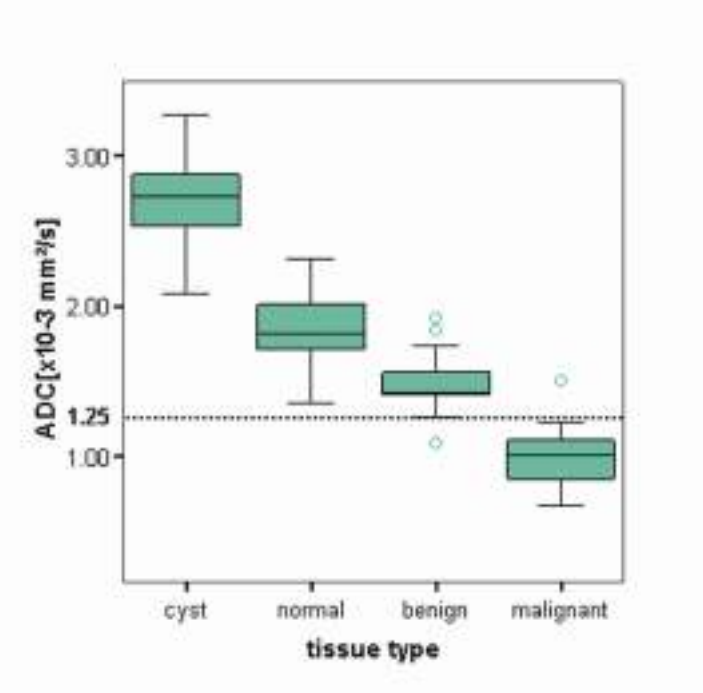
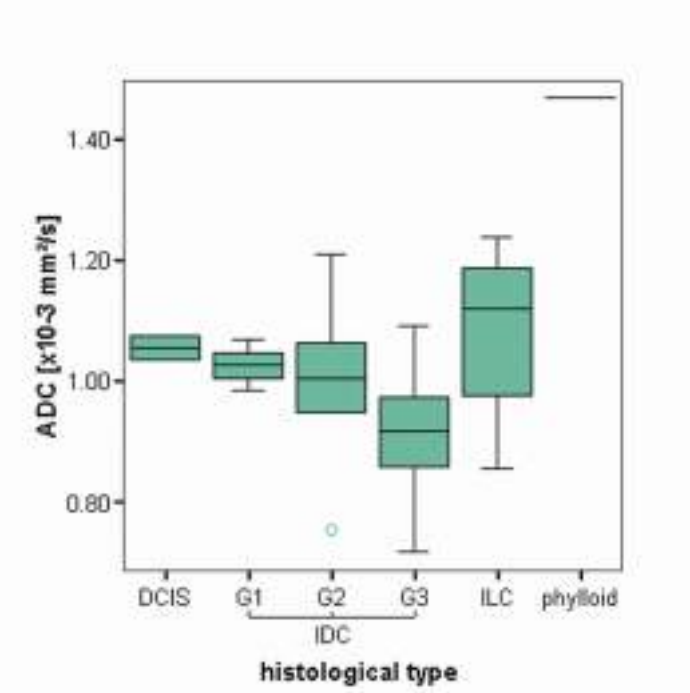
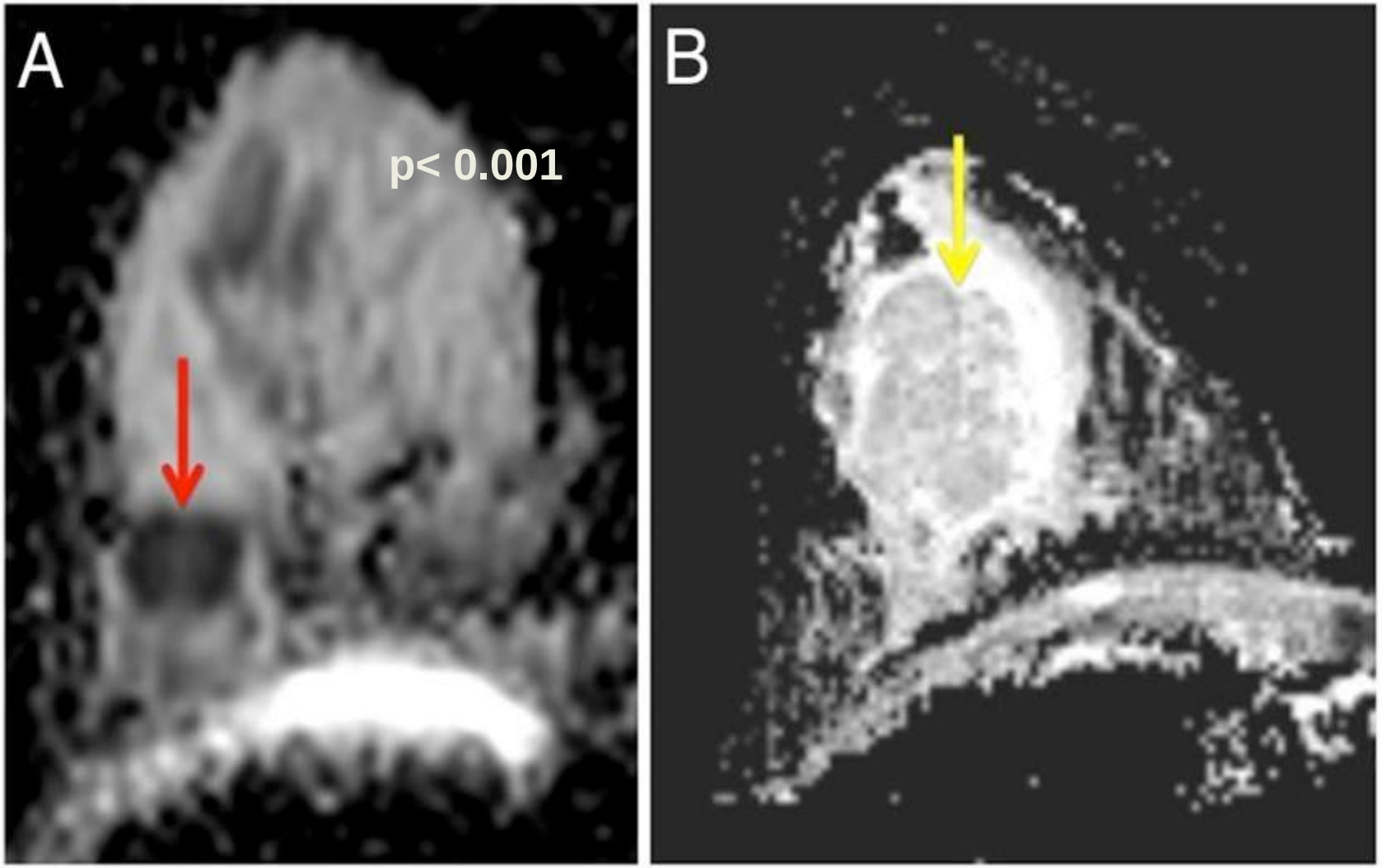
- for 2 b-values (50/850 s/mm²) (~ 2:30 min)
- ADC threshold of 1.25 × 10^{-3} mm^2/sec

→ sensitivity – 96%
specificity – 94%





ADC: „POTENT“ Imaging Biomarker



Bickel H., T. Helbich et al. Investigative Radiology 2014

ADC – an imaging-biomarker for breast cancer invasiveness (n= 176)

		ADC mean (SD)	Statistical test	p-value
Histopathology:				
Invasive (n=155)		.90 (.15)	t-Test	0,005
Non-invasive (n=21)		1.24 (.23)		
DCIS (n=21)		1.24 (.23)		
IDC (n=130)		.91 (.14)	ANOVA	<.001
ILC (n=25)		.86 (.21)		
DCIS VS IDC				<.001
DCIS VS ILC			t-Test	<.001
IDC VS ILC				0,805
Grades:				
Invasive	I (n=14)	.94 (.11)		
	II (n=62)	.88 (.17)	ANOVA	0,272
	III (n=79)	.92 (.15)		
Non-invasive	I (n=7)	1.23 (.20)		
	II (n=9)	1.20 (.25)	ANOVA	0,593
	III (n=5)	1.33 (.23)		

Table 1: Overview on ADC-value by histopathologic subtype, invasiveness and grade. Abbreviations: ADC - apparent diffusion coefficient; DCIS - ductal carcinoma in situ; IDC - invasive ductal cancer; ILC - invasive lobular cancer; SD - standard deviation; ADC-values are displayed in $\times 10^{-3}$ mm^2/s

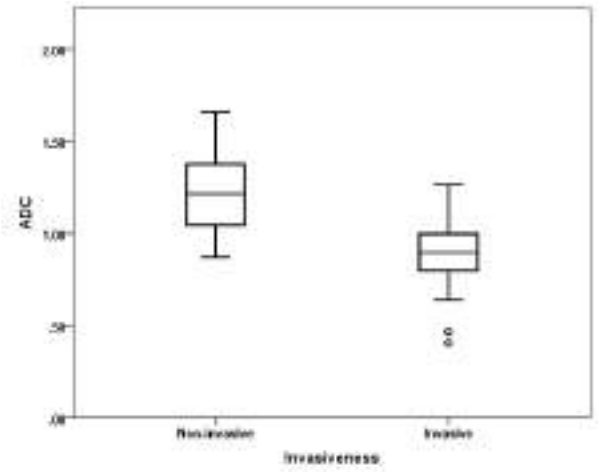
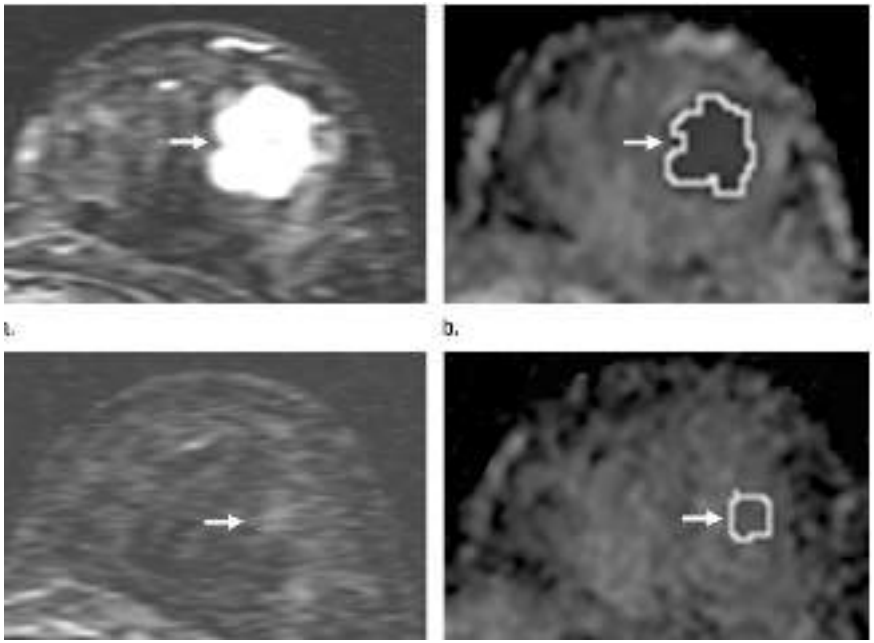


Figure 2: Boxplot displaying the distribution of apparent diffusion coefficient (ADC) values of all cancers. ADC-values are displayed in $\times 10^{-3}$ mm^2/s. Mean ADC-values differ significantly (p<.001) between invasive and non-invasive cancers.

