



Fast, Low Contrast, and No Contrast Techniques for Breast MRI

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Conflicts of interest

- I have no conflicts of interest to declare

Outline

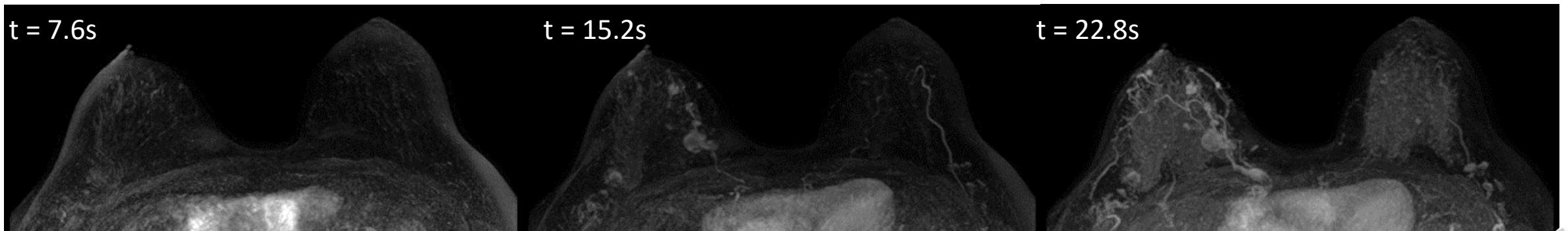
- Ultrafast DCE-MRI
- Low Gd-dose DCE-MRI
- Non-contrast breast MRI techniques:
 - DWI
 - High spectral and spatial resolution imaging
 - Other techniques

Ultrafast Dynamic Contrast-Enhanced MRI



High-temporal resolution breast DCE-MRI

- Breast dynamic contrast-enhanced MRI protocols typically have high spatial resolution and relatively low temporal resolution (≥ 1 min)
- Early studies looking into trade-offs between spatial and temporal resolution concluded that spatial resolution should be favored¹
- Wash-in of contrast media is an important diagnostic parameter
- Faster acquisition protocols offer: better characterization of wash-in kinetics, greater lesion conspicuity^{2,3}, and increased accuracy of pharmacokinetic analysis



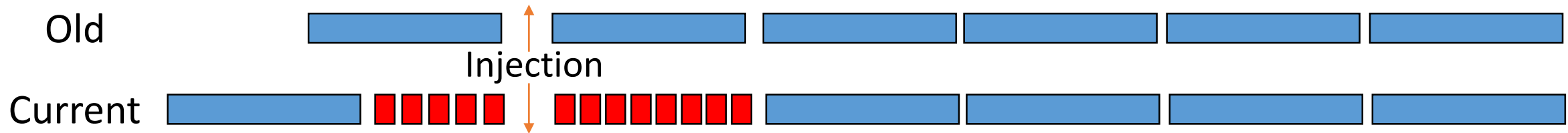
Decreasing acquisition time

- There are a few options to increase the temporal resolution of DCE-MRI
 - Smaller coverage
 - Lower spatial resolution
 - Parallel imaging
 - Partial Fourier
 - Modified acquisition techniques



UChicago acquisition protocol

- We achieved a temporal resolution of ~ 3.5 s on our 3T scanners (Philips Achieva and Ingenia) with a 16-channel bilateral phased array coil using standard Fourier imaging techniques



'Standard'

Acquisition time: 60 s

Acq. voxel size: 0.8 mm x 0.8 mm x 1.6 mm

SENSE factor (RL) : 2.5

Halfscan: 0.85 (ky), 1 (kz)

TR/TE: 4.7 / 2.4 ms

'Ultrafast'

Acquisition time: 3.5 s

Acq. voxel size: 1.5 mm x 1.5 mm x 4 mm

SENSE factor (RL) : 3

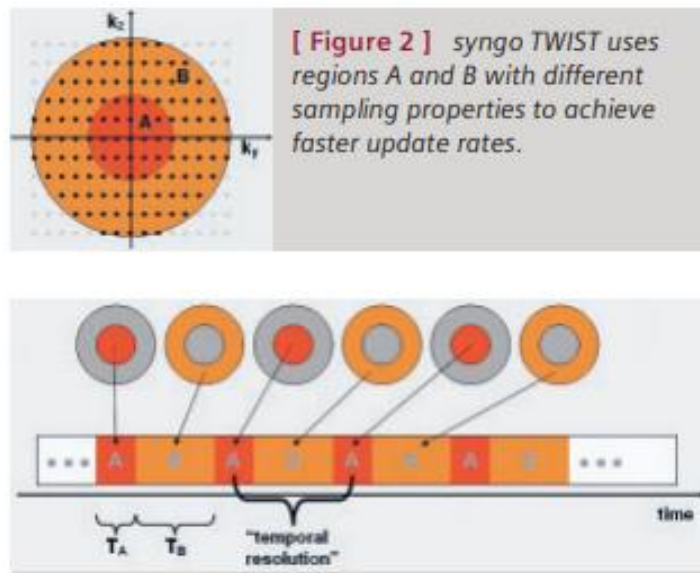
Halfscan: 0.65 (ky), 0.7 (kz)

TR/TE: 2.8 / 1.4 ms

Other ultrafast acquisition techniques

- Modified acquisition and reconstruction techniques can be used to increase the temporal resolution of DCE-MRI while minimizing sacrifices in spatial resolution

TWIST (Laub et al. 2006)



Acquisition voxel size: $1 \times 0.9 \times 2.5 \text{ mm}^3$

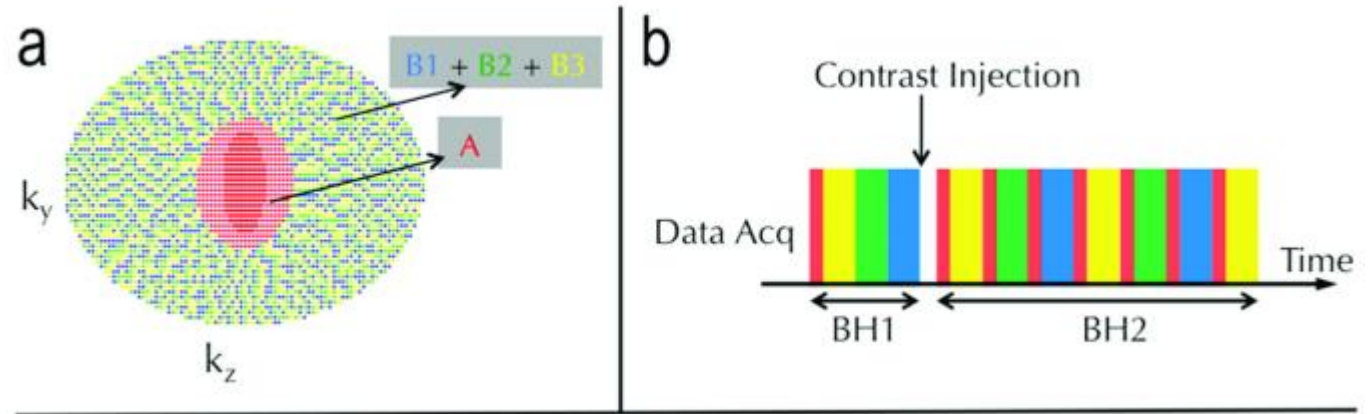
Temporal resolution: 4.32s

A region: 15%

B sampling density: 10%

(Mus et al. 2017)

DISCO (Saranathan et al. 2012)



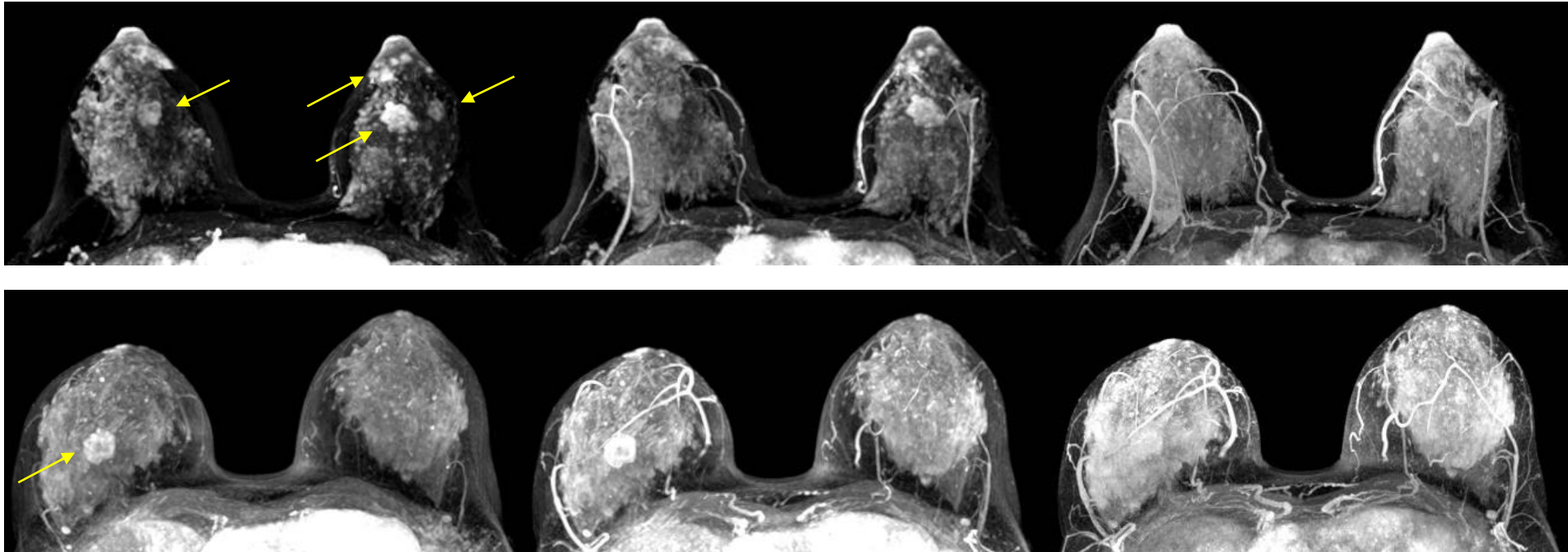
Acquisition voxel size: $1.6 \times 1.6 \times 1.6 \text{ mm}^3$

