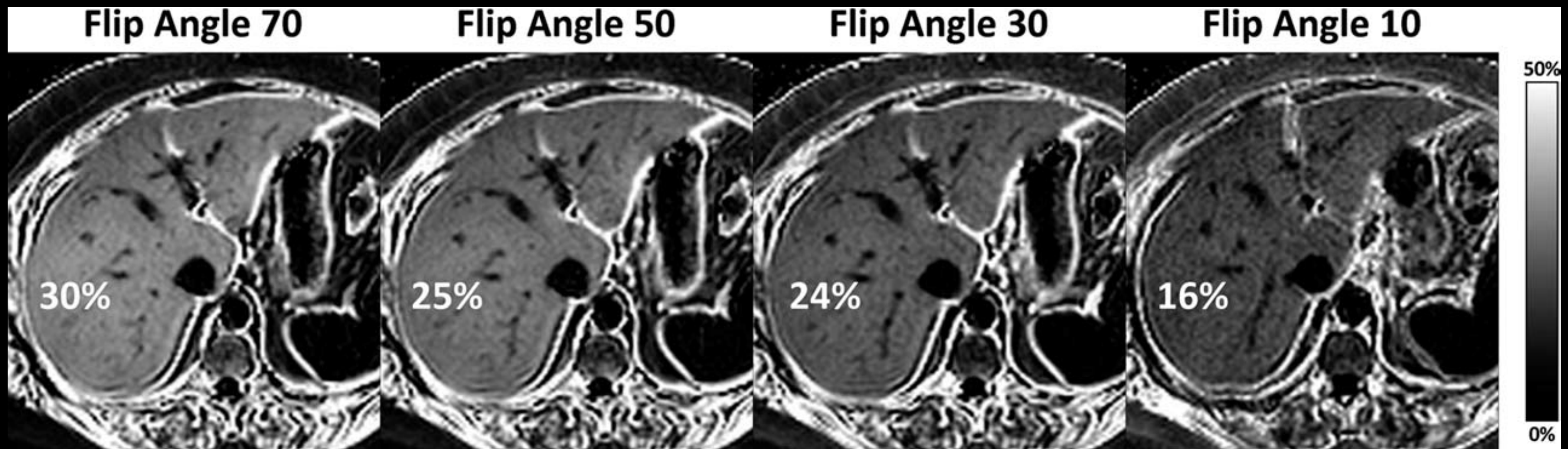


R_2^*



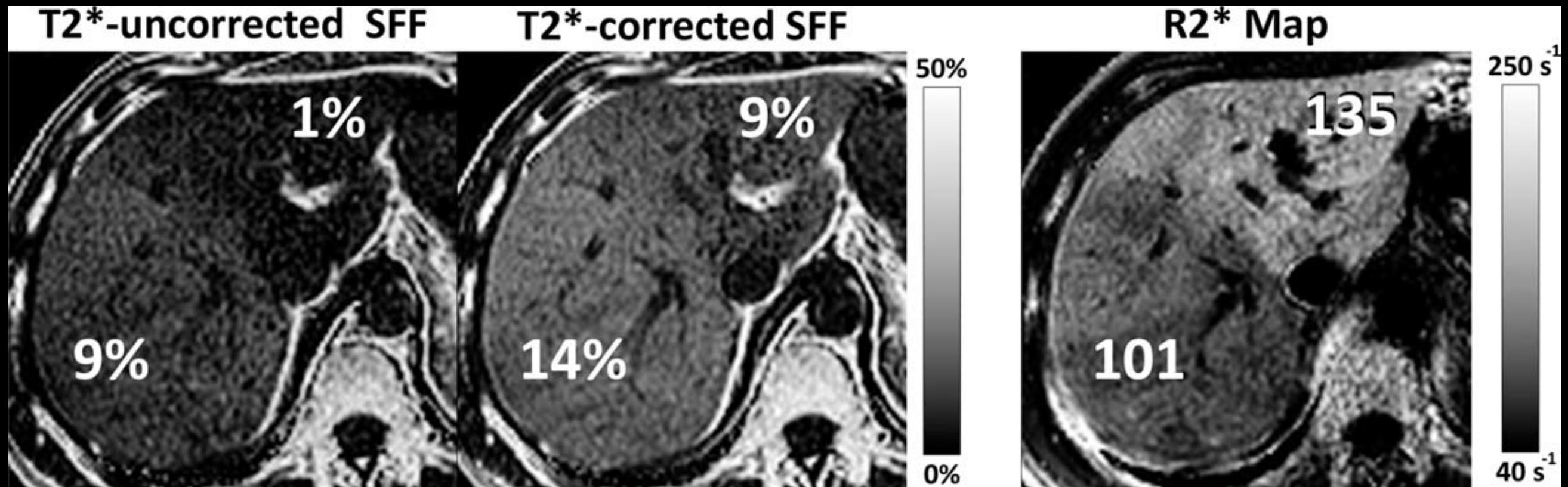
Liver Fat Quantification

Reduce T_1 bias by using low flip angle



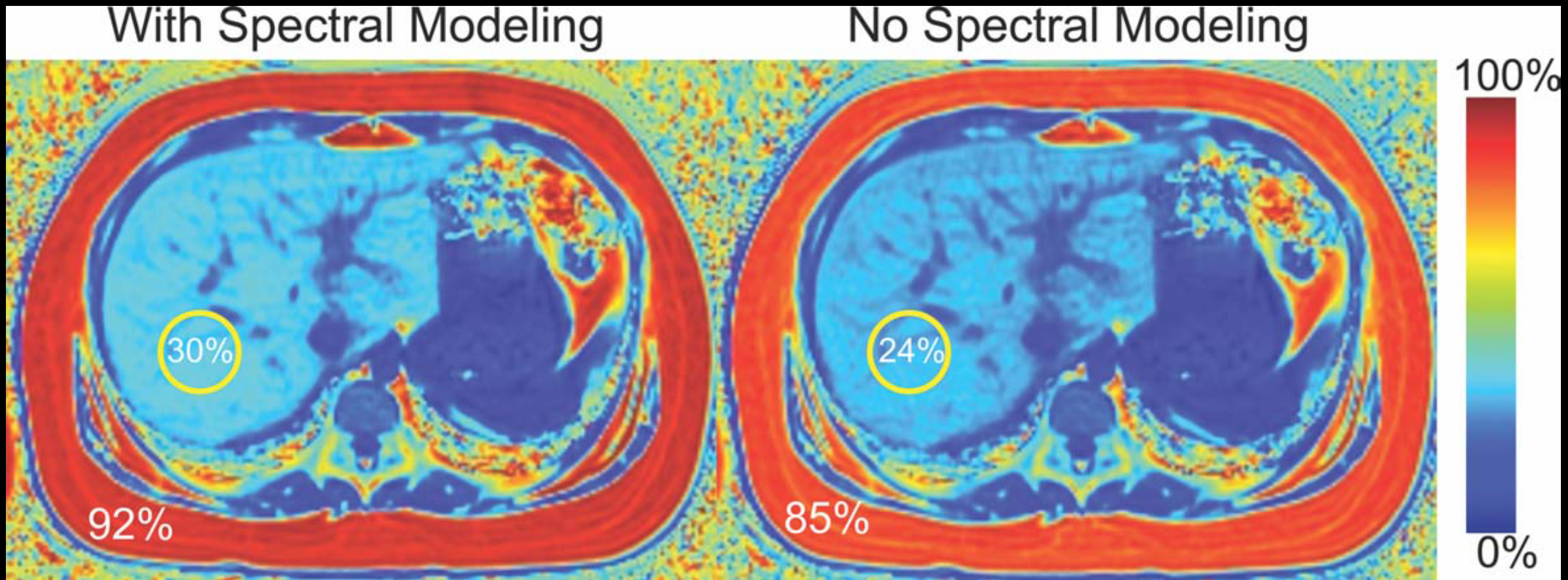
Liver Fat Quantification

Account for T_2^* effects



Liver Fat Quantification

