Multiparametric MRI for Precision Oncology and Radiation Oncology: A Physician's Perspective

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Nobel Prizes in Magnetic Resonance

MRI play an important role in medicine.

1930s: Discovered mag… prop… nuclei

1940s: NMR measurement in

1950s: Pulsed NMR in

1970s: Obtained first 2D MRI

The role of Multiparametric MRI is growing rapidly.

1st revolution: *in vivo* spectroscopy

2nd revolution: magnetic field gradients for spatial encoding → Image resolution: mm

Poster r… ISMRM

Courtesy of Yuenan Wang

MpMRI for Precision Oncology and Radiation Oncology (RT): A Physician's View

- Multiparametric MRI in precision oncology
  - Precision screening, diagnosis, staging, treatment response and recurrent assessment
- Multiparametric MRI in precision RT
  - Precision simulation, target delineation and RT plan
  - Precision treatment delivery
  - Precision treatment response prediction
  - Precision detection of tumor recurrence
- Multiparametric MRI future potential

What is Multiparametric Magnetic Resonance Imaging (mpMRI)?

What Is MpMRI?

- "A multiparametric MRI (mpMRI) is a combination of two or more sequences, and/or including other specialized MRI configurations such as spectroscopy"

The Wiki Definition https://en.wikipedia.org/wiki/MRI_sequence

No definition from official organizations like AAPM, ACR,RSNA….

MpMRI Multiple MRI Sequences

- Anatomic T1 weighted, T2 weighted sequences
- Additional MRI sequences:
  - Diffusion-Weighted Images (DWI)
  - Dynamic Contrast Images (DCI)
  - Proton Density Images (PDI)
  - Flow sensitive images like MR angiography, MR venography, CSF flow study
  - Cholangiopancreatography (MRCP), MR Spectroscopy, MR perfusion, functional MRI…

In general, MRI sequences vary with diseases and anatomic sites. Selection of MRI Sequence shall be individualized to the site and function.

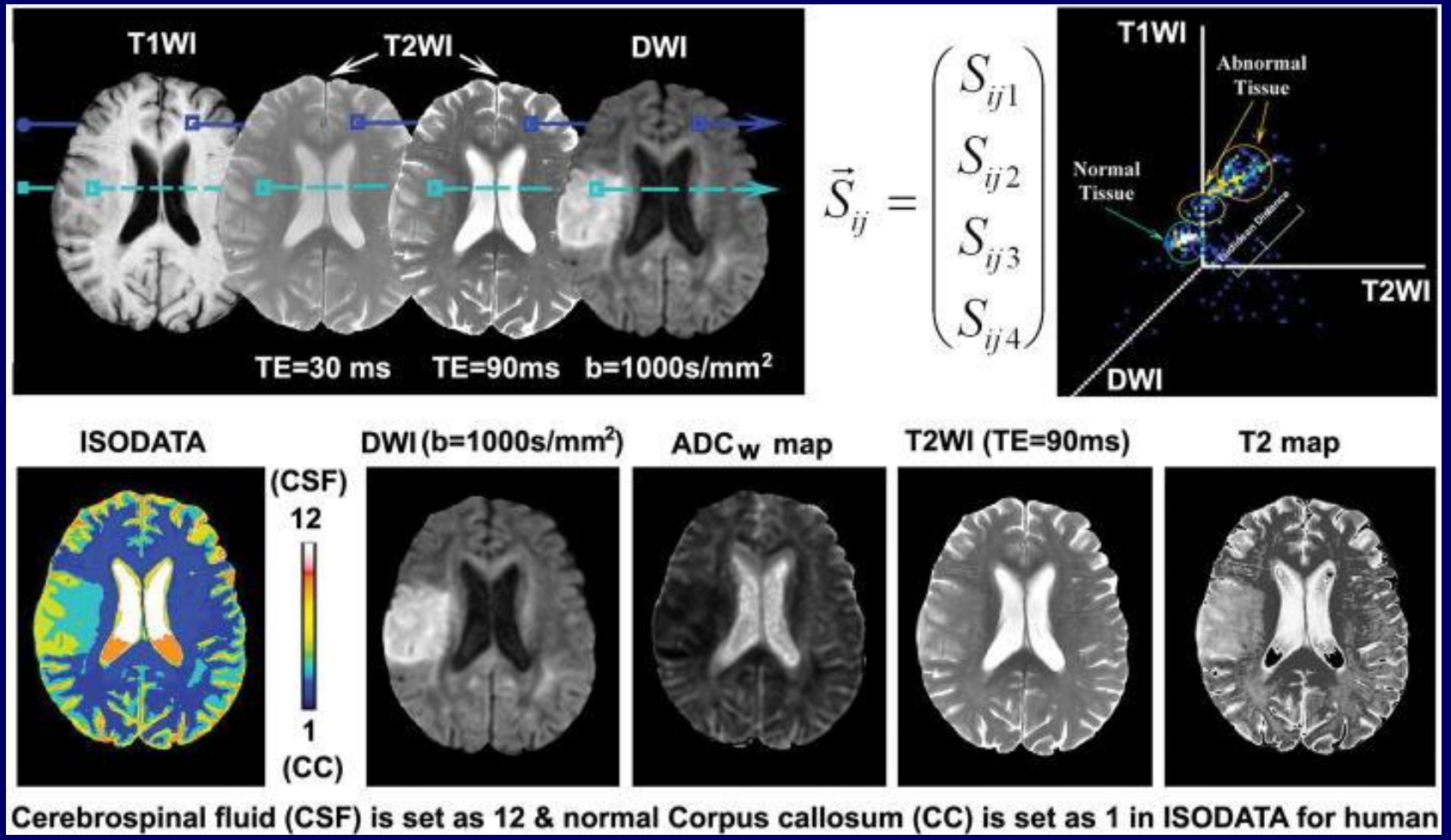
https://radiopaedia.org/articles/mri-sequences-overview

MpMRI for the Brain

- "Combining multiple imaging contrasts that reflect different aspects of pathophysiological processes ..."