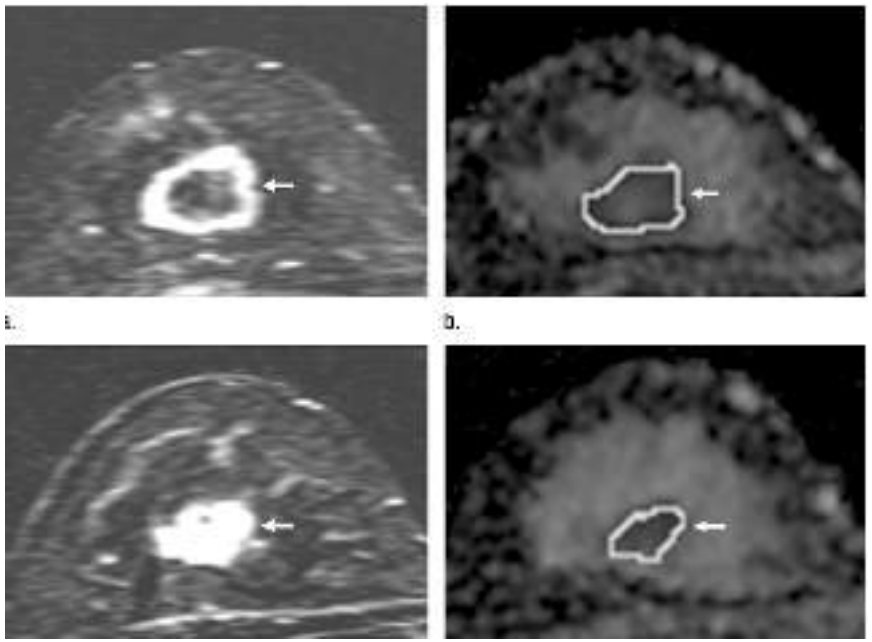
Bickel H., T. Helbich et al. Investigative Radiology 2014

Diffusion-weighted imaging (DWI)

Responder



NON-Responder



Park et al; Radiology 2010

Diffusion-weighted imaging (DWI)
„motion of molecules“

ADC increase indicates treatment response

- Why?

  Cell damage compromises cell membrane & allows greater mobility
- Influenced by type & duration of therapy

Tumor Diameters and ADCs

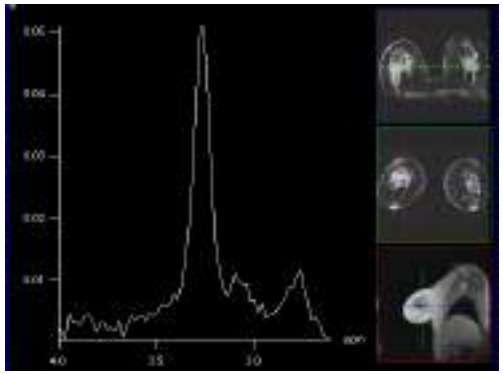
Parameter	Responders	Nonresponders	*P* Value
Maximal tumor diameter* (cm)			
Pretreatment	4.9 ± 0.4	5.3 ± 0.5	.537
Posttreatment	2.0 ± 0.2	4.8 ± 0.5	<.001
ADC (× 10^{-3} mm^2/sec)			
Pretreatment	1.035 ± 0.015	1.299 ± 0.079	.004
Posttreatment	1.524 ± 0.046	1.535 ± 0.110	.913
Increase in ADC (%)	47.9 ± 4.8	18.1 ± 4.5	<.001

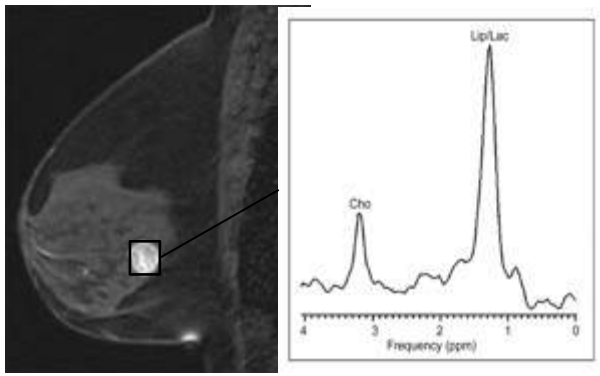
Park et al; Radiology 2010

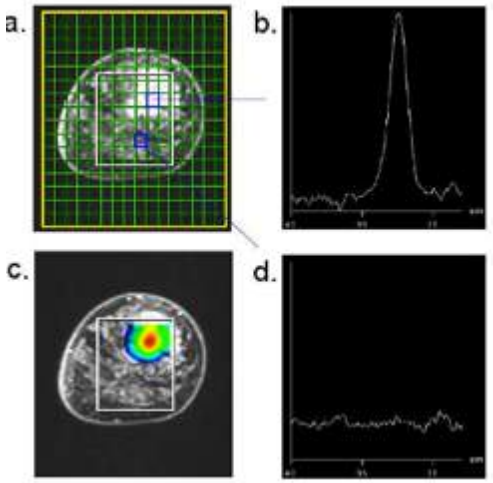
Sharma et al, NMR in biomedicine 2009

Proton MR Spectroscopy (1H-MRSI)

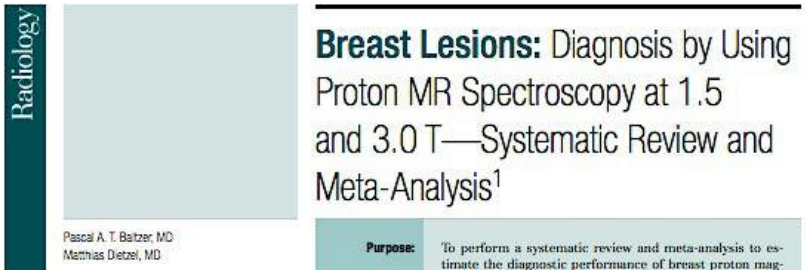
- Detection of elevated levels of Choline (Cho) compounds = Choline Peak
- Cho compounds are markers for BC
- Compounds: cholin, phosohocholin, taurin, glucose, etc
- Resonance frequency at 3.2ppm







Proton MR Spectroscopy (^{1}H-MRSI)


Radiology

Pascal A. T. Baltzer, MD
Matthias Dietzel, MD

Breast Lesions: Diagnosis by Using Proton MR Spectroscopy at 1.5 and 3.0 T—Systematic Review and Meta-Analysis[1]

Purpose: To perform a systematic review and meta-analysis to estimate the diagnostic performance of breast proton mag-

- Meta-analysis (n=19)
- SENS: 73%; SPEC: 88%
- Results NOT influenced by technique:

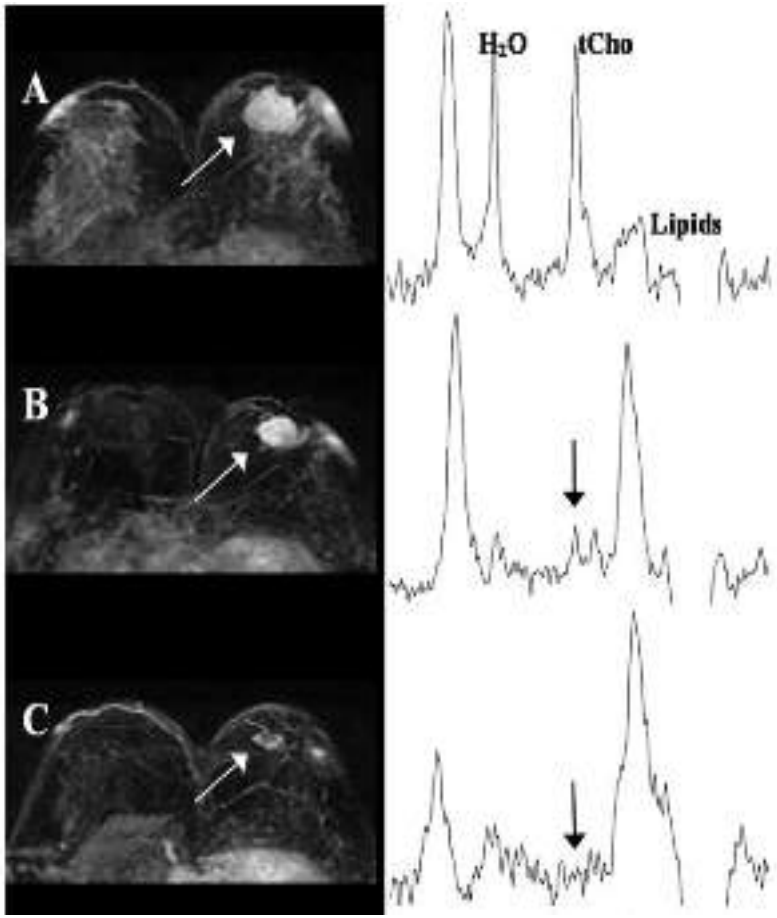
(Field strength, single vs. multi voxel, quantification!)

- HIGH SPECIFICITY: multicenter studies!

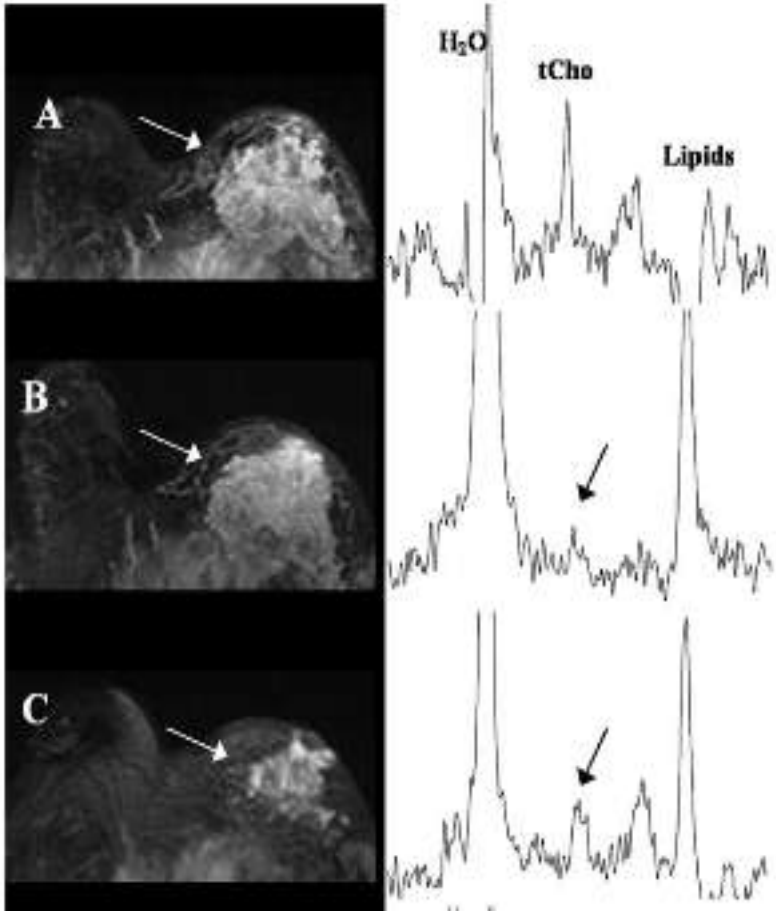
Baltzer et al. Radiology 2013

Proton MR Spectroscopy (^{1}H-MRSI)

