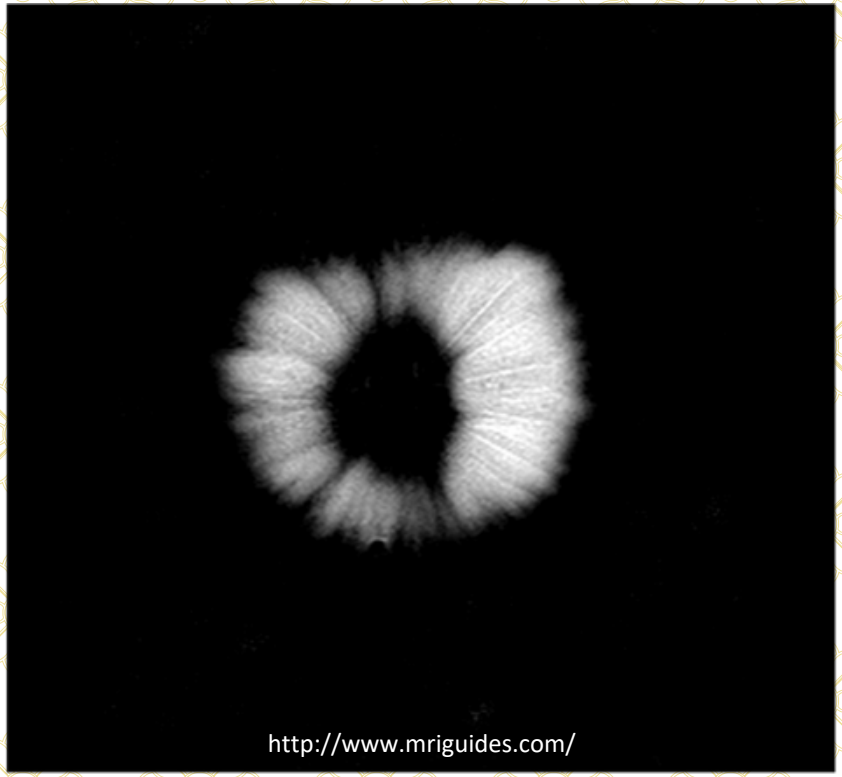
High-resolution Breast DWI

with improved Nyquist Ghost Correction and Simultaneous Multislice Imaging

Jessica McKay, Ph.D.

https://twitter.com/OHSUBrain

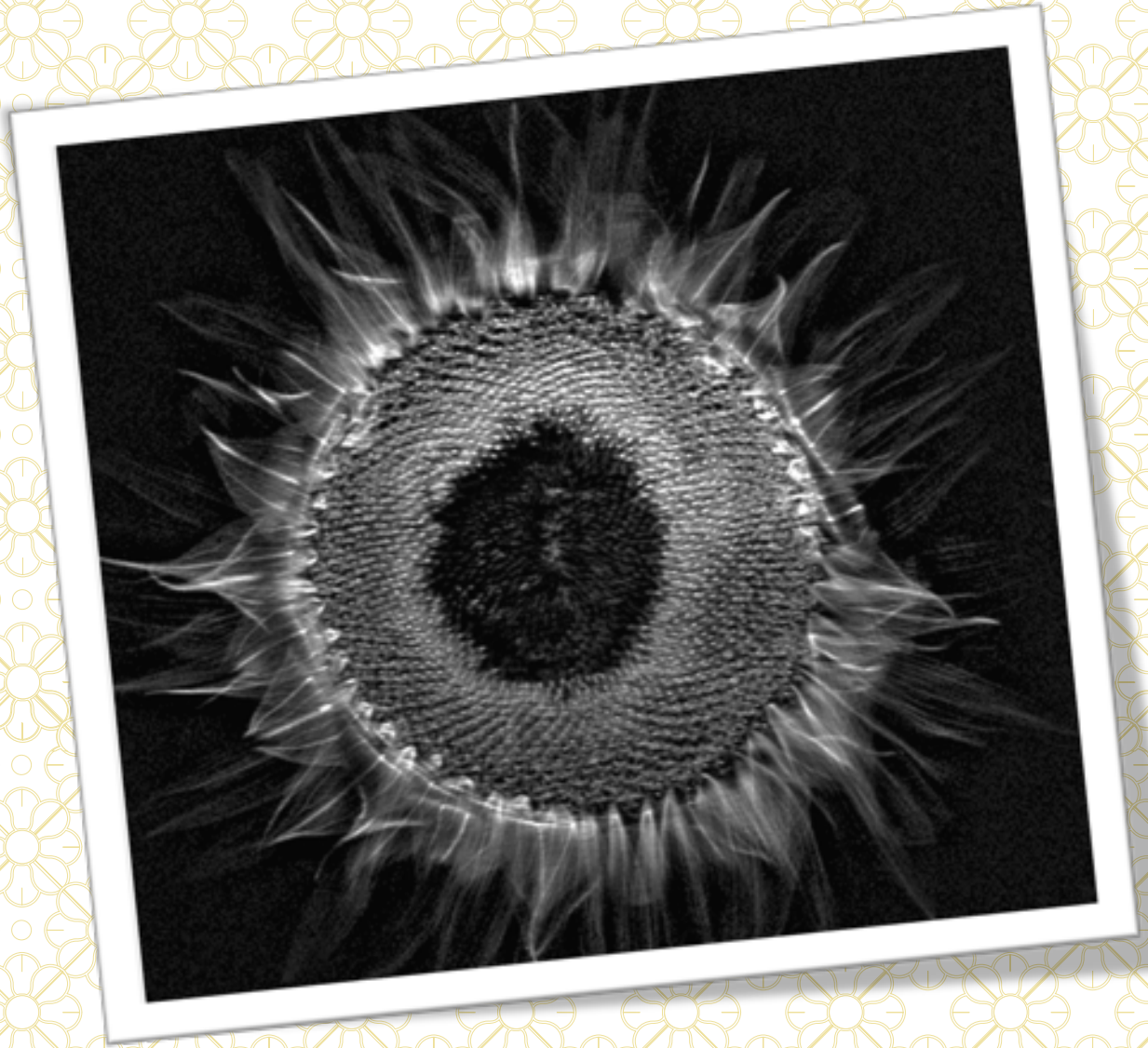


http://www.mriguides.com/

Stanford Cancer Imaging Training (SCIT) Seminar
RSL Meeting

Mentored by **Drs. Brian Hargreaves** and **Bruce Daniel**
Ph.D. work advised by **Dr. Patrick J Bolan**

October 21st, 2020



Goal:

To develop a strategy for breast DWI with high resolution and image quality within a clinically acceptable scan time.

OUTLINE

Motivation

- MRI background
- Diffusion weighting
- Why breast DWI?
- Problems with SE-EPI: distortion, Nyquist ghosts, limited resolution

Part 1: Ghost correction

- The Nyquist ghost
- Referenceless ghost correction

Part 2: High Resolution

- Axially reformatted SMS
- Phantom study
- Reader study

Discussion, future directions, & summary

MRI in three steps:

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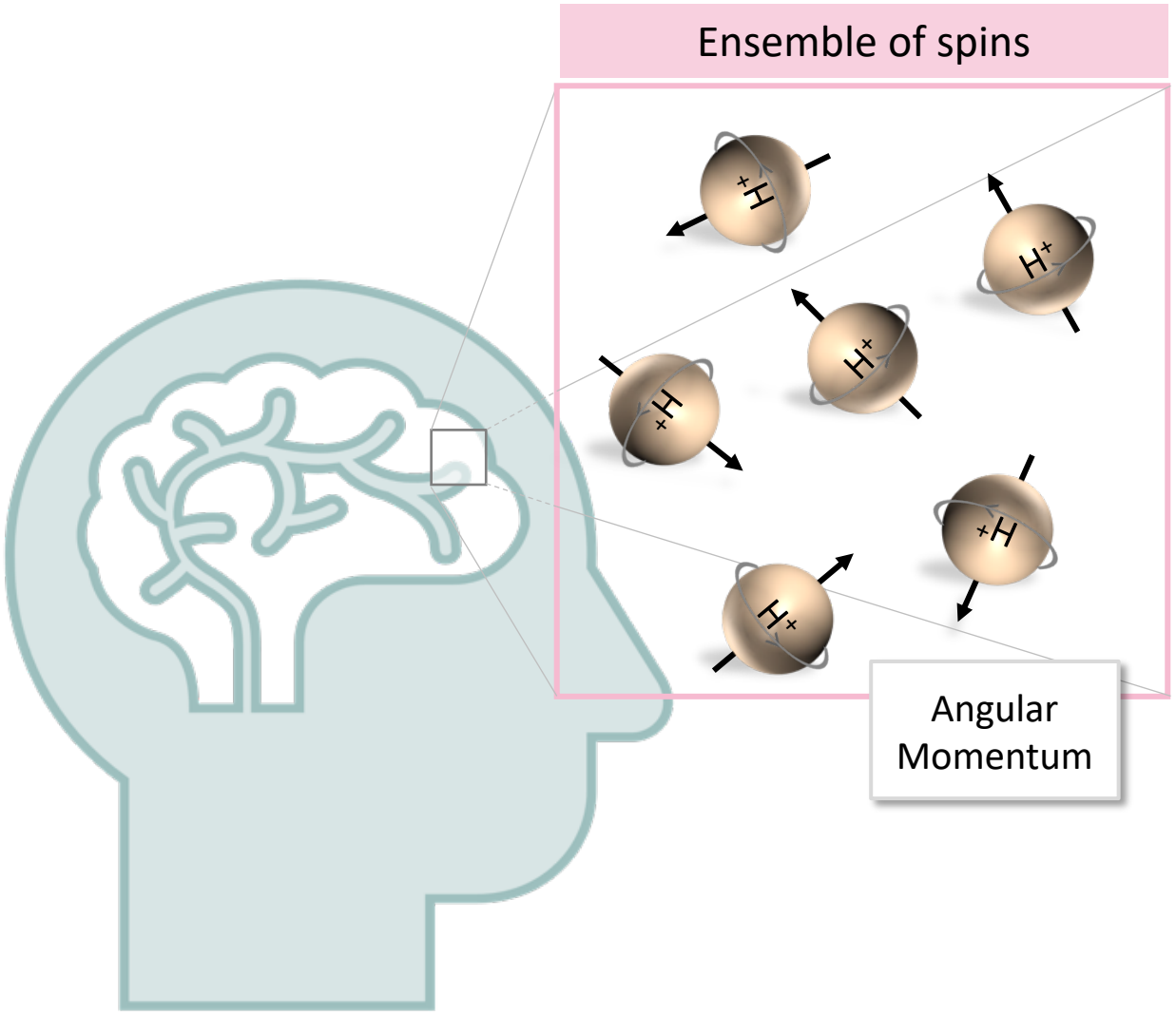
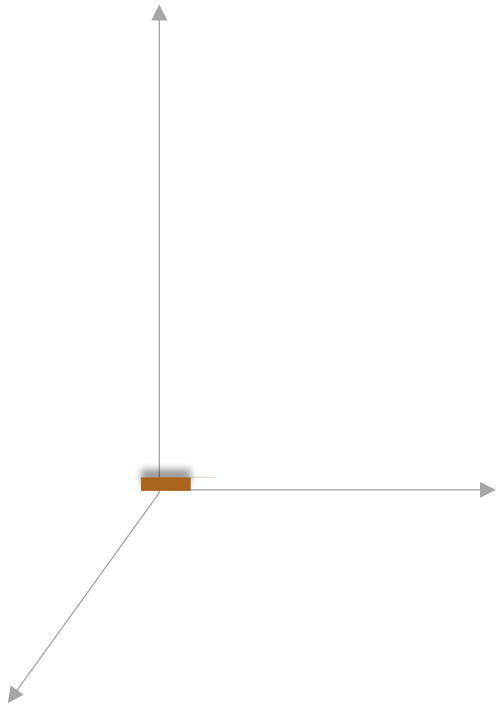


Net Magnetization



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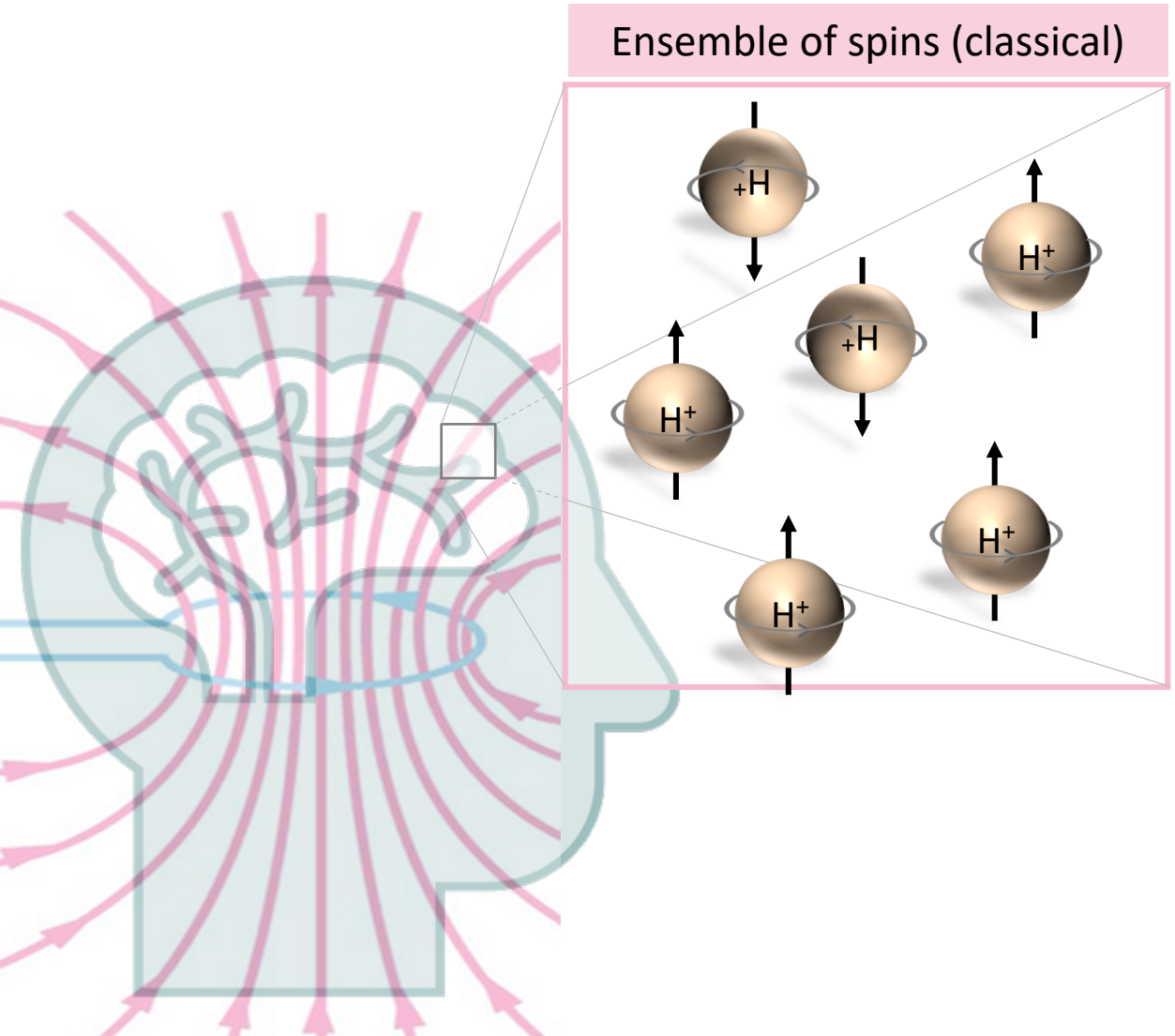

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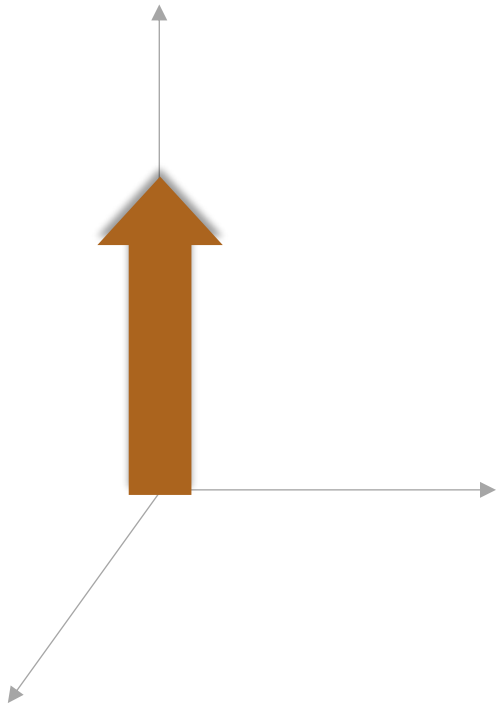

Effect #1: The net magnetic moment **aligns** with B_0

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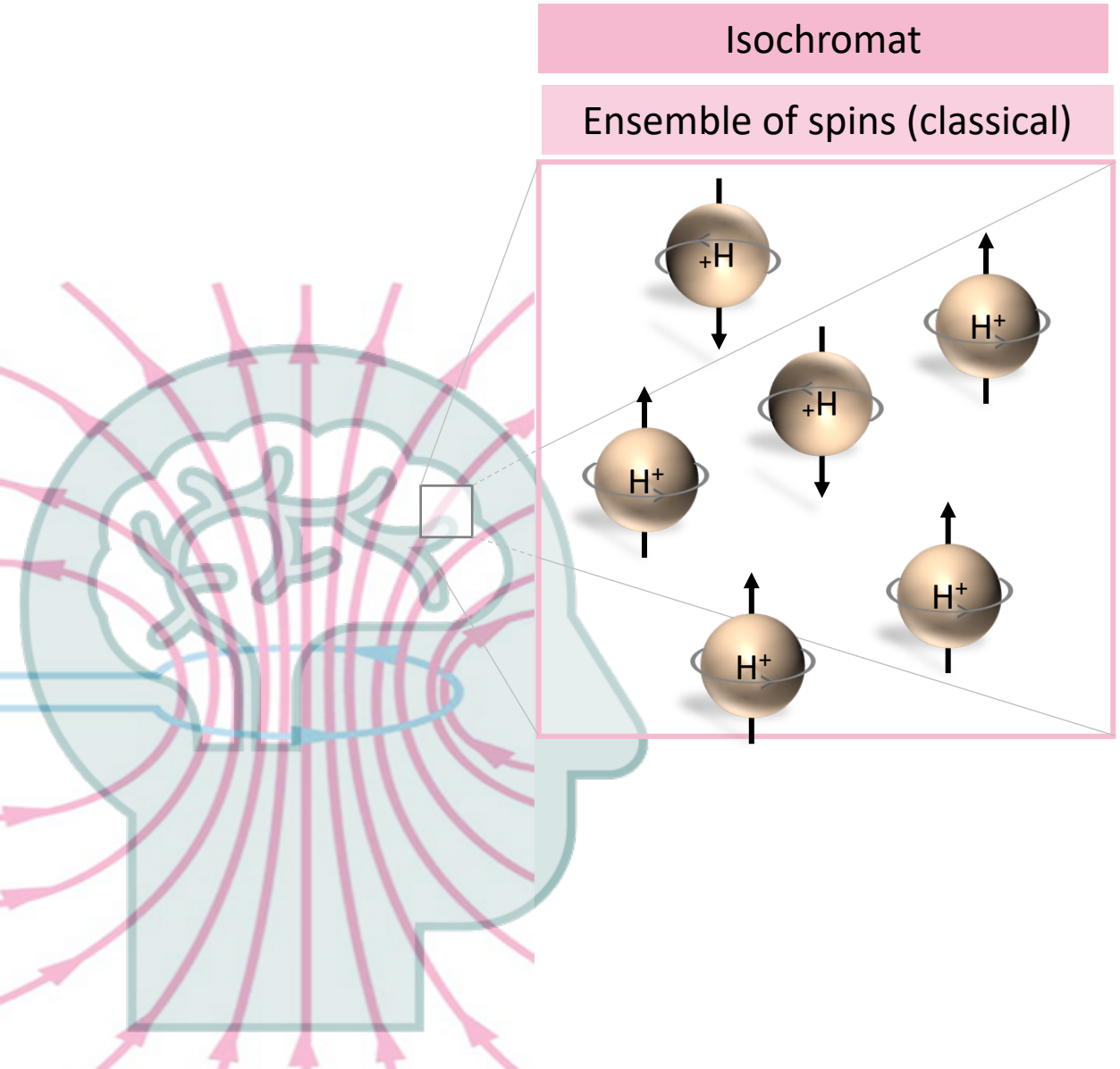

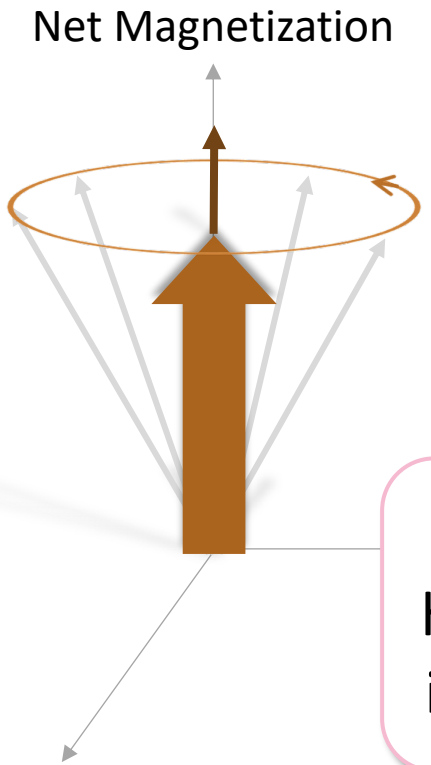

Effect #2:
Precession at Larmor frequency:
γB_0

for water

B_0 homogeneity is important!