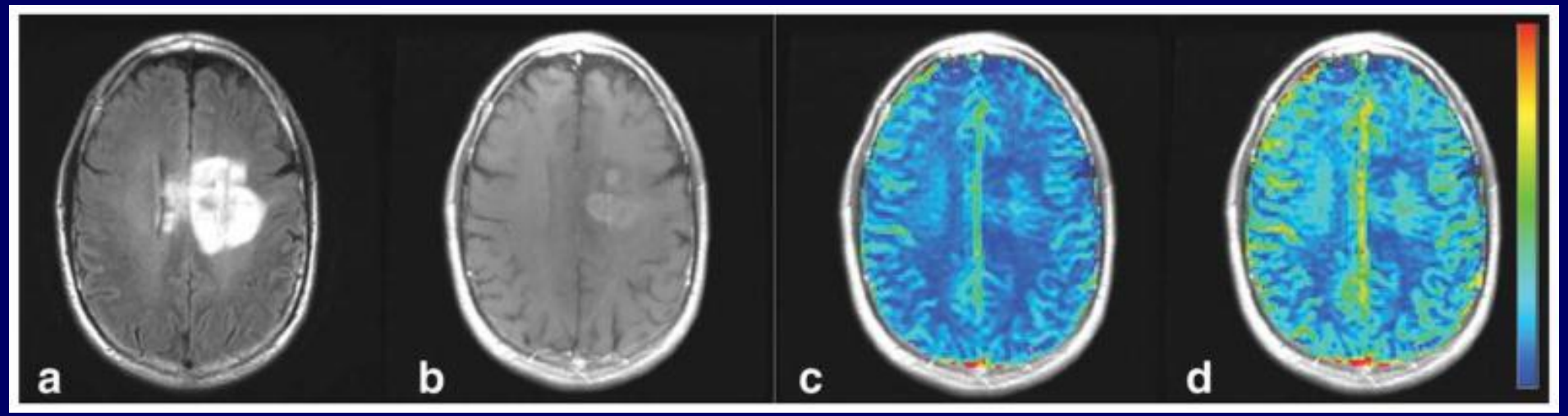
ADC=Apparent diffusion coefficient)

ISODATA=Iterative Self-Organizing Data Analysis Technique



Wu et al, 2010 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3319343/

Relative Cerebral Blood Volume (rCBV)



Fluid-Attenuated Inversion Recovery Images (FLAIR)

Post-contrast T1*WI*

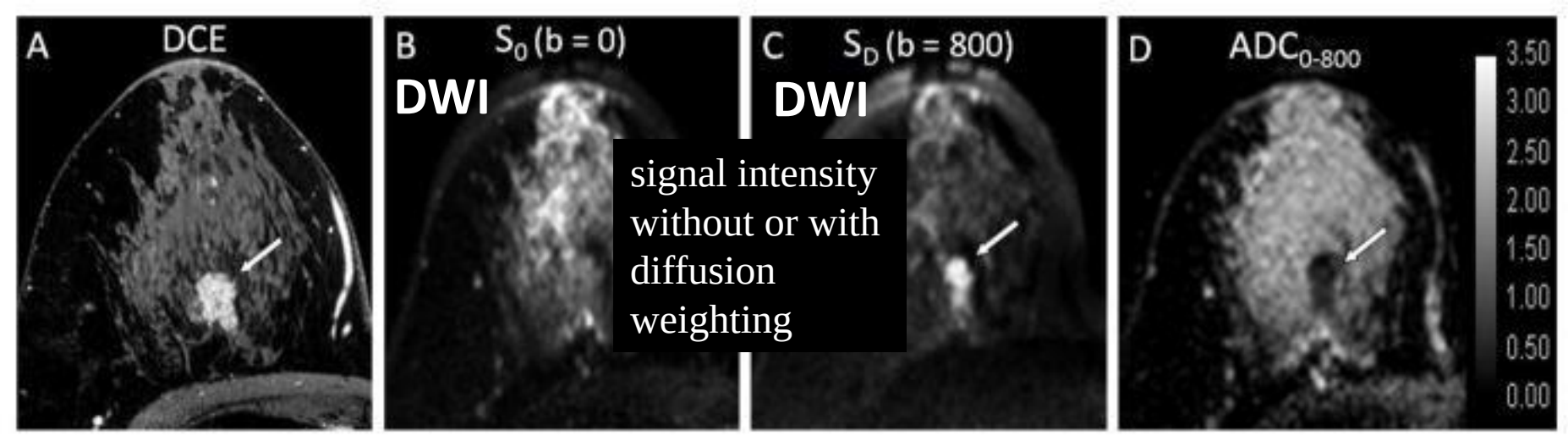
Pre-STD rCBV maps

post-STD rCBV maps

Bedekar et al: Magn Reson Med. 2010 Sep; 64(3): 907–913.