Responder



NON-Responder



tCho reduction indicates treatment response

Baek et al; Radiology 2009

Proton MR Spectroscopy (^{1}H-MRSI)

tCho reduction indicates treatment response

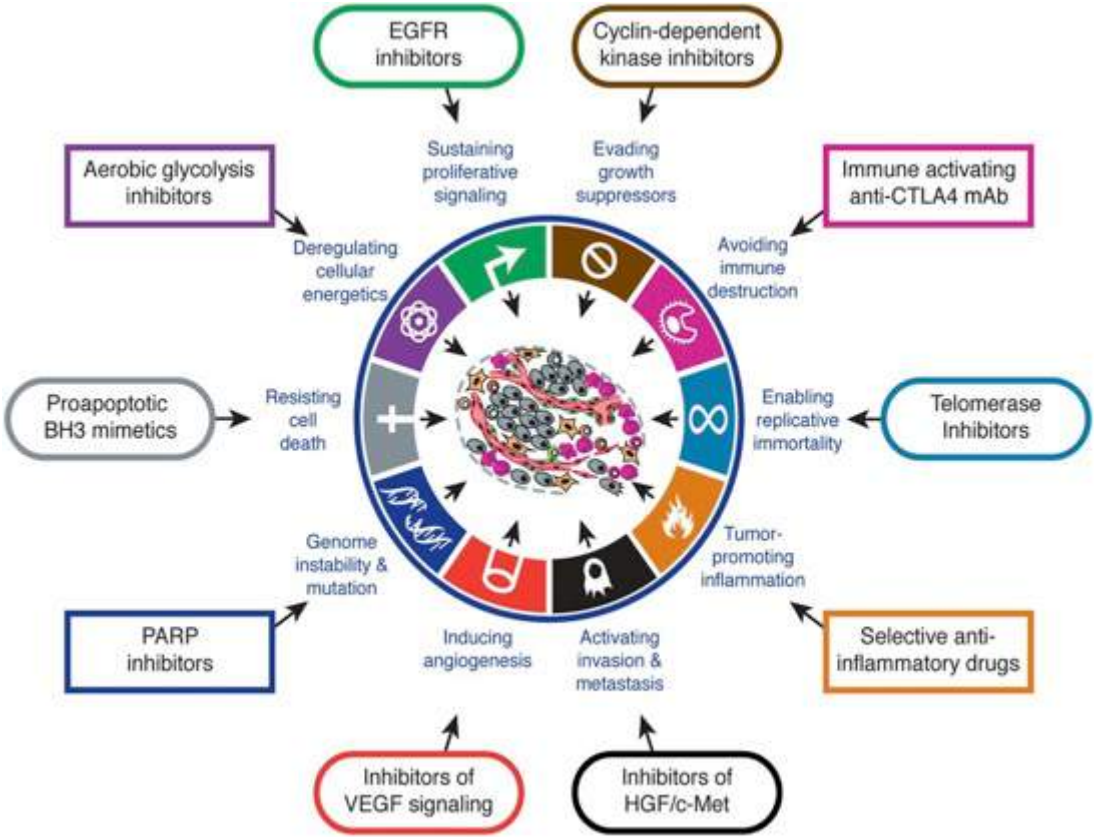
- Assessment of response to NAC:

- *tCho changes already 24h after onset of therapy*
- *Changes in tCho earlier than in tumor size*

Meisamy et al, Radiology 2004
Gruber et al, ISMRM 2013

Altered Metabolism

[^{18}F]FDG PET
MRSI
Hyperpolarized MRI
[^{18}F] MISO PET
BOLD MRI



Hanahan D. et al.
Cell 2011;144:646-74.

Metastasis

[^{18}F]FDG PET
DWIBS
Bone Scan
CT/MRI

Angiogenesis

[^{18}F]FDG PET
DWIBS
Bone Scan
CT/MRI

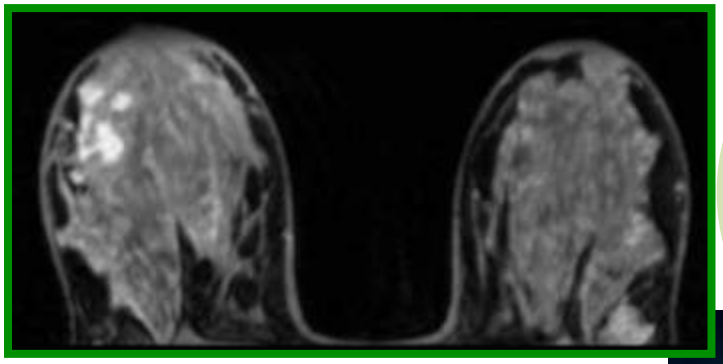
Cell Death

Annexin
Diffusion MRI
Hyperpolarized MRI

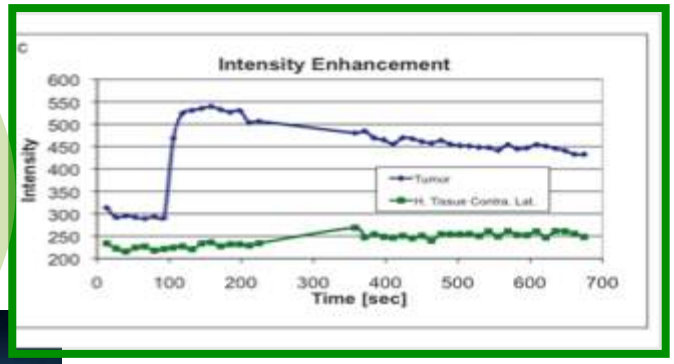
Proliferation

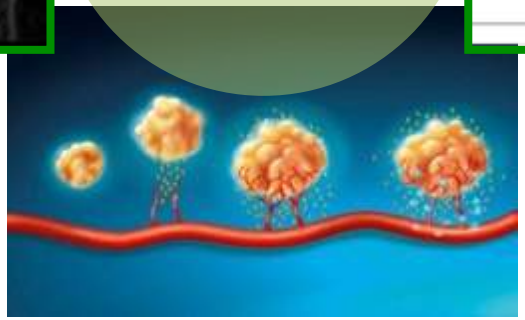
[^{18}F]FLT PET, MRSI, Diffusion MRI

Multiparametric MRI

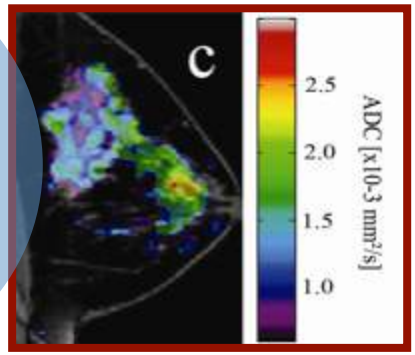


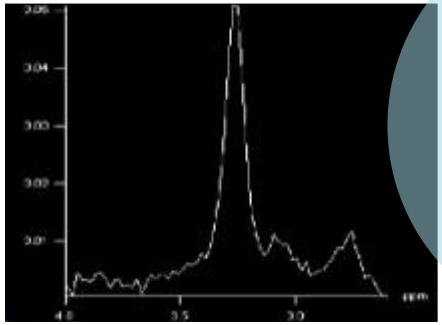
DCE-MRI
morphology &
neoangiogenesis





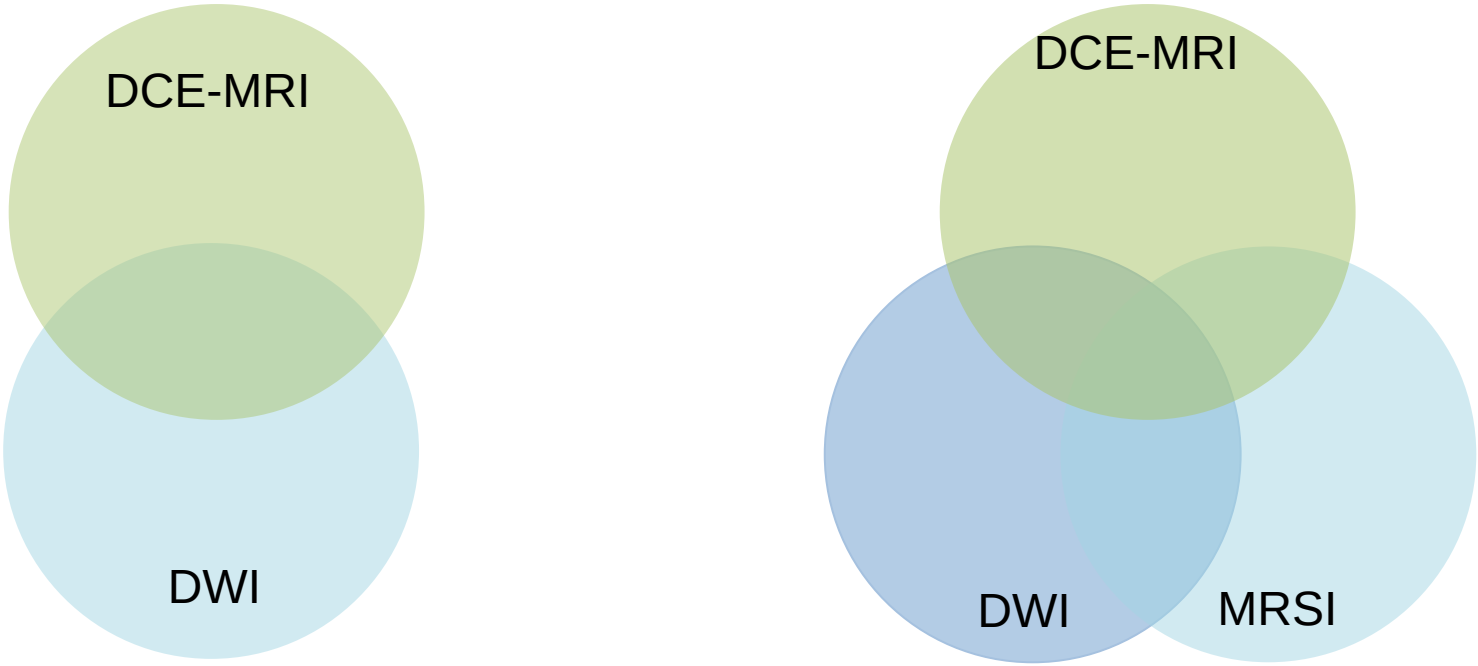
DWI
microstructural
changes





^{1}H-MRSI
metabolism

Multiparametric MRI



Hypothesis

Multiparametric MRI increases diagnostic accuracy in breast cancer diagnosis

Multiparametric MRI: CE-MRI & DWI

Single Reading:

	Sensitivity	Specificity	PPV	NPV	Accuracy
CE-MRI	97.6%	70.6%	89.1%	92.3%	89.8%
DWI	91.9%	89.4%	95.5%	81.7%	91.2%