Temporal resolution: 2.7s

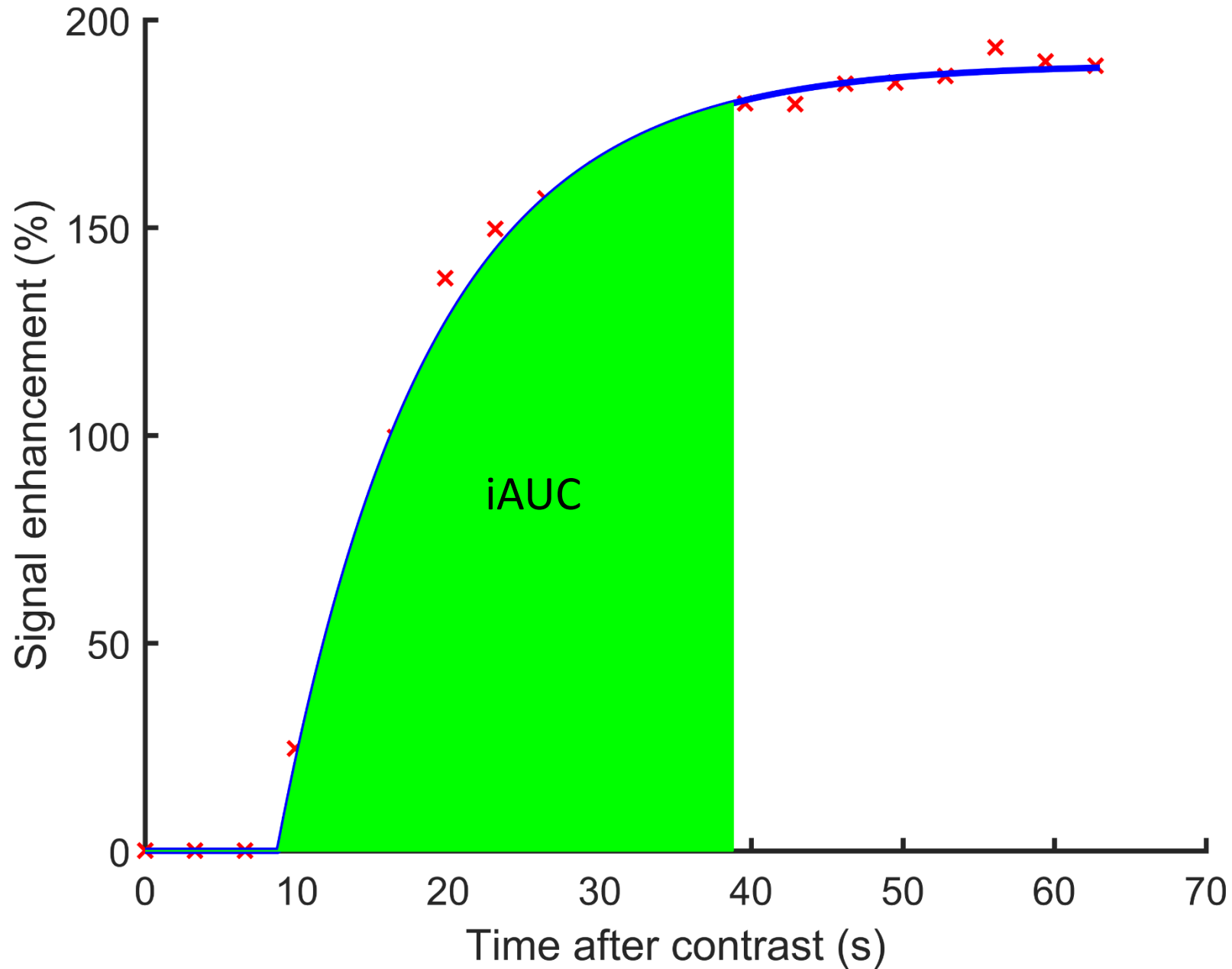
(Onishi et al. 2020)

Lesion conspicuity

- Given the slower enhancement rate of normal parenchyma, lesion conspicuity is often highest in early images, this is especially pronounced in cases with marked BPE

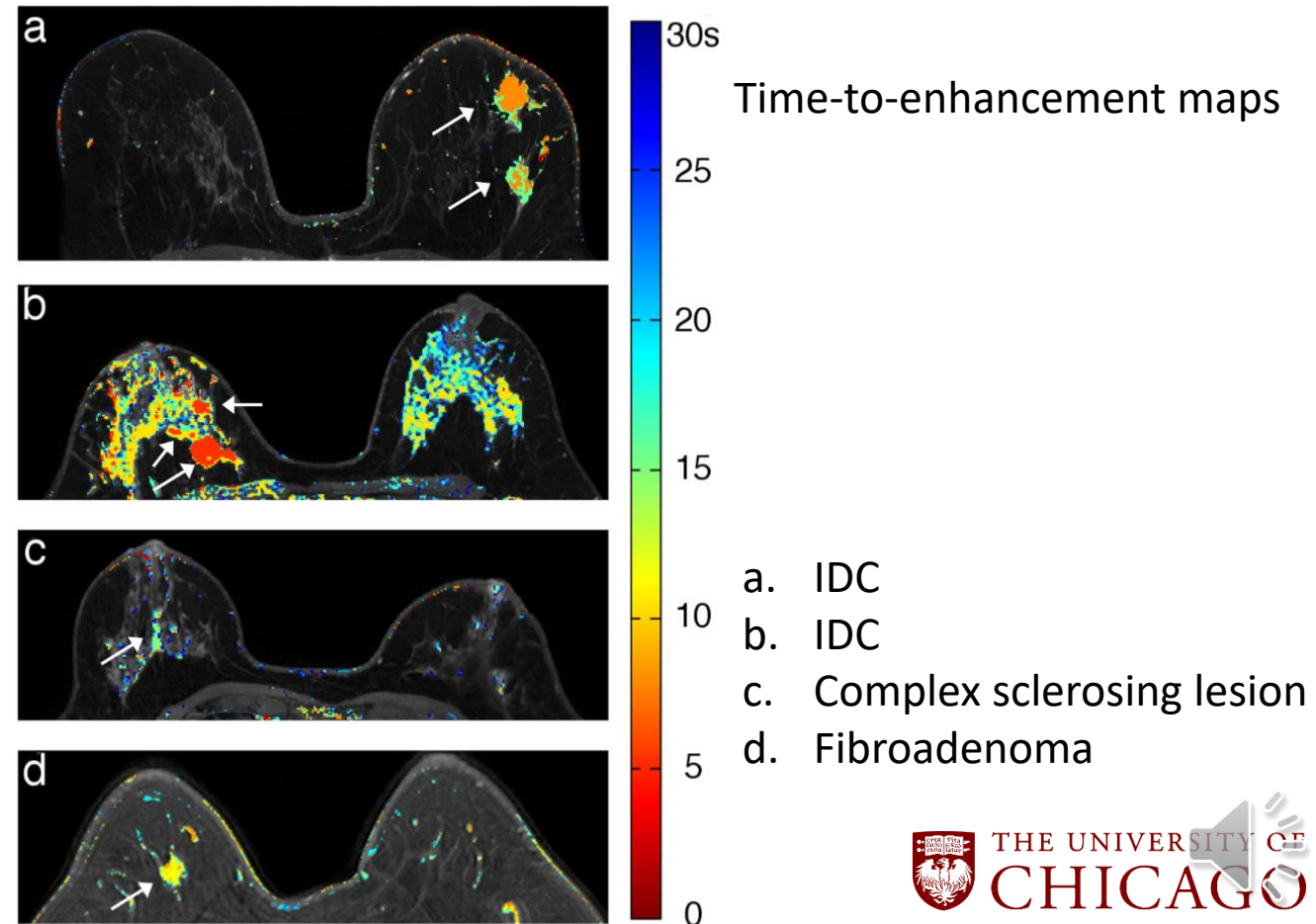
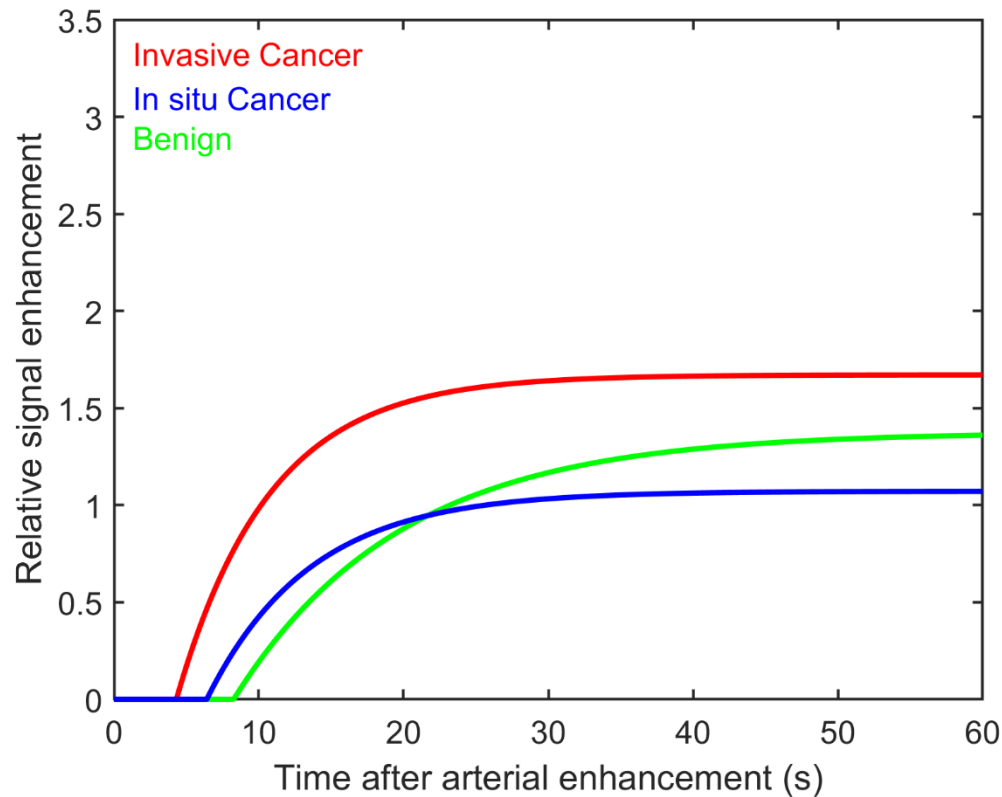