MpMRI for Breast

- MpMRI of breast, can be done by different field strengths (1.5-7 T), include DWI, MRS, with Novel MRI parameters (sodium imaging, chemical exchange saturation transfer imaging, blood oxygen level-dependent), and hybrid imaging with PET/MRI and different radiotracers.



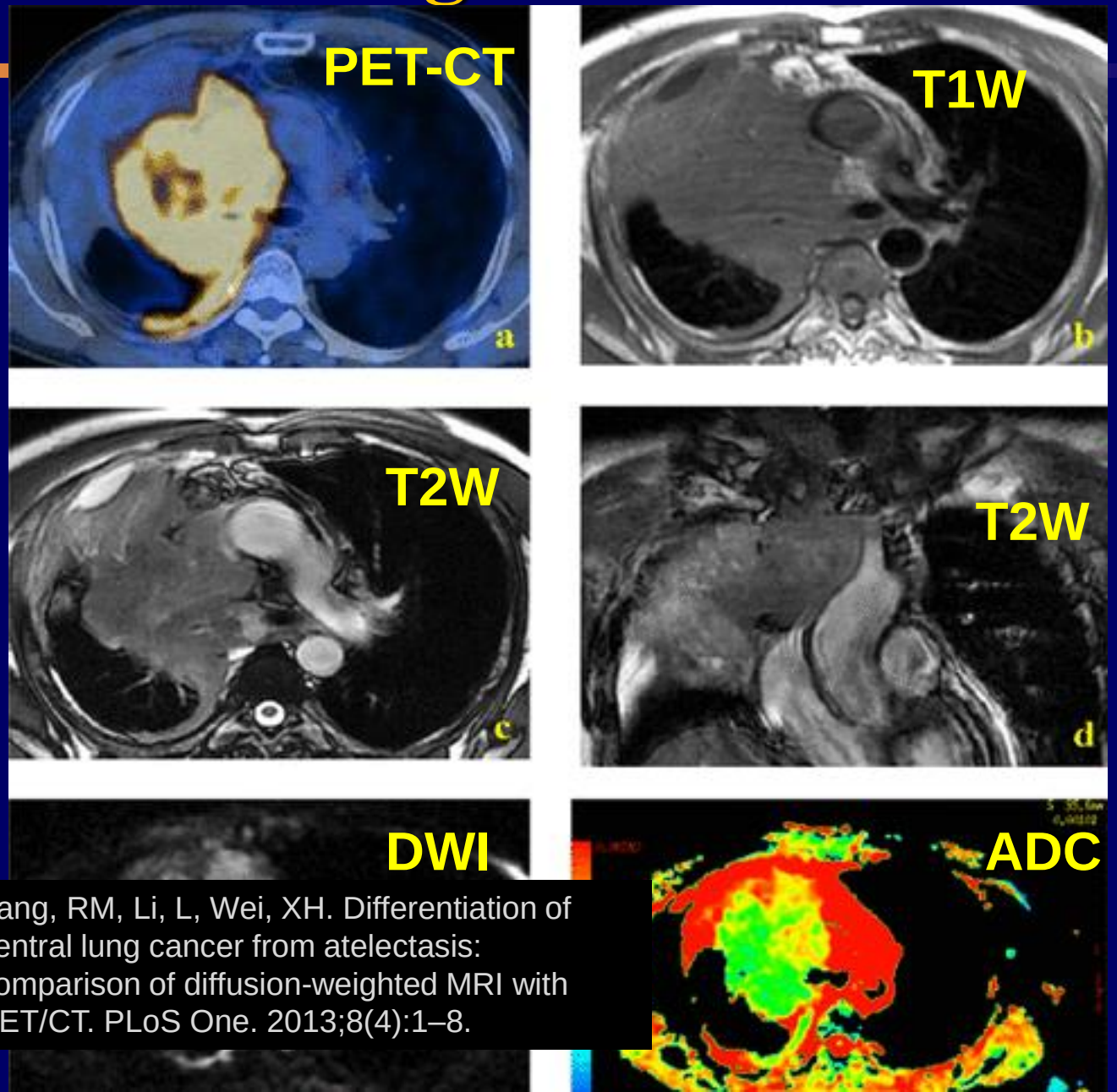
Rahbar et al, Magn Reson Imaging Clin N Am. 2016 Feb; 24(1): 223–238.