$\neq \omega_{fat}$

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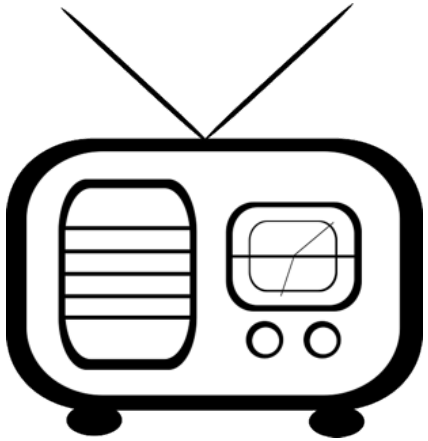
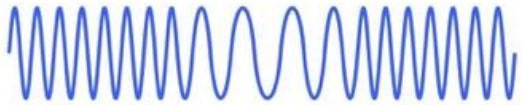
Consider the rotating frame

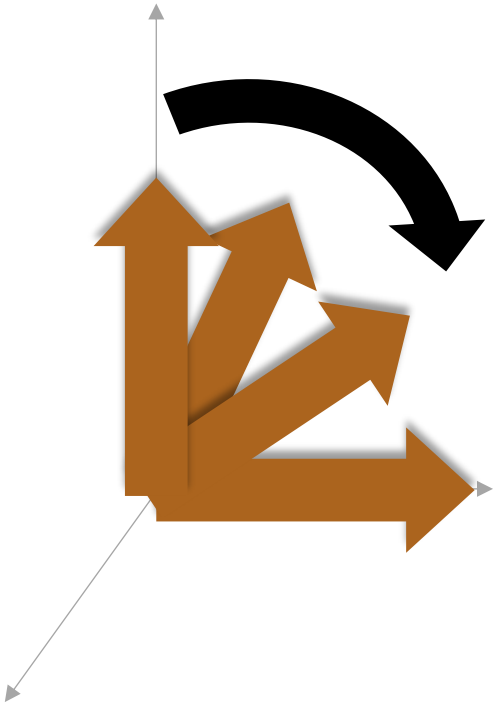


AM pulse



FM pulse

Net Magnetization



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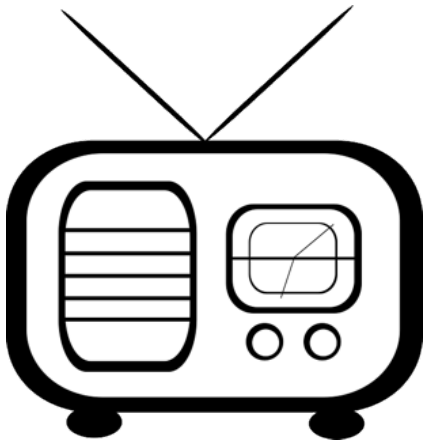
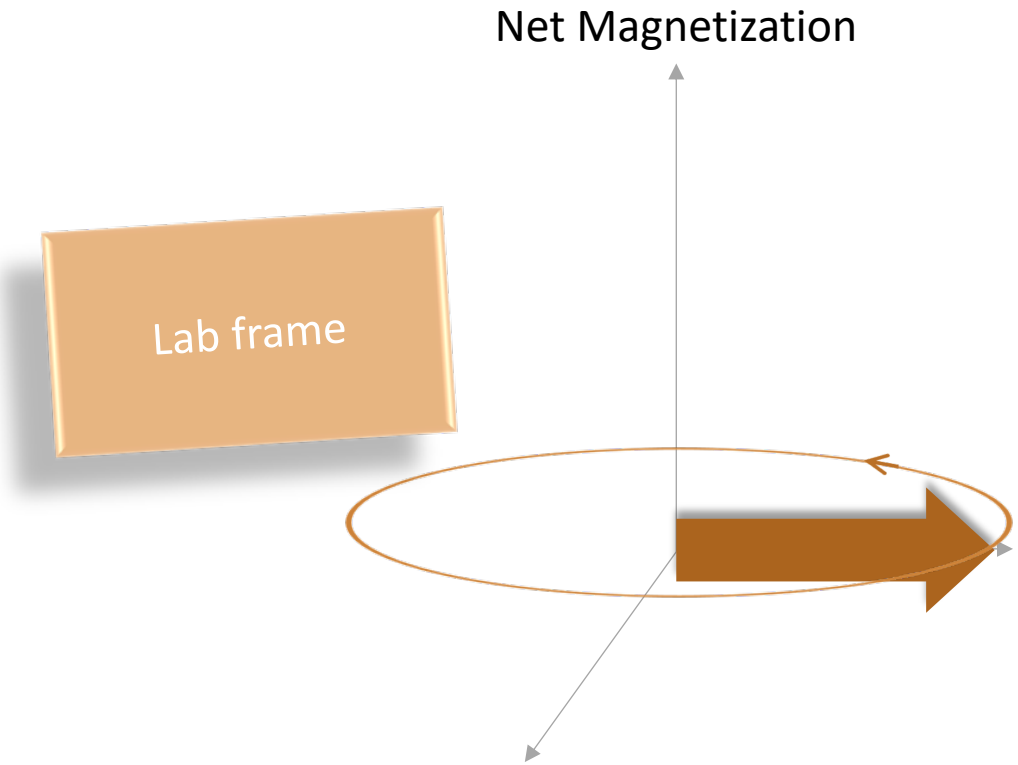
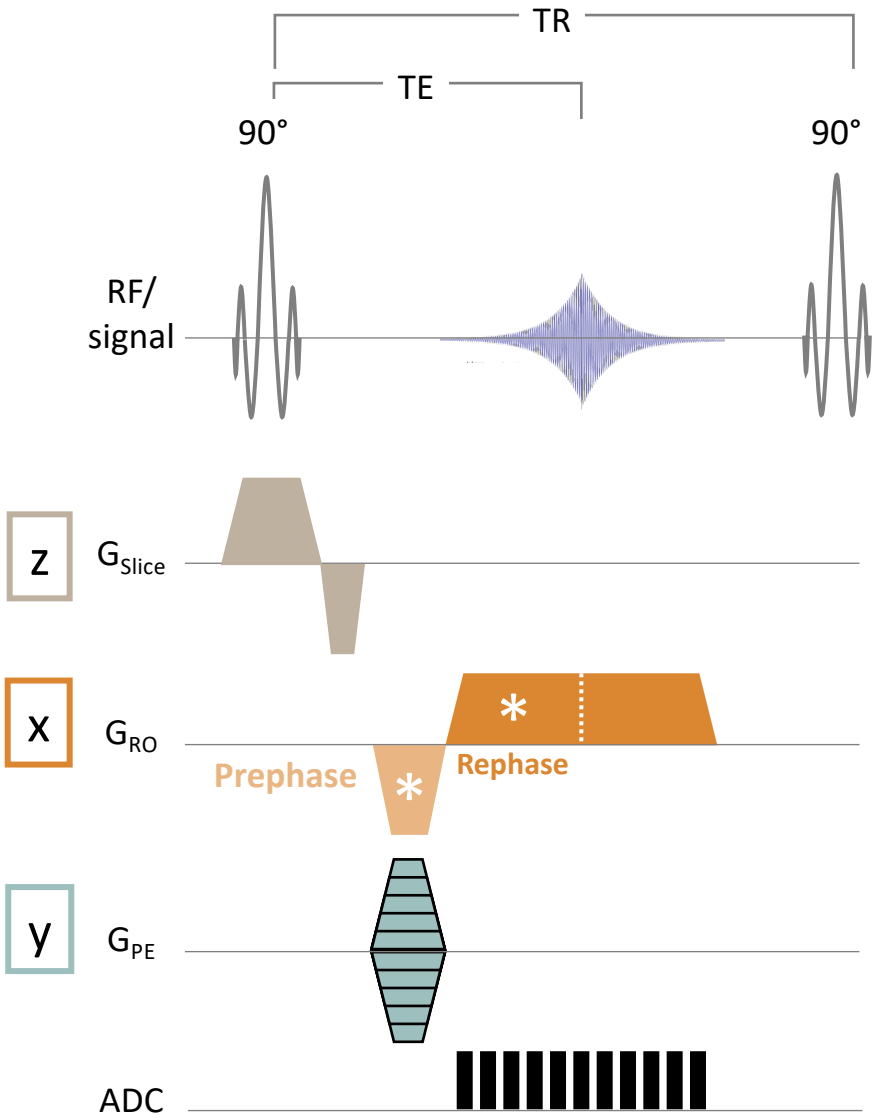
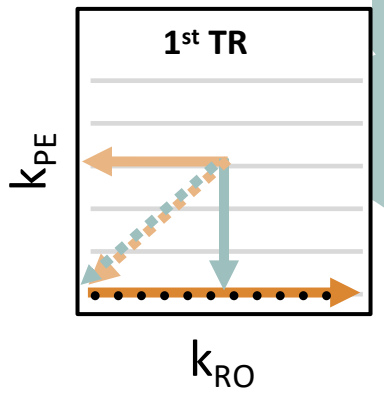


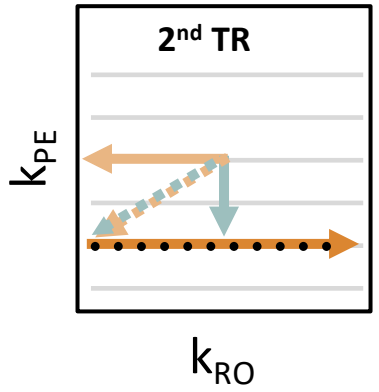


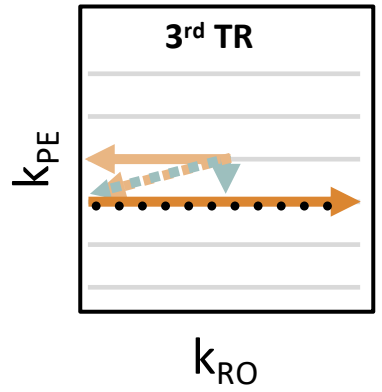
Signal!

Gradient Echo









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$$k(t) = \gamma \int_0^t G(x,y,t)dt$$

$$k_{RO} = k_x$$
$$k_{PE} = k_y$$

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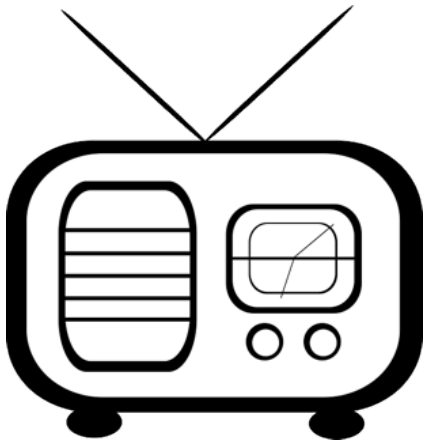

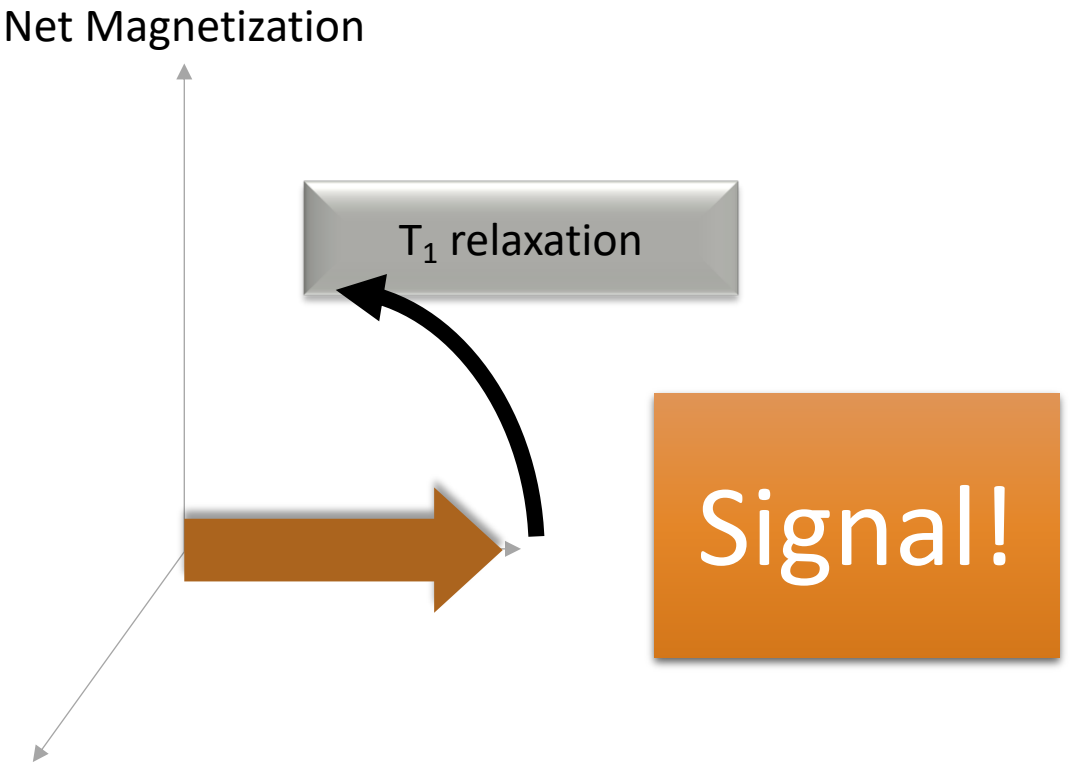

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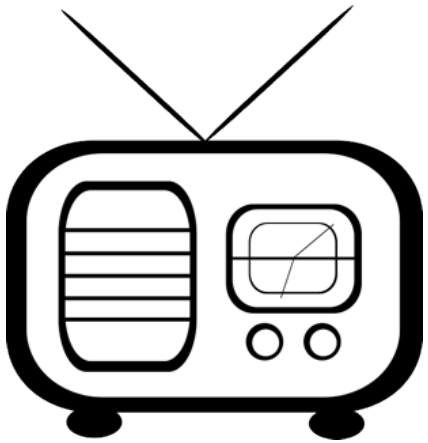
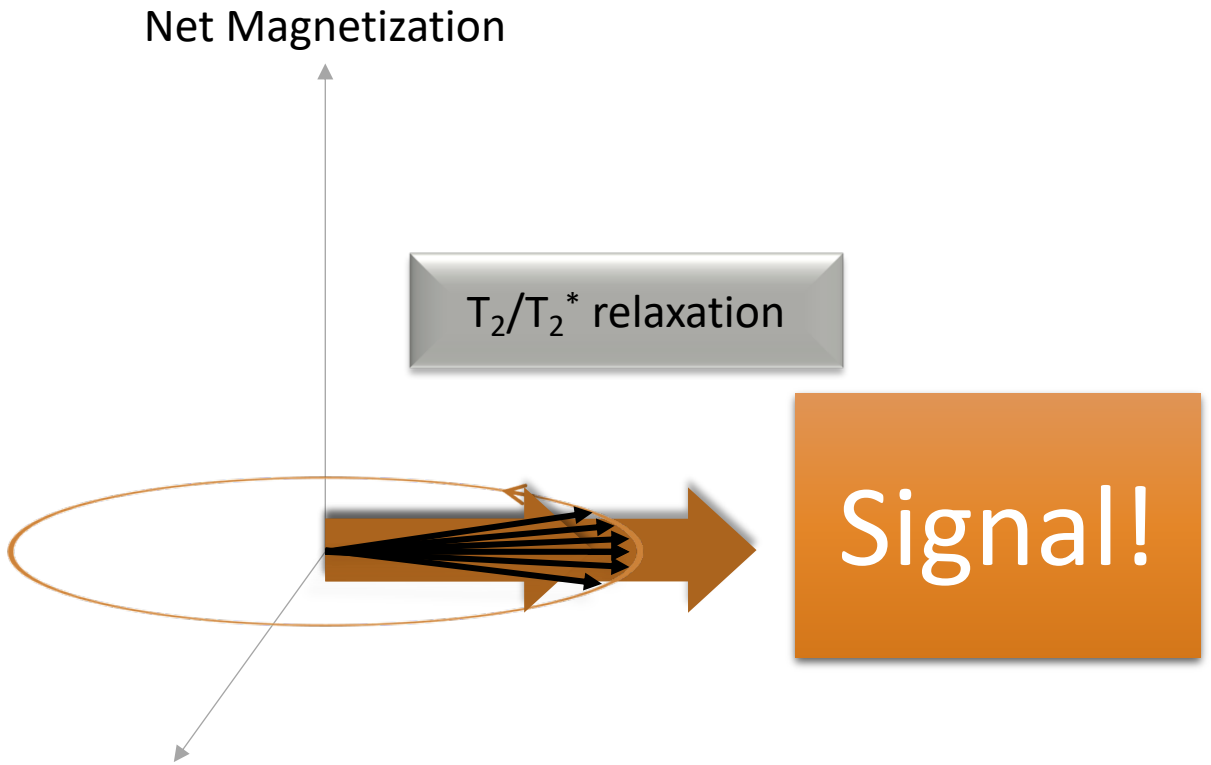
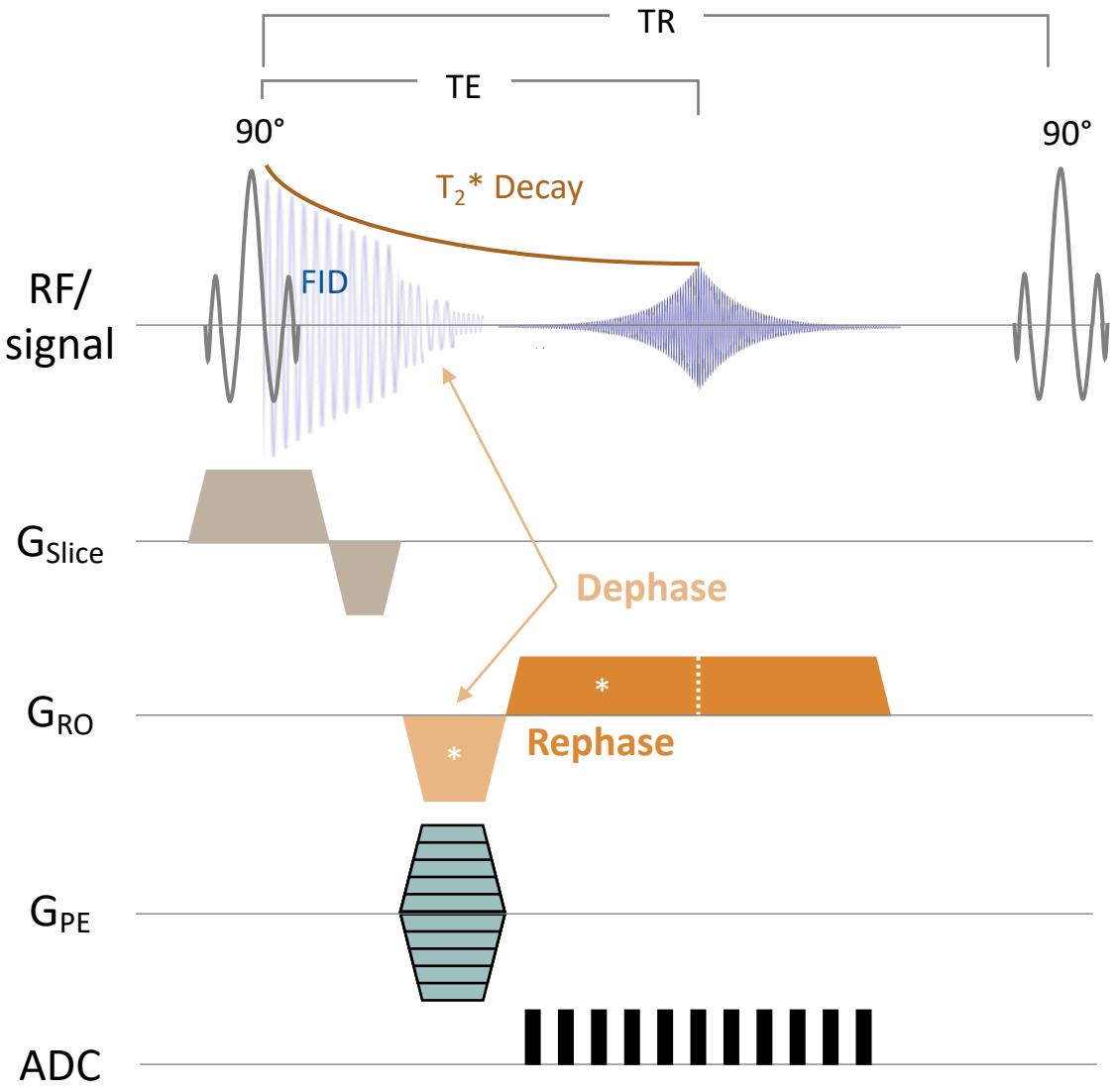