Account for multiple peaks in fat spectrum



fat peaks near water account for ~8% of fat signal

Liver Fat Quantification

Account for multiple peaks in fat spectrum

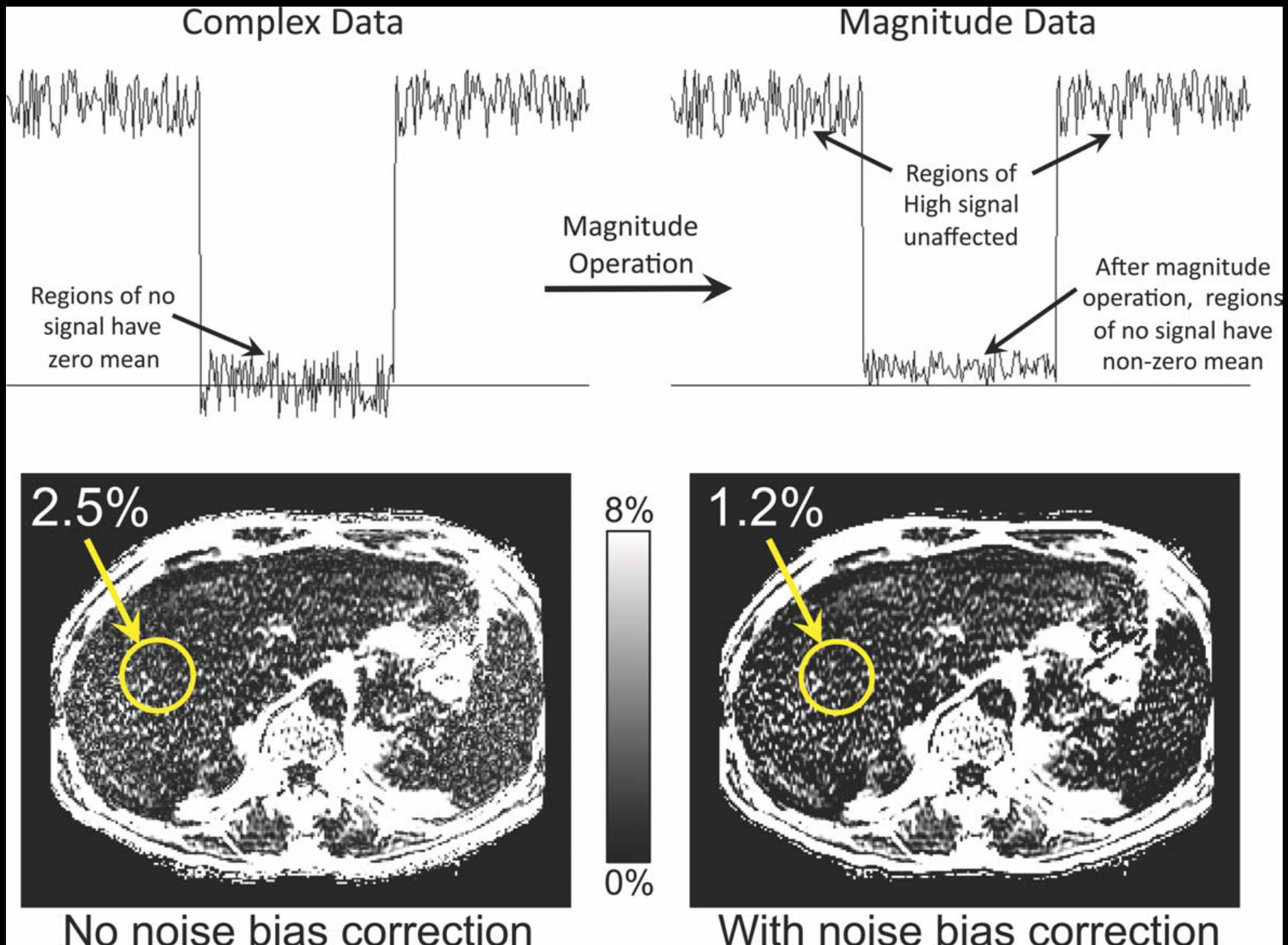
Table 1
Proton MR Spectrum of Liver Triglycerides