MpMRI for Lung

- Conventional T1W,T2W
- T2-weighted fast spin echo (FSE) imaging with and without fat saturation
- Inversion recovery techniques
- T1-spin echo sequence
- Gradient echo sequence (GRE)

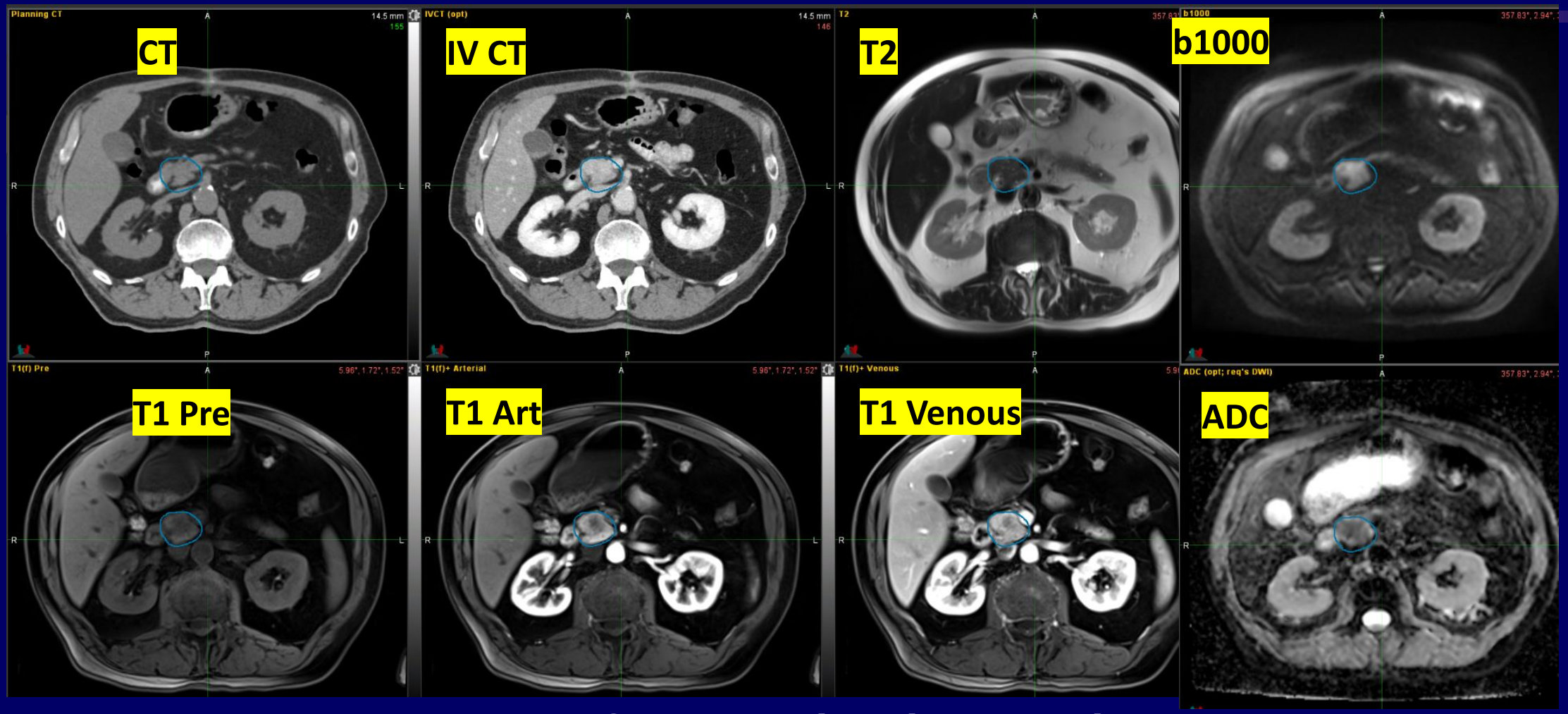
Bierder et al, Insights Imaging, 2012 Aug; 3(4): 355–371.

T2W FSE-MRI is favorable for the mediastinum. Normal lung tissue can be seen on single-shot sequences (HASTE or TrueFISP). Lung nodules are ideally visualized with a volumetric interpolated 3D-GRE sequence (e.g. VIBE)
~Bierder et al, 2003



Yang, RM, Li, L, Wei, XH. Differentiation of central lung cancer from atelectasis: comparison of diffusion-weighted MRI with PET/CT. PLoS One. 2013;8(4):1–8.