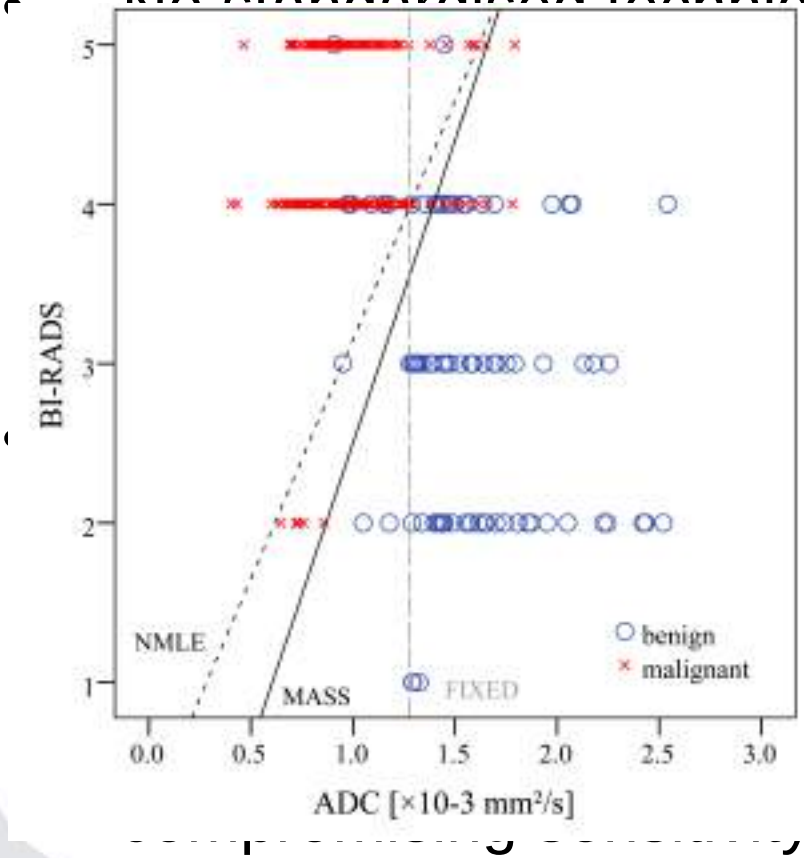
Combined Reading:

	Sensitivity	Specificity	PPV	NPV	Accuracy
Own Results	96.2%	89.4%	89.1%	92.3%	89.9%
Kul et al.	95.2%	80.0%	92.1%	87.2%	90.8%
Yabuuchi et al.	95.7%	77.6%	91.3%	88.0%	90.5%
Ei Kouhli et al	97.1%	89.4%	95.8%	92.7%	94.9%
Partridge et al	97.6%	70.6%	89.1%	92.3%	89.8%

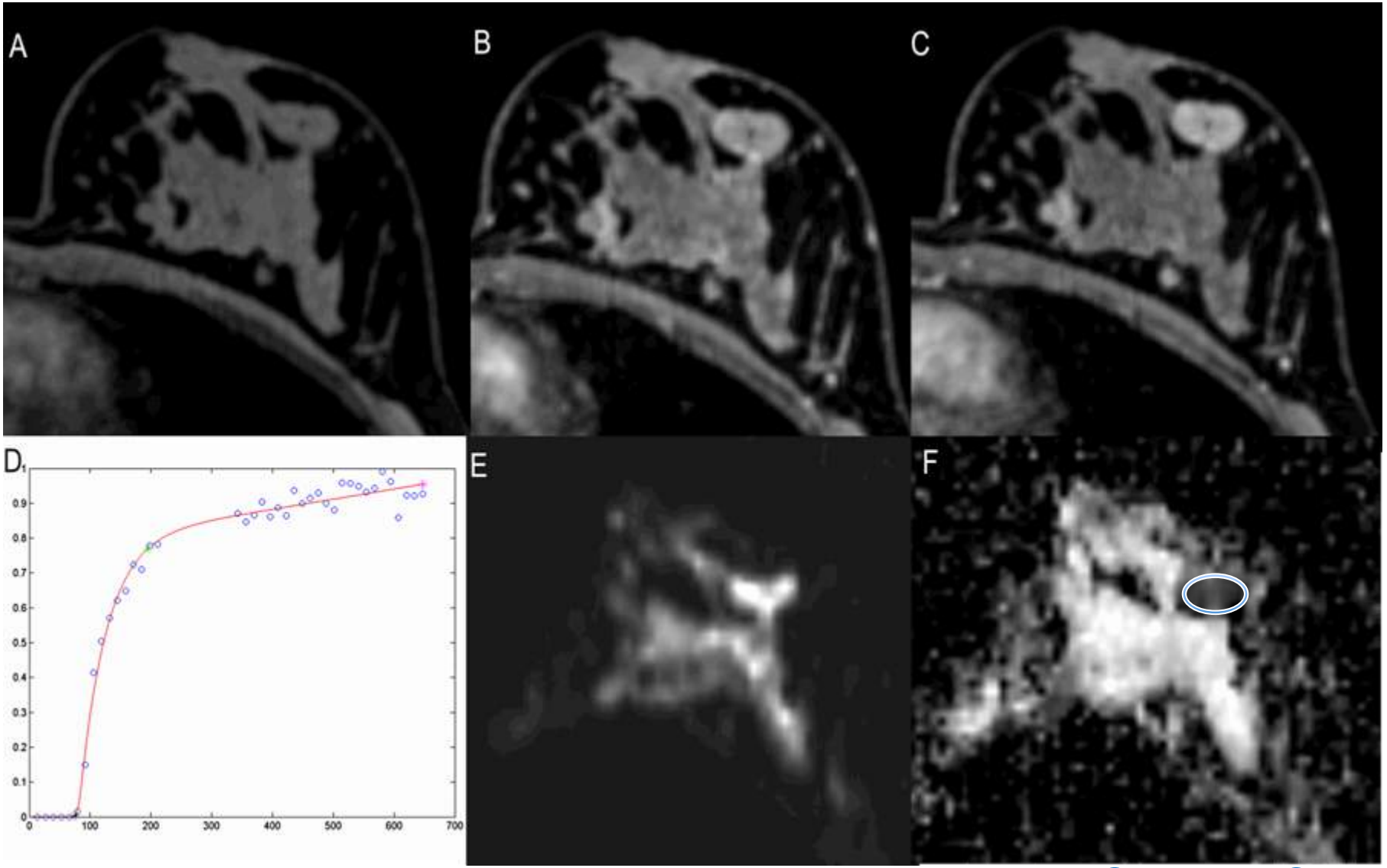
Diffusion Weighted Imaging (DWI)

Pinker et al., Eur Radiol 2013

- No standardised technique
- To develop a reading for CE-MRI and DWI adapted to established BI-RADS® classification



BI-RADS® classification	ADC threshold (x10^{-3} mm^{2}/s)	
	Masses	NMLE
BI-RADS® 1	0.61	0.28
BI-RADS® 2	0.87	0.62
BI-RADS® 3	1.13	0.95
BI-RADS® 4	1.39	1.28
BI-RADS® 5	1.66	1.62



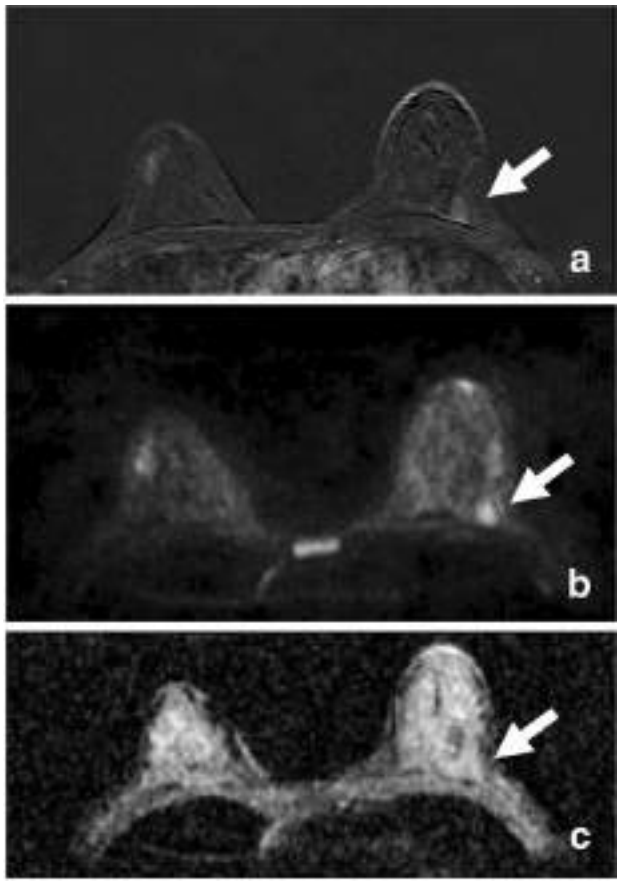
ADC: 0.6 ($x10^{-3}$ mm^2)

Eur Radiol (2014) 24:1204–1210
DOI 10.1007/s00330-014-3153-6

BREAST

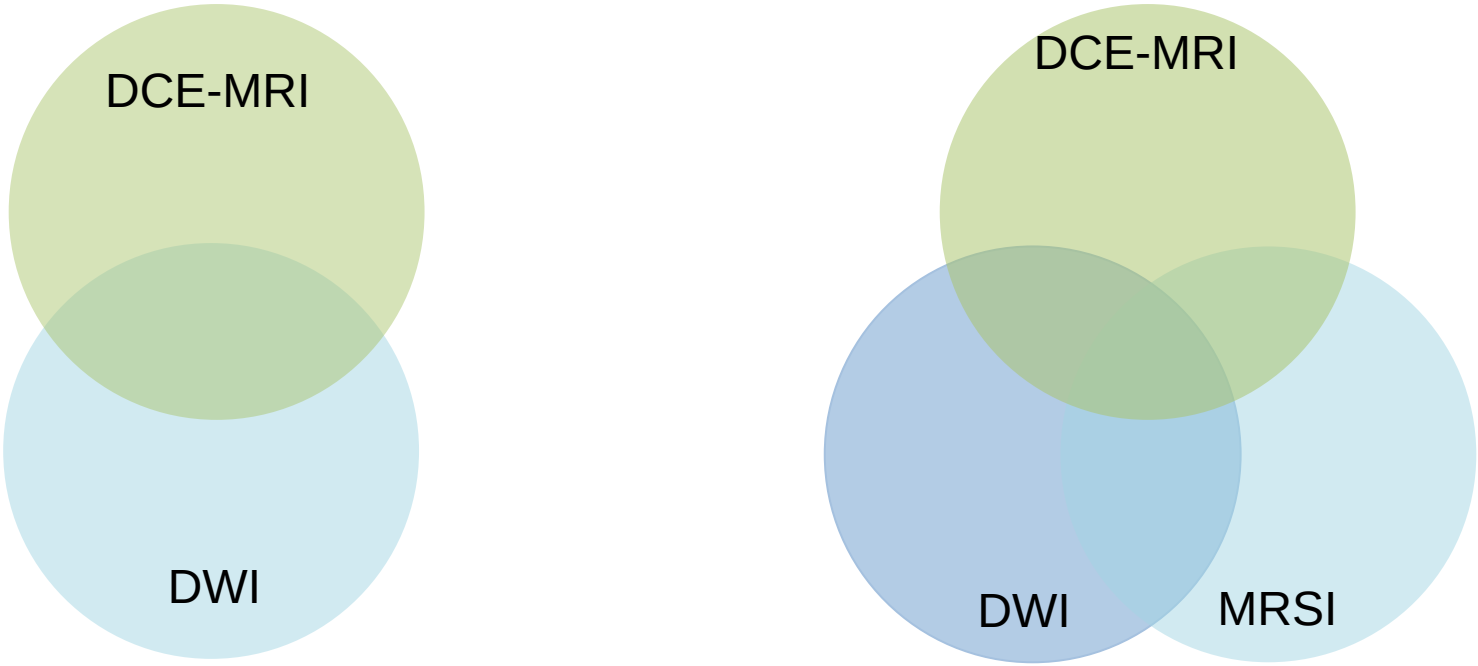
MRI-only lesions: application of diffusion-weighted imaging obviates unnecessary MR-guided breast biopsies