Kinetic analysis



Diagnostic utility of initial enhancement

- Several studies⁴⁻¹⁰ have shown that – on average – malignant lesions, relative to benign lesions, have: faster time-to-enhancement, higher initial/maximum slope of enhancement, higher initial area under the uptake curve



Discussion - Ultrafast DCE-MRI

- Ultrafast imaging during the initial phase of breast DCE-MRI offers several advantages:
 - Increased lesion conspicuity in cases with marked BPE
 - Accurate measurement of initial enhancement kinetics
 - Measurement of kinetic parameters relative to bolus time-of-arrival in the aorta or arteries – reducing influence from global variables
- Hybrid ultrafast/high spatial resolution protocols can be implemented clinically
- There are various techniques for the acquisition of ultrafast DCE, protocols should be tailored for each site/scanner

Low-dose Imaging Technique (LITE) MRI:
imaging with low doses of Gd



Gadolinium retention

- Recent studies have reported that gadolinium can deposit in the brain after repeated administrations of gadolinium based contrast agents (GBCA) in patients with normal renal function
- Although no long-term consequences for patient health have been identified this is of growing concern in the patient and imaging communities
- The accumulation of Gd is dose-dependent
- Reducing the dose of Gd used may help alleviate some of these concerns

GBCA dosage

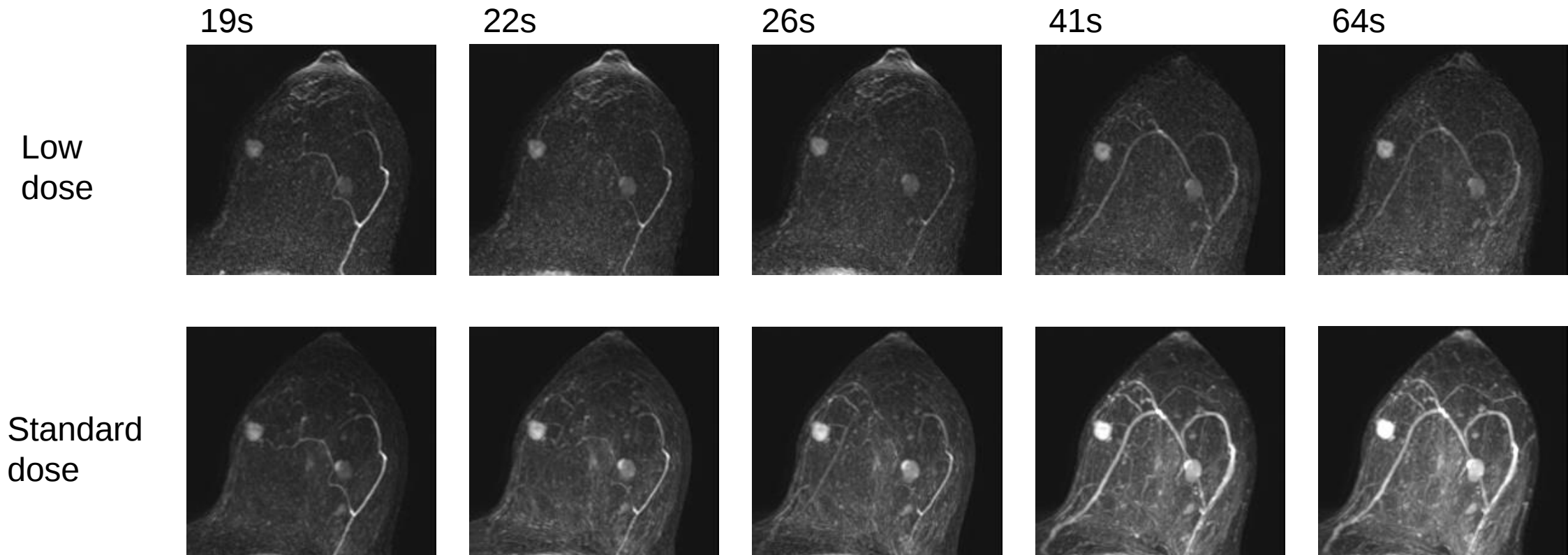
- The standard dose of GBCAs used currently (0.1 mM/kg) was determined in the 1980s after initial experience showed it was well-tolerated and effective for imaging
 - Minimum effective dose was not determined
- At the time, the field strengths at which MRI was performed were lower (0.35T – 0.5T) than those used nowadays (1.5T – 3T)
 - Native tissue T1's higher at higher field strengths
- The standard dose of 0.1 mM/kg may not be optimal for modern-day breast DCE-MRI

Study design

- 8 patients (ages 18-60 years) with a total of 10 lesions with imaging features most compatible with fibroadenoma were imaged with a protocol combining ultrafast and 'standard' DCEI¹¹
 - Fibroadenomas selected for rapid enhancement and lower inter-lesion variability
- The first injection consisted of 15% of a standard dose (0.015 mM/kg)
- The second injection delivered 85% of a standard dose (0.085 mM/kg)
- Injection flow rates (2 ml/s) and flush volume (20 ml) were the same for both administrations

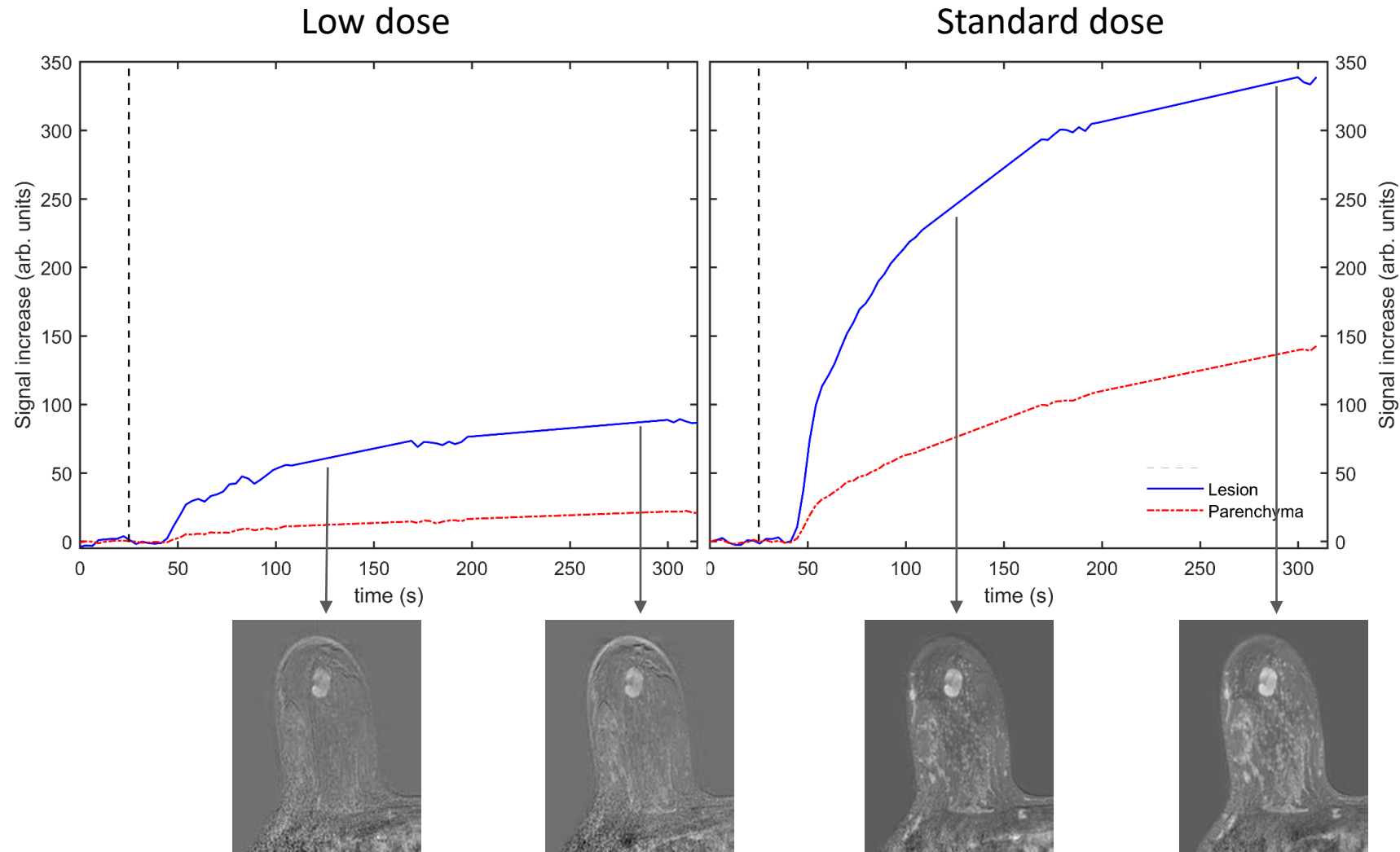
Results - detectability

- 9 of the 10 lesions had measurable enhancement on both series of images
 - 1 lesion did not enhance in either series
- While enhancement was higher in the standard dose images, lesions were well-visualized on LITE as well