MpMRI for Pancreas



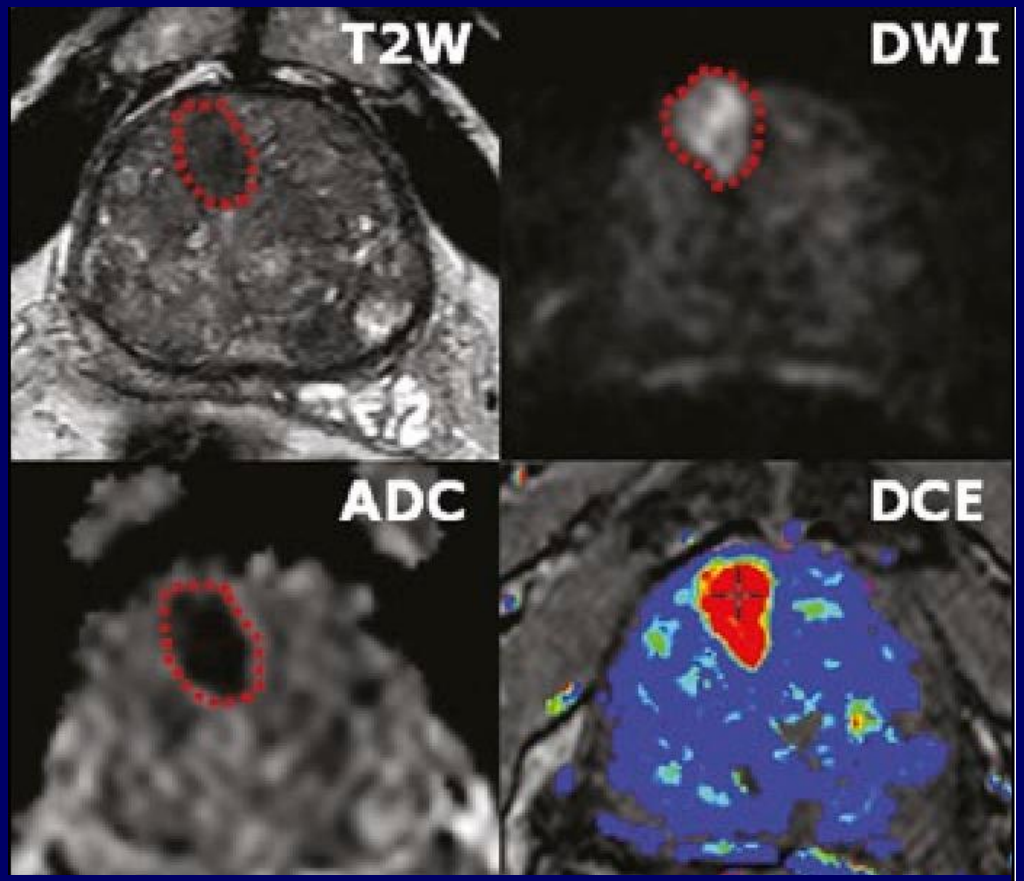
A case of Pancreatic adenocarcinoma

Slide courtesy of Allen Li

Froedtert & Medical College of Wisconsin

MpMRI for Prostate

- **MpMRI of the prostate** combines anatomic information from T1-weighted and T2-weighted sequences with functional information from Diffusion-Weighted imaging (DWI) ±ADC and dynamic contrast enhancement (DCE),±MRS



Bjurlin et al, 2016,
DOI:10.5173/ceju.2016.734
Corpus ID: 17680536

Stabile et al, 2019, **https://www.nature.com/articles/s41585-019-0212-4**
https://radiopaedia.org/articles/multiparametric-mri-mpmri-of-the-prostate

MpMRI for Precision Oncology

MpMRI for Precision Oncology

- Precision cancer screening, diagnosis, and staging
- Precision multidisciplinary treatment decision
- Precision treatment response prediction
- Precision post-treatment response assessment
- Precision detection of recurrent diseases

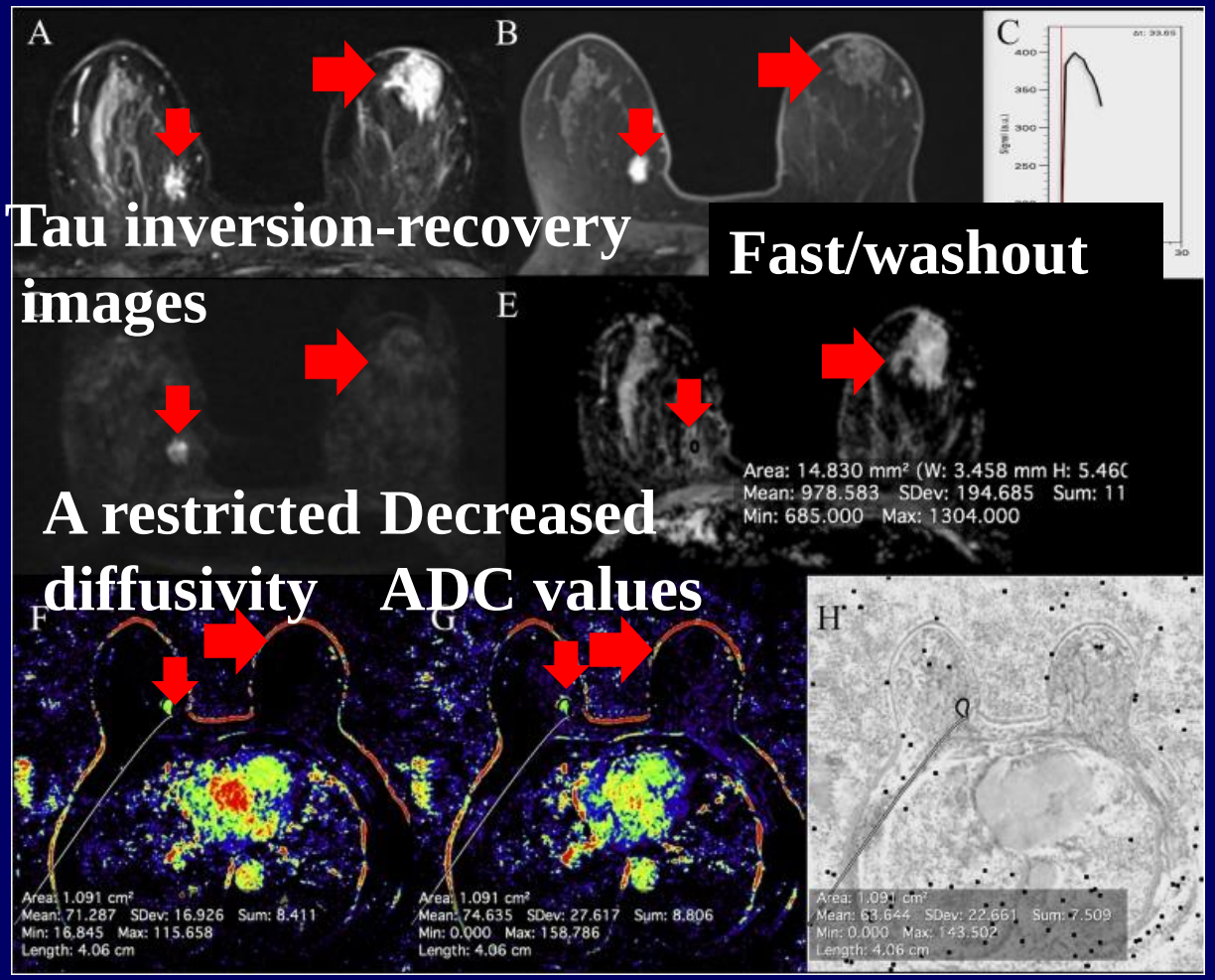
MRI is being used in clinic in almost all solid tumors