Gradient Echo



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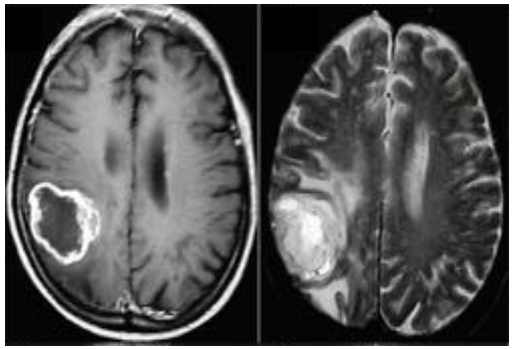
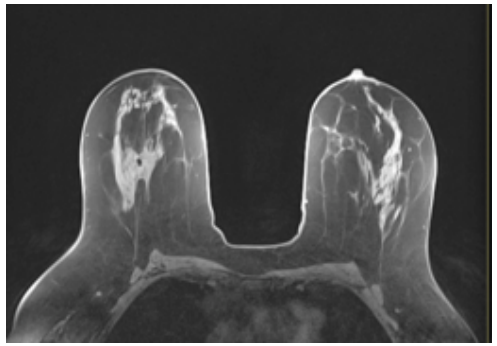
T_1-weighted T_2-weighted

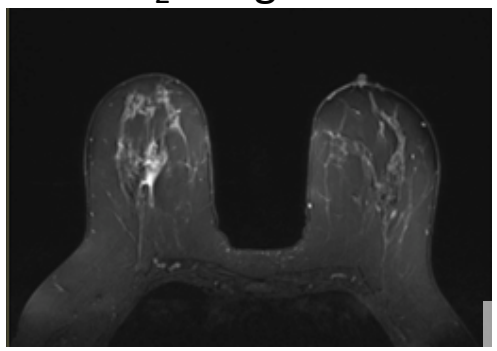


Liu, Jin Li, et al. (2014).

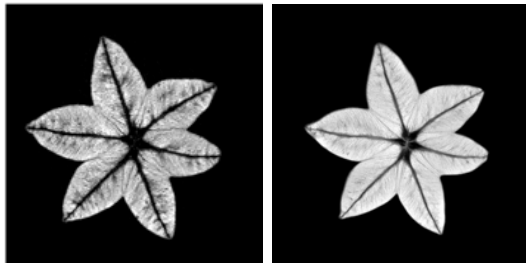
T_1-weighted

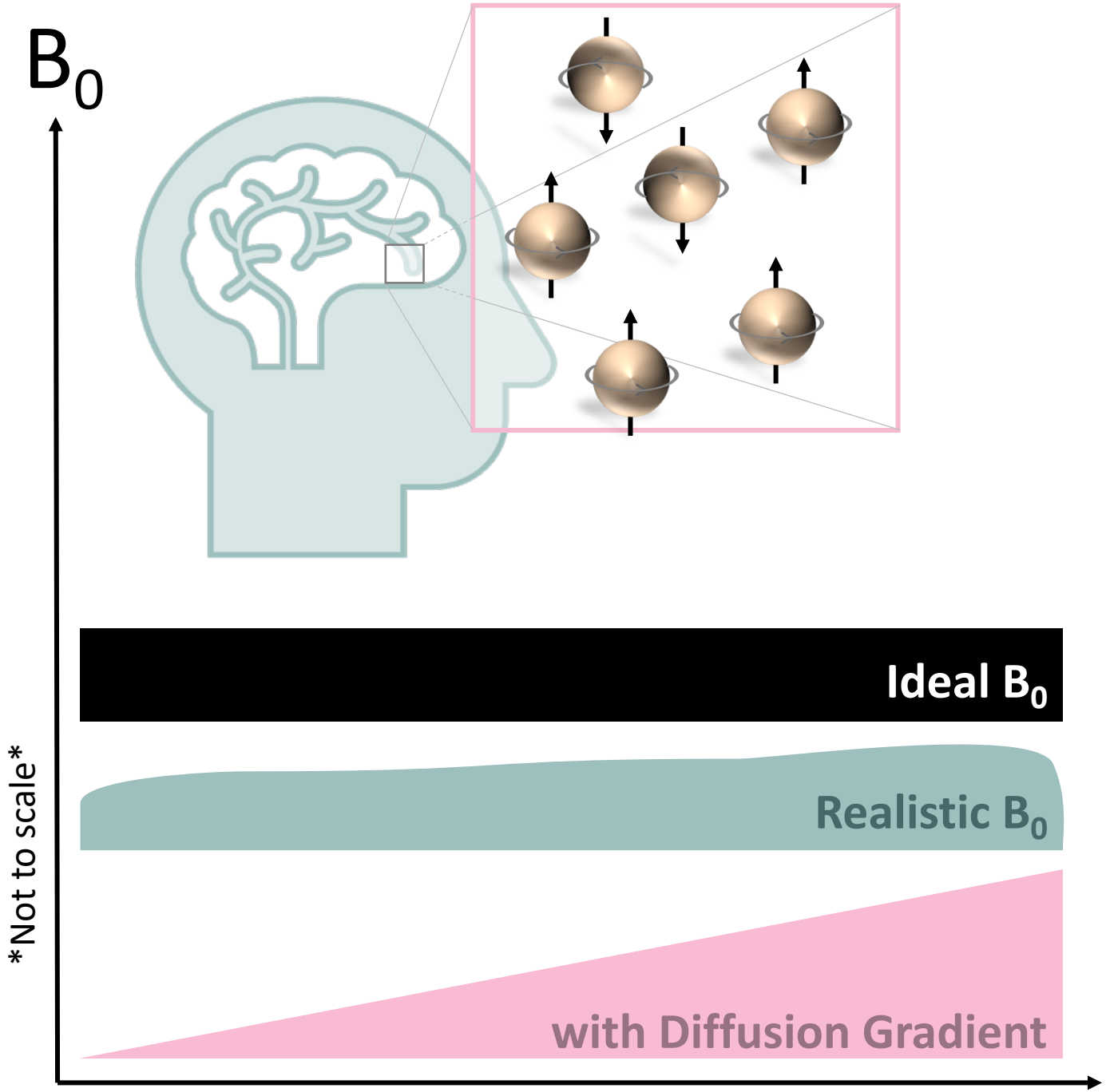


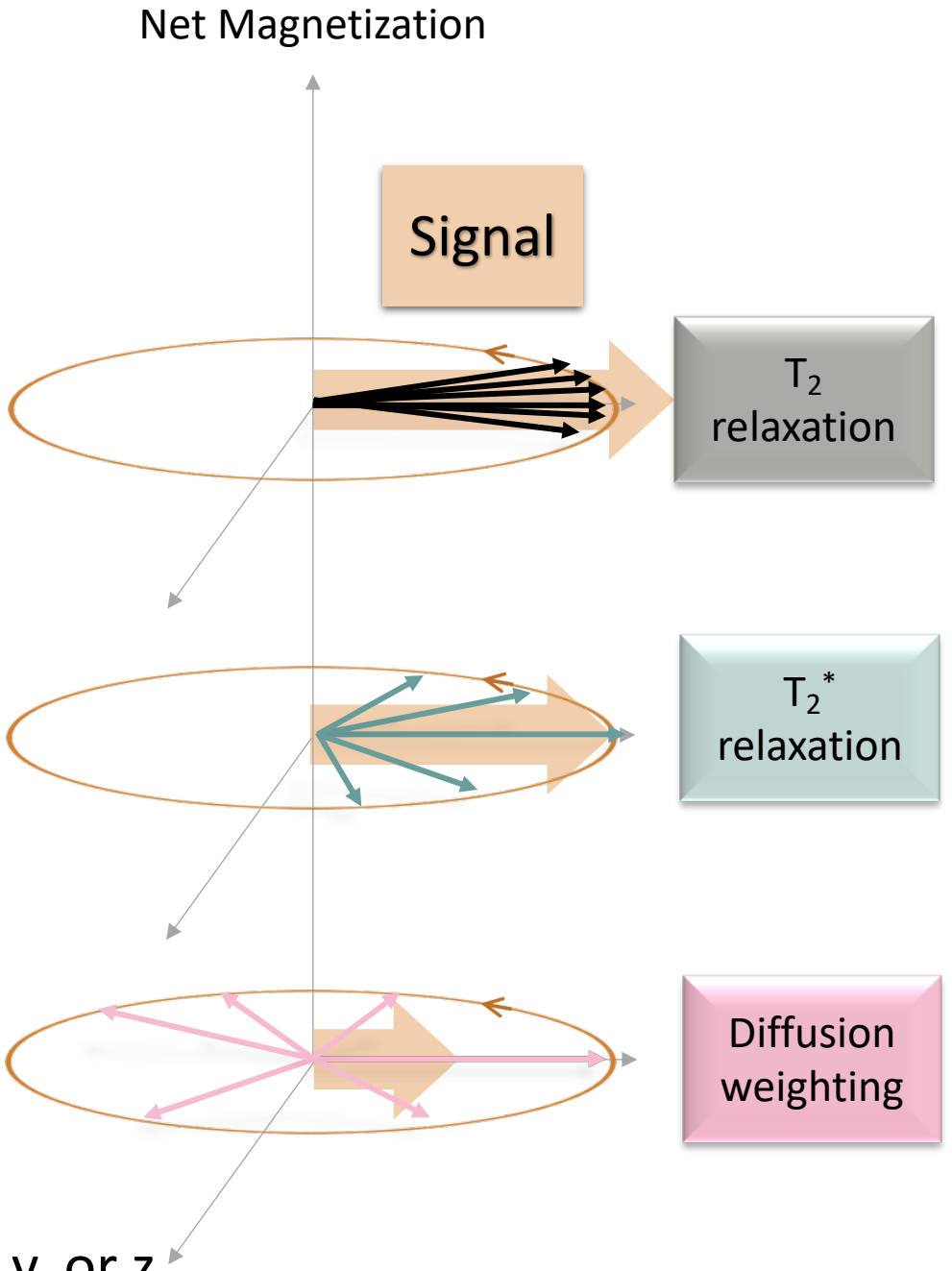
T_2-weighted



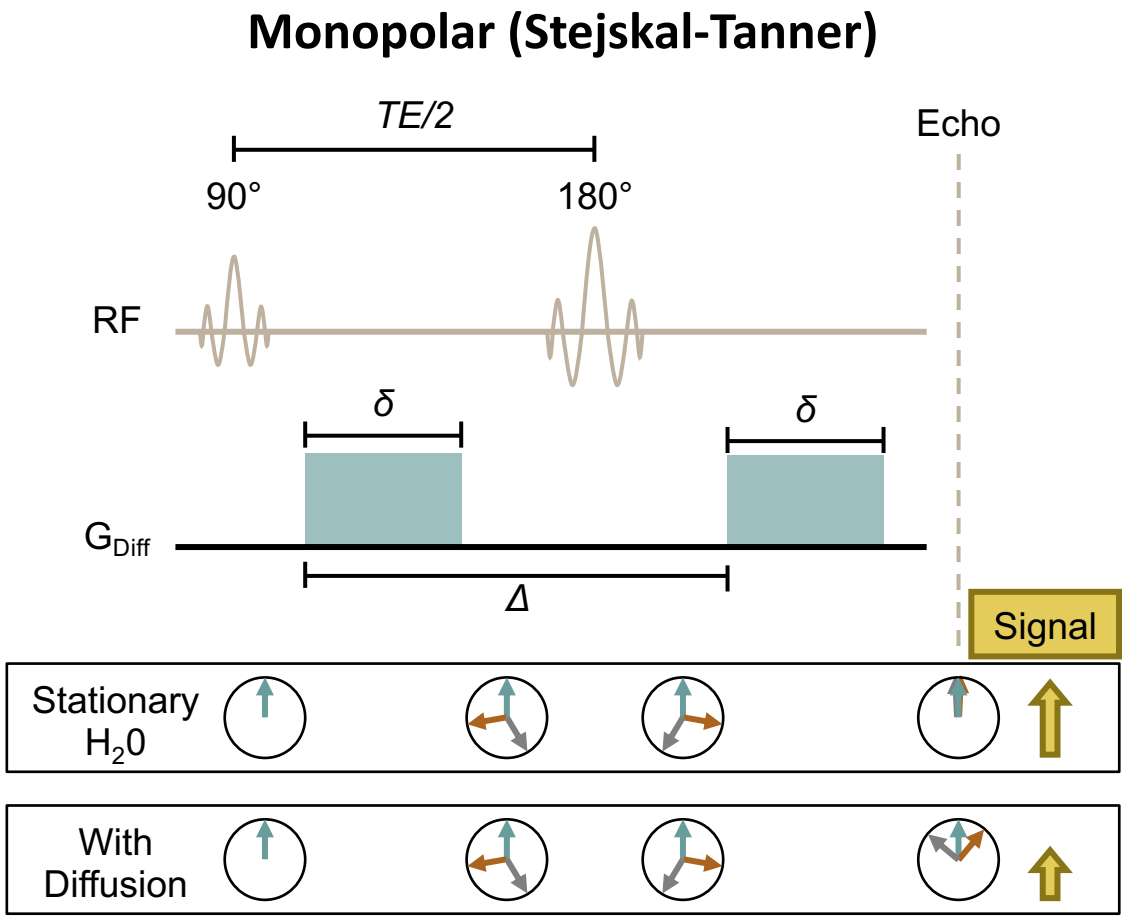
Gradient Echo Spin Echo




B_0
Ideal B_0
Realistic B_0
with Diffusion Gradient
Not to scale
x, y, or z


Net Magnetization
Signal
T_2 relaxation
T_2^* relaxation
Diffusion weighting

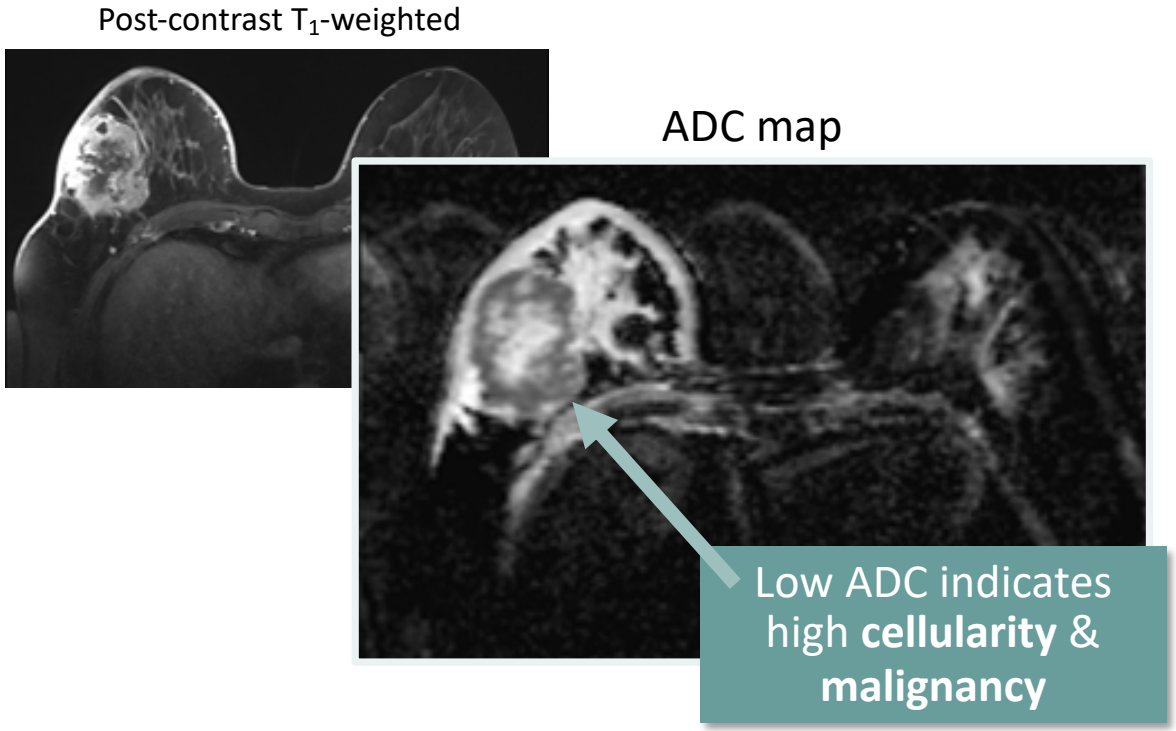
Diffusion Encoding



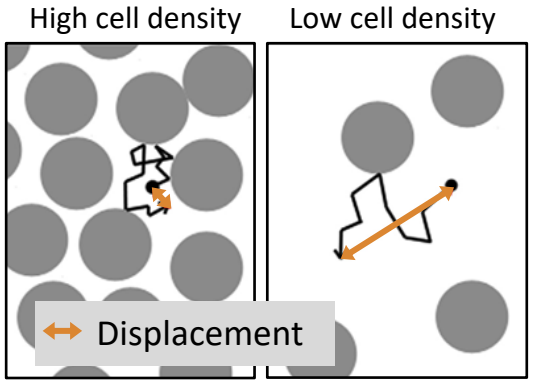
$$S(b) = S_0 e^{-b*ADC}$$

For Monopolar: $b = \gamma^2 {G_{Diff}}^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right)$

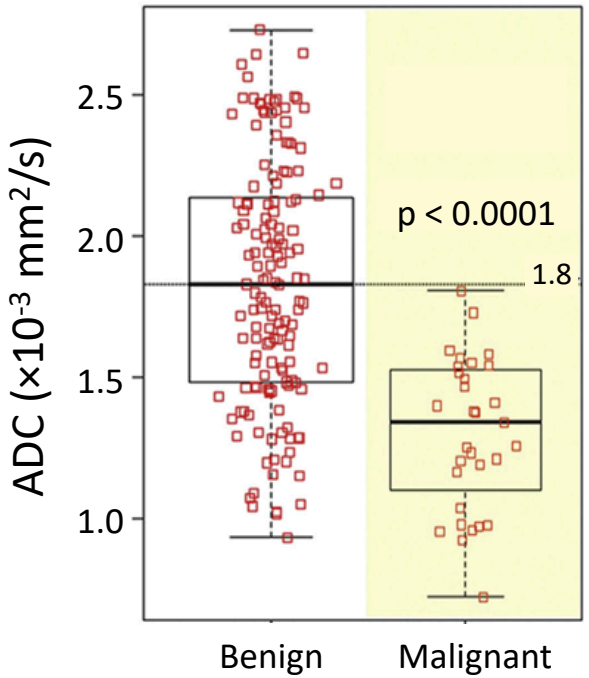
Breast DWI & ADC



ADC reflects cell density



ADC reflects malignancy



El Khouli, R.H. *et al.* (2010)

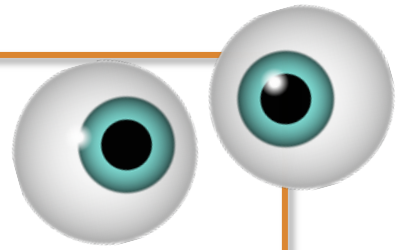
Clinical applications of DWI for breast cancer