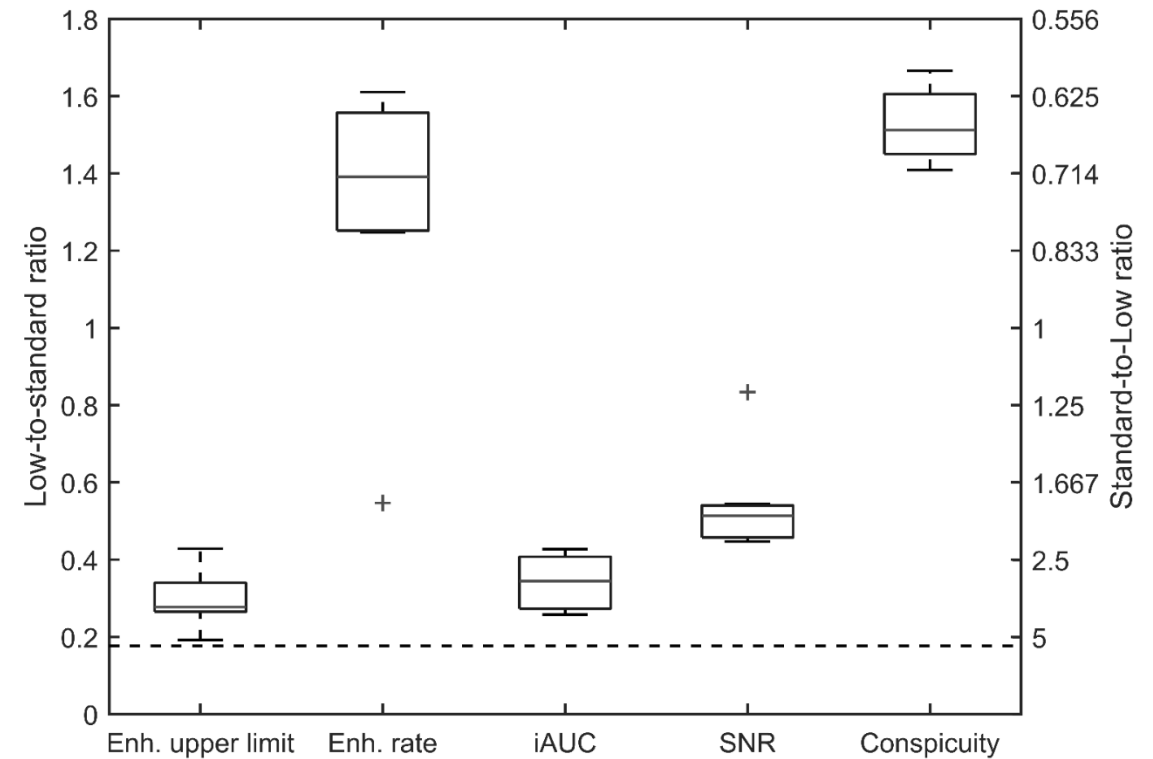
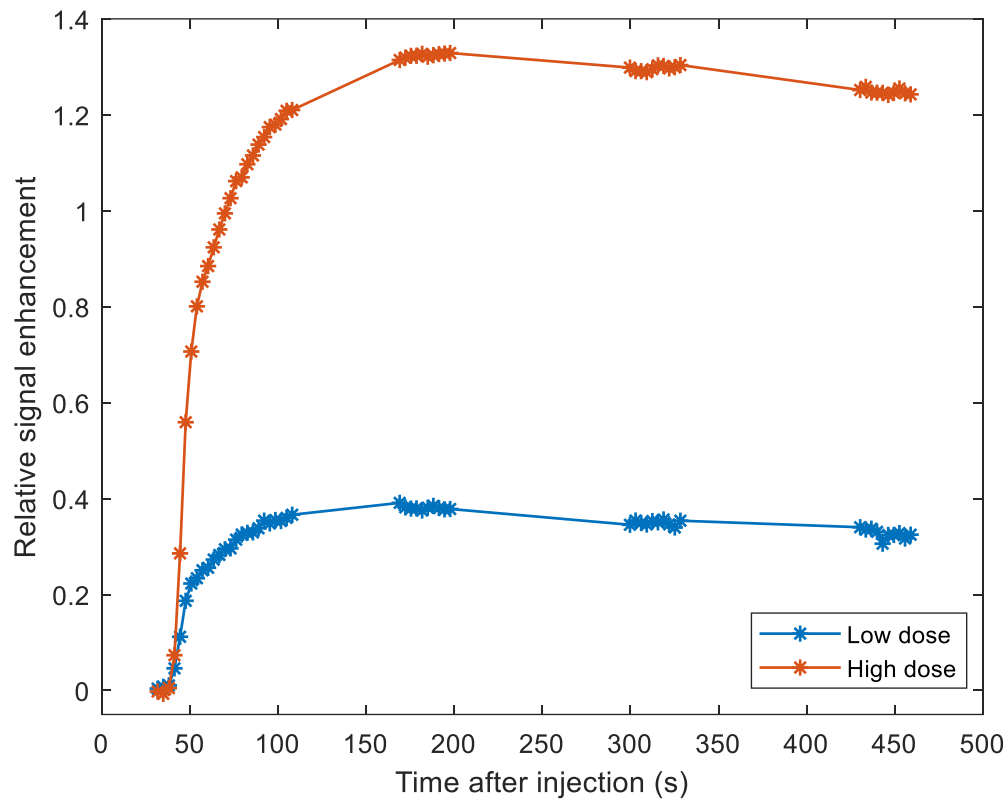
Results - conspicuity

- Due to lower BPE, conspicuity of lesions was higher in the LITE images



Results – kinetic parameters

- While the (low-to-standard) ratio of doses administered was ~ 0.18 , this was not reflected in the ratios of the parameters measured



Discussion - LITE MRI

- Study limitations:
 - Low number of cases
 - Only suspected fibroadenomas
 - All scans performed at 3T
- Low-dose breast imaging is feasible and may offer some advantages to standard doses of contrast media
- LITE MRI may provide enhanced sensitivity to contrast media dynamics
- Concerns with Gd deposition could be addressed with low-dose administrations, increasing screening compliance
- Results need to be validated in a larger study
- The optimal dose of contrast media will depend on several factors

Non-contrast techniques for Breast MRI



Diffusion-weighted imaging (DWI)

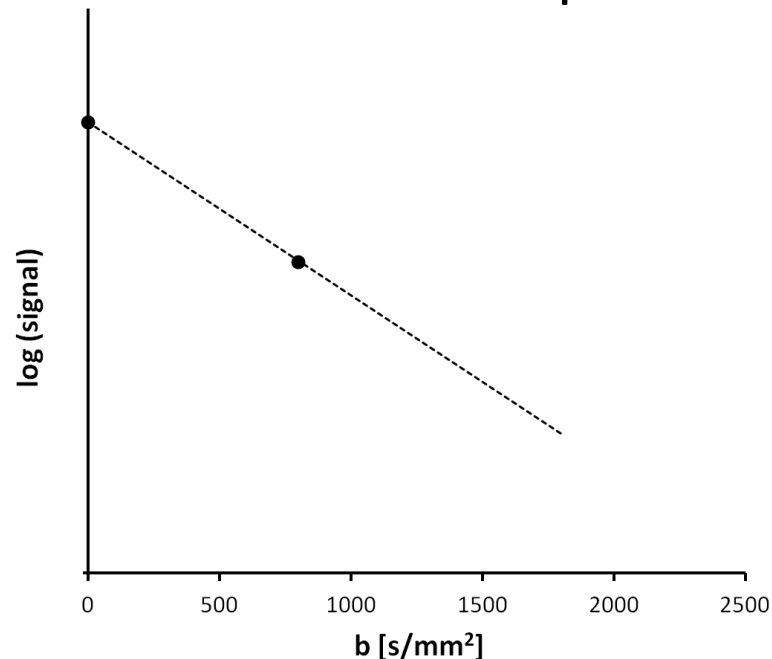
- In DWI motion-sensitizing gradients are applied and the resulting images depend on the diffusion of water molecules

$$S_b = S_{b=0} e^{-b \times ADC}$$

b = strength of diffusion gradient (s/mm²)

ADC = apparent diffusion coefficient (mm²/s)

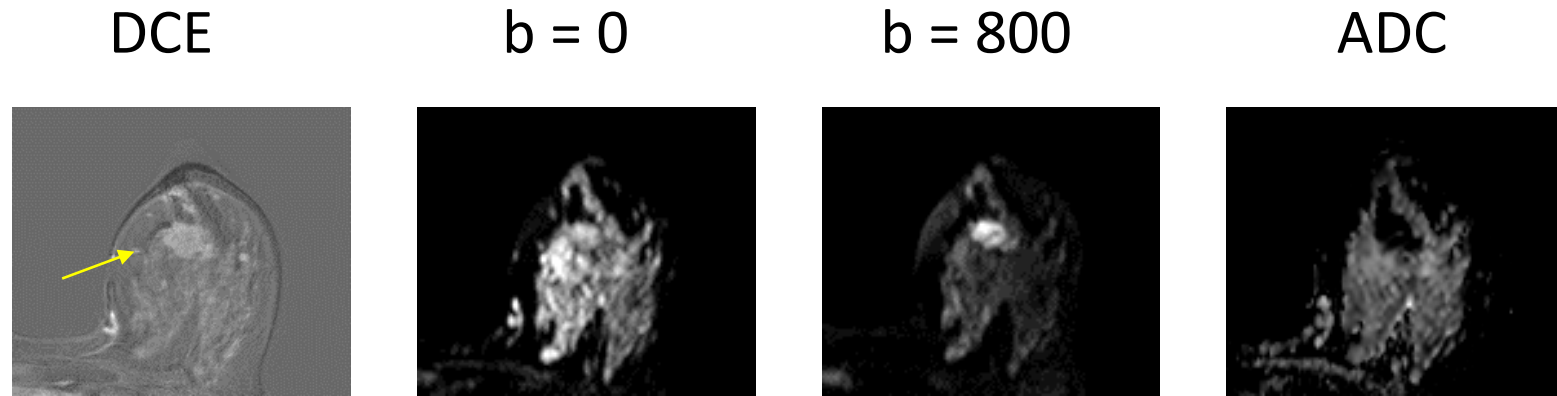
- Higher cellularity in cancers leads to restricted diffusion and lower ADC's than benign lesions and normal parenchyma