Peak	In vivo ppm	Ex vivo ppm	Chemical environment	Type	Relative magnitude
1	5.3	5.29	-CH =CH-	Olefinic	4.7%
		5.19	-CH-O-CO-	Glycerol	
Water	4.7	4.70	H ₂ O	—	—
2	4.2	4.20	-CH ₂ -O-CO-	Glycerol	3.9%
3	2.75	2.75	-CH=CH-CH ₂ -CH=CH-	Diacyl	0.6%
4	2.1	2.24	-CO-CH ₂ -CH ₂ -	α-Carboxyl	12.0%
		2.02	-CH ₂ -CH=CH-CH ₂ -	α-Olefinic	
5	1.3	1.60	-CO-CH ₂ -CH ₂ -	β-Carboxyl	0.7
		1.30	-(CH ₂) _n -	Methylene	
6	0.9	0.9	-(CH ₂) _n -CH ₃	Methyl	0.088

fat peaks near water account for ~8% of fat signal

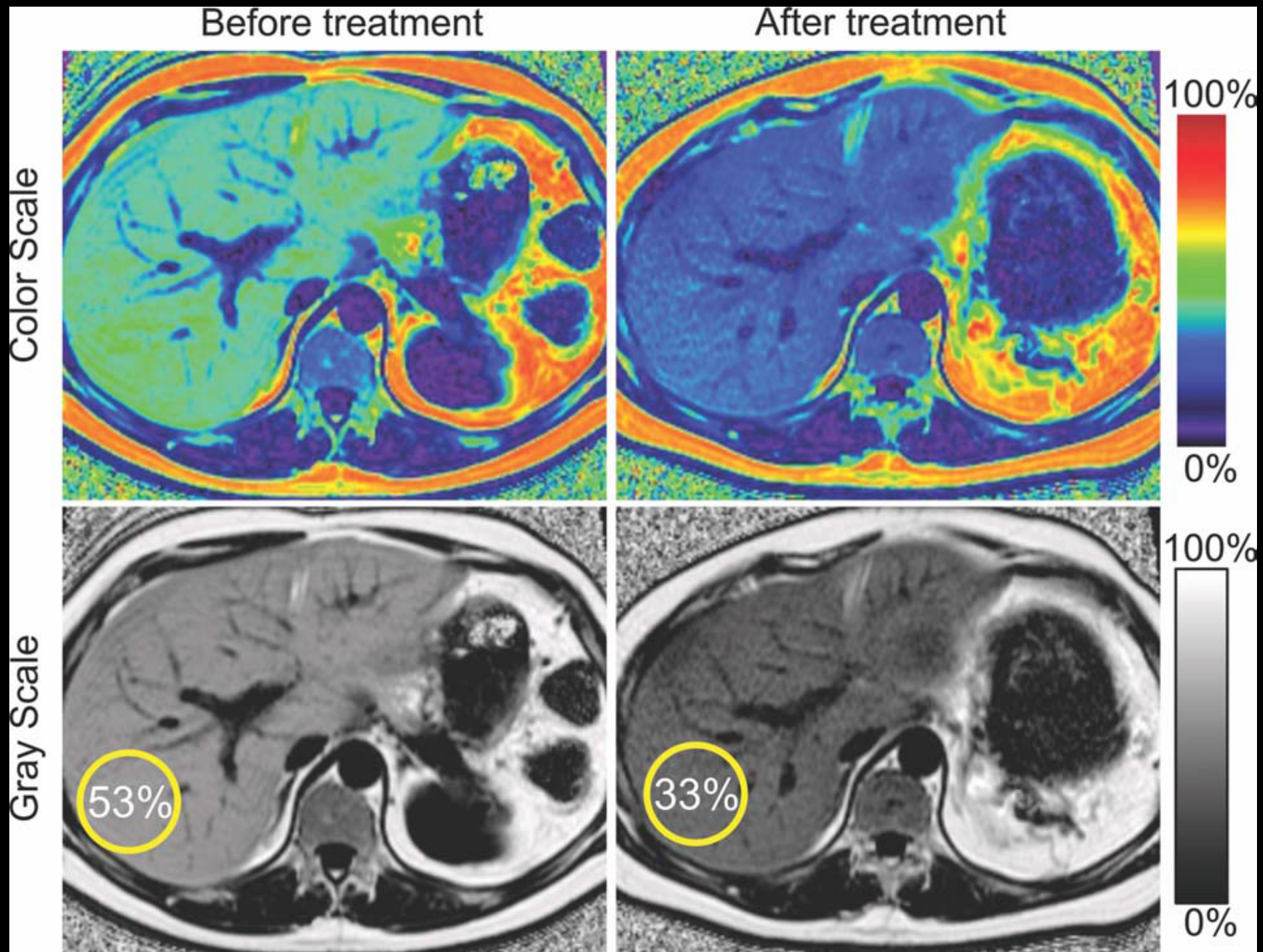
Liver Fat Quantification