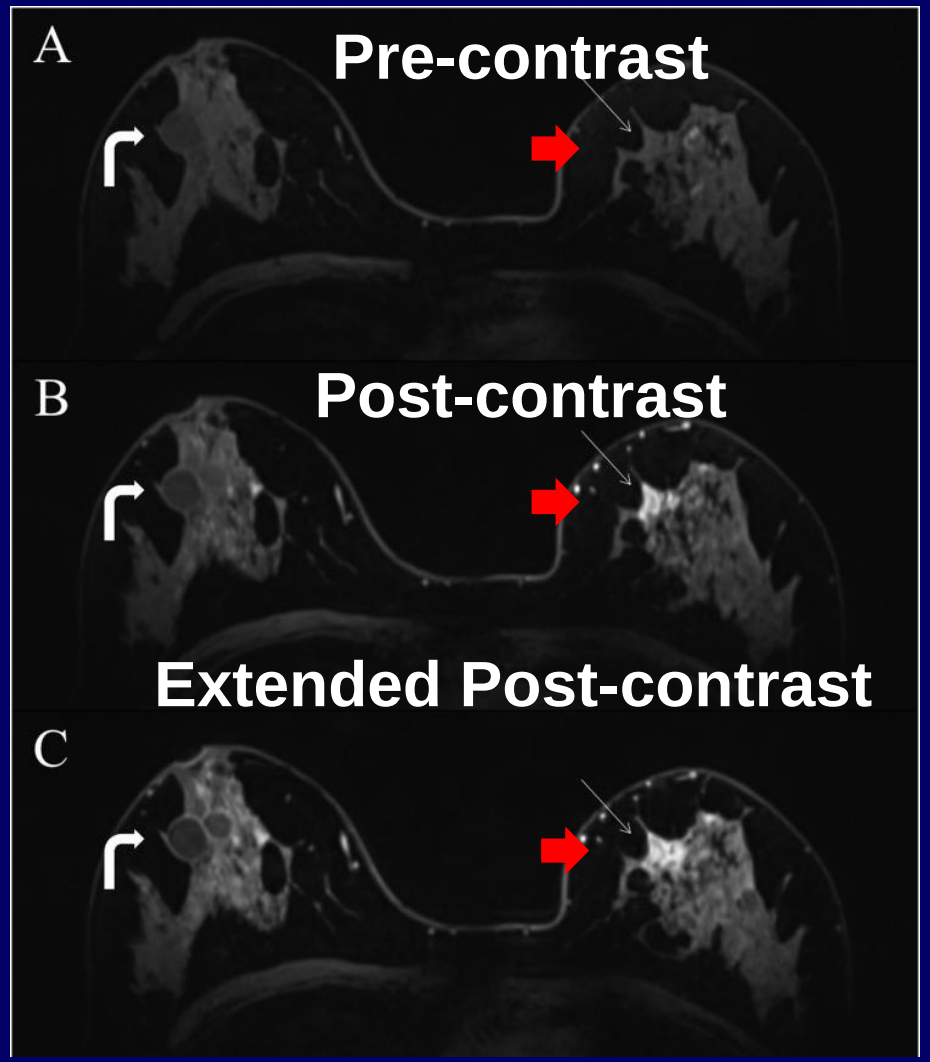
MpMRI in Breast Cancer Precision Care

- DCE-MRI is the most sensitive test for breast cancer detection, with a good specificity.
- DWI, sometimes MRS and higher field strengths (≥3T), has demonstrated improved sensitivity and specificity of breast cancer detection.
- MpMRI can quantify the functional processes of cancer development and progression at multiple levels
- MpMRI of the breast improves diagnostic accuracy in breast cancer and obviates unnecessary breast biopsies
- MpMRI of the breast enables an improved assessment and prediction of response to neo-adjuvant therapy.