Claudio Spick · Katja Pinker-Domenig · Margaretha Rudas · Thomas H. Helbich · Pascal A. Baltzer



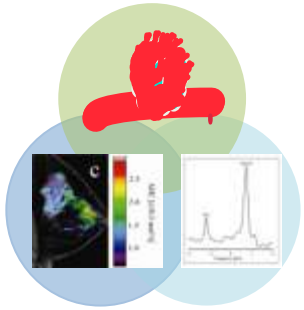
- At 1.5 Tesla
- Malignant: 1.06 x10-3 mm2/s
- Benign: 1.53 x10-3 mm2/s
- AUC : 1.58 x10-3 mm2/s value for exclusive benign lesions
- Obviates unnecessary breast biopsies recommended by MRI alone in 34.5%

Multiparametric MRI



Hypothesis

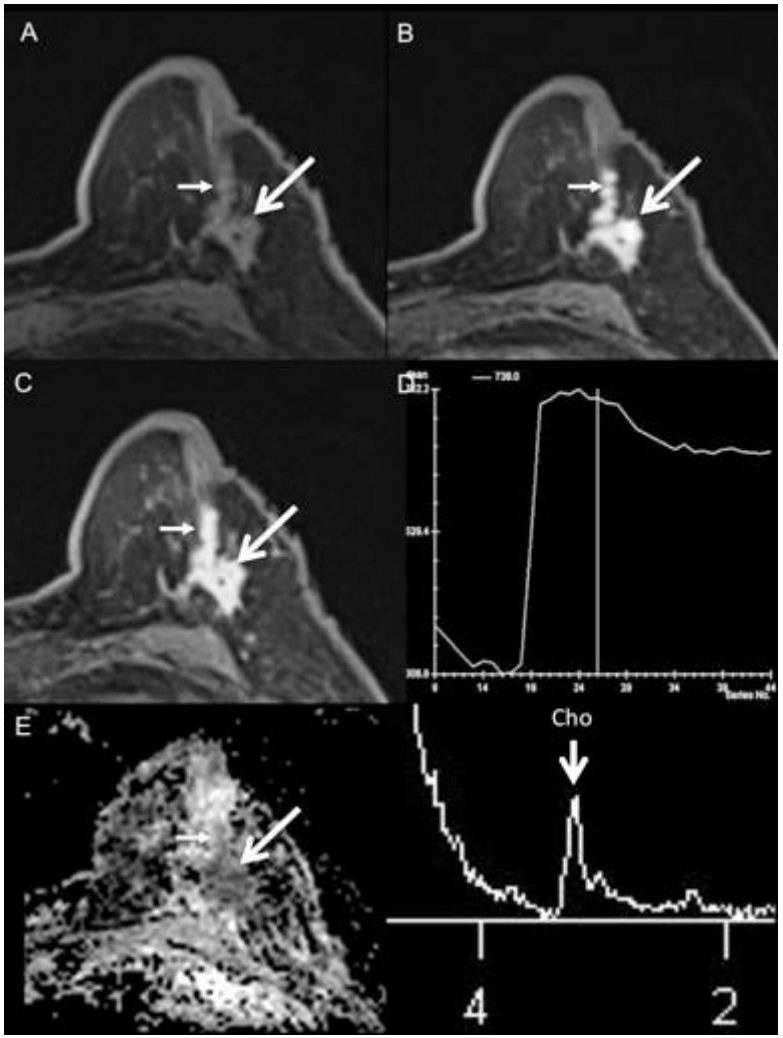
Multiparametric MRI increases diagnostic accuracy in breast cancer diagnosis

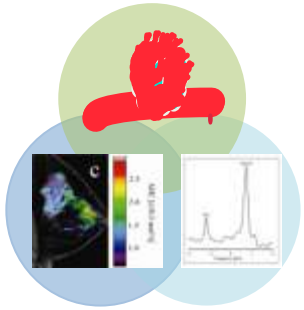


Multiparametric MRI

Pinker, Helbich et al., Invest Radiol 2014

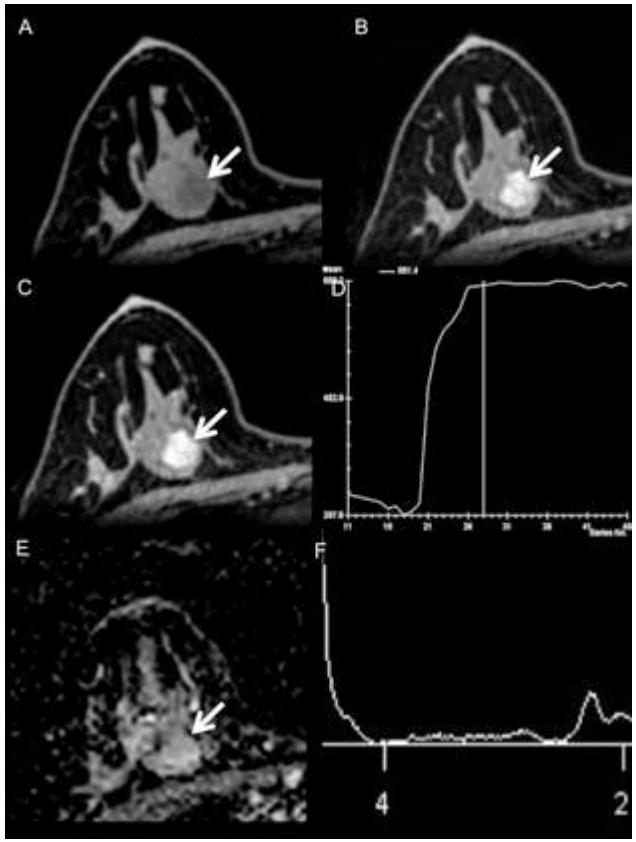
- To compare the diagnostic accuracy of DCE with 2 (DCE, DWI) and three (DCE, DWI, 3D ^{1}H-MRSI) parameters in breast cancer diagnosis
- IRB-approved prospective study
- 113 patients examined with multiparametric MRI at 3T





Multiparametric MRI

- Sensitivity 100%
- Specificty 87.2%
- Diagnostic accuracy 95.6%
- PPV significantly higher with multiparametric MRI (93.7%) than DCE-MRI alone (83.9%) ($p<0.001$)
- Potential to obviate almost two thirds of unnecessary breast biopsies



Multiparametric MRI with three parameters increases the diagnostic accuracy of breast cancer in comparison to DCE-MRI alone and MP MRI with two parameters.

Multi-parametric MRI of the breast should become standard

TAKE HOME MESSAGE

Prostate Cancer

Advances in Magnetic Resonance Imaging: How They Are Changing the Management of Prostate Cancer

A. Sciarra, J. Barentsz, A. Bjartell, J. Eastham, H. Hricak, V. Panebianco, J.A. Witjes

Published data underline an emerging role for multiparametric magnetic resonance imaging (MRI), in particular with the combination of T2-weighted imaging, magnetic resonance spectroscopic imaging, diffusion-weighted imaging, and dynamic contrast-enhanced MRI, as the most sensitive and specific tool available for imaging prostate cancer.

Sciarra et al. Eur Urol. 2011;60:962-77.

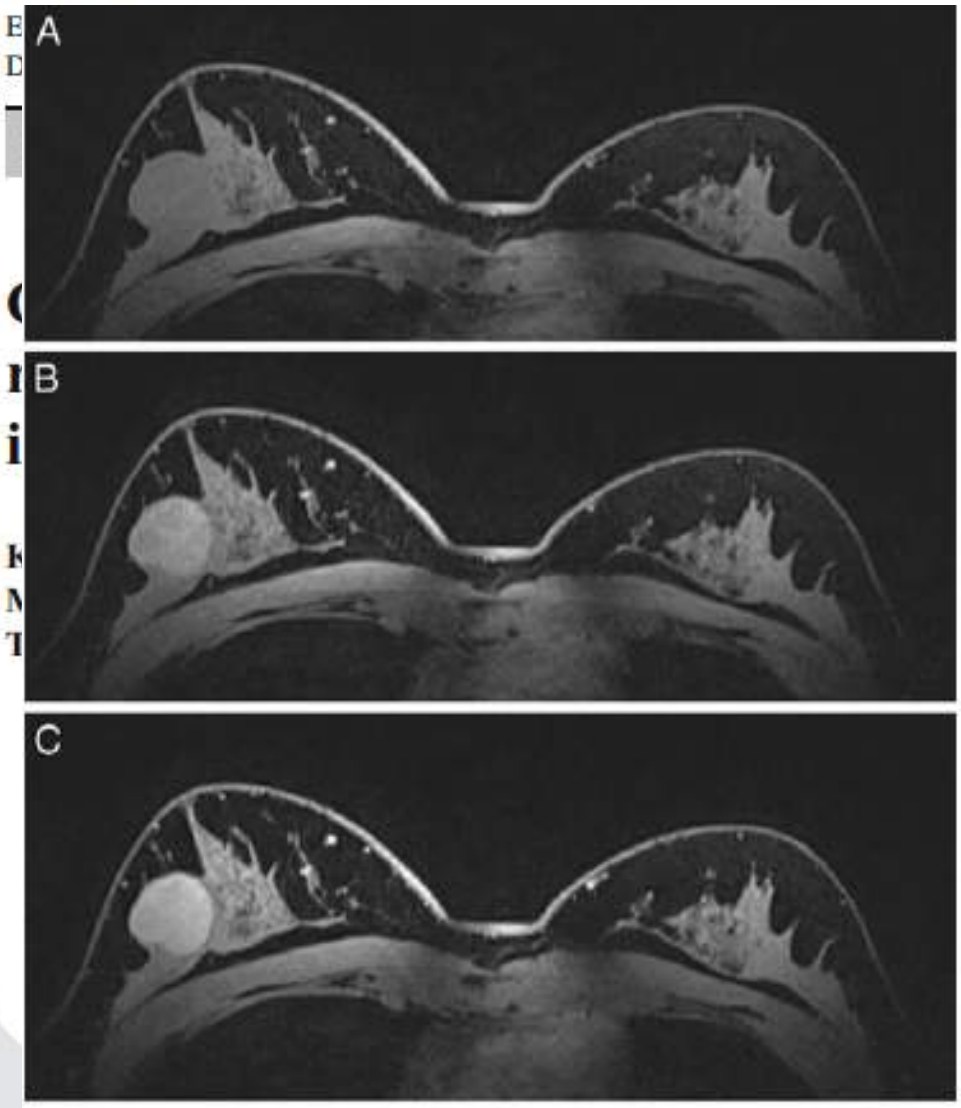
MRI of the breast at 7T

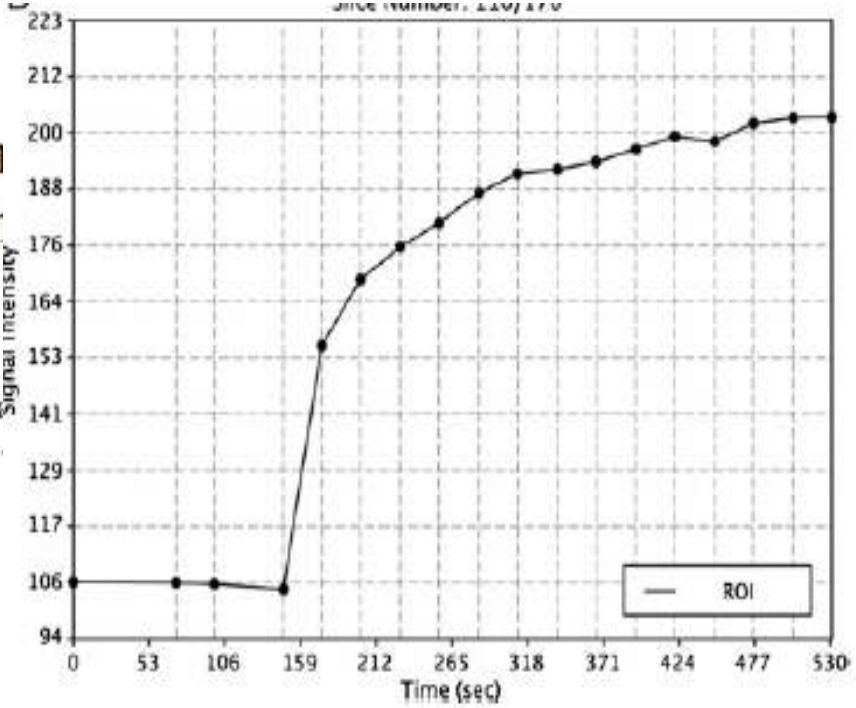
1.5 Tesla

3 Tesla

7 Tesla

MRI of the breast at 7T





Gruber et al. Investigative Radiology 2014
Pinker et al. European Radiology 2014

MRI of the breast at 7T

Dynamic Contrast-Enhanced Magnetic Resonance Imaging of Breast Tumors at 3 and 7 T