- **Treatment monitoring**: Increasing ADC values indicate treatment response earlier than conventional measurements
- **Diagnosis and staging**: Increase specificity and reduce unnecessary biopsies??
- **Screening**: detection without contrast

Problems with Breast DWI

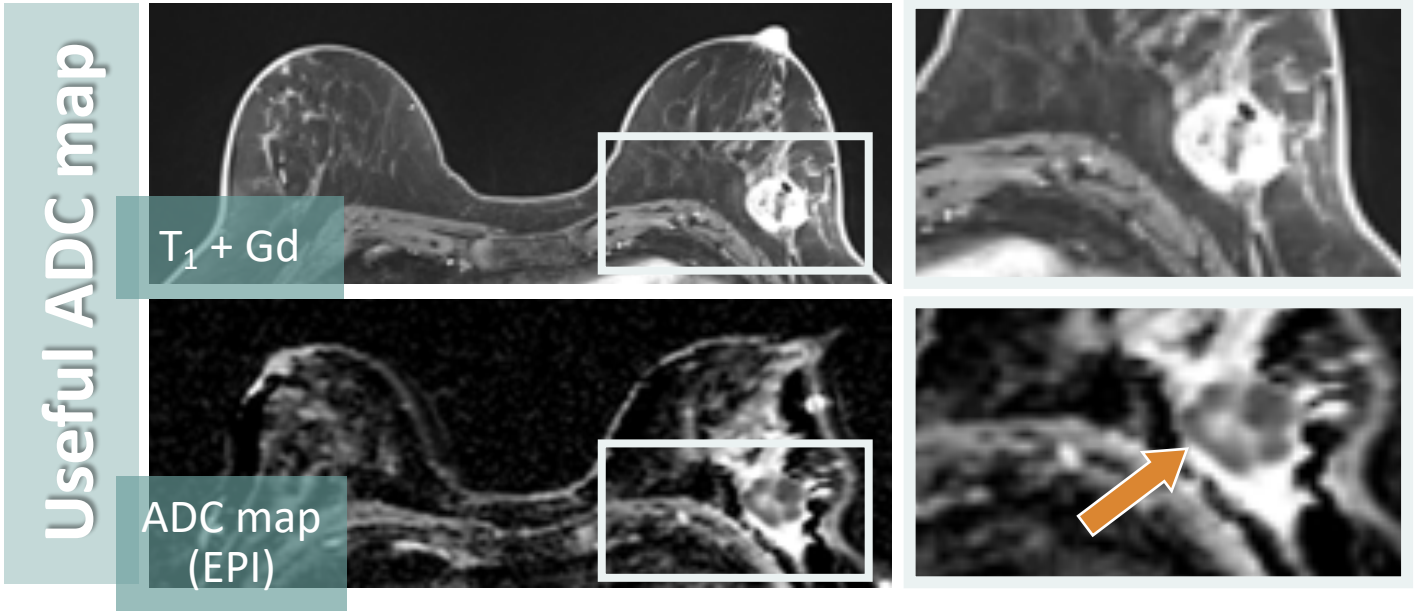
Typically acquired using **single shot SE-EPI**

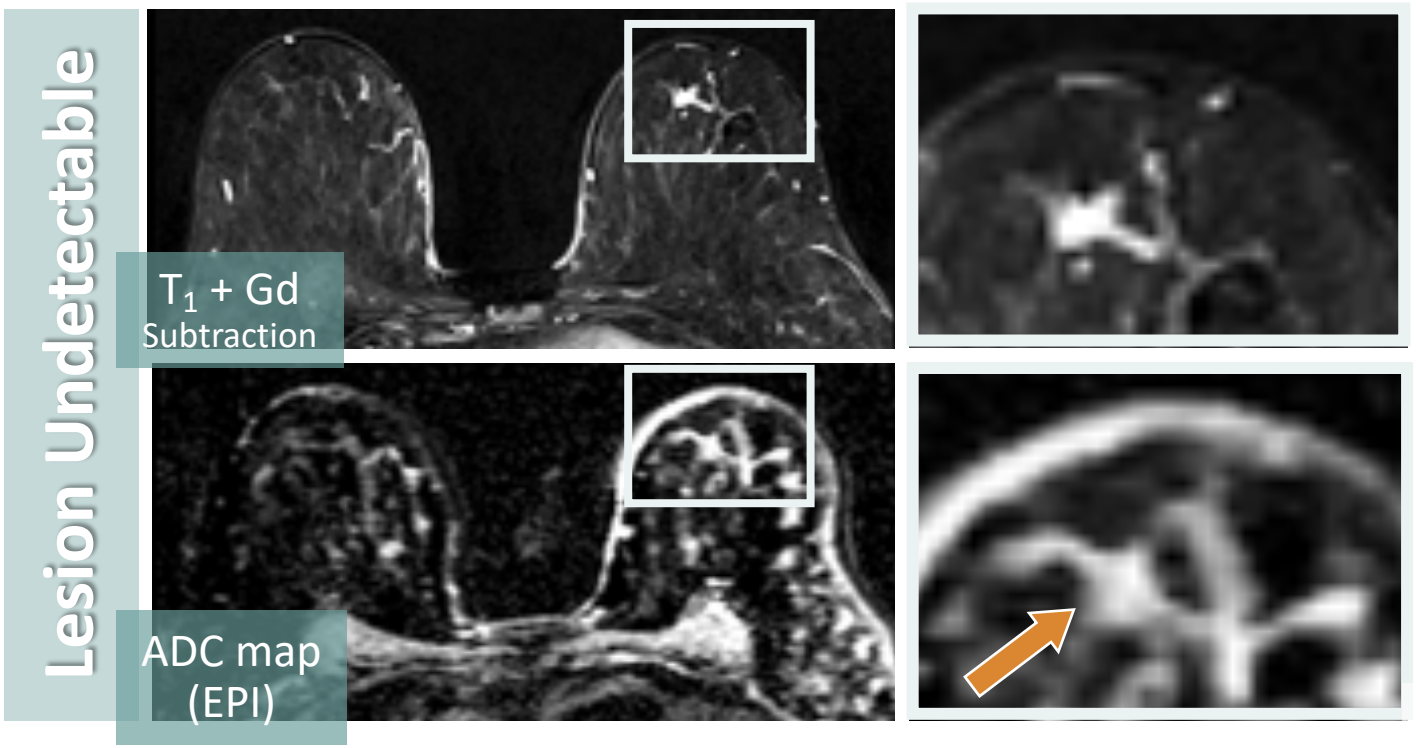
- Fast, no shot-to-shot phase errors, and low power deposition



But…

1. **Low resolution**
2. Geometric distortion and chemical shift
3. Nyquist ghosts





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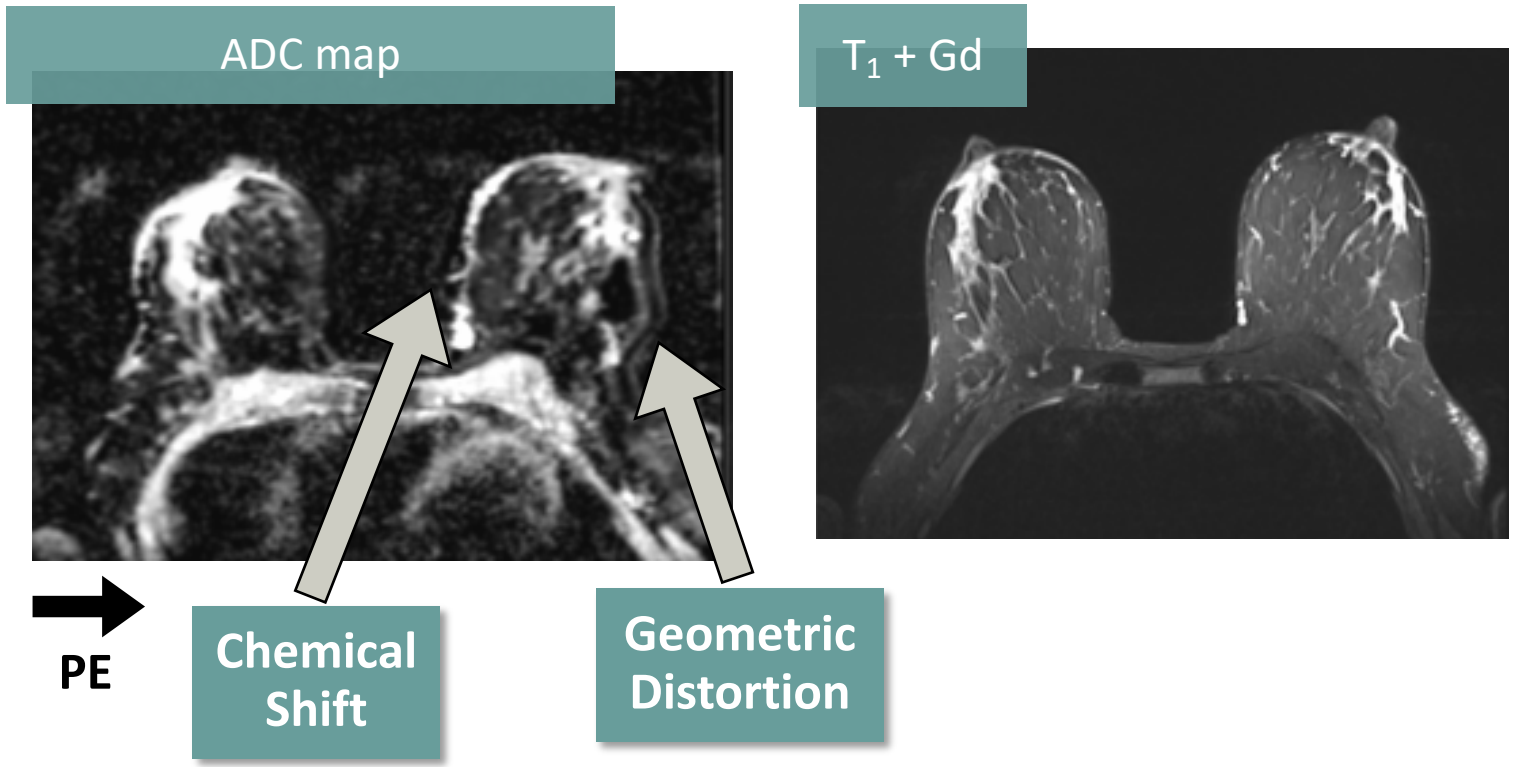

But…

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2. **Geometric distortion and chemical shift**
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Phase accrual ➔ geometric shift in PE direction:

$$\Delta y_{PE} = \frac{\Delta f}{BW_{PE}} FOV_{PE}$$

Δf: off resonance (Hz)
Major sources:
1. Fat (chemical shift)
2. B_0 inhomogeneity

$\frac{1}{t_{esp}}$: effective BW in PE direction

Problems with Breast DWI

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But…

1. Low resolution
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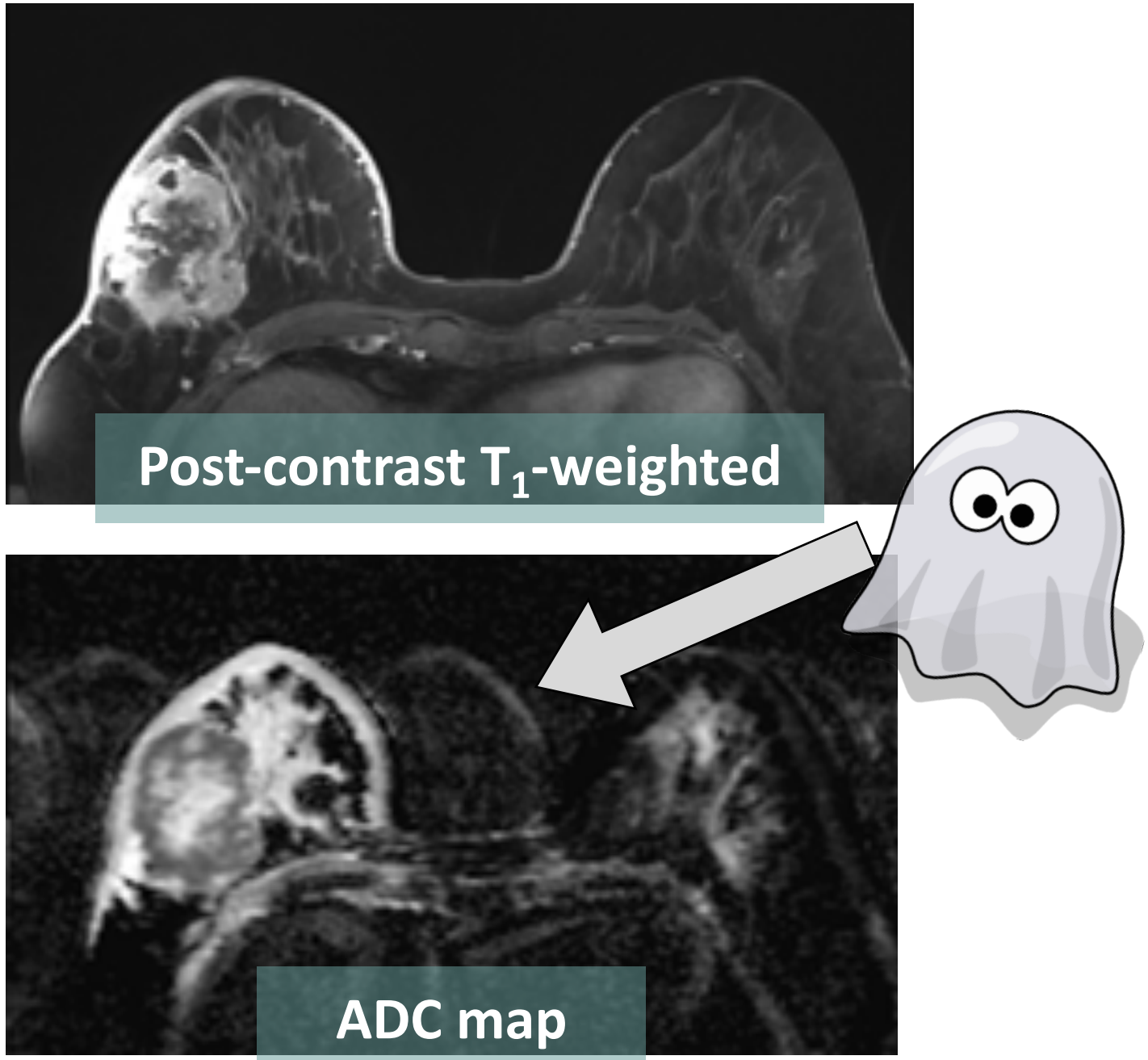

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- Why breast DWI?
- Problems with SE-EPI: distortion, Nyquist ghosts, limited resolution

Part 1: Ghost correction

- The Nyquist ghost
- Referenceless ghost correction

Part 2: High Resolution

- Axially reformatted SMS
- Phantom study
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Discussion, future directions, & summary

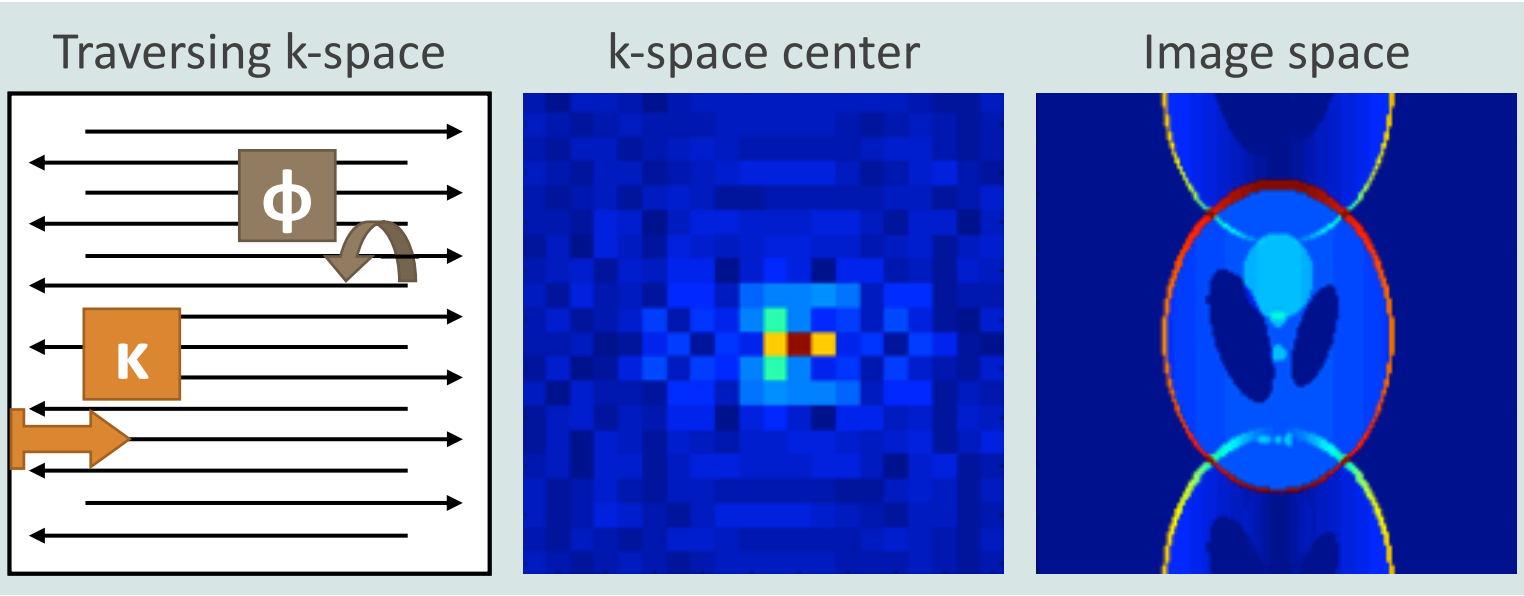
Flashback to 1984…
I mean, 2015

Purpose:

1. To **characterize** the Nyquist ghost artifact
2. To assess **referenceless** methods compared to the standard **3-line navigator** in **standard SE-EPI** breast DWI

Background: Nyquist Ghosts in EPI

Actual k-space



Caused by **RO+/RO- inconsistencies**

- Eddy currents
- Imperfect gradients
- Timing errors

Modeled as a 1st-order phase difference

In image space:

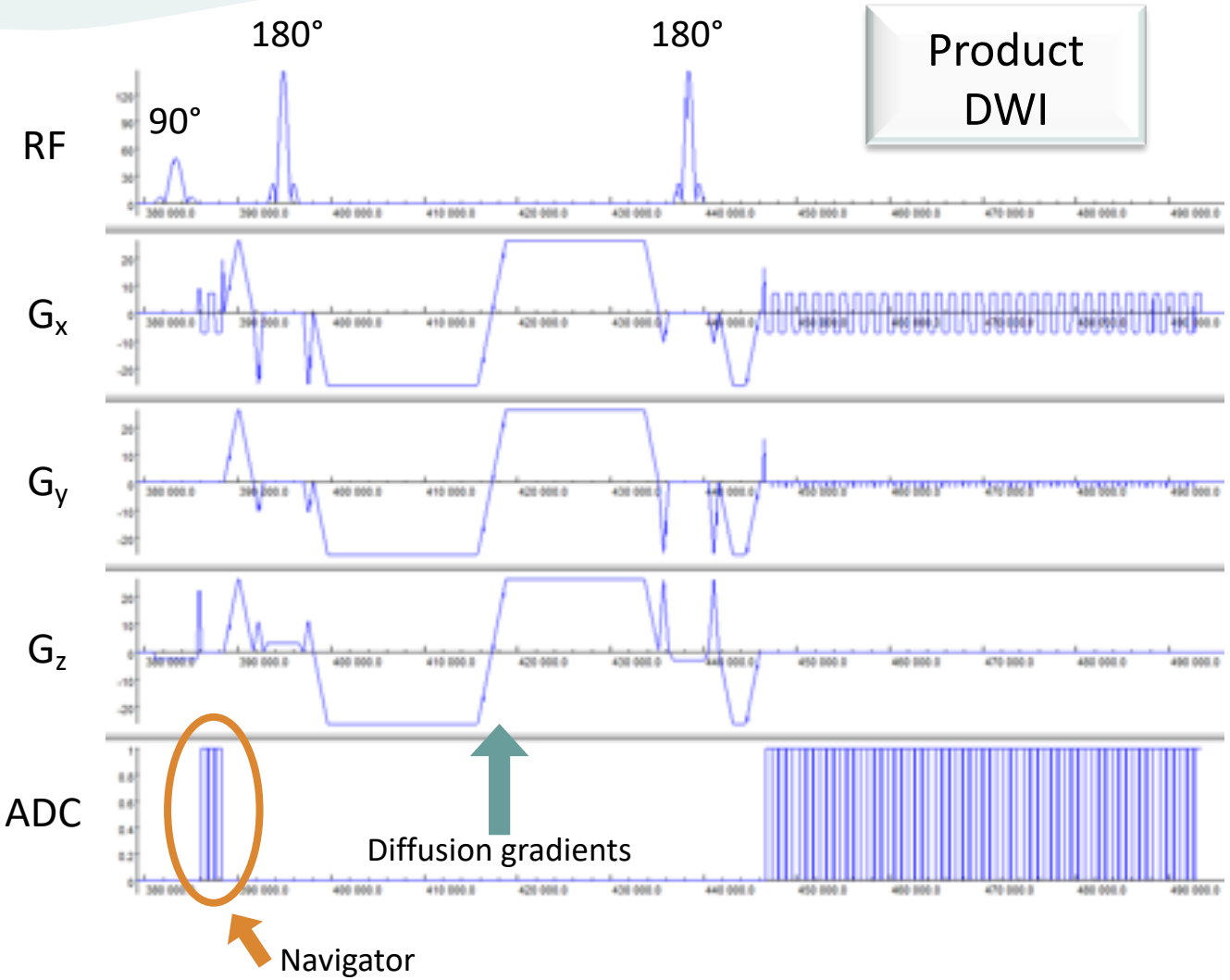
$$I_{meas}(x,y) = I_0(x,y)\cos\left(\frac{\pi\kappa x}{N_x}+\phi\right) + iI_0\left(x, y-\frac{FOV}{2}\right)\sin\left(\frac{\pi\kappa x}{N_x}+\phi\right)$$