Correct for noise bias



Liver Fat Quantification

Hepatic PDFF as an imaging biomarker



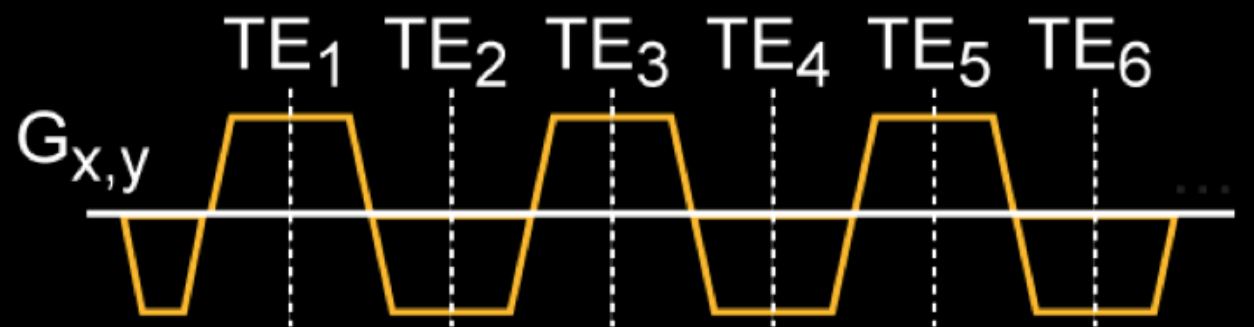
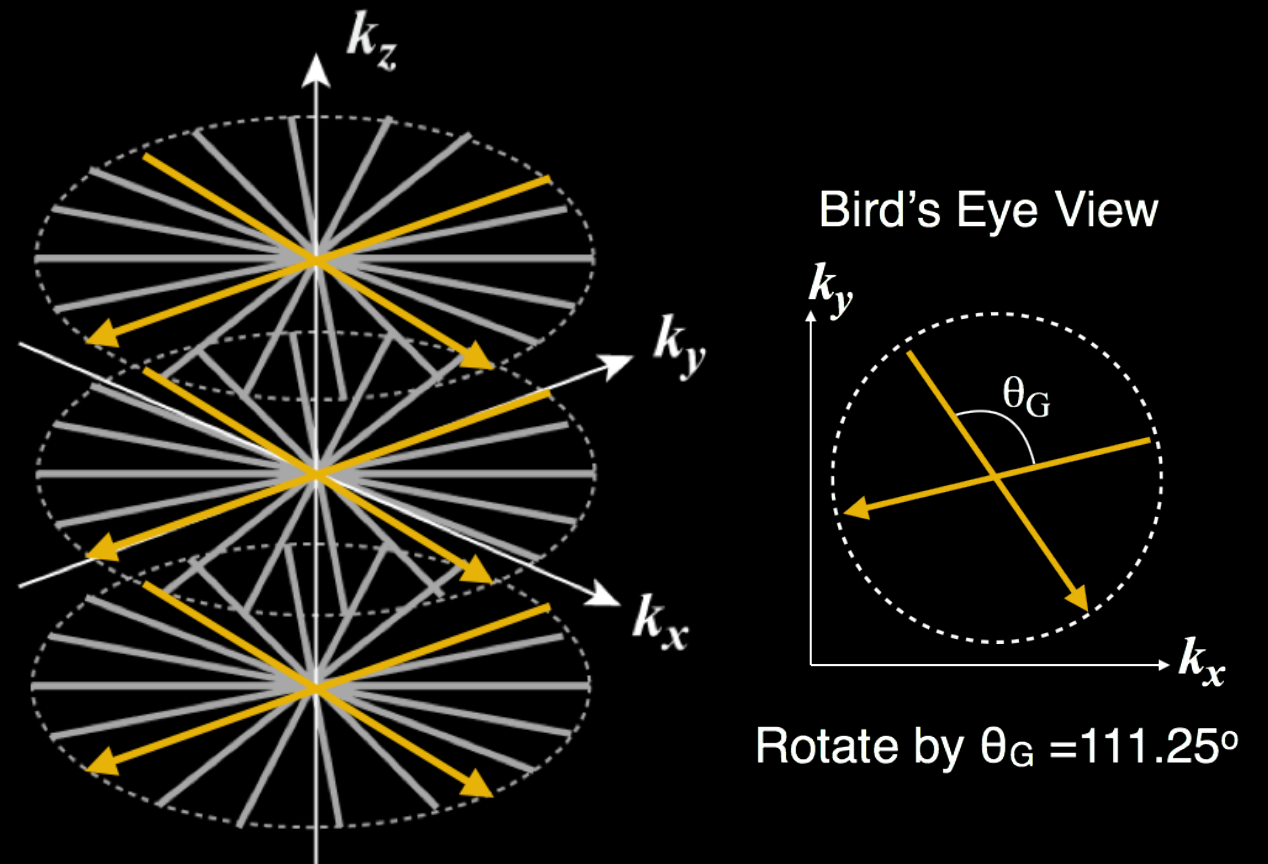
Free-Breathing Fat Quantification

- Cartesian acquisitions limited by motion
 - Breath-hold (BH) imaging, 10-30 sec
- BH imaging limits image quality and fat quantification performance
- Many patients cannot BH

Free-Breathing Fat Quantification

3D Stack-of-Radial MRI

- golden angle ordering
- bipolar multi-echo
- gradient calibration
- multi-peak F/W and R_2^*
- proton density fat fraction