A Comparison

Stephan Gruber, PhD, Katja Pinker, MD,*† Olgica Zaric, MSc,*† Lenka Minarikova, MSc,* Marek Chmelik, PhD,* Pascal Baltzer, MD,† Roland N. Boubela, MSc,‡ Thomas Helbich, MD,† Wolfgang Bogner, PhD,* and Siegfried Trattnig, MD**

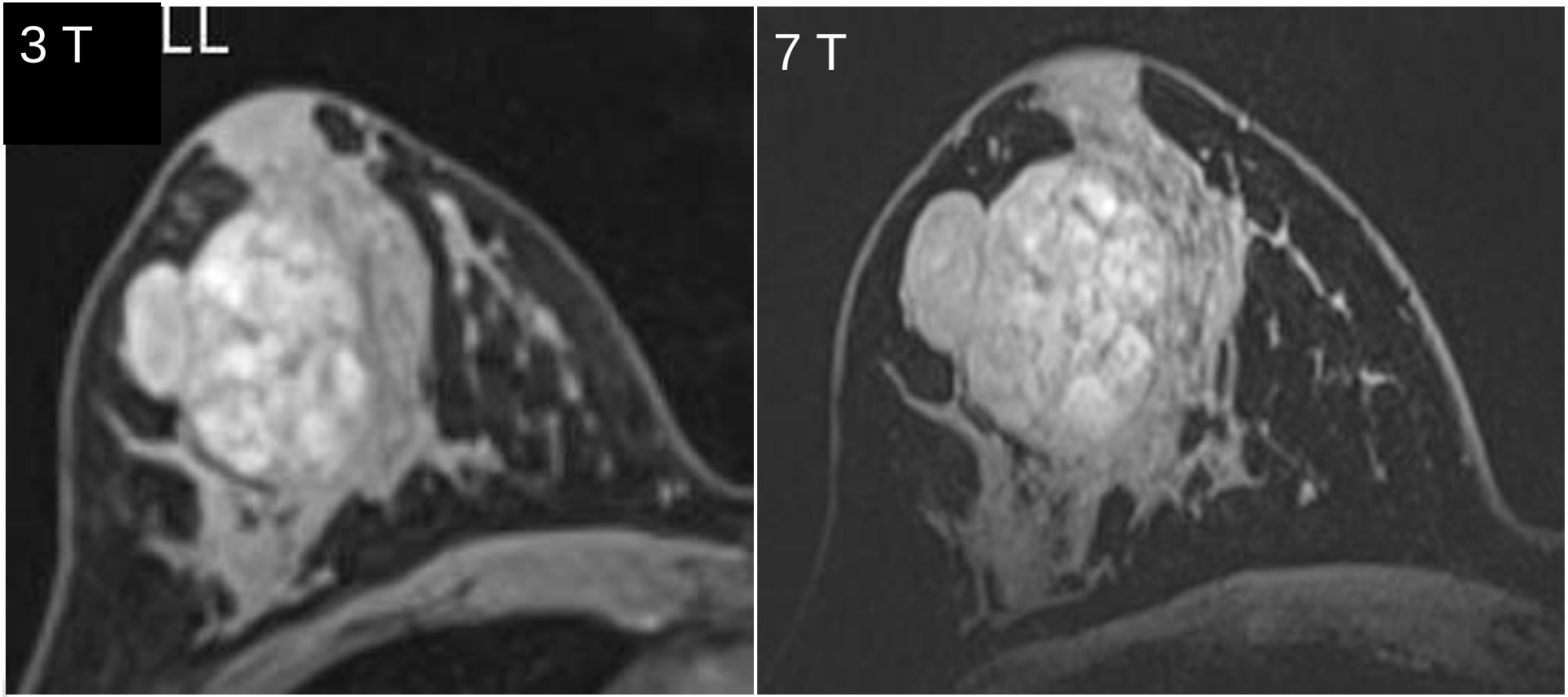
Objectives: The objective of this study was to compare the image quality, contrast enhancement behavior, and diagnostic value of bilateral 3-dimensional

Key Words: breast MRI, breast cancer, 7 T, contrast-enhanced MRI

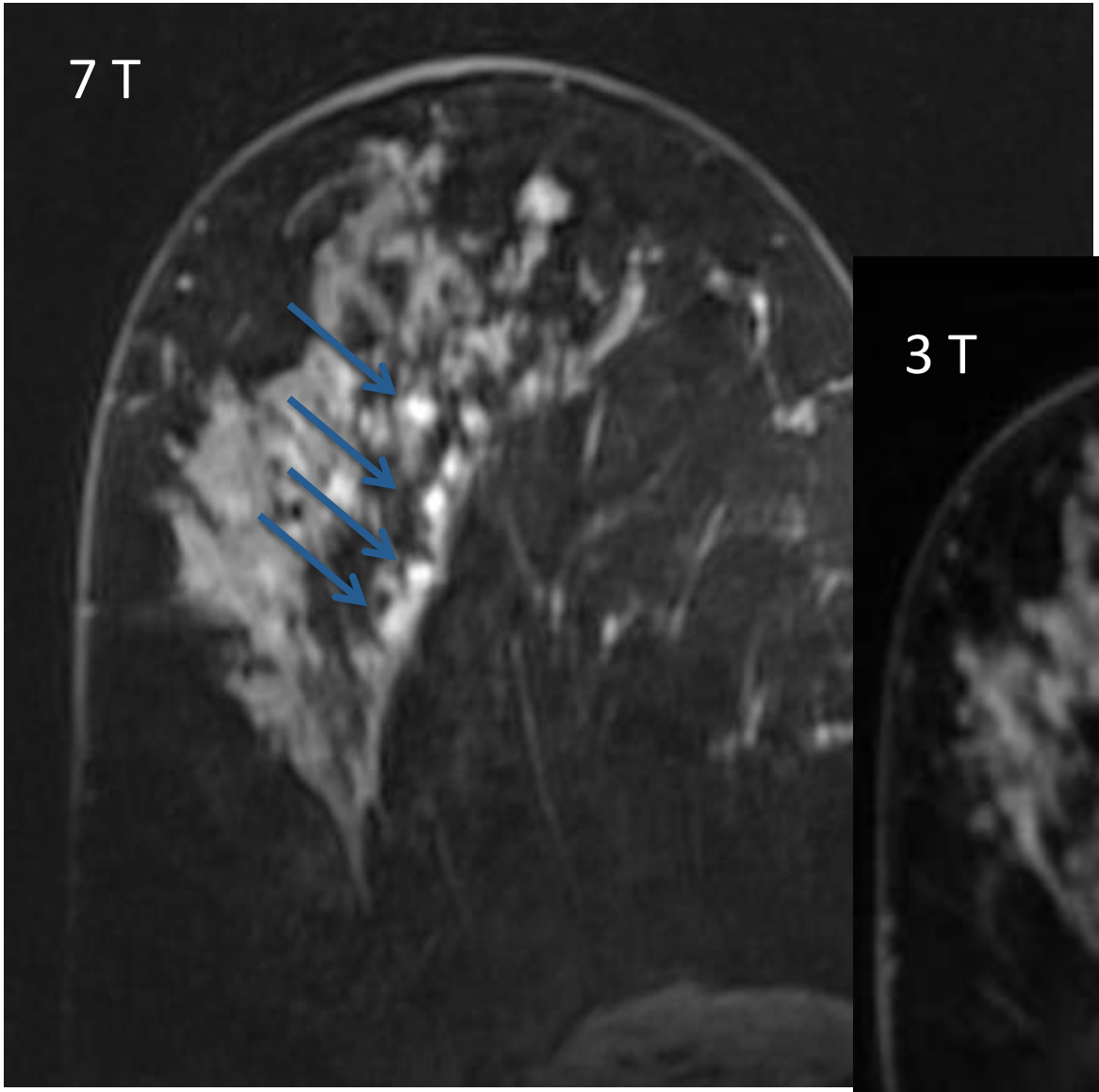
(*Invest Radiol* 2014;49: 354–362)

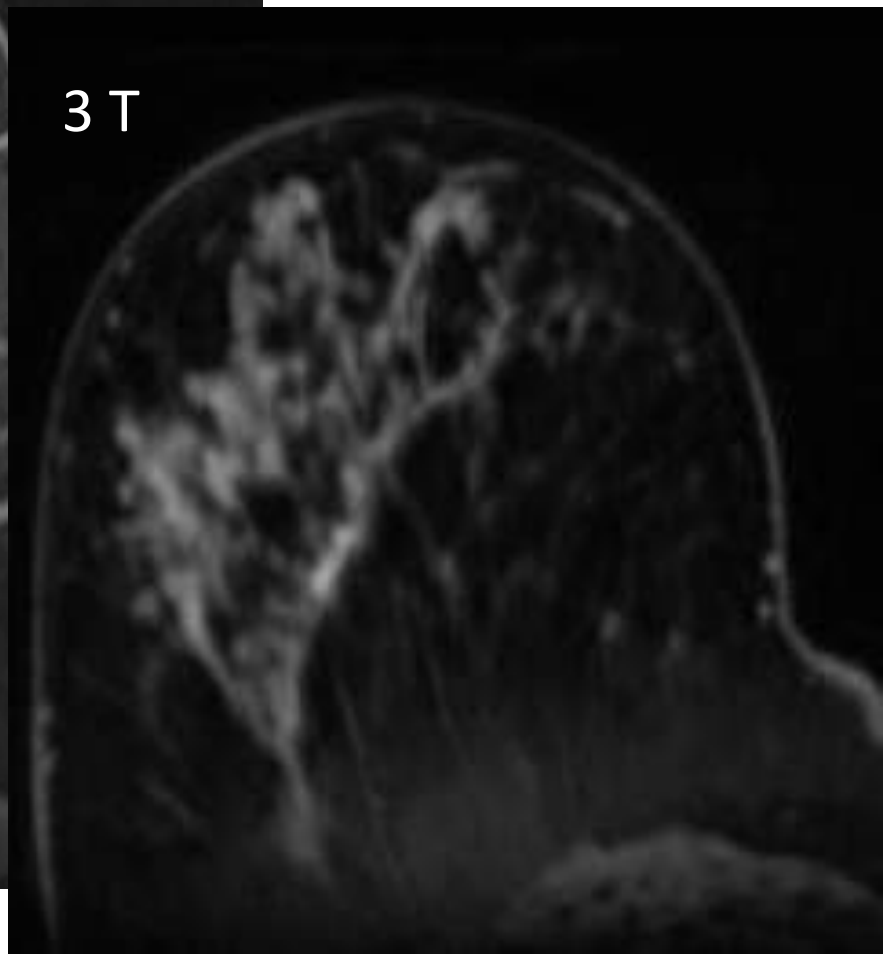
Gruber et al. Investigative Radiology 2014