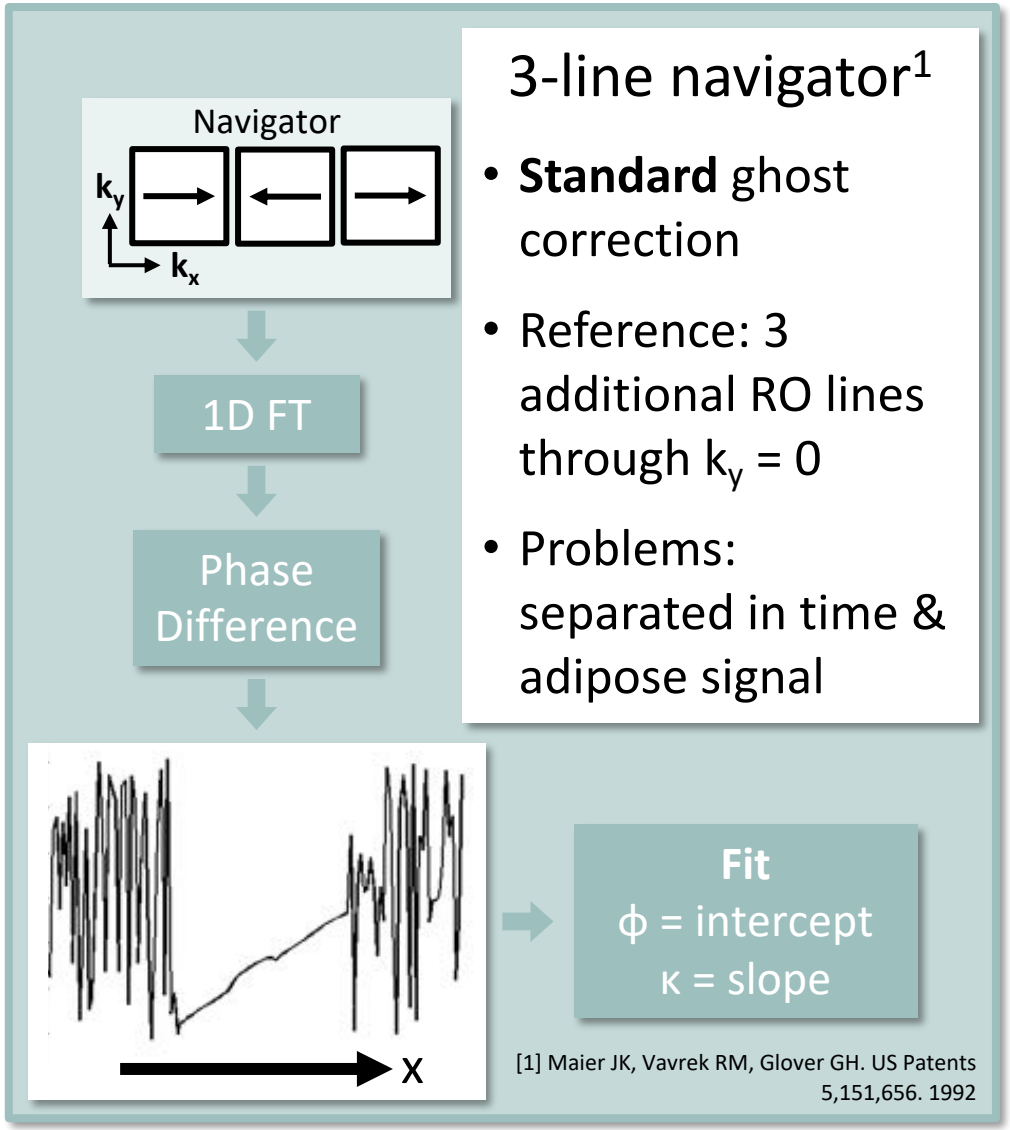
Object **Ghost**

Bernstein MA, King KF, Zhou XJ. Handbook of MRI pulse sequences. 2004.

I_0 = Ideal Image
I_{meas} = Ghosted Image
N_x = # of odd points
κ = shift in k_{RO}
ϕ = even/odd phase difference

Background: Three-line Navigator





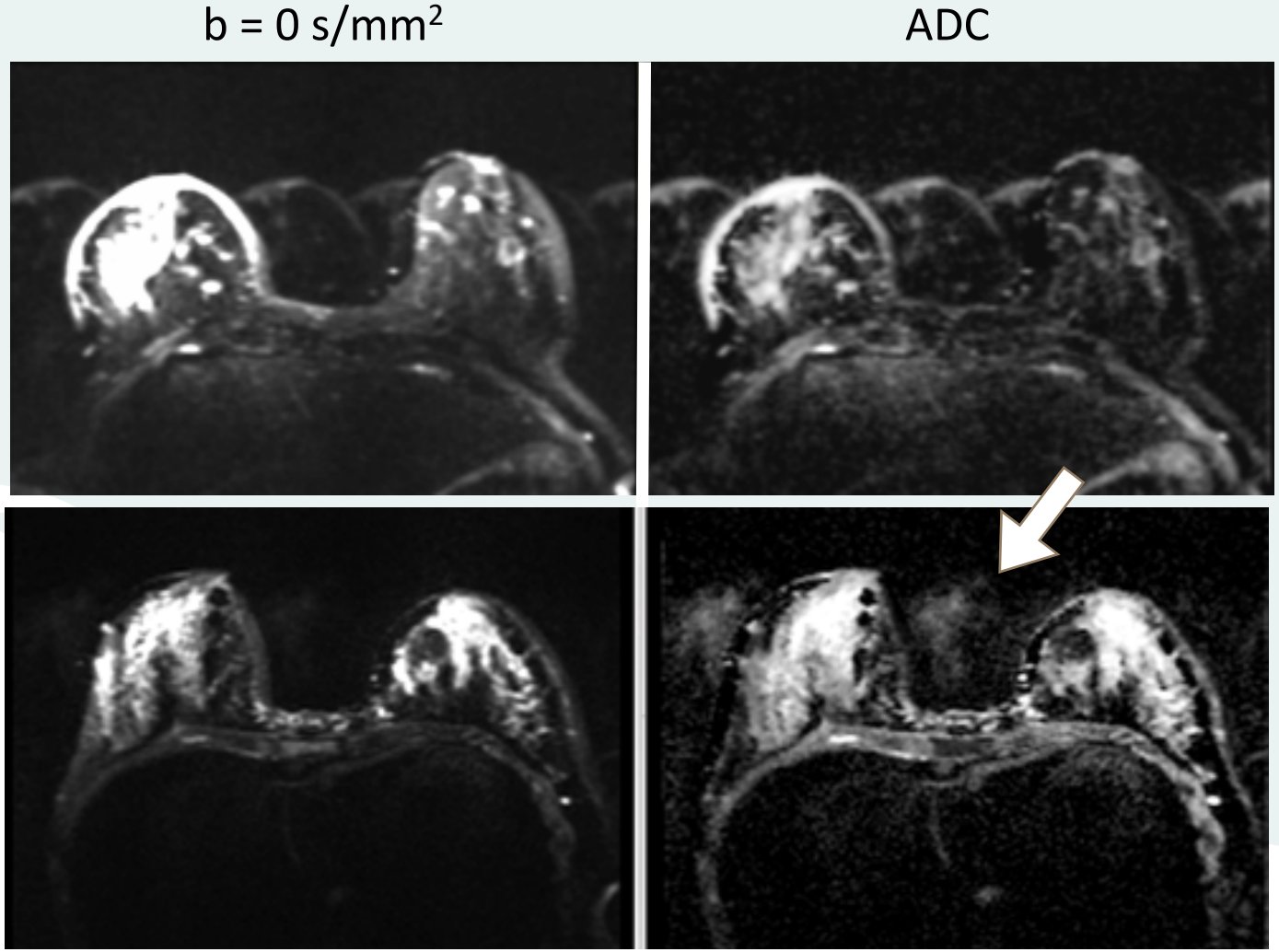
3-line navigator[1]

- **Standard** ghost correction
- Reference: 3 additional RO lines through $k_y = 0$
- Problems: separated in time & adipose signal

[1] Maier JK, Vavrek RM, Glover GH. US Patents 5,151,656. 1992

Background: Three-line Navigator

- Often **fails in breast imaging**
  - Unsuppressed fat, bigger B_0 inhomogeneity, respiratory motion, etc.
- Even small ghosts can have a **large impact on the ADC maps** and bias ADC values

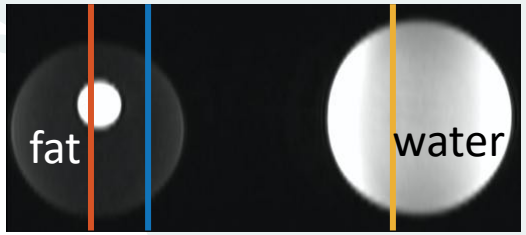


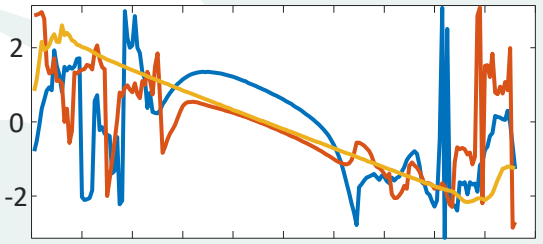
Preliminary Studies: Discussion

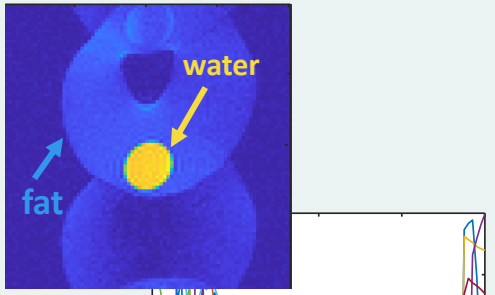
- Bimodal coil distribution
- Fat affects the navigator even when it is suppressed in the image
- Linear but time varying – the 3-line navigator measures the beginning of the echo train

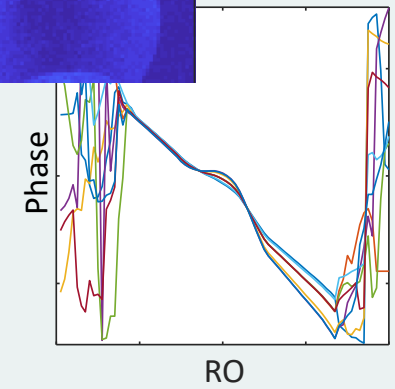
Why referenceless?!

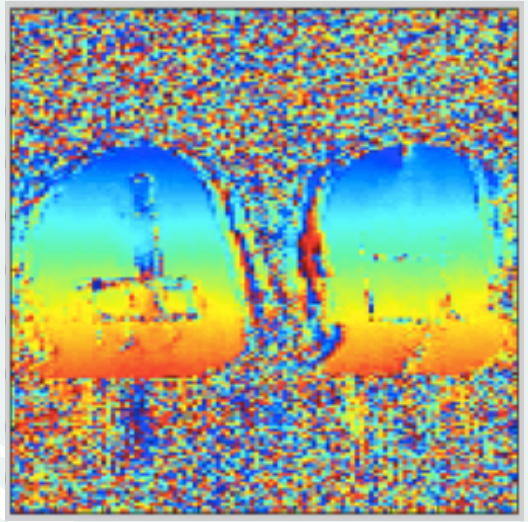
- Measures the weighted readout "average"
- Insensitive to fat because it does not rely on fitting

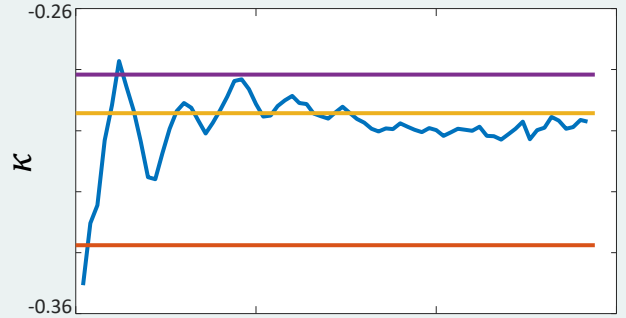


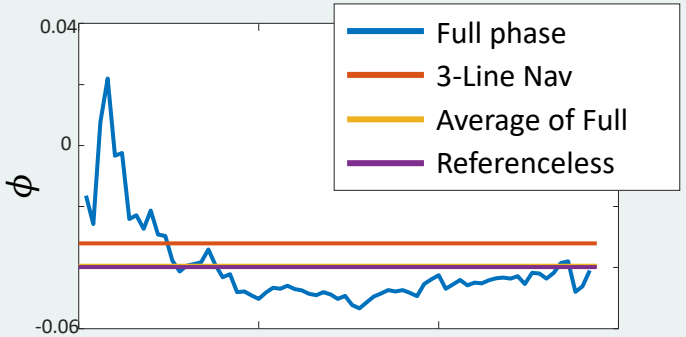












Preliminary Studies: Discussion

- Bimodal coil distribution
- Fat affects the navigator even when it is suppressed in the image
- Linear but time varying – the 3-line navigator measures the beginning of the echo train

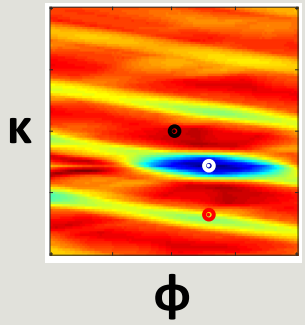
Why referenceless?!

- Measures the weighted readout "average"
- Insensitive to fat because it does not rely on fitting

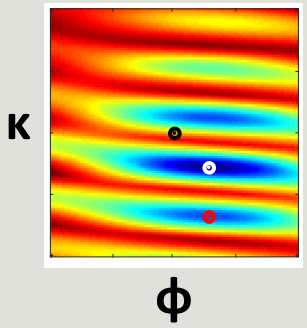
Referenceless methods

- **Data-driven** approach (no reference scans needed)
- **Optimization** over ϕ and κ for a given cost function:

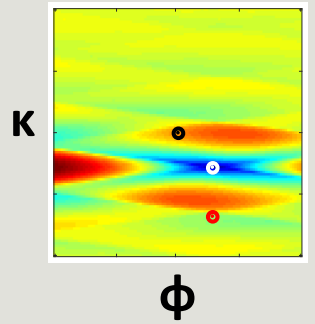
Entropy[1,2]: image entropy

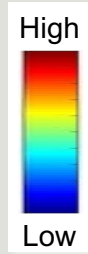


SVD[3]: enforce low rank of k-space



Ghost/Object (G/O): an image space ratio





Minima correspond to **ghost-free** image

[1] Clare S. Proc ISMRM, 2003. p.1041. [2] Skare S, et al Proc ISMRM, 2006. p.2349. [3] Peterson E, et all. Proc ISMRM 23; 2015 p.75

Contact me for code!

In Vivo Study: Methods

- 41 female subjects
- Single-shot 2D SE-EPI DWI derived from ACRIN 6698 clinical trial[1,2]
- Siemens Prisma^{fit} 3T system with a Sentinelle 16-channel breast coil
- TR = 8 s, TE = 51/74 ms (monopolar/bipolar diffusion, N = 12/29)
- GRAPPA acceleration R = 3, acquisition time ≤ 5 min

Offline ghost correction with five **1st-order** methods (all coil-, slice-, and acquisition-specific)

A) Standard 3-line navigator[3]

B) Entropy Minimization[4,5]

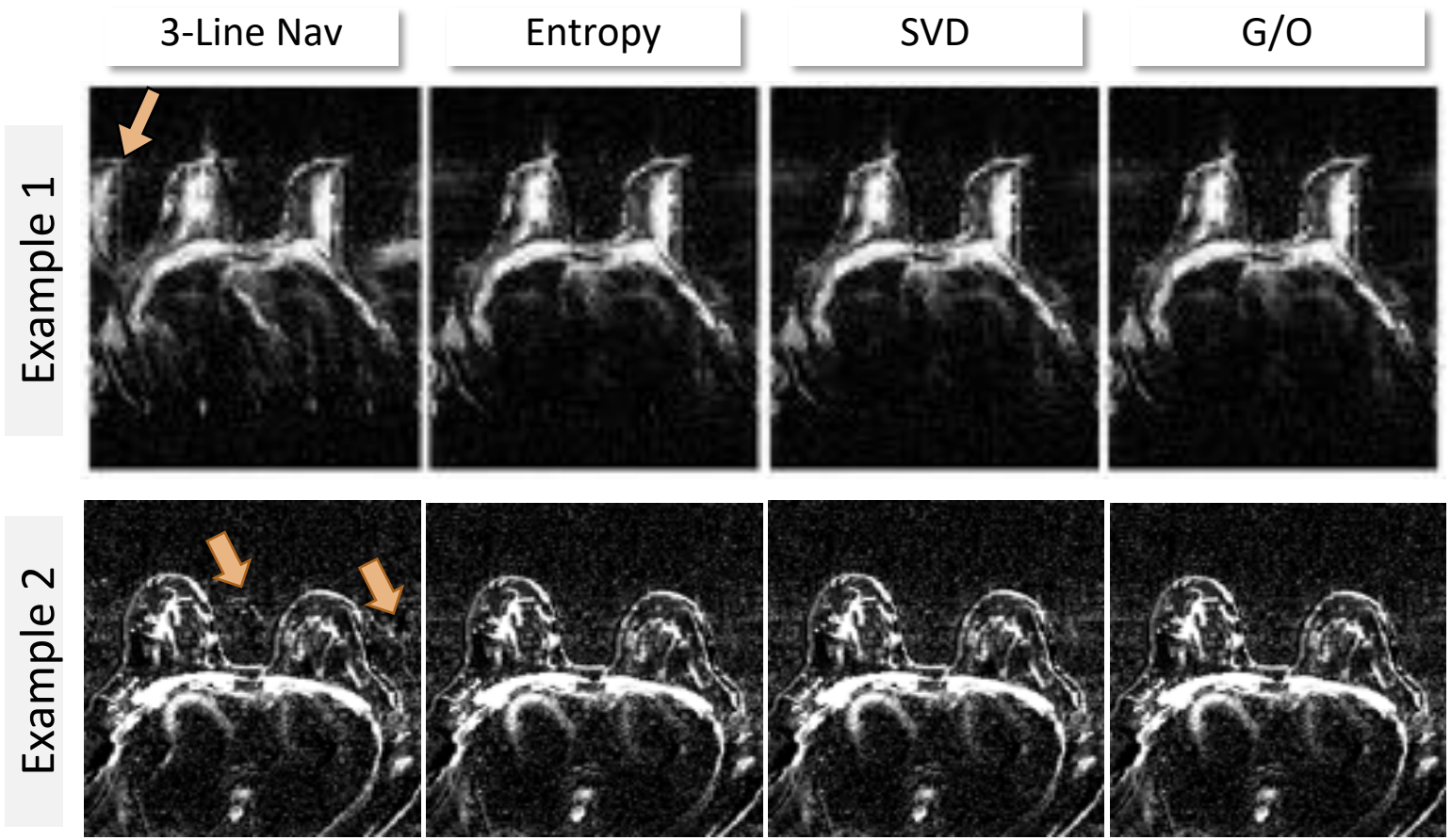
C) Singular Value Decomposition (SVD)[6]

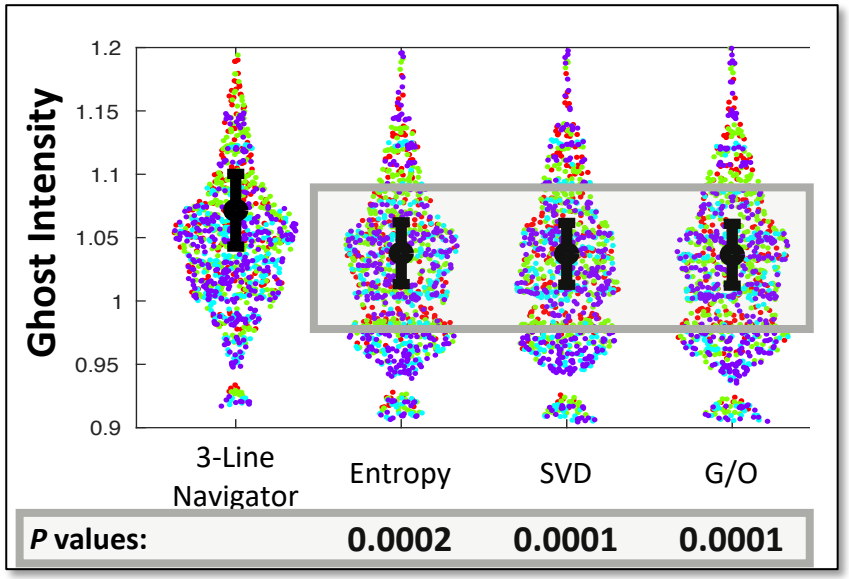
D) Ghost/Object (G/O)

E) Median ~ median(B, C, D)

[1] Hylton N, Partridge SC. 2012. | [2] Partridge SC, et al. Radiology 2018:180273. | [3] Maier JK, Vavrek RM, Glover GH. US Patents 5,151,656. 1992 | [4] Clare S. ISMRM, Toronto, 2003. p. 1041 | [5] Skare S, Clayton DB, Newbould R, Moseley M, Bammer R. Seattle, 2006. p. 2349. | [6] Peterson E, Aksoy M, Maclaren J, Bammer R. ISMRM, Toronto, 2015. p. 75. | [7] McKay JA, et al. ISMRM, Paris, 2017, p. 5339.