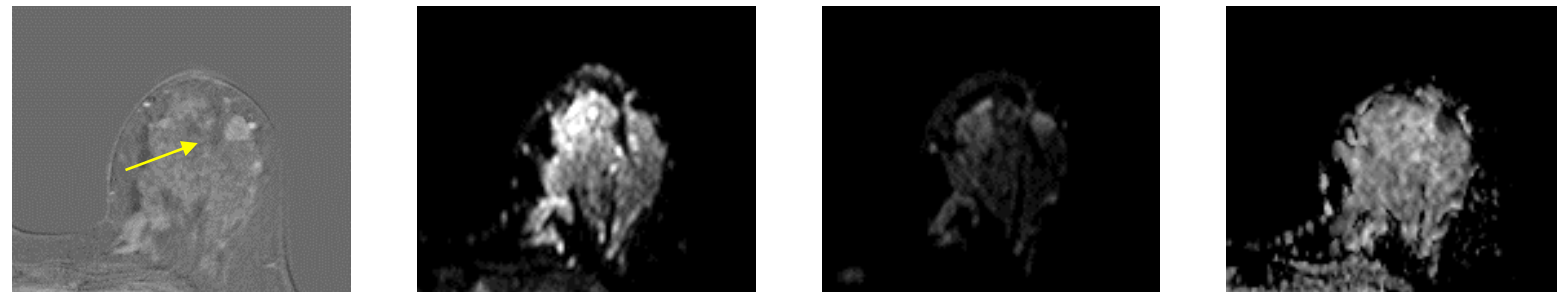
$$\ln \left(\frac{S_b}{S_{b=0}} \right) = -ADC \times b$$

Breast DWI

Invasive ductal carcinoma



Fibroadenoma



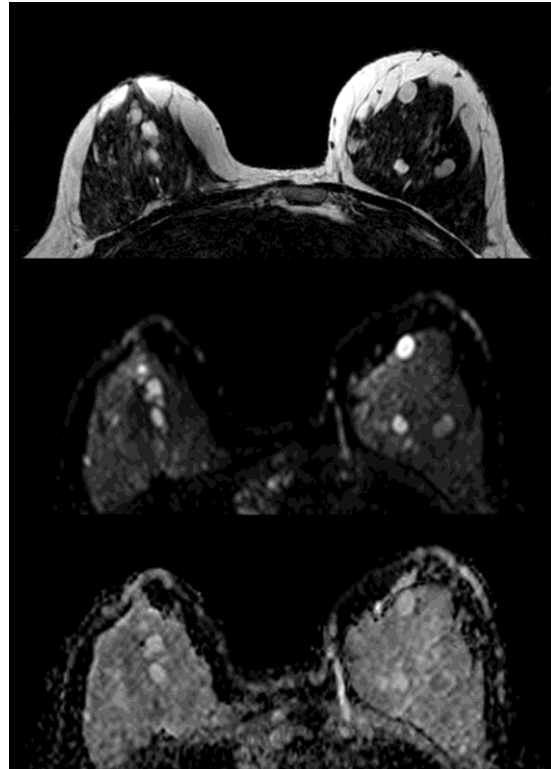
T2 shine through

- Lesions that appear hyperintense on T2-weighted images (e.g. cysts) may also appear hyperintense relative to parenchyma on high b-value images
- Looking at ADC maps can differentiate these lesions from malignancies

T2-weighted image

$b = 800 \text{ s/mm}^2$

ADC map

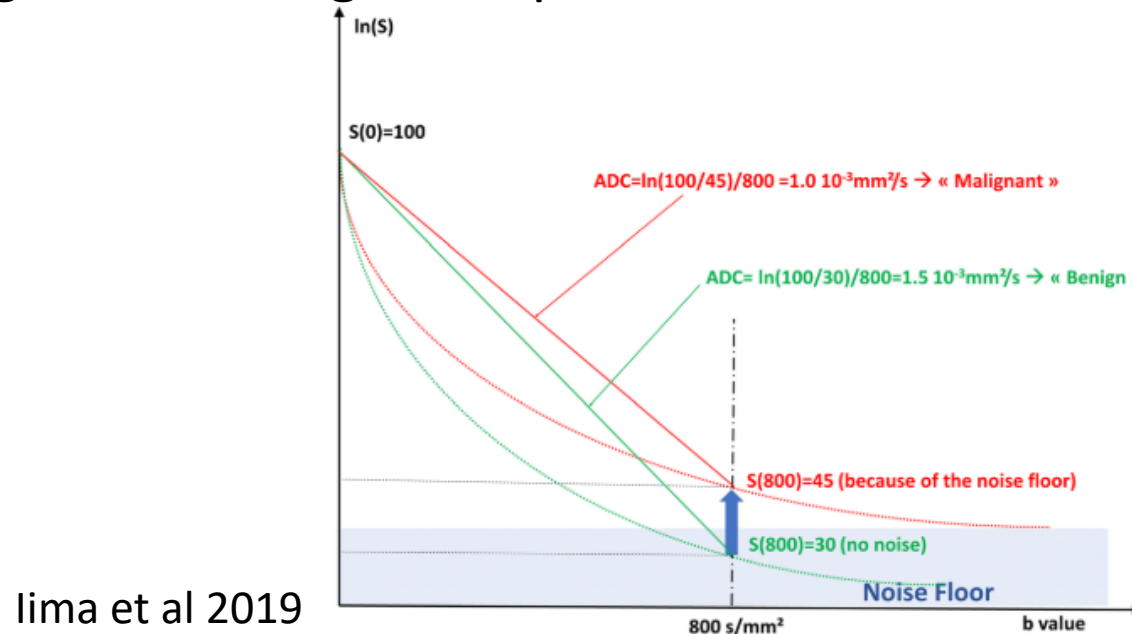


Technical considerations for breast DWI

- Good quality shimming and uniform fat suppression are essential to minimizing image artifacts
- Proper patient positioning can avoid tissue folds and minimize local B0 gradients
- Current protocols typically have low spatial resolution, limiting the detection of small lesions
- SNR can be improved by: scanning at higher field strength, increasing the number of signal averages, shortening TE, increasing voxel size, and by appropriate choices of b-values

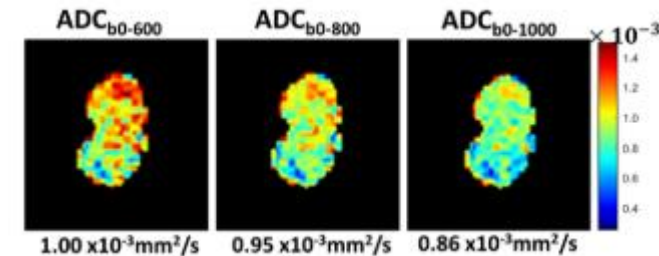
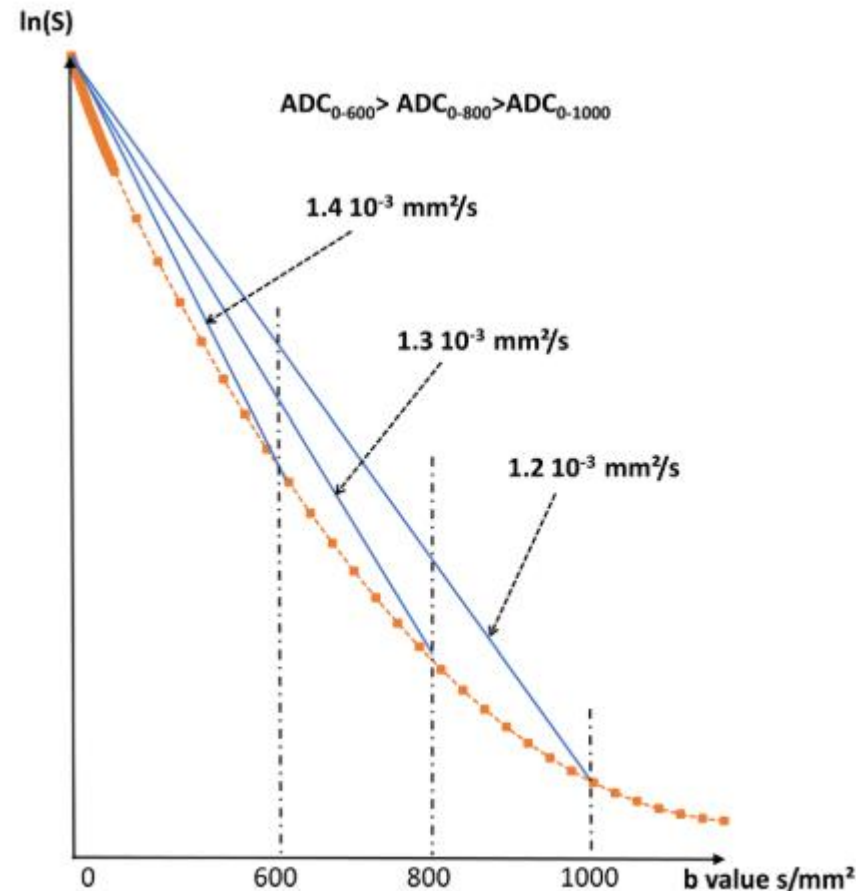
b-value selection