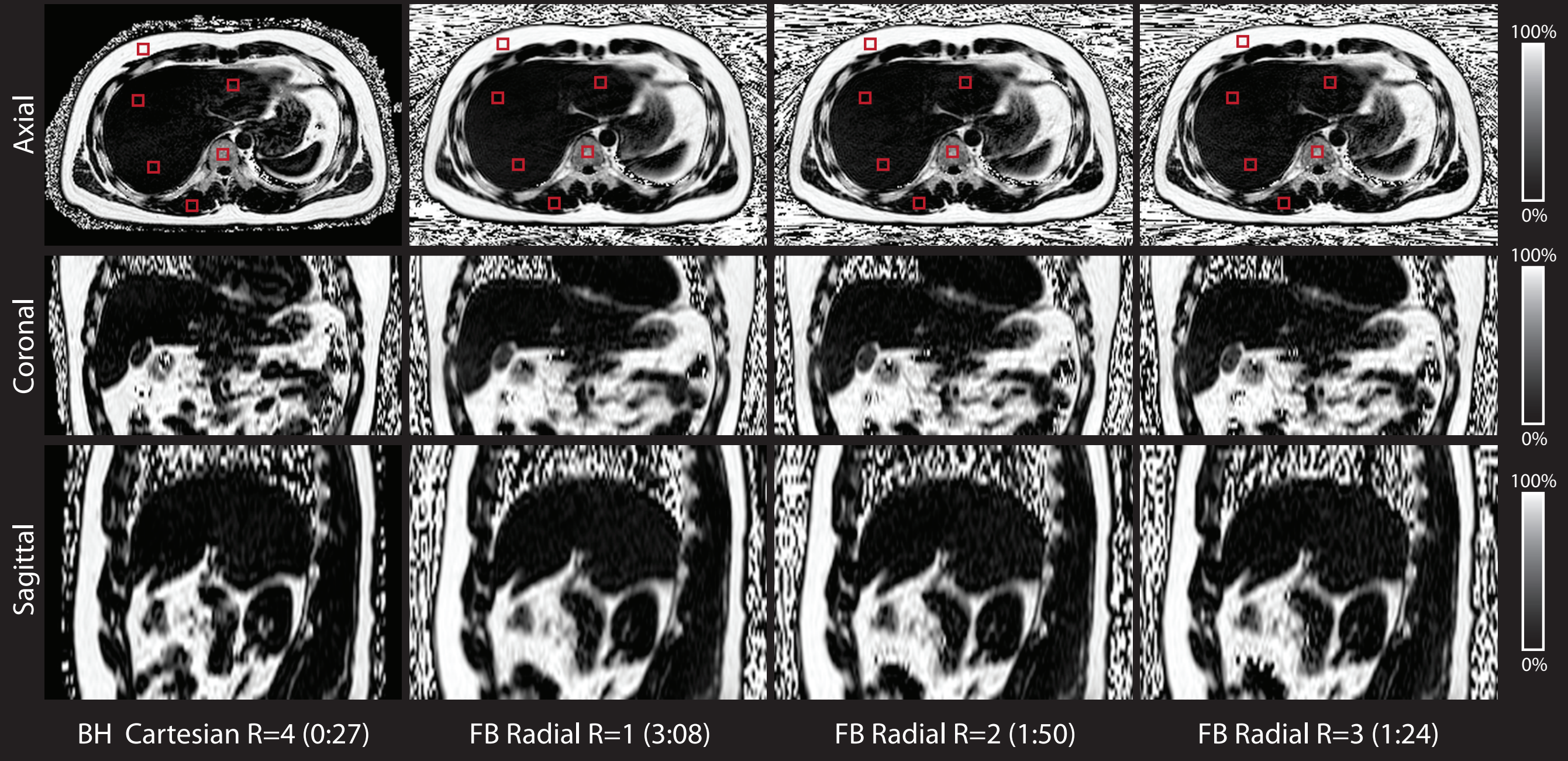


Free-Breathing Fat Quantification

Imaging Parameters (3T)	BH Cartesian	FB Radial
TE (ms)	1.23, 2.46, 3.69, 4.92, 6.15, 7.38	
Δ TE (ms)	1.23	1.23
TR (ms)	8.85	8.85
Matrix (Nx x Ny x Nz)	256 x 256 x 40	256 x 256 x 40
FOV (mm x mm x mm)	400 x 400 x 200	400 x 400 x 200
Slice Thickness (mm)	5	5
Radial Spokes	N/A	403 / 202 / 135
Flip Angle (degrees)	5	5
Bandwidth (Hz/pixel)	1150	1150
Acceleration Factor (R)	4	1 / 2 / 3
Scan Time (min:sec)	0:27	3:08* / 1:50* / 1:24*