Results





All referenceless methods yield **reduced ghosts** compared to the standard approach

Part 1: *Summary*

Understand the ghost

- Characterized the ghost
  - Mostly linear but is affected by eddy currents
  - The 3-line navigator is unreliable, especially in the presence of fat

2016 ISMRM abstract: McKay JA, Moeller S, Ramanna S, Auerbach EJ, Nelson MT, Ugurbil K, Yacoub E, Bolan PJ. Improving EPI Phase Correction for Breast DWI.

Referenceless methods

- Implemented several referenceless methods
- Developed Ghost/Object minimization

2018 ISMRM abstract: McKay JA, Moeller S, Zhang L, Auerbach EJ, Nelson MT, Bolan PJ. Comparison of Referenceless Methods for EPI Ghost Correction in Breast DWI.

2018 ISMRM abstract: McKay JA, Moeller S, Ramanna S, Auerbach EJ, Metzger G, Nelson MT, Ugurbil K, Yacoub E, Bolan PJ. Novel Image-based Nyquist Ghost Correction of Diffusion-Weighted Echo Planar Imaging using Ghost/Object Minimization.

U.S. Patent Application, Filed June 3, 2019: McKay JA, Bolan PJ. System and Method for Nyquist Ghost Correction in Medical Imaging.

Assessment

- Referenceless methods reduced ghosts in breast DWI

MRM Note: McKay JA, Moeller S, Zhang L, Auerbach EJ, Nelson MT, Bolan PJ. Nyquist Ghost Correction of Breast Diffusion Weighted Imaging using Referenceless Methods. 2019.

2018 ISMRM Breast Workshop abstract: McKay JA, Moeller S, Zhang L, Auerbach EJ, Nelson MT, Bolan PJ. Referenceless Nyquist Ghost Correction of Breast Diffusion Weighted Imaging.

OUTLINE

Motivation

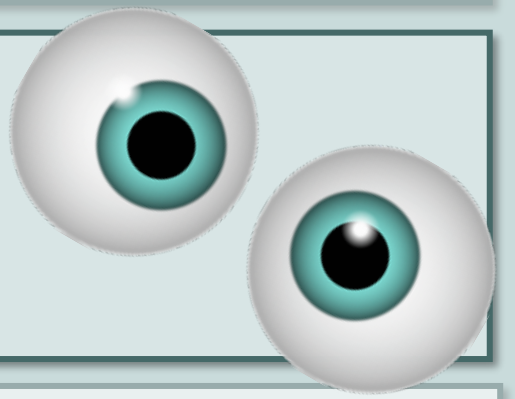
- MRI background
- Diffusion weighting
- Why breast DWI?
- Problems with SE-EPI: distortion, Nyquist ghosts, limited resolution

Part 1: Ghost correction

- The Nyquist ghost
- Referenceless ghost correction

Part 2: High Resolution

- Axially reformatted SMS
- Phantom study
- Reader study

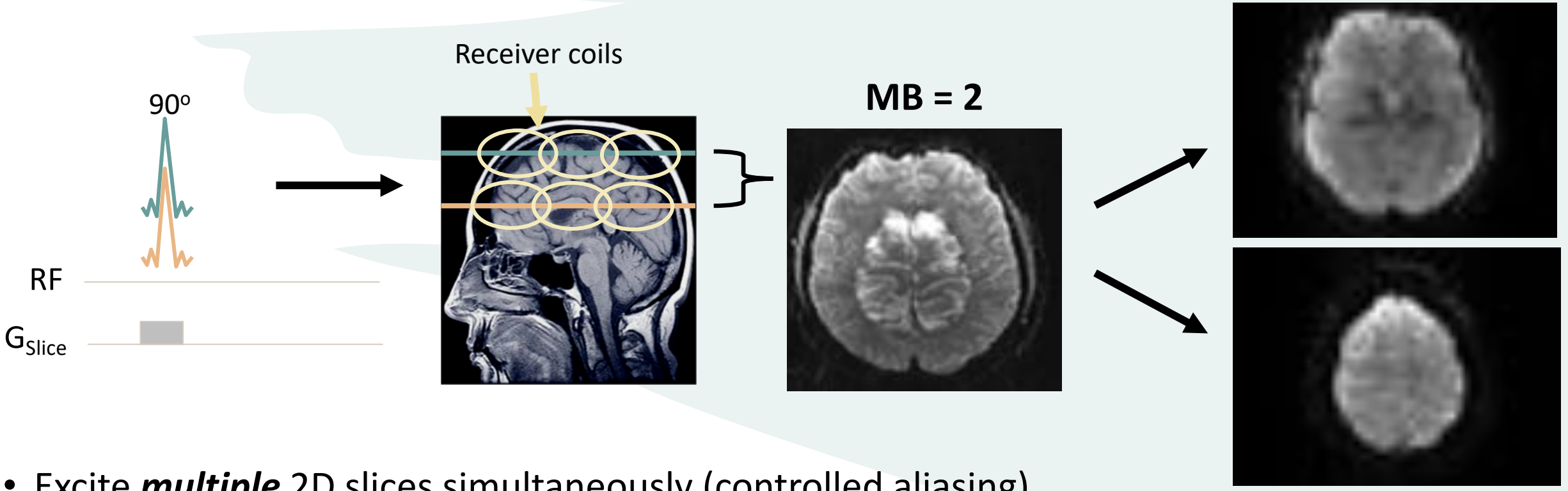


Discussion, future directions, & summary

1. To utilize **Simultaneous Multislice (SMS)** imaging to achieve high resolution breast DWI
2. To evaluate **AR-SMS** with a **reader study**

Simultaneous Multislice (SMS) Imaging

(aka Multiband)



- Excite ***multiple*** 2D slices simultaneously (controlled aliasing)
- Also acquire a fully sampled reference scan (called **Single Band reference**)
- Each coil yields a linear combination of different slices (weighted by sensitivity profiles)
- Matrix inversion separates slices (GRAPPA)

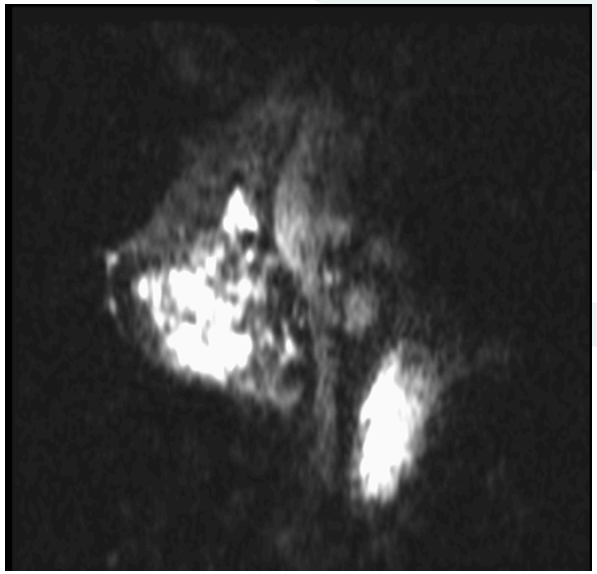
Larkman et al JMRI 2001 (leg), Moeller et al ISMRM 2008, MRM 2010 (brain)

Slide courtesy of Patrick Bolan

Axially Reformatted (AR) -SMS

- Radiologists prefer **axial** images
- **PE** is low-quality encoding

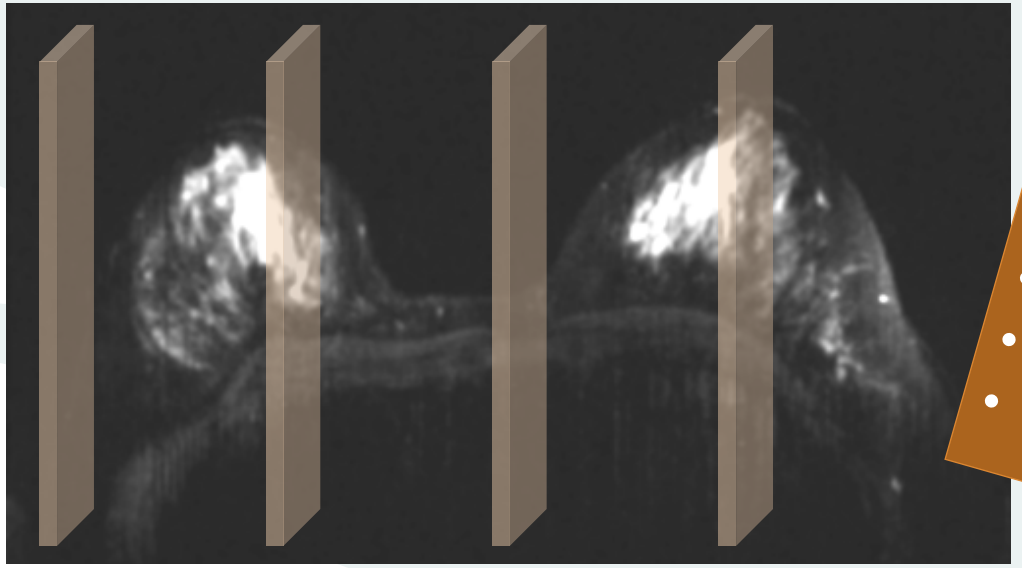
Acquired



PE

RO

Reformatted



RO

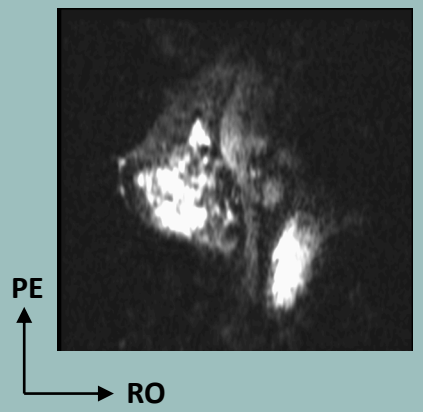
Slice

- 1.25 mm x 1.25 mm x 2.5 mm nominal resolution
- 4 at b = 0, 24 at b = 800
- 5-minute scan time
- Full coverage

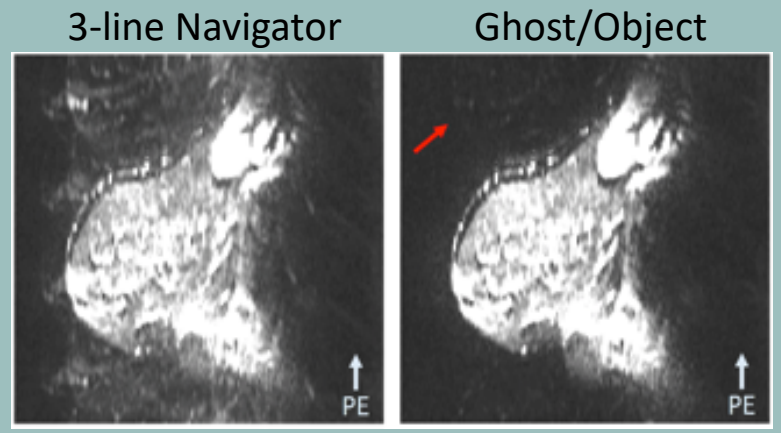
TR / TE [ms]	PE	Echo spacing	# of echoes acquired	b-values (dir/avg)	Diffusion Scheme	Nominal resolution (RO x PE)	Coverage [mm] (R/L, A/P, H/F)	Slice: number, thickness, gap	GRAPPA and SMS	Partial Fourier	Acquisition Time [min:sec]
6500 / 60.80	H/F (Sagittal)	0.93 ms	38	4 at 0 s/mm^2, 24 at 800 s/mm^2	Monopolar	1.25 mm x 2.5 mm	320 (slice) x 240 (RO) x 240 (PE)	256 slices, 1.25 mm, 0 mm	R = 2 MB = 4 (R/L)	6/8 phase	4:52

Reconstruction Details

Acquire sagittal images, save raw data



Ghost correction with Ghost/Object Minimization (per slice, coil, acquisition)

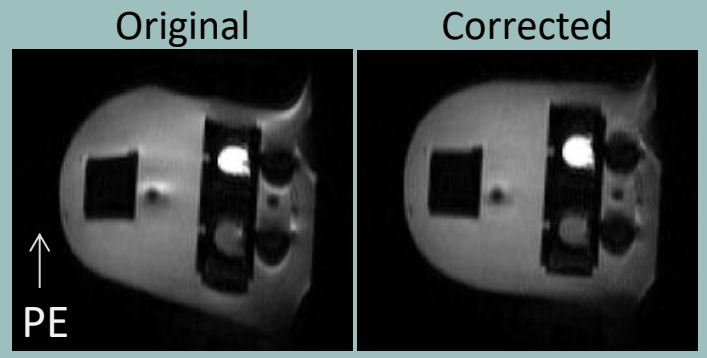


SMS unaliasing (slice GRAPPA)

2nd iteration: slice-specific ghost correction

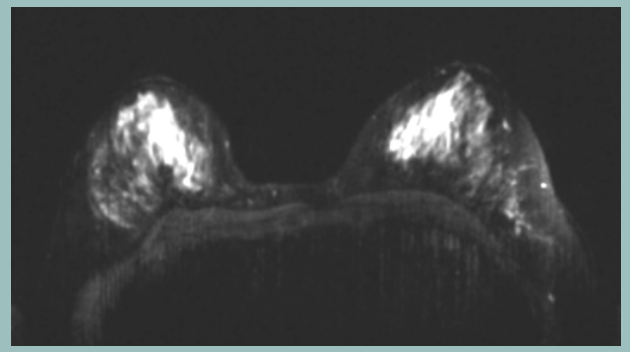
GRAPPA unalias and combine coils
(Also explored: SENSE, LORAKS, E-SPIRiT, and combined GRAPPA and MB recon)

Topup distortion correction



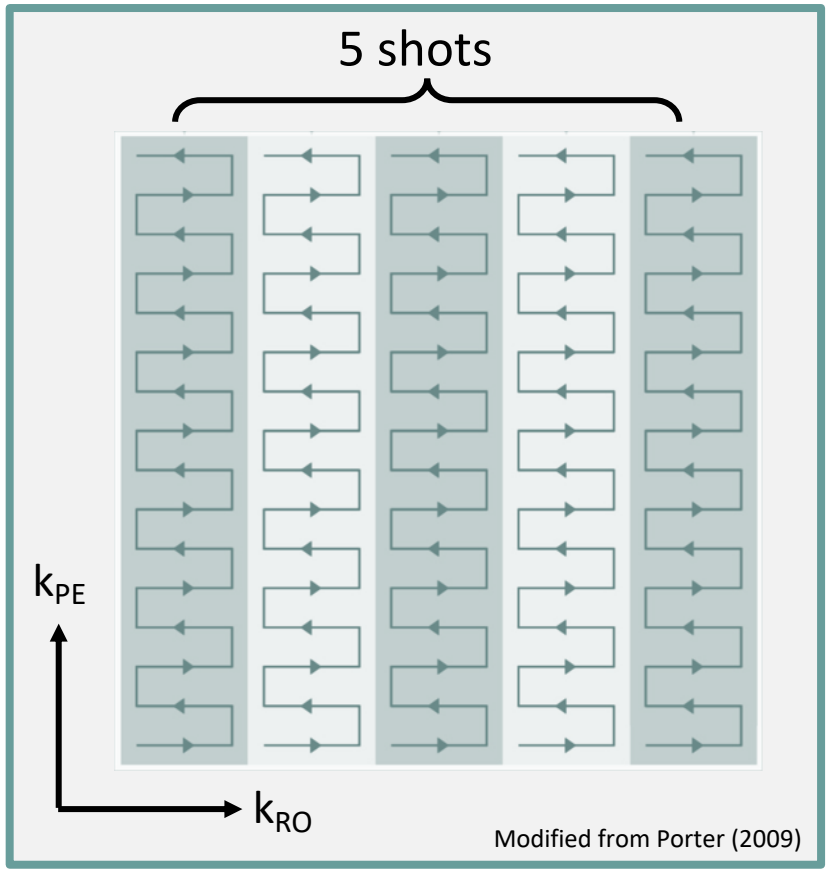
"topup," *FSL*. http://fsl.fmrib.ox.ac.uk/fsl/fslwiki/topup.

Reformat for axial images



Write images and ADC maps to DICOM and send to PACS for **reader study**

RO-segmented EPI for Comparison



Motion between shots can cause artifacts

- Acquire a low-res navigator through the center of k-space to correct phase differences

Benefits

- Higher SNR
- Reduced geometric distortion and chemical shift artifact
- Potential gain in resolution

Disadvantages

- Slower in time
- Demanding on RO gradient

High Res Comparison: Methods

- 3 T Siemens Prisma^{Fit} with 16-ch Sentinelle breast coil
- **15 breast cancer patients + breast phantom with resolution grid**
- DWI within ~5 min each
  - **Standard**: single-shot, axial SE-EPI, ACRIN 6698
  - **RS-EPI**: RO-segmented EPI, 5 segments, Wisner *et al.*'s
  - **AR-SMS**: Sagittal SE-EPI with simultaneous multislice (MB = 4)
- T_2-weighted (T_2w) for comparison

Parameter	Standard	RS-EPI	AR-SMS	T_2-weighted
Sequence	Single-shot SE-EPI	SE-EPI, 5 RO segments	Single-shot SE-EPI	Turbo spin echo
TR/TE (ms)	8000/74	7800/64	6500/60.80	4500/72
Nominal Resolution	1.7 x 1.7 mm	1.8 x 1.8 mm	1.25 x 1.25 mm	0.8 x 0.8 mm
Slice thickness	4 mm	2.4 mm	2.5 mm	3 mm
PE	R → L	A → P	H → F	R → L
RO x PE FOV	320 x 320 mm	350 x 156.8 mm	240 x 240 mm	320 x 320 mm
# of Slices	36	56	256	60
Acceleration	R = 3	R = 2	R = 2 MB = 4	R = 2

[1] Partridge SC, et al. Radiology 2018:180273. [2] Wisner DJ, et al. JMRI 2014;40:674–681. [3] McKay JA, et al. Proc ISMRM. 25; 2017. p. 2115.