- A b-value of approximately $1.1/\text{ADC}$ may provide ideal SNR
 - Breast cancers typically have ADCs in the range of 0.9 to $1.5 \times 10^{-3} \text{ mm}^2/\text{s}$
 - This corresponds to optimal b-values in the range of 700 to 1200 s/mm^2
- High b-value images have lower SNR and the signal in some voxels may be below the noise floor, affecting the ADC calculated in these voxels
 - A common strategy to deal with this issue is to increase the number of averages for the high b acquisition



ADC and b-value selection

- Calculation of ADC assumes free water diffusion, however in most tissues diffusion is non-Gaussian due to obstacles such as cell membranes
- This means that $\ln(S/S_0)$ is no longer a straight line

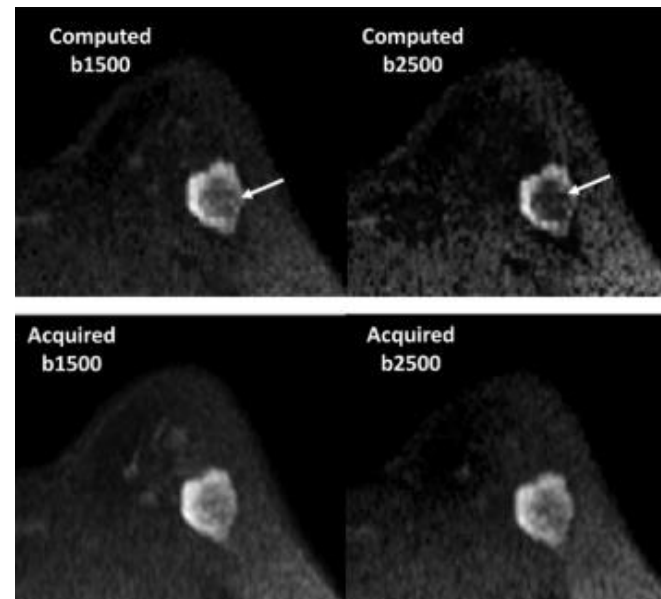


ADC and ROIs

- The mean ADC of a lesion can be measured either by drawing an ROI on the calculated ADC map, or by drawing the ROI on the DW-images and calculating the ADC based on the mean signal
- These two approaches can lead to different ADC values
- Signal averaging by calculating the ADC from the mean ROI signal reduces the effect of noise and leads to an ADC closer to the true value
- Image registration and noise thresholding also increase the accuracy of ADC measurements
- Measurements can vary widely depending on the method of ROI selection (2D, 3D, “hotspot”)
- Semi-automated ROIs may improve accuracy and reproducibility of measurements

Synthetic DWI

- Some vendors offer the option to generate synthetic DWI images
- These images extrapolate the signal from the acquired images to simulate images acquired with a higher b-value
 - For example if a protocol is set up with $b = 0, 800 \text{ s/mm}^2$, a synthetic DW-image may be generated for $b = 1500 \text{ s/mm}^2$
- In theory, at high enough b-values the signal from the background drops to 0, and only the areas with restricted diffusion will be visible
- However these images rely on the assumption of free water diffusion and are not reflective of the true tissue microstructure



Diagnostic performance of DWI

- A meta analysis¹³ of 14 studies (2008-2014) for lesion classification: sensitivity 86% ,specificity 75.6% for DWI versus 92% and 86% for DCE
- 6 blinded studies¹⁴ looked at DWI for screening: sensitivity 45-94%, specificity 79-95%
- 3 studies¹⁴ that evaluated reader performance on DW MRI vs DCE: DW sensitivity 78.9% vs 93.4% for DCE
- Mutisite ECOG-ACRIN trial¹⁵: DWI lowered the biopsy rate by 20.9% while maintaining the same sensitivity
- Studies¹⁴ have also shown increased diagnostic accuracy when adding DWI to mammography for screening
- Advances in DWI acquisition can lead to higher diagnostic accuracy (e.g. readout segmented EPI)

Intravoxel incoherent motion (IVIM)

- In IVIM analysis we do not treat the DWI signal decay as a mono-exponential, and account for the effect of microperfusion

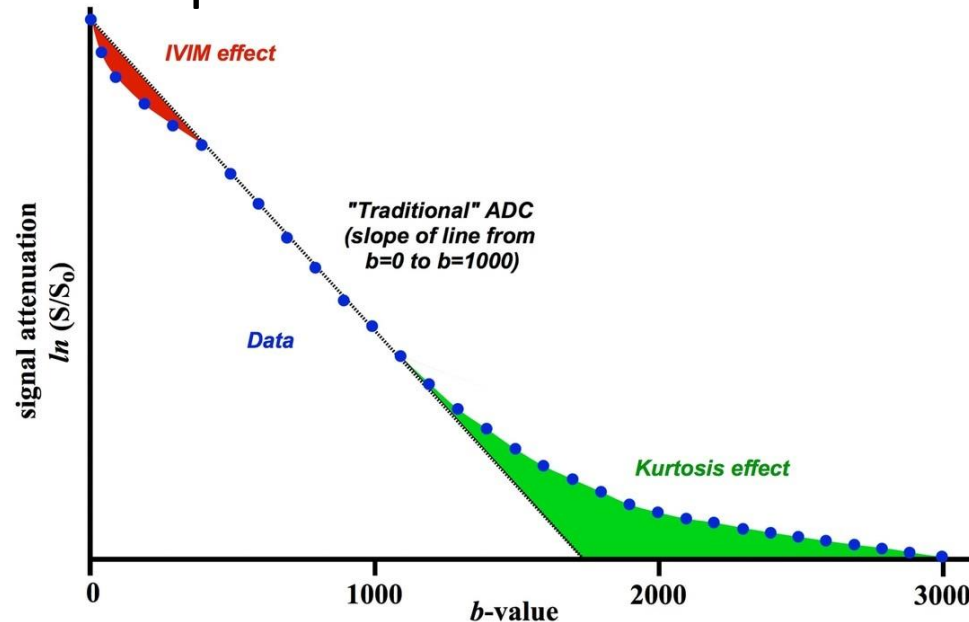
$$\frac{S}{S_0} = f e^{-b(D+D^*)} + (1-f)e^{-bD}$$

f = perfusion fraction

D = ADC

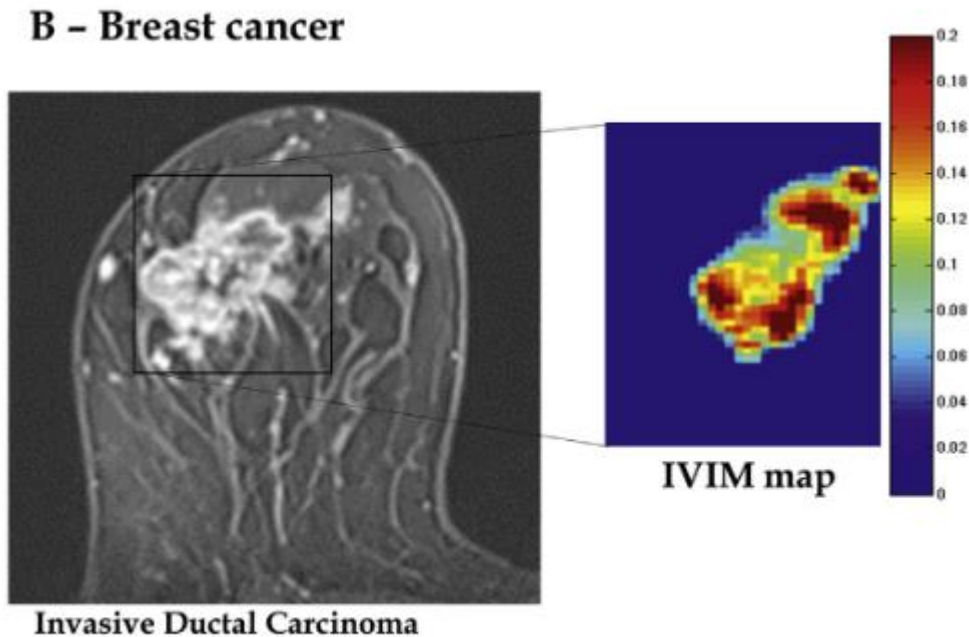
D^* = pseudodiffusion coefficient

- Data are acquired at multiple b-values and the signal fit to the equation above to get estimates for all the parameters

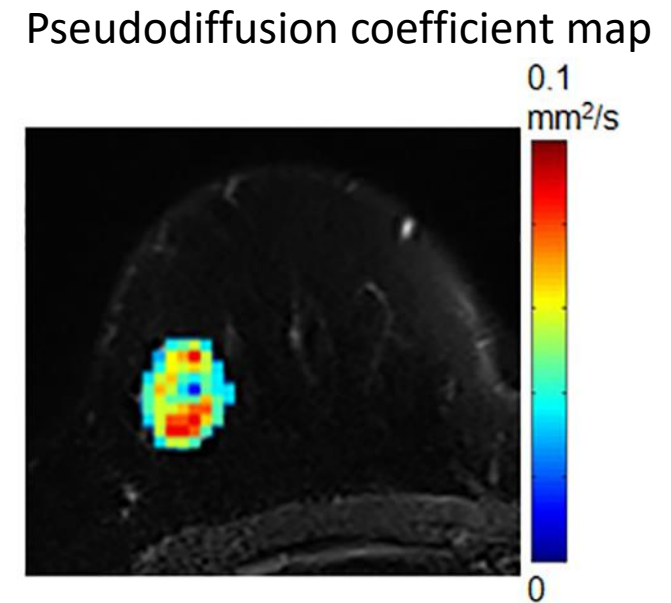


IVIM in breast

- Preliminary studies¹⁶ have shown increased perfusion fraction in invasive breast cancers