** already includes radial gradient calibration*

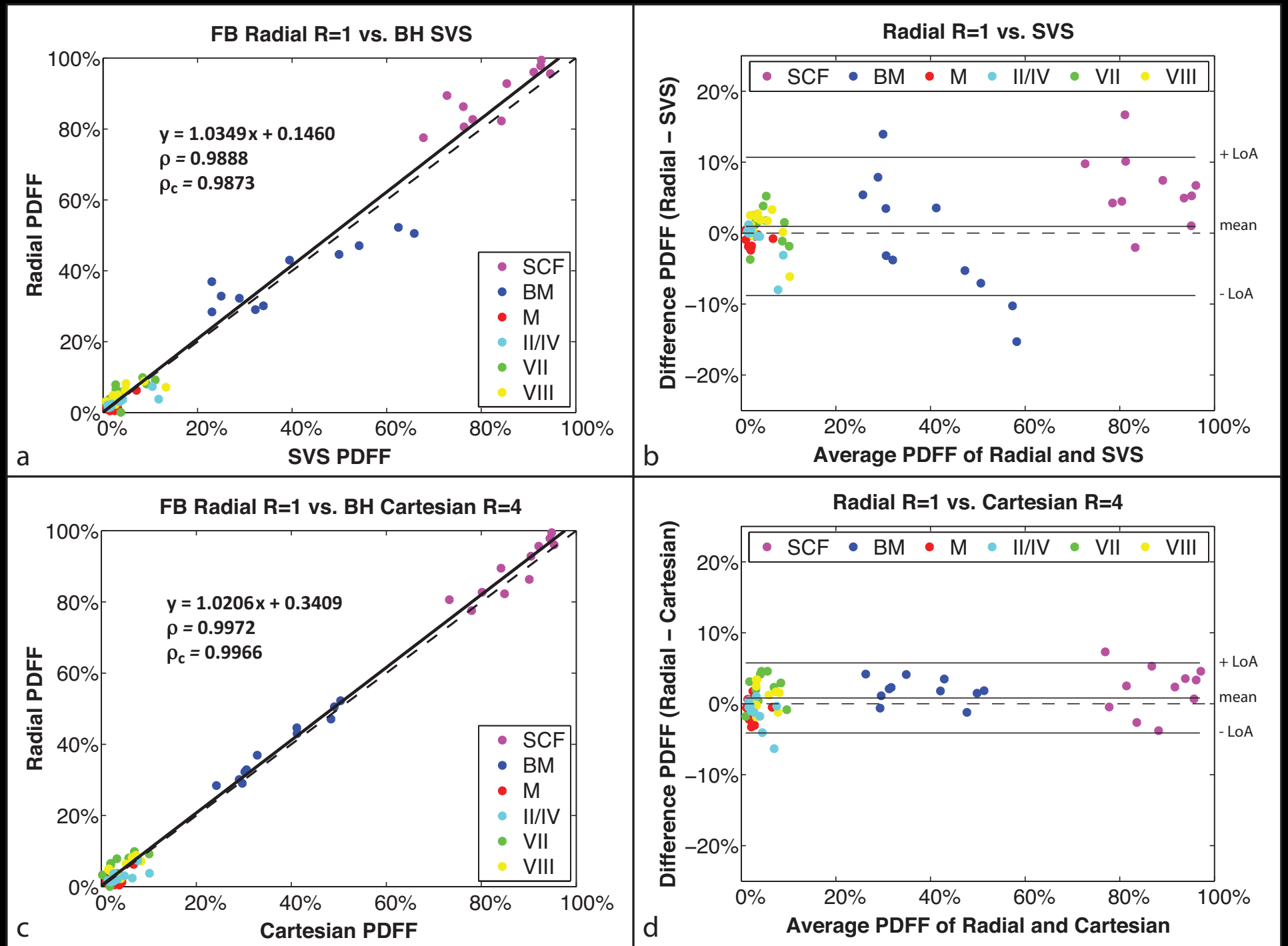
Free-Breathing Fat Quantification



Free-Breathing Fat Quantification

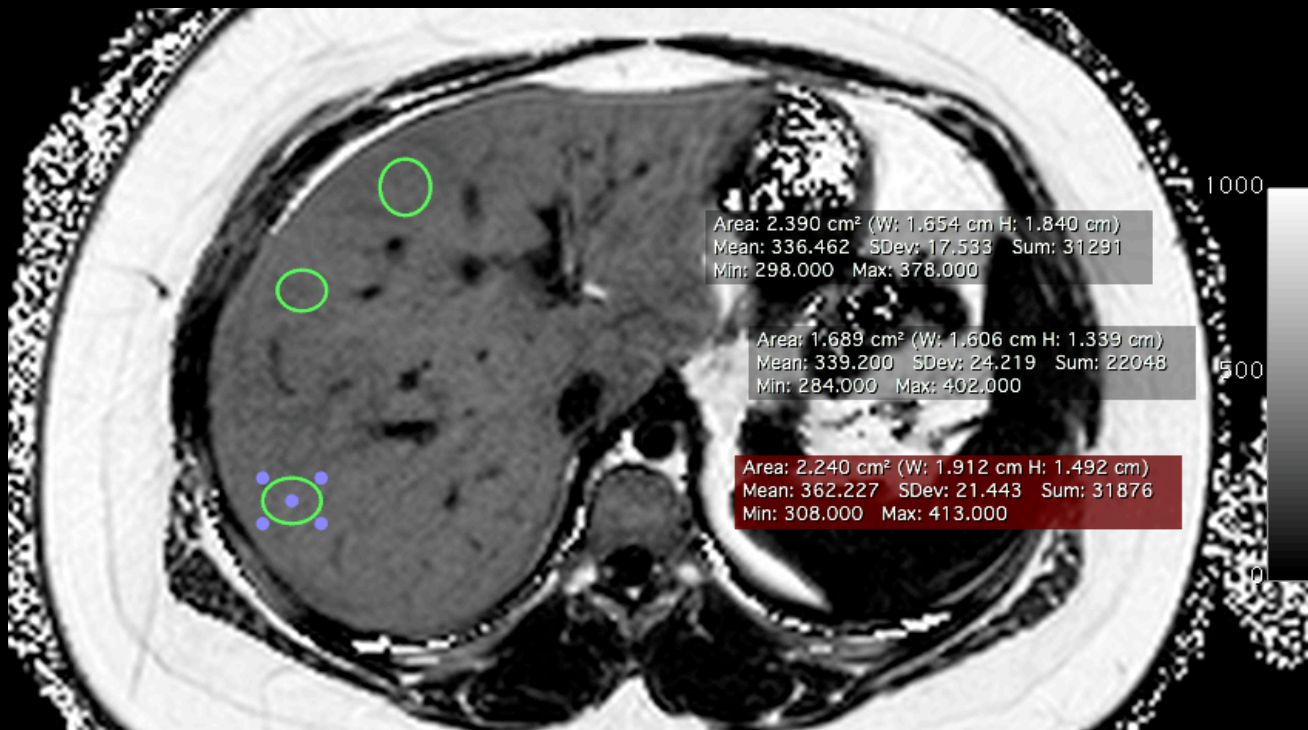
N = 11 subjects

- BH MRS
- BH Cartesian
- FB Radial



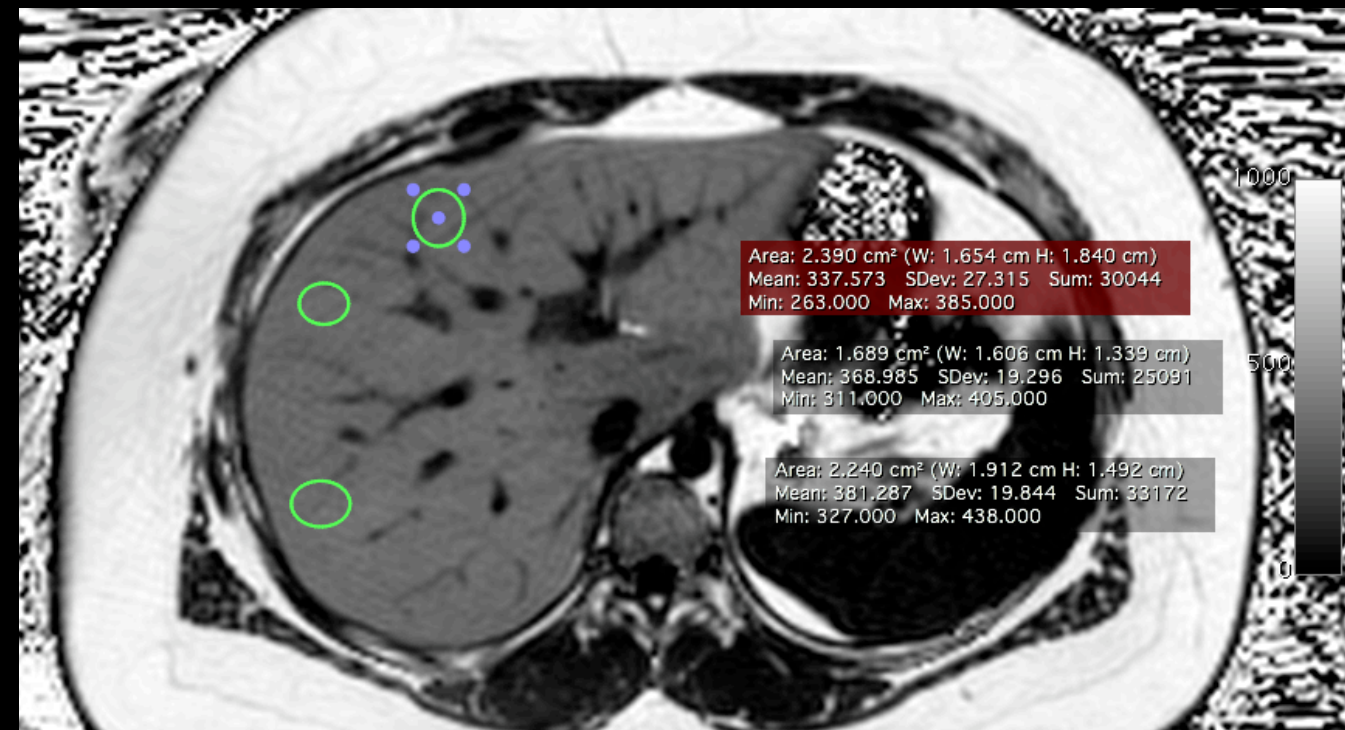
Free-Breathing Fat Quantification

Pediatric Patient 1



BH Cartesian

mean PDFF = 34.6%

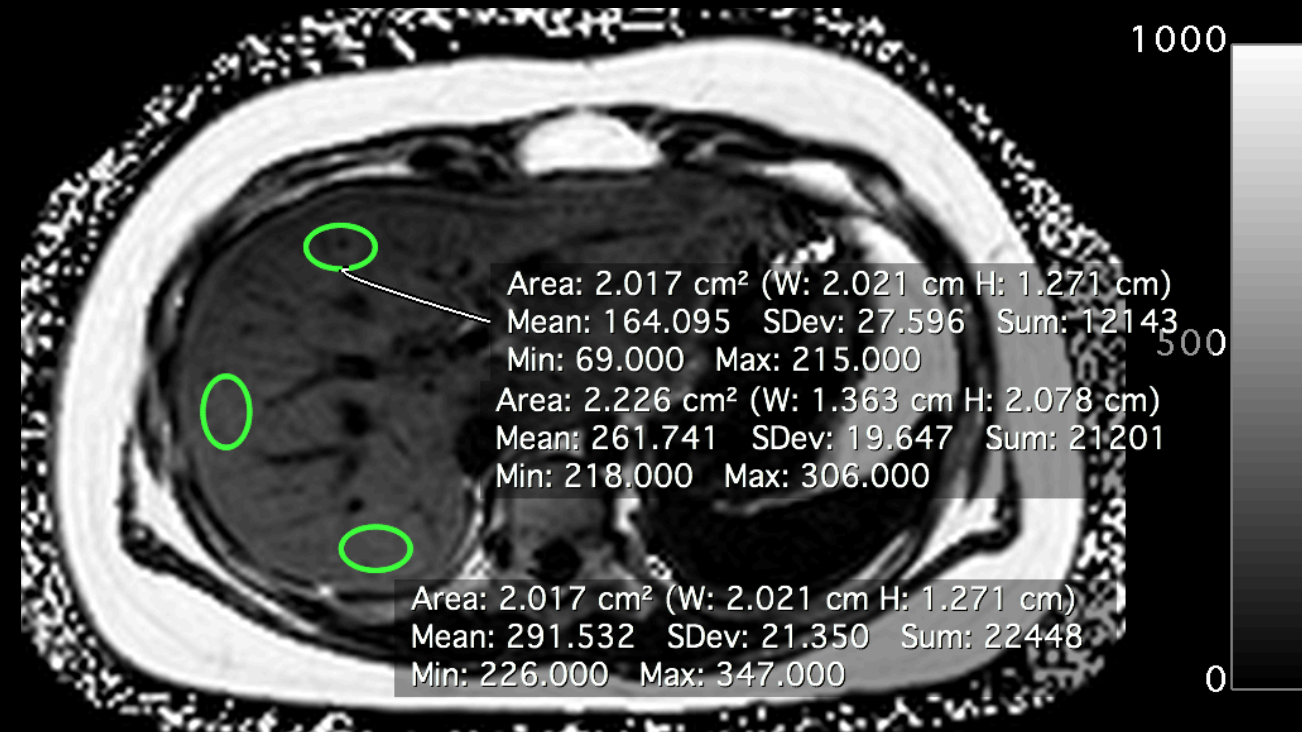