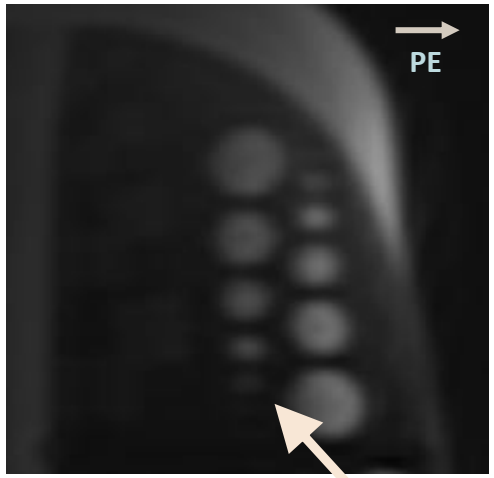
Results: *resolution phantom*

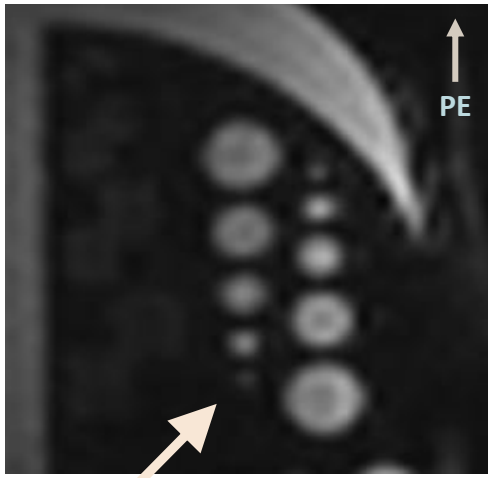
Standard
b = 0 s/mm²

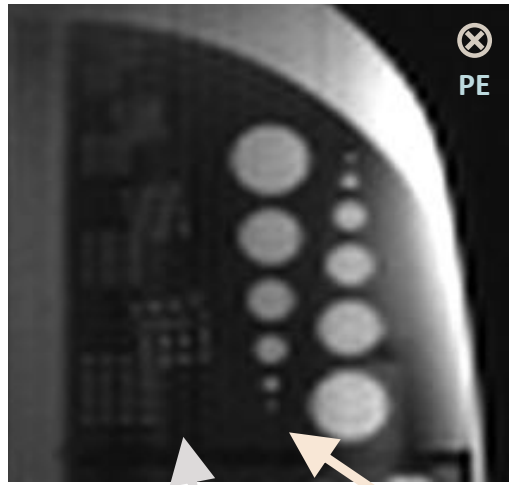
RS-EPI
b = 0 s/mm²

AR-SMS
b = 0 s/mm²

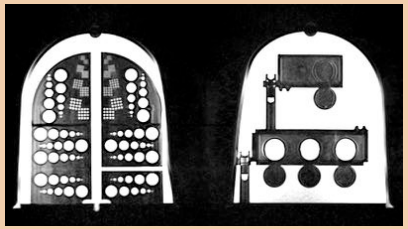
T_2-weighted anatomical

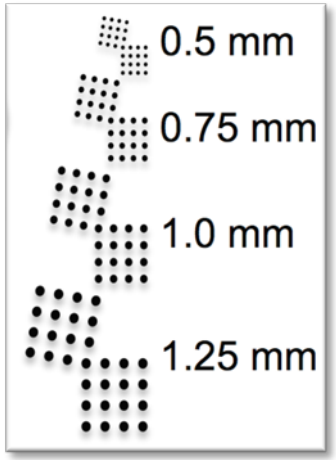


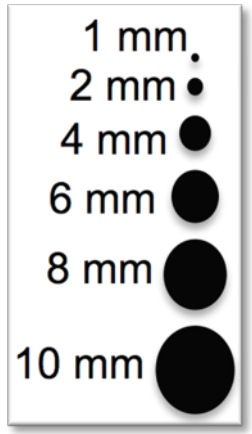




Breast phantom







2 mm feature

1.25 mm grid

1 mm feature

Reader Study

- 3 readers
- 28 subjects (8 screening, 20 ISPY) with 30 lesions
- See 3 methods side-by-side in random order (not blinded)
- Measure size and ADC and score confidence in measurements
- Rank overall quality
- Rate overall quality
- Linear mixed model

reader:_____ case:_____

Size on **CE-MRI:** LD (mm):_____

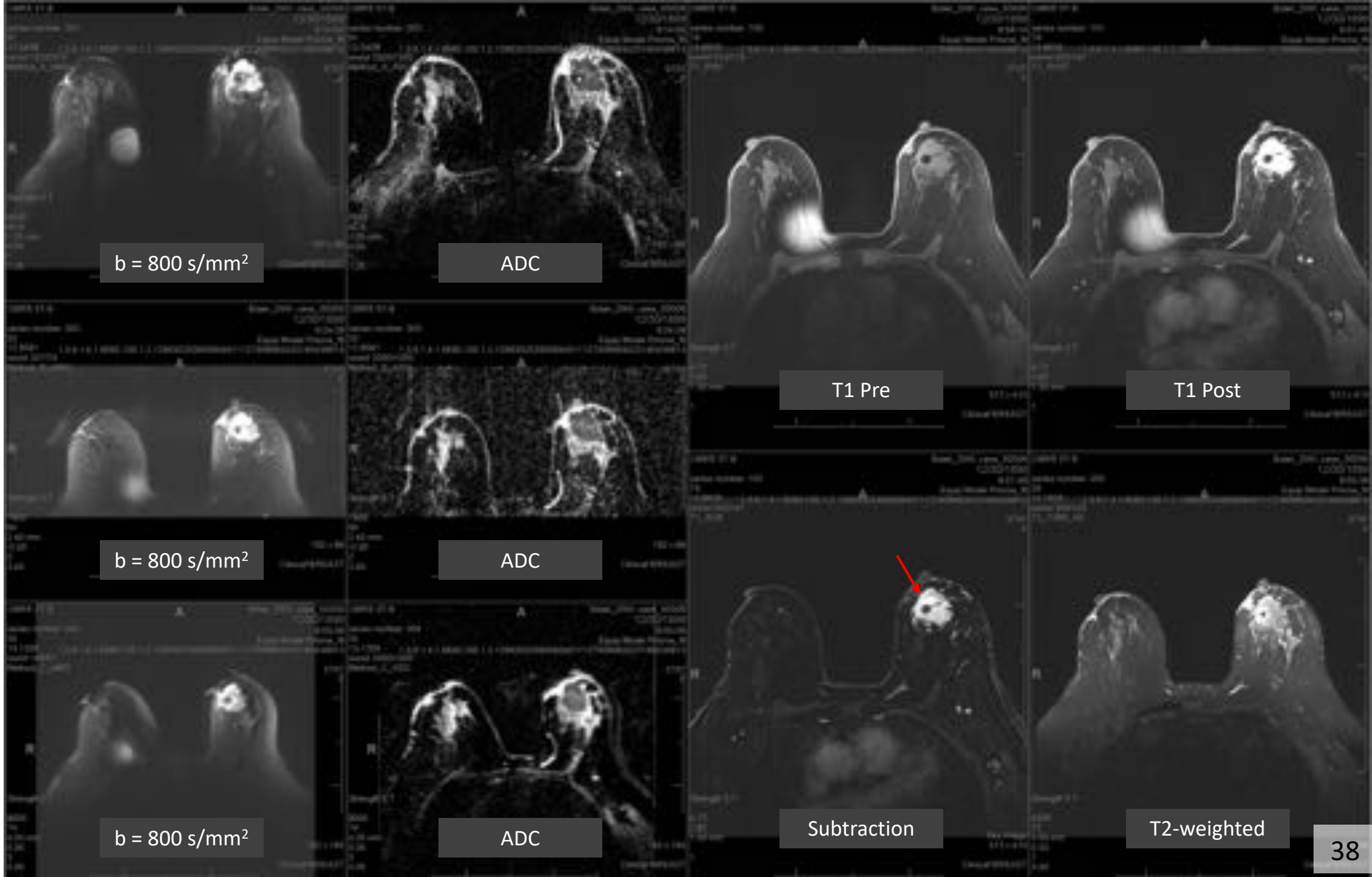
	Method A	Method B	Method C
Size on b=800:	LD (mm):_____	LD (mm):_____	LD (mm):_____
Mean ADC value:	mean:_____	mean:_____	mean:_____
Lesion Correspondence Confidence:	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5
ADC confidence:	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5

overall quality rank (1st, 2nd, 3rd):	_____	_____	_____
overall quality:	1 2 3 4 5	1 2 3 4 5	1 2 3 4 5

Method A (AR-SMS)

Method B (RS-EPI)

Method C (Standard)

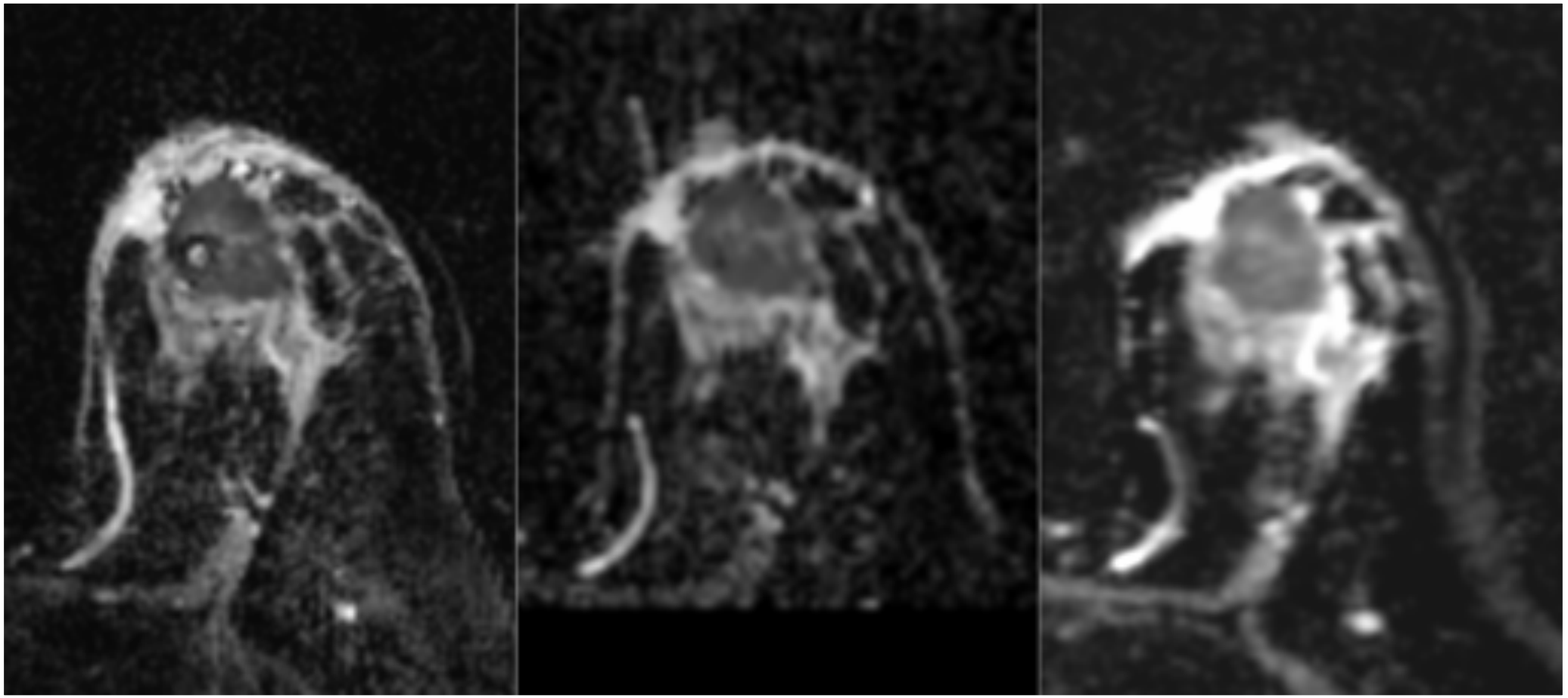


ADC Maps

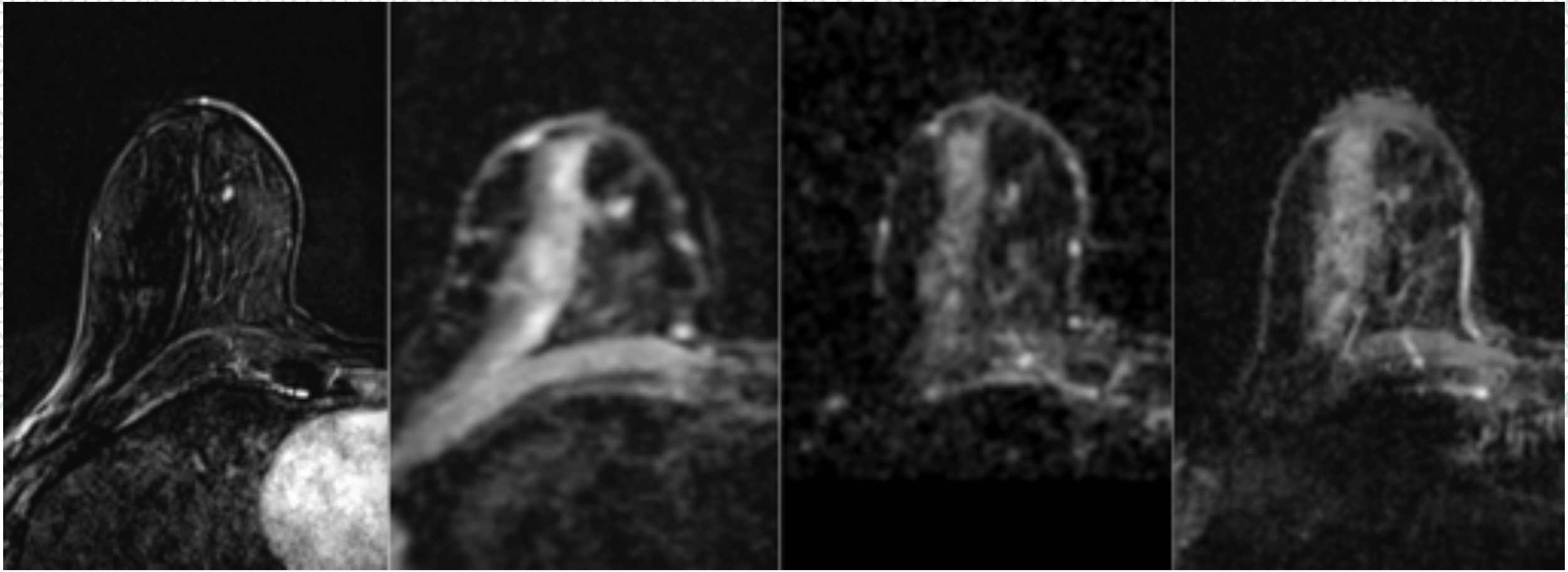
Method A: AR-SMS

Method B: RS-EPI

Method C: Std



ADC MAPS

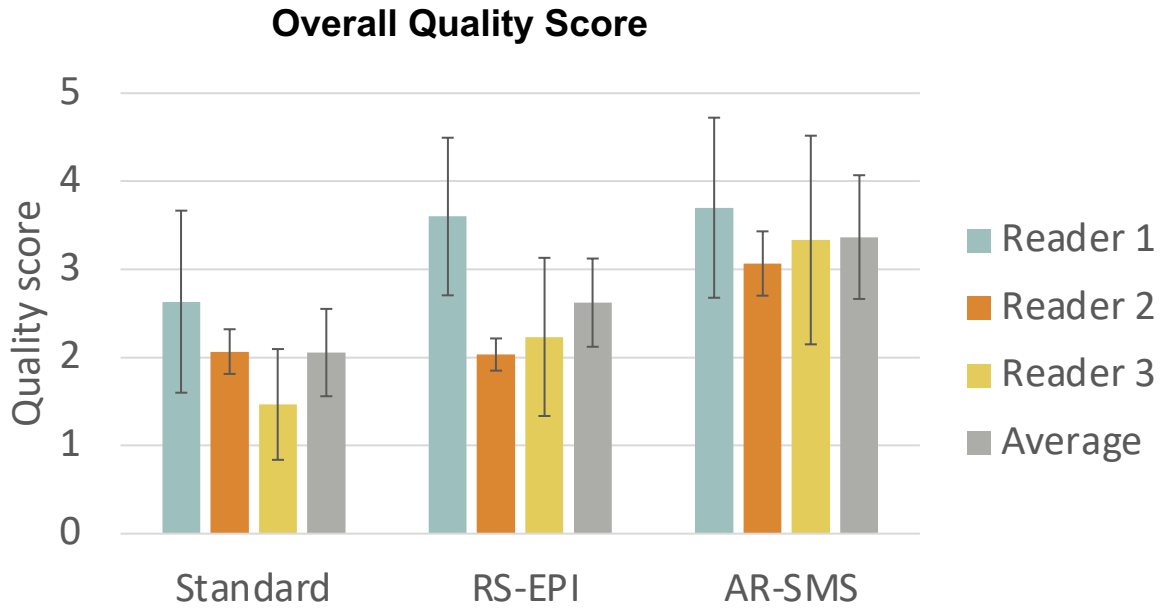


T_1 Subtraction **Standard** **RS-EPI** **AR-SMS**

Results

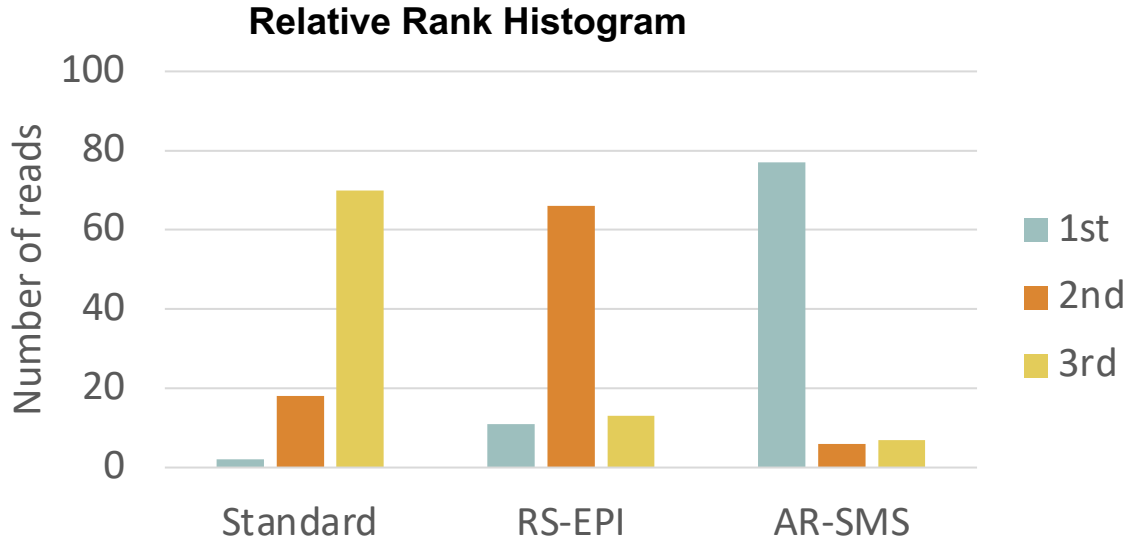
Quality Comparison by Linear Mixed Model

Method Comparison	Effect (95% CI)	p-value
RS-EPI vs. Standard	0.57 (0.36, 0.77)	**<0.001***
AR-SMS vs. Standard	1.31 (1.10, 1.52)	**<0.001***
AR-SMS vs. RS-EPI	0.74 (0.54, 0.95)	**<0.001***