Pinker et al. European Radiology 2014



Fibroadenoma





DCIS, high grade

Gruber et al. Investigative Radiology 2014

MRI of the breast at 7T

Bilateral Diffusion-weighted MR Imaging of Breast Tumors with Submillimeter Resolution Using Readout-segmented Echo-planar Imaging at 7 T[1]

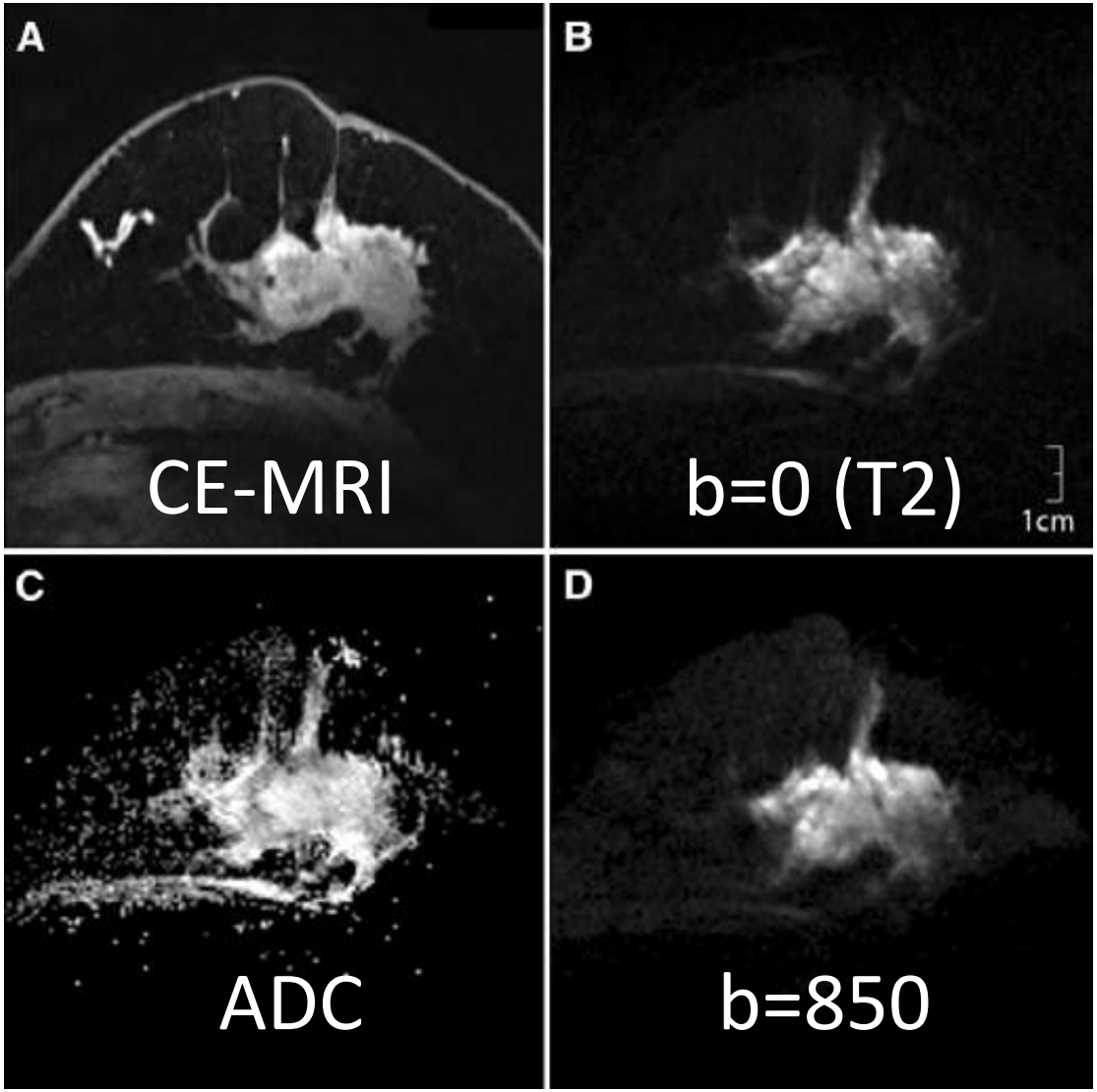
Wolfgang Bogner, PhD[2]
Katja Pinker, MD
Olgica Zaric, MSc
Pascal Baltzer, MD
Lenka Minarikova, MSc
David Porter, PhD
Zsuzsanna Bago-Horvath, MD, PhD
Peter Dubsky, MD
Thomas H. Helbich, MD
Siegfried Trattnig, MD
Stephan Gruber, PhD

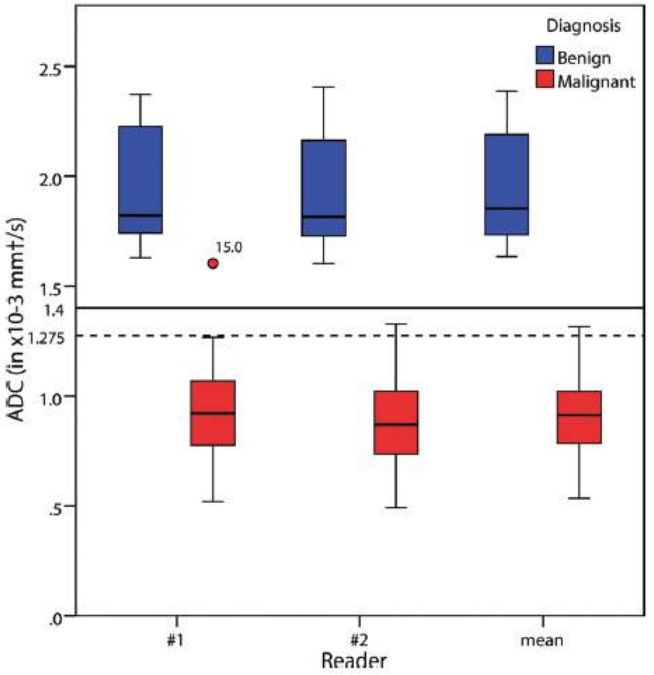
radiology.rsna.org ▪ **Radiology:** Volume 274: Number 1—January 2015

tic
sion-weighted (DW) magnetic resonance (MR) imaging at 7 T in the assessment of breast tumors.

Materials and Methods: Institutional review board approval and written informed consent of five volunteers and 33 patients with 33 breast lesions (31 with histopathologic confirmation, two with confirmation at follow-up) were obtained. Image quality optimization and comparisons of readout-segmented echo-planar imaging (rs-EPI) and single-shot echo-planar imaging (ss-EPI) with or without parallel imaging were

Bogner et al. Radiology 2015





Bogner et al. Radiology 2015

Multiparametric MRI at 7T

Multiparametric MR Imaging with High-Resolution Dynamic Contrast-enhanced and Diffusion-weighted Imaging at 7 T Improves the Assessment of Breast Tumors: A Feasibility Study[1]

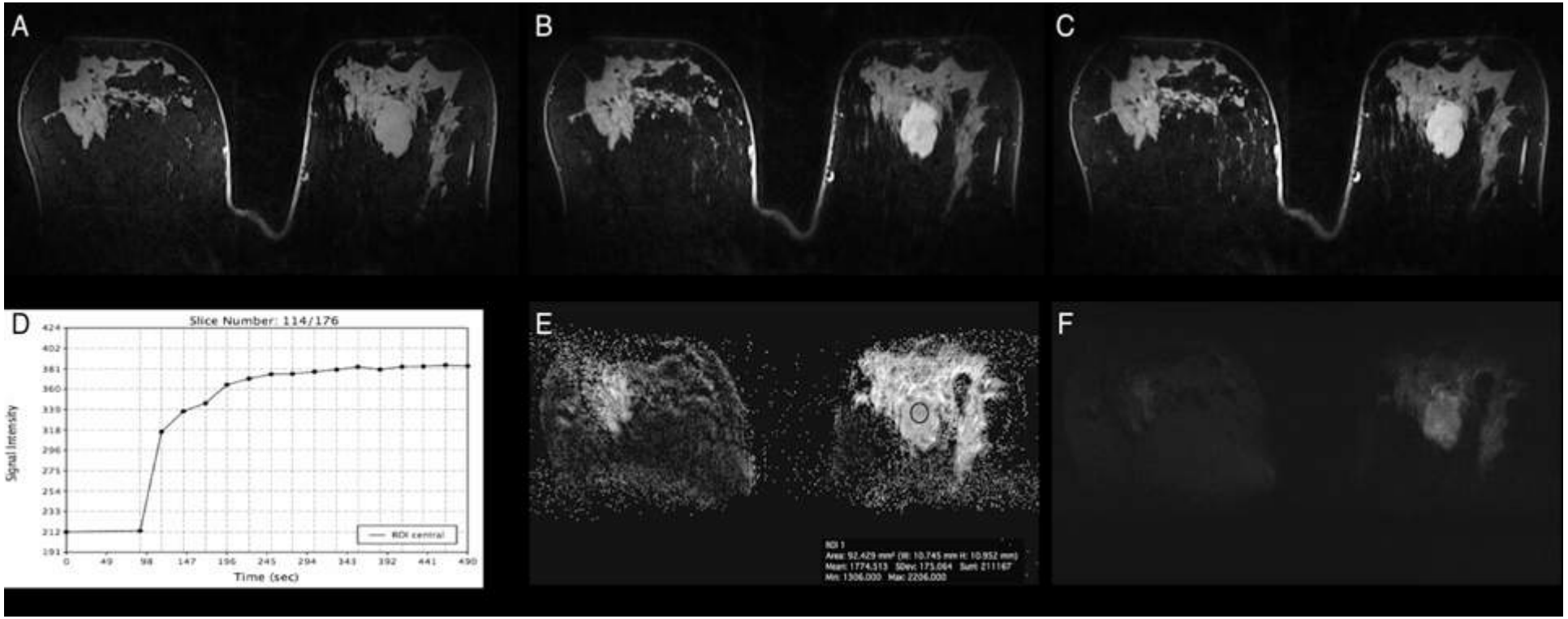
Katja Pinker, MD
Pascal Baltzer, MD
Wolfgang Bogner, PhD
Doris Leithner, MD
Siegfried Trattnig, MD
Olgica Zaric, PhD
Peter Dubsky, MD
Zsuzsanna Bago-Horvath, MD
Margaretha Rudas, MD
Stephan Gruber, PhD
Michael Weber, PhD
Thomas H. Helbich, MD

Purpose: To ascertain whether multiparametric magnetic resonance (MR) imaging of the breast in combination with dynamic contrast material–enhanced (DCE) imaging and diffusion-weighted imaging (DWI) at 7 T is feasible and improves diagnostic accuracy.