FB Radial

mean PDFF = 36.3%

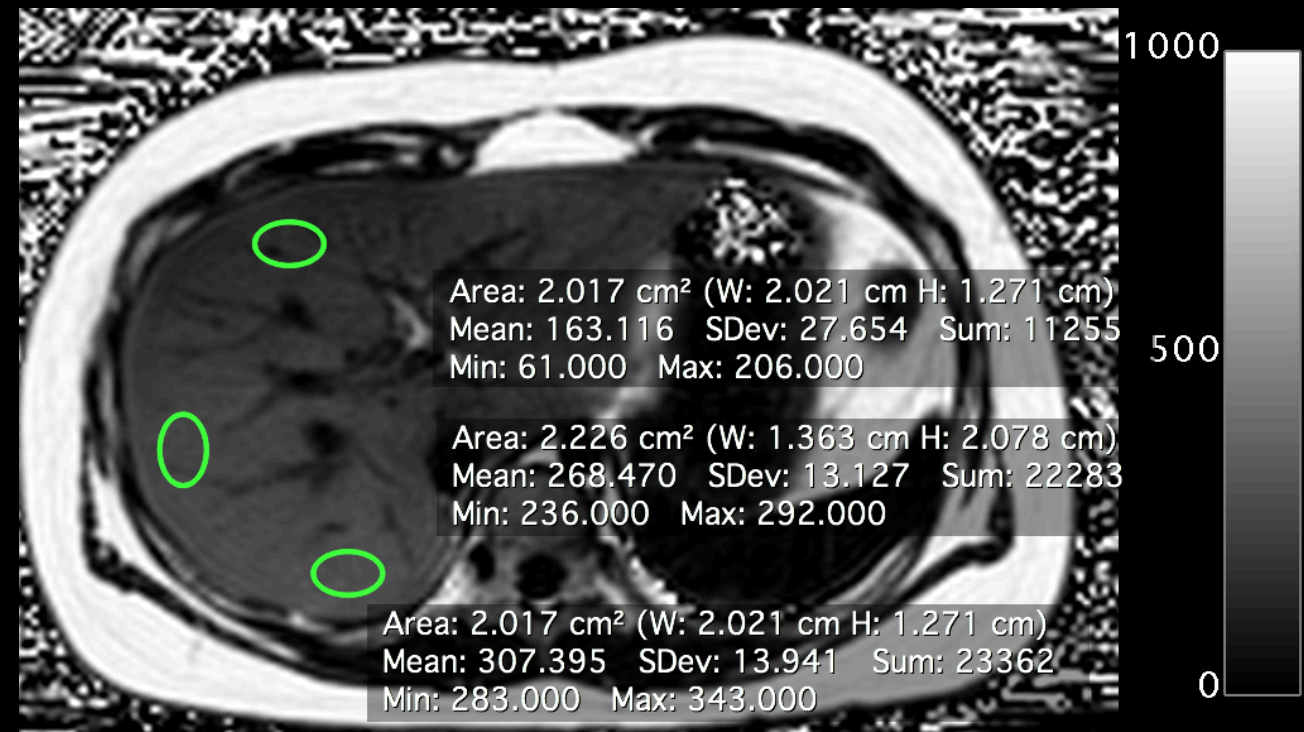
Free-Breathing Fat Quantification

Pediatric Patient 2



BH Cartesian

PDFF = 16.4%, 26.2%, 29.2%



FB Radial

PDFF = 16.3%, 26.8%, 30.7%

Summary: What We Learned

- Fat in MRI
 - chemical shift
- Fat Suppression
- Fat-Water-Separated MRI
 - multi-echo Dixon techniques
- Fat Quantification
 - liver fat quantification
- Free-Breathing Fat Quantification

Summary: Water-Fat MRI Research

Signal Model

Pulse Sequence

Reconstruction

Fat-Water Separation

Registration

Quantitative Analysis

Validation

Application

Thanks!

- Further reading
 - Handbook of MRI Pulse Sequences, Ch17.3
 - references on each slide
 - ISMRM Fat-Water Toolbox (2012)
- PBM229 Advanced Topics in MRI

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<http://mrrl.ucla.edu/wulab>