lima et al. 2013



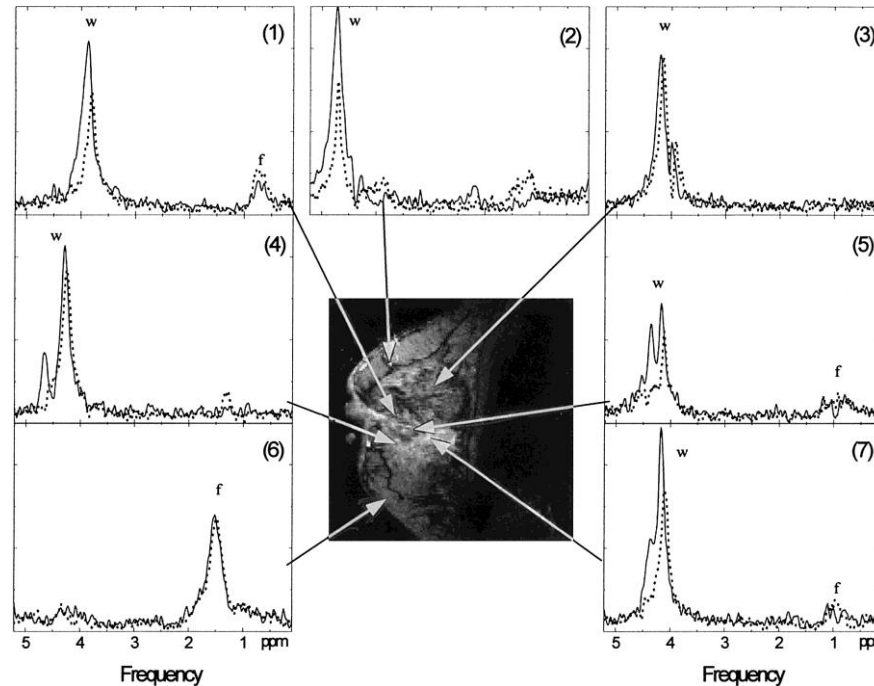
lima et al. 2018

High Spectral and Spatial (HiSS) resolution MRI



HiSS MRI

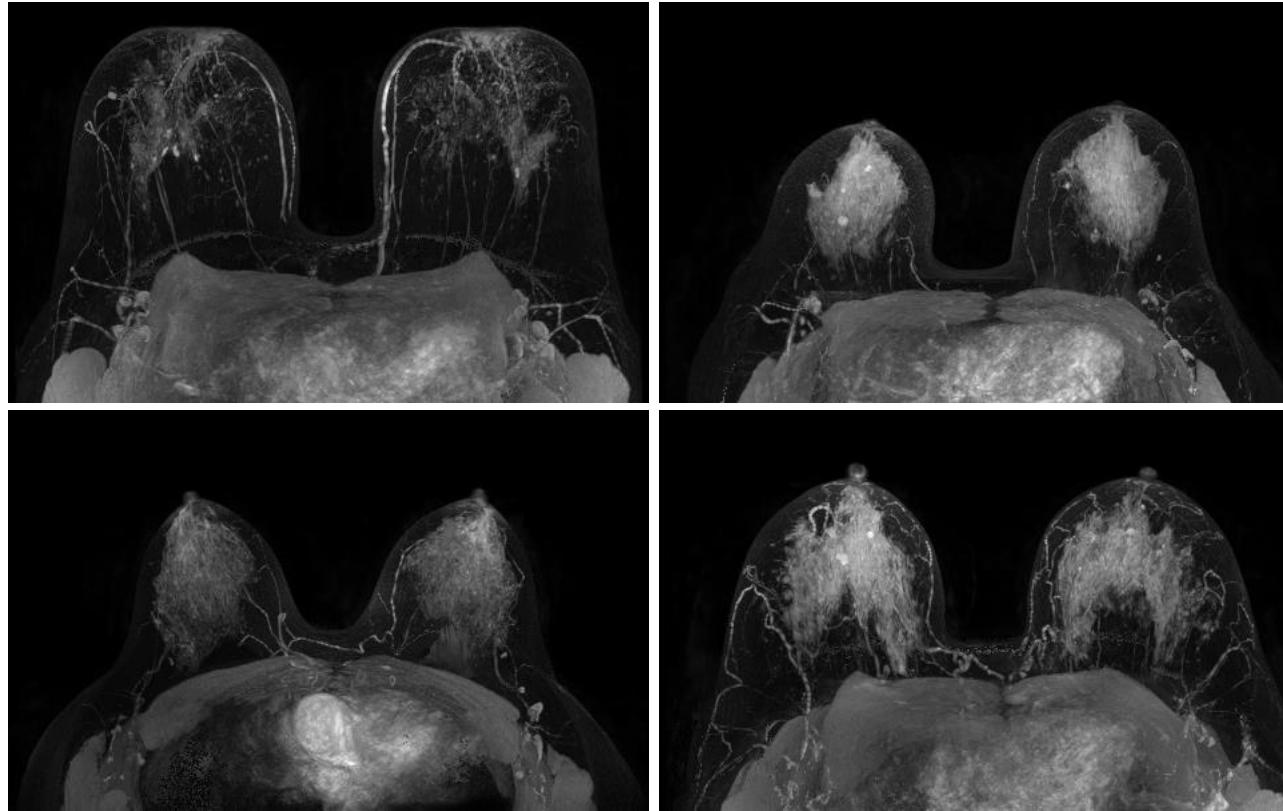
- HiSS is based on an Echo-Planar Spectroscopic Imaging (EPSI) acquisition, with small voxel size and no suppression of fat and water peaks
- To process the images a Fourier transform is applied in the temporal direction (along the train of gradient-echo images), and a spectrum is obtained in every voxel



Du et al. Radiology 2002

HiSS images

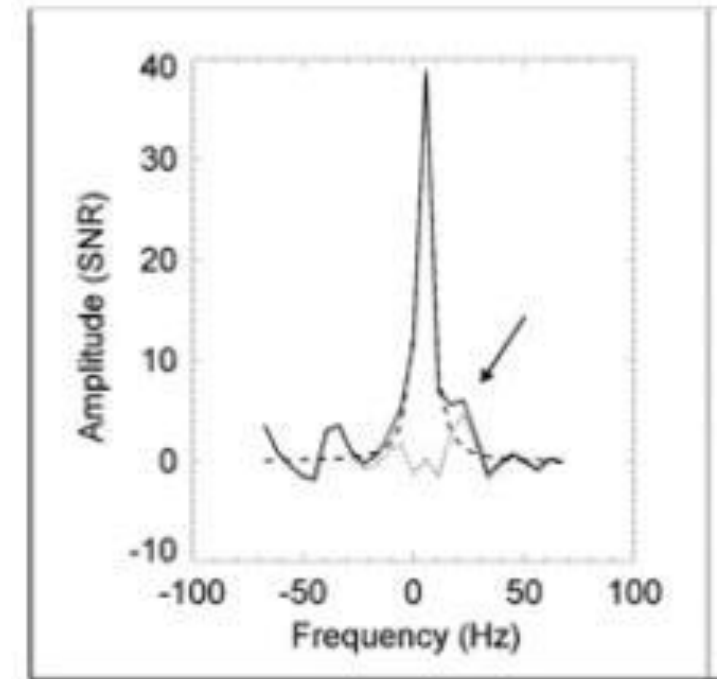
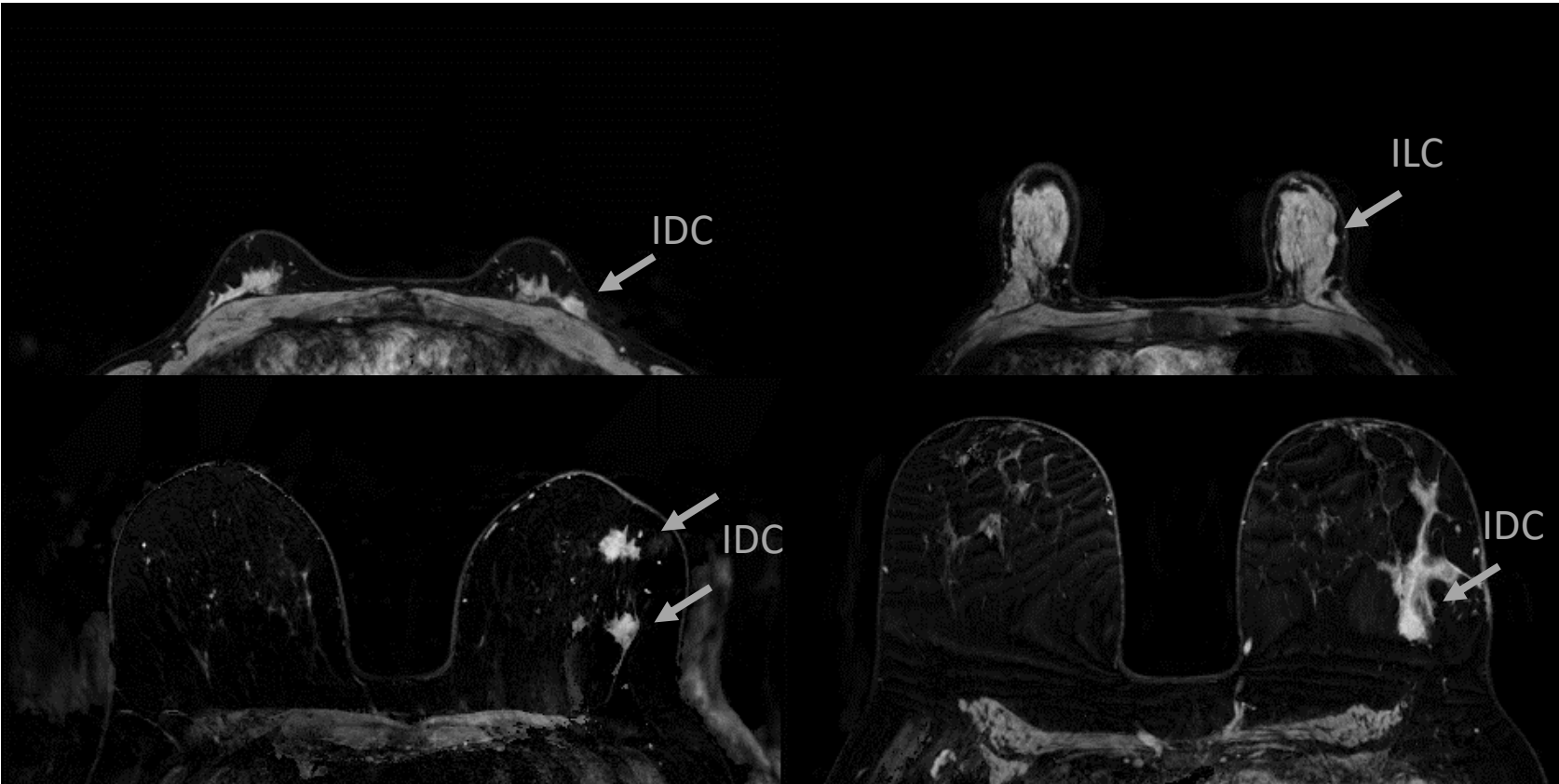
- HiSS water peak height images provide excellent fat suppression