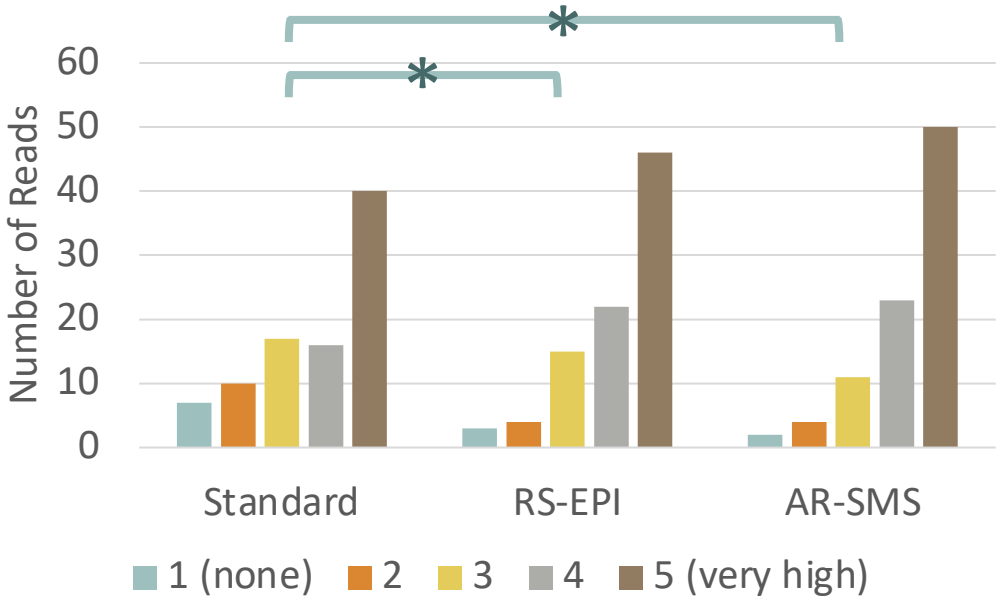
Rank Comparison by Linear Mixed Model

Method Comparison	Effect (95% CI)	p-value
RS-EPI vs. Standard	-0.73 (-0.89, -0.58)	**<0.001***
AR-SMS vs. Standard	-1.53 (-1.69, -1.40)	**<0.001***
AR-SMS vs. RS-EPI	-0.80 (-0.95, -0.65)	**<0.001***



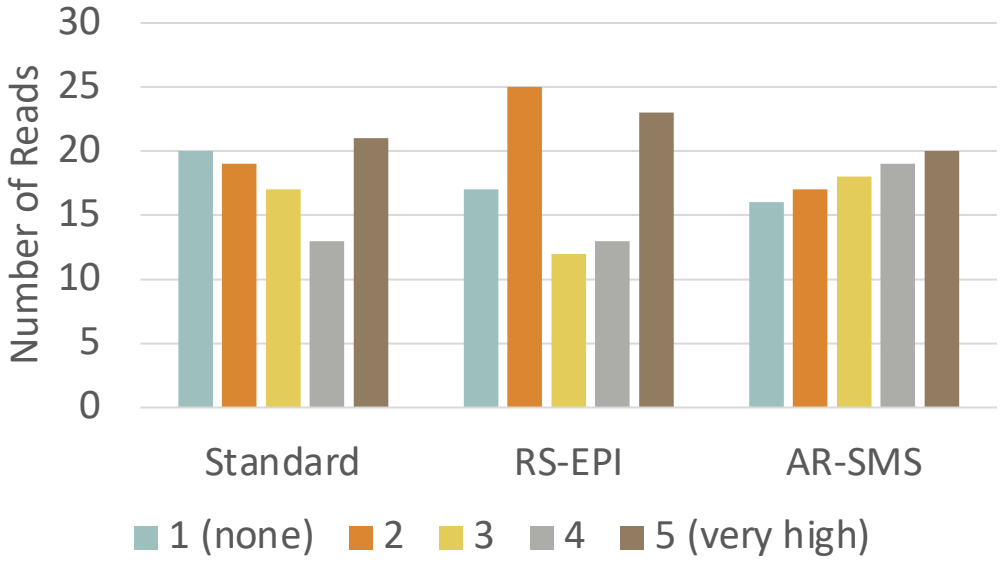
Results

Confidence in measurement of lesion size



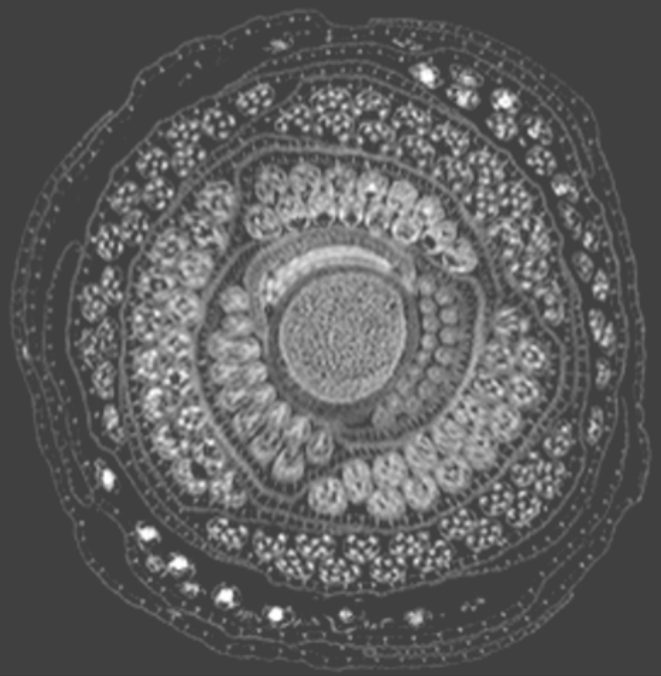
Method Comparison	Effect (95% CI)	p-value
RS-EPI vs. Standard	0.36 (0.15, 0.56)	**0.002***
AR-SMS vs. Standard	0.48 (0.28, 0.68)	**<0.001***
AR-SMS vs. RS-EPI	0.12 (-0.08, 0.32)	0.460

Confidence in ADC measurement



Method Comparison	Effect (95% CI)	p-value
RS-EPI vs. Standard	0.04 (-0.16, 0.25)	0.908
AR-SMS vs. Standard	0.16 (-0.05, 0.36)	0.309
AR-SMS vs. RS-EPI	0.11 (-0.10, 0.32)	0.296

Part 2: *Summary*



Development

- Used SMS with axially reformatting (AR) to achieve high resolution breast DWI
- Ghost/Object referenceless method reduced ghosts
- Applied topup (FSL) for distortion correction

Acknowledgement: Patrick Bolan, Eddy Auerbach, Essa Yacoub, Steen Moeller, Christophe Lenglet

2017 ISMRM abstract: McKay JA, Moeller S, Ramanna S, Auerbach EJ, Metzger G, Ugurbil K, Yacoub E, Bolan PJ. Comparison of methods for high spatial-resolution breast diffusion imaging.

2019 ISMRM abstract: McKay JA, Moeller S, Ramanna S, Church AL, Nelson MT, Auerbach EJ, Ugurbil K, Bolan PJ. Nyquist Ghost Correction of High-Resolution SMS Breast DWI with Ghost/Object Minimization.

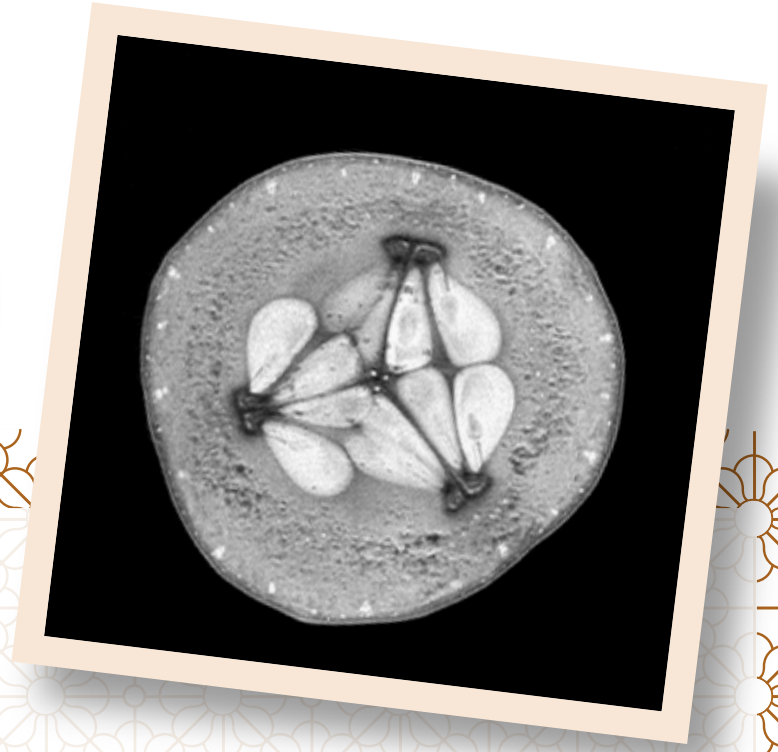
Reader Study

- Conducted a reader study with 30 lesions
- 3 breast radiologists preferred the overall image quality of AR-SMS, followed by RS-EPI and Standard SE-EPI ~ with statistical significance
- Saw improved confidence in lesion size measurement

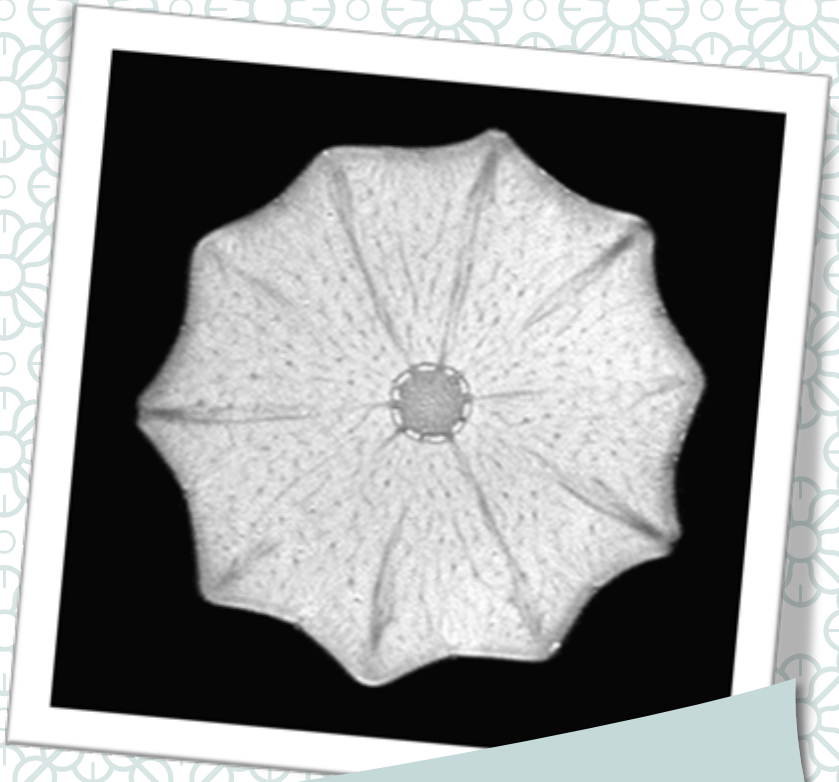
Radiology: McKay JA, Church AL, Rubin N, Emory TH, Hoven NF, Kuehn-Hajder JE,Nelson MT, Ramanna S, Auerbach EJ, Moeller S, and Bolan PJ. A comparison of methods for high spatial resolution diffusion weighted imaging in breast MRI. 2020;297:304–312

2020 ISMRM abstract: McKay JA, Church AL, Rubin N, Emory TH, Hoven NF, Kuehn-Hajder JE, Nelson MT, Bolan PJ. A Reader Study Comparing the Quality of High-Resolution Diffusion Weighted Imaging Methods for Breast MRI.

Final Summary



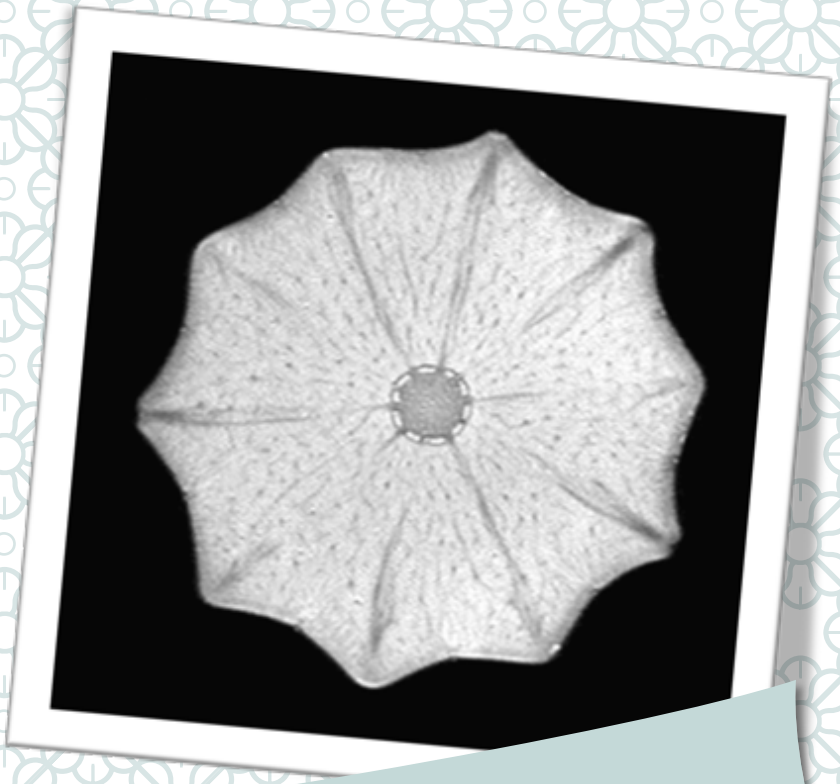
- Characterized the Nyquist ghost in breast DWI
- Implemented referenceless ghost corrections
- Developed Ghost/Object minimization
- Demonstrated that referenceless methods improve ghost correction in standard SE-EPI and AR-SMS
- Proposed a novel acquisition strategy for high resolution full coverage breast DWI in 5 minutes
  - Axially-Reformatted SMS
- Implemented reconstruction pipeline for AR-SMS
- Compared AR-SMS with standard and RS-EPI with phantom study and reader study
  - AR-SMS improved feature detection and SNR
  - Radiologist consistently preferred AR-SMS



Discussion Points

SMS provides very fast encoding, which allows us to reach high resolution breast DWI in a reasonable scan time.

DWI has clinical promise, but it isn't commonly used in the clinic. We need significant improvements to get the radiologists on board! Then we can assess the clinical usefulness.



Now what?

SMS provides very fast encoding, which allows us to reach high resolution breast DWI in a reasonable scan time.

With the Hargreaves lab:

- Combine SMS with multishot EPI with shot LLR reconstruction to reduce distortion (Yuxin Hu and Kitty Moran)
- Apply AR-SMS in other body regions – especially liver and female pelvic imaging

DWI has clinical promise, but it isn't commonly used in the clinic. We need significant improvements to get the radiologists on board! Then we can assess the clinical usefulness.

With the Hargreaves lab:

- Assess the clinical performance in the context of non-contrast screening and the detection of invasive cancer in patients with DCIS

Acknowledgements

UNIVERSITY OF MINNESOTA
Center for Magnetic Resonance of Research

Especially…

- ***Advisor:* Pat Bolan**
- Mike Garwood, Mehmet Akçakaya, and Greg Metzger
- Steen Moeller
- Sudhir Ramanna
- Eddie Auerbach
- Kamil Ugurbil
- Essa Yacoub
- Christophe Lenglet
- Gosia Marjanska
- Ivan Tkáč
- *Clinicians*: Mike Nelson, An Church, and Doug Yee
- *Readers*: Noelle Hoven, Jessica Kuehn-Hajder, and Tim Emory
- *Statisticians:* Lynn Eberly, Nathan Rubin, and Lei Zhang

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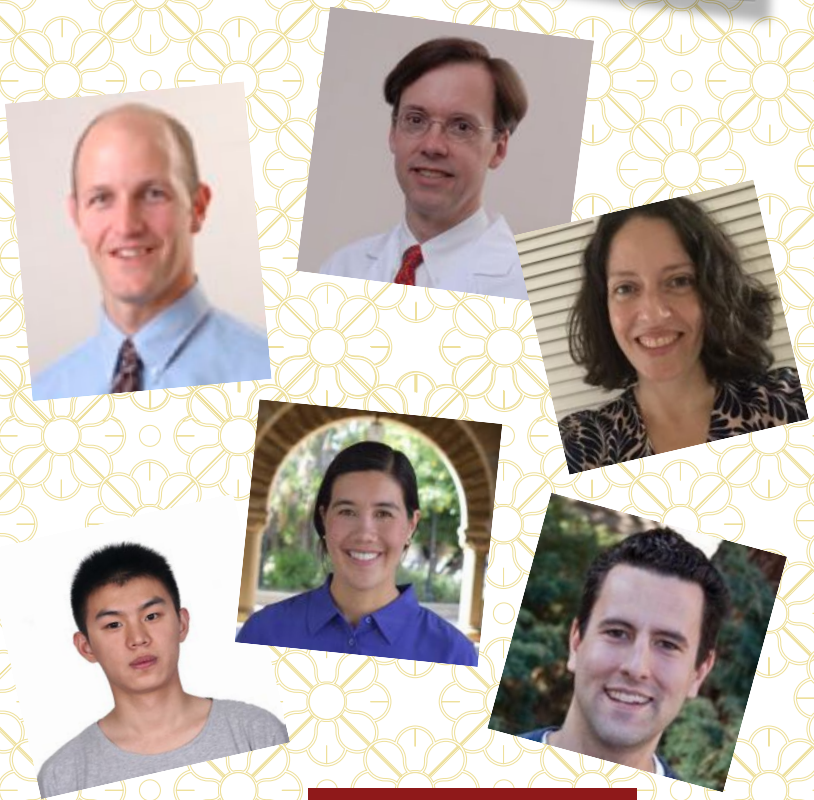
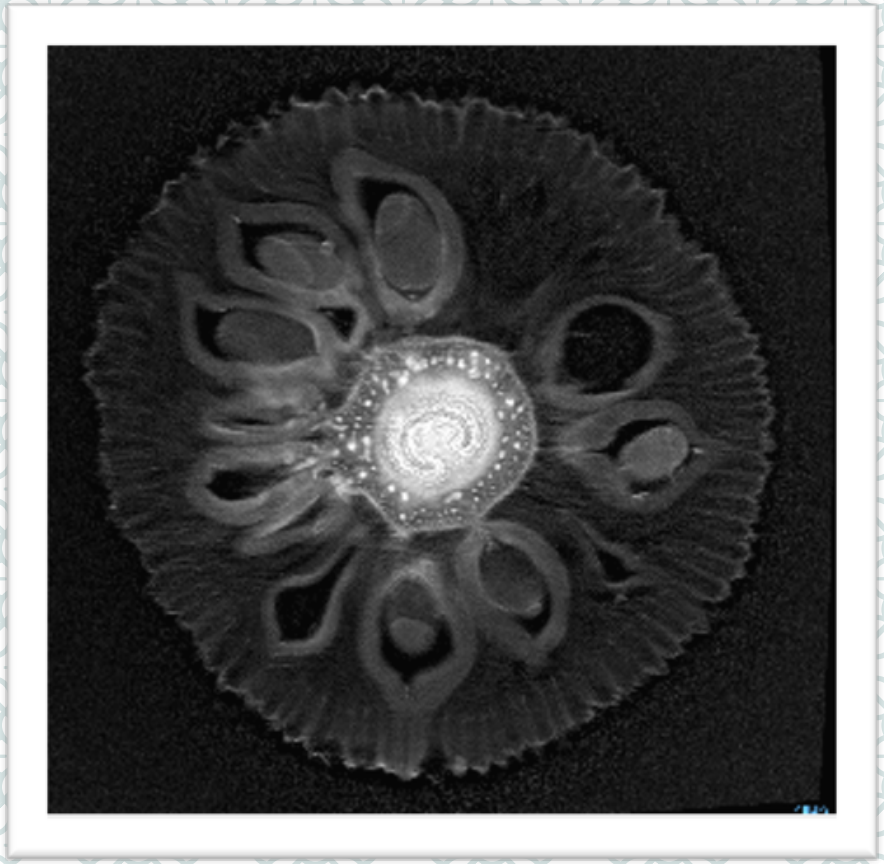


…and others!

Grant support: NIH P41 EB015894 (NIBIB) | NIH R21 CA201834 (NCI) | NIH S10 OD017974-01 (OD) | UL1 TR002494

Miscellaneous MR images: http://insideinsides.blogspot.com



Thank you!