Materials and Methods: From December 2011 to December 2013, 40 patients with suspicious breast lesions were included in this institutional review board–approved prospective study. Before bilateral multiparametric MR imaging of the breast at 7 T, all patients gave written informed consent. Lesions were classified according to Breast Imaging Reporting and Data System (BI-RADS) and assessed for apparent diffusion coefficient (ADC) values by two readers independently. For combined analysis of DCE MR imaging and

Radiology: Volume 000: Number 0—■ ■ ■ 2015 ▪ radiology.rsna.org

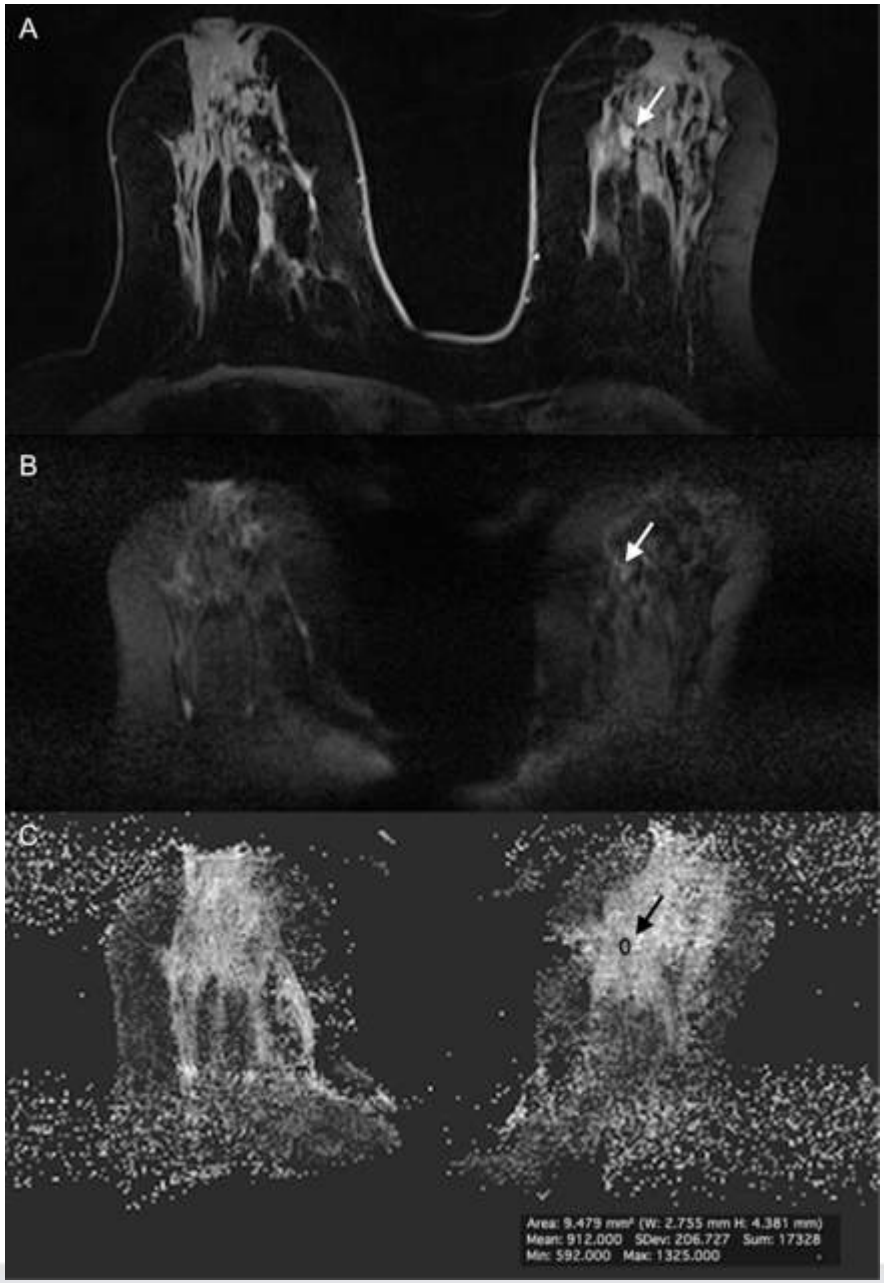
Pinker et al. Radiology 2015



- Fibroadenoma in a 50-year-old woman centrally in the left breast
  - Irregular shaped and partially irregularly marginated mass
  - Initial fast/persistent (II) heterogeneous contrast enhancement
  - In DWI the mass no decreased ADC values (1.774 $\times 10^{-3}$ mm^2/s)

DCE MRI and DWI were discordant

Multiparametric MRI correctly classified mass as benign

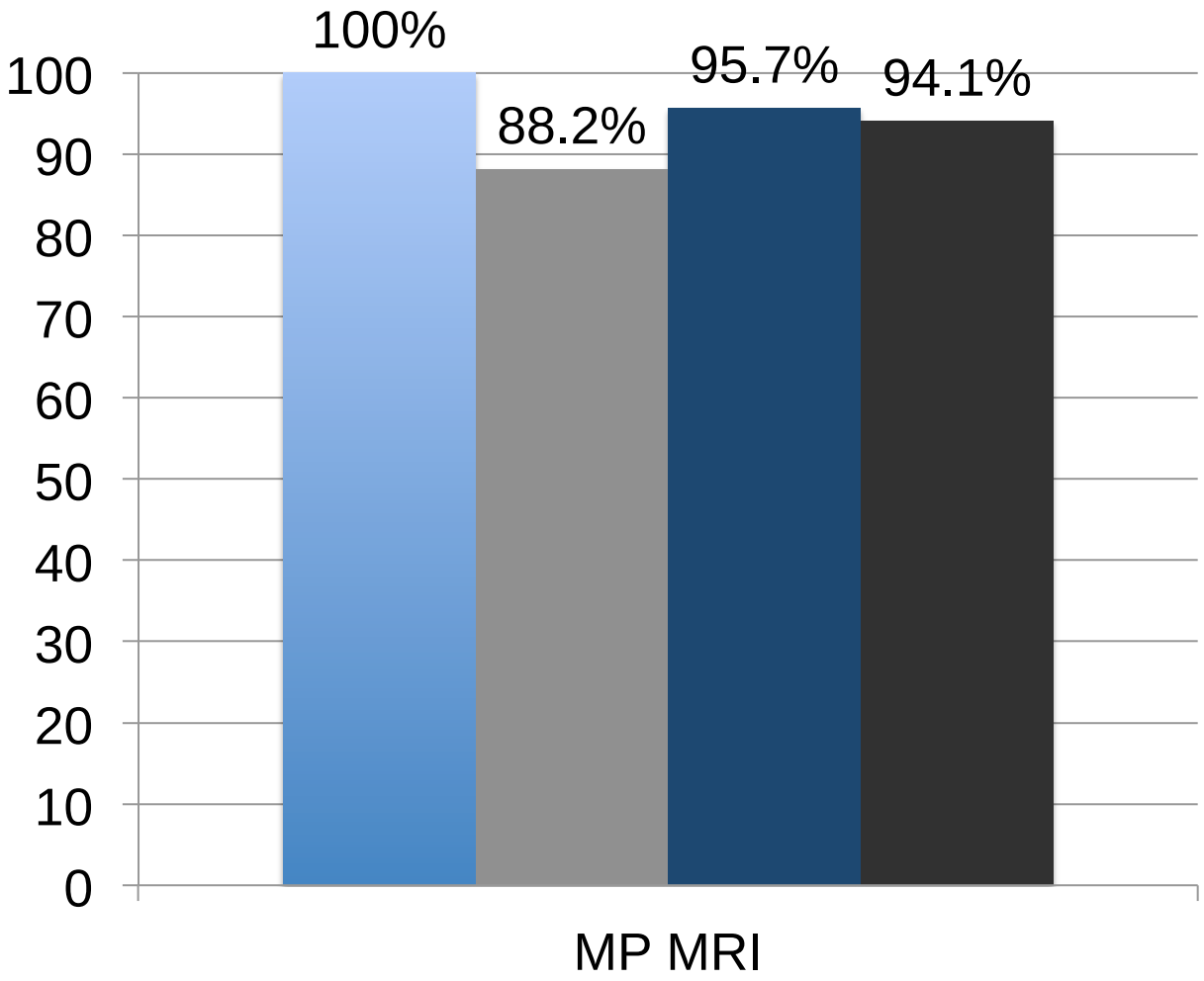


- Invasive lobular carcinoma in a 55-year-old woman centrally in the left breast
  - Focal and heterogeneous NME
  - Restricted diffusivity (ADC values 0.912×10^{-3} mm^2/s)

DCE MRI and DWI were concordant

Multiparametric MRI confidently classified NME as malignant.

Multiparametric MRI at 7T



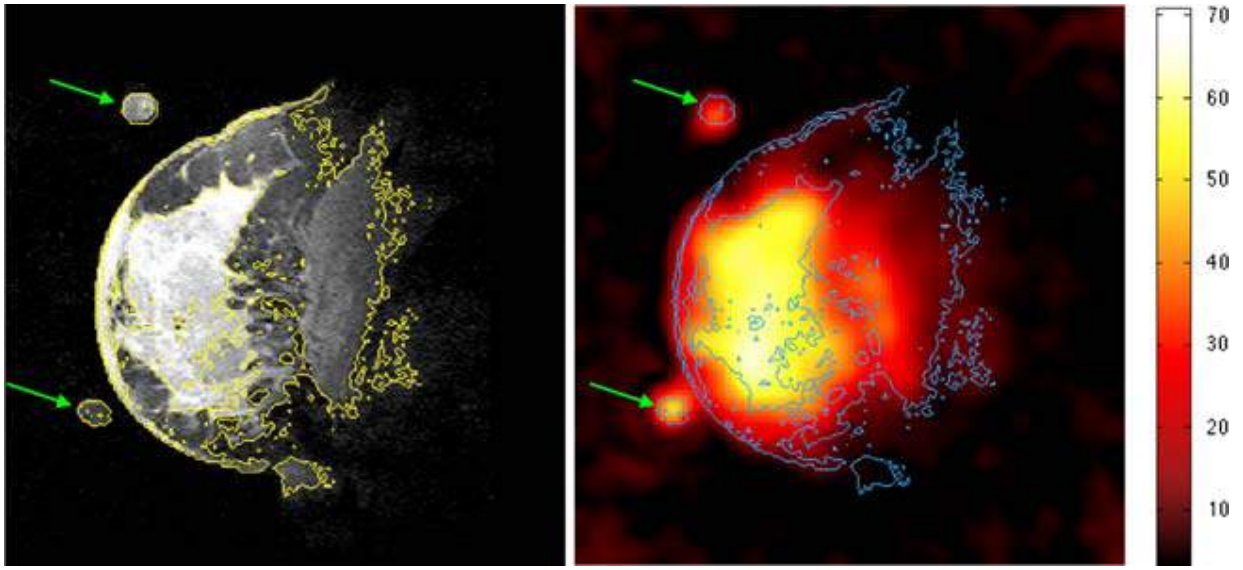
Sensitivity
Specificity
Diagnostic Accuracy
AUC

N= 40

- 29 malignant
- 17 benign lesion
- Size 6-95mm
- Mean size 23.3mm

Emerging techniques:
Sodium Imaging

- Sodium concentration is sensitive indicator of cellular integrity and cellular energy metabolism
- Tissue sodium concentration (TSC) is increased in cancer
- Potential to increase specificity in breast cancer diagnosis
- Promising radiologic biomarker for therapy monitoring



Ouwerkerk et al. Breast Cancer Res Treat (2007)

Elevated tissue sodium concentration in malignant breast lesions detected with non-invasive 23Na MRI at 1.5 T