MIPs of water peak height images in healthy volunteers

HiSS and cancer detection

- Morphological and functional analysis of HiSS images have been shown in studies to have high diagnostic accuracy (AUC's of 0.83-0.92) ¹⁸⁻²³

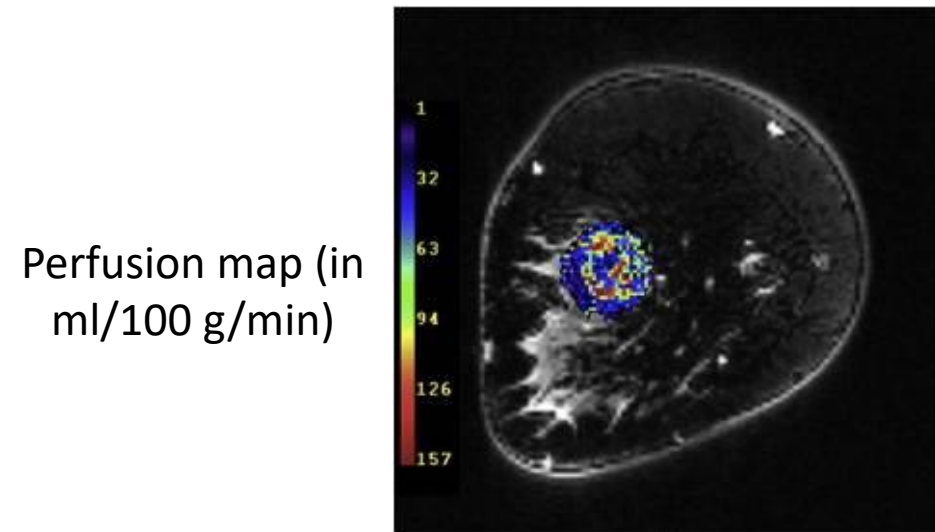


Other non-contrast techniques

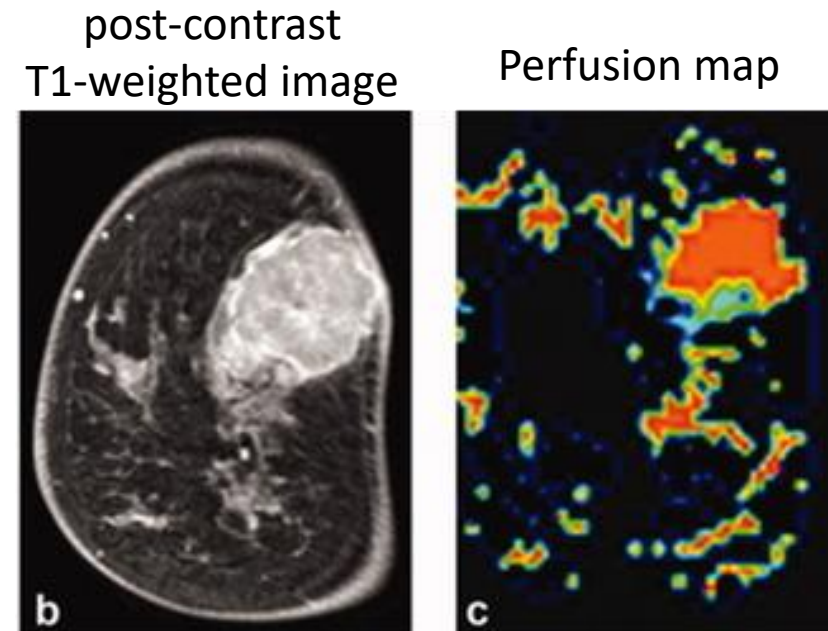


Arterial spin labeling (ASL)

- ASL is not commonly used in breast MRI but offers a technique to study perfusion without the use of GBCAs
- Arterial blood spins are tagged near the chest wall, a delay is built in to allow the labeled spins to arrive to the area of interest and images are acquired coronally
- The signal difference between labeled and non-labeled images is proportional to perfusion



Buchbender et al., Clinical Radiology
2013



Kawashima et al., JMRI 2012

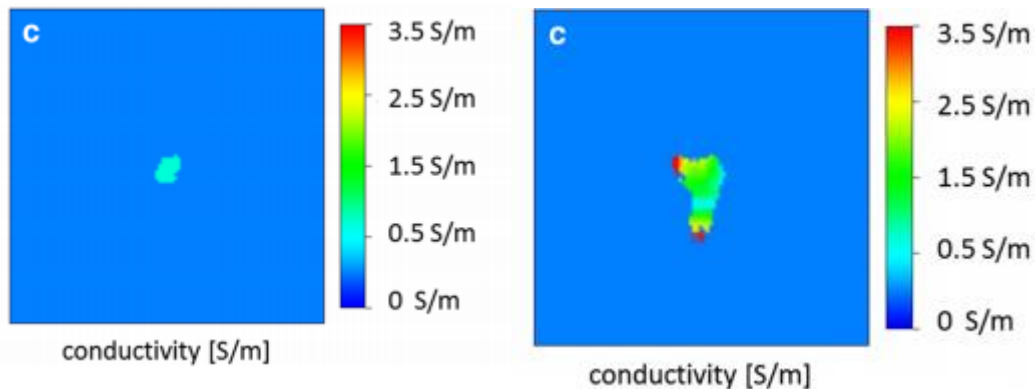
Electric Properties Tomography

- EPT is a novel technique that can be used to analyze the electrical conductivity of tissues
- Increased concentration of sodium, potassium, calcium along with changes in water content lead to higher conductivity in malignant tumors
- The conductivity of tissues is estimated via the phase of the transmit field $B1^+$

Mori et al. 2019

Significantly higher conductivity in malignant lesions

AUC of EPT was 0.71 vs. 0.80 using SER from DCE

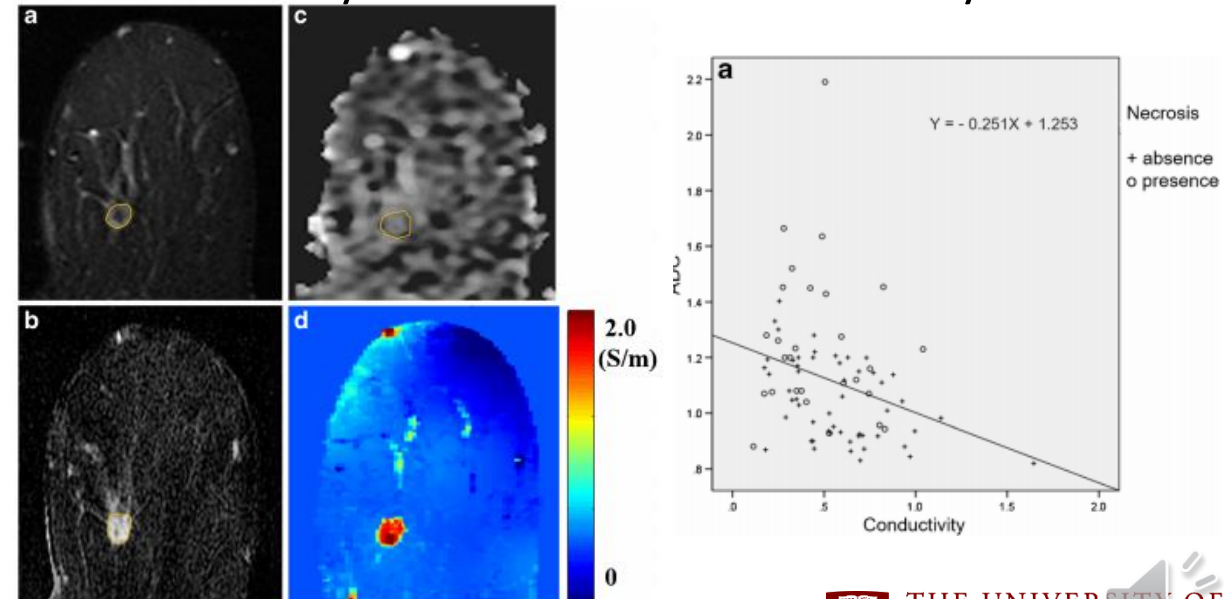


Sclerosing adenosis

IDC

Kim et al. 2018

ADC is inversely correlated with conductivity



Conclusions: Non-contrast breast MRI

- DWI is a promising technique for non-contrast breast cancer screening and lesion classification
- The factors that affect estimates of ADC need to be understood before setting thresholds for malignancy
- Diagnostic performance of DWI does not match DCE currently, but advanced acquisition and analysis techniques could increase DWI's accuracy
- HiSS is an experimental technique that can be used to obtain images with high morphological details as well as functional information
- ASL and IVIM are two non-contrast techniques that could be used to assess perfusion
- EPT may provide novel markers for malignancy
- A non-contrast MRI protocol will require the combination of several sequences



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Thank you!

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