Marino et al https://pubmed.ncbi.nlm.nih.gov/28639300/

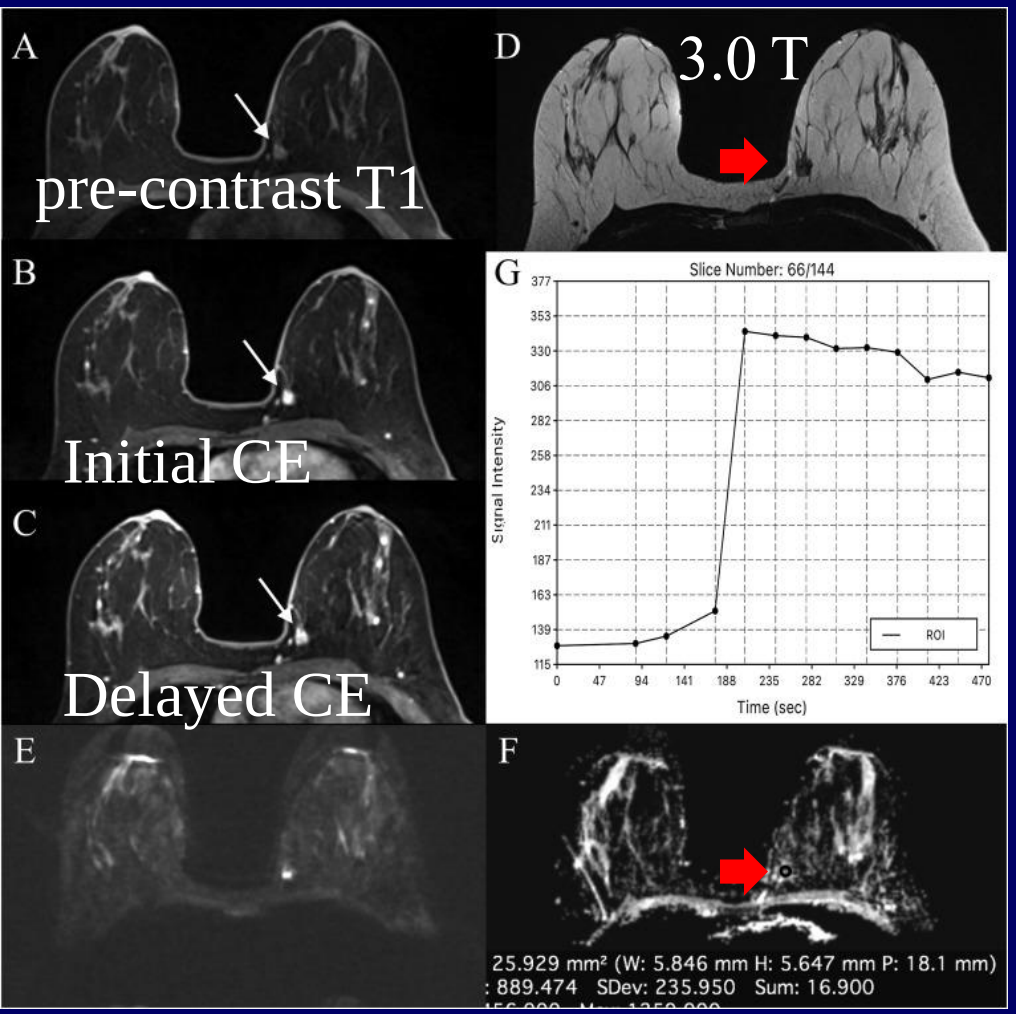
MpMRI for Breast Cancer Diagnosis

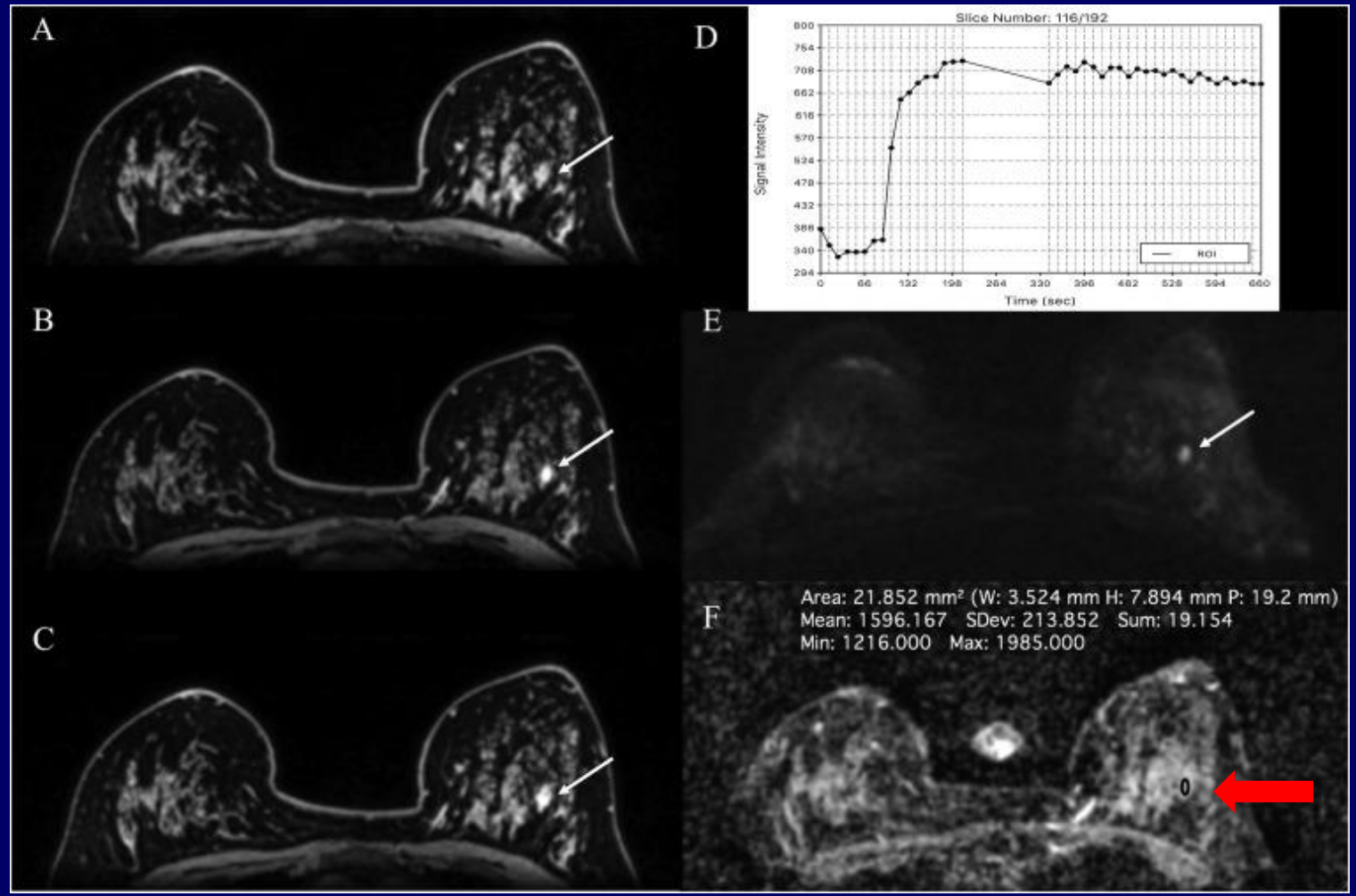




Pinker et al, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5605035/

MpMRI in Breast Cancer Diagnosis





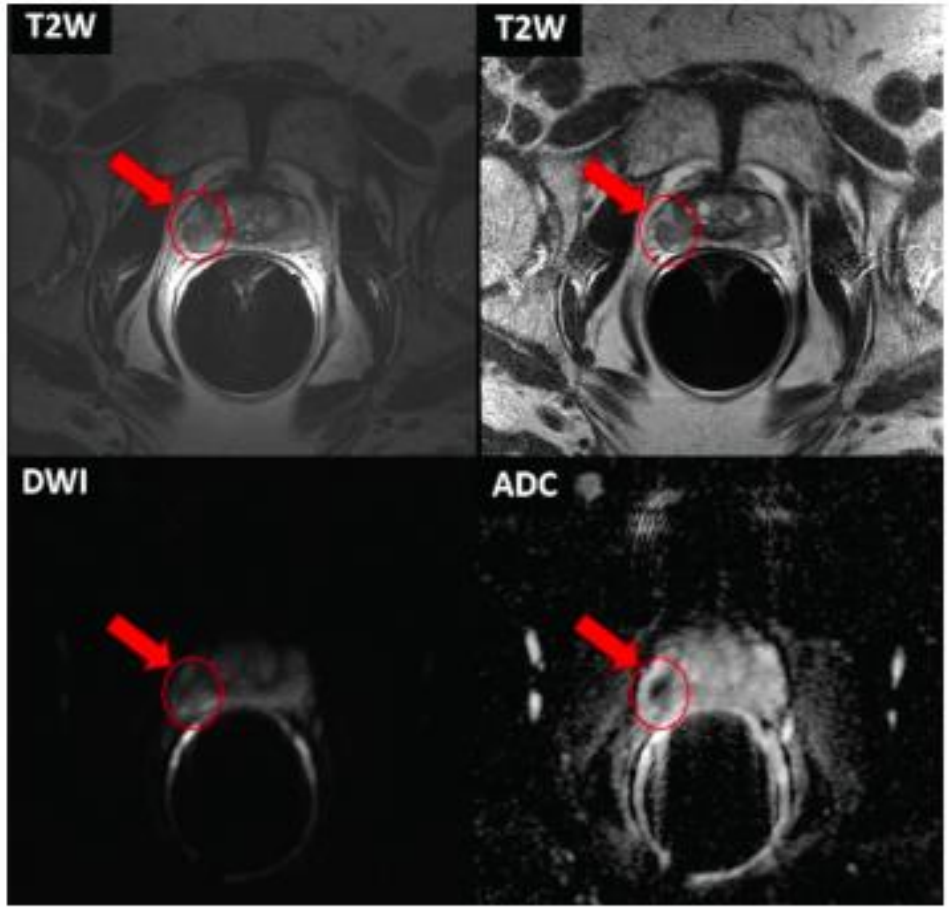
Low apparent diffusion coefficient values suggest breast cancer

Pinker et al, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5605035/

Multiparametric MRI in Prostate Cancer

- Frequently studied and almost routinely used during daily practice
- Has advantage over conventional CT,
  - Screening
  - Surveillance
  - Lesion localization for biopsy
  - Cancer extent assessment (staging)
  - Treatment response assessment

MpMRI Can Accurately Detect Prostate Cancer Nodules



MRI fusion Ultrasound 3D image of same lesion on fusion device screen

Demirel and Davis, 2018 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5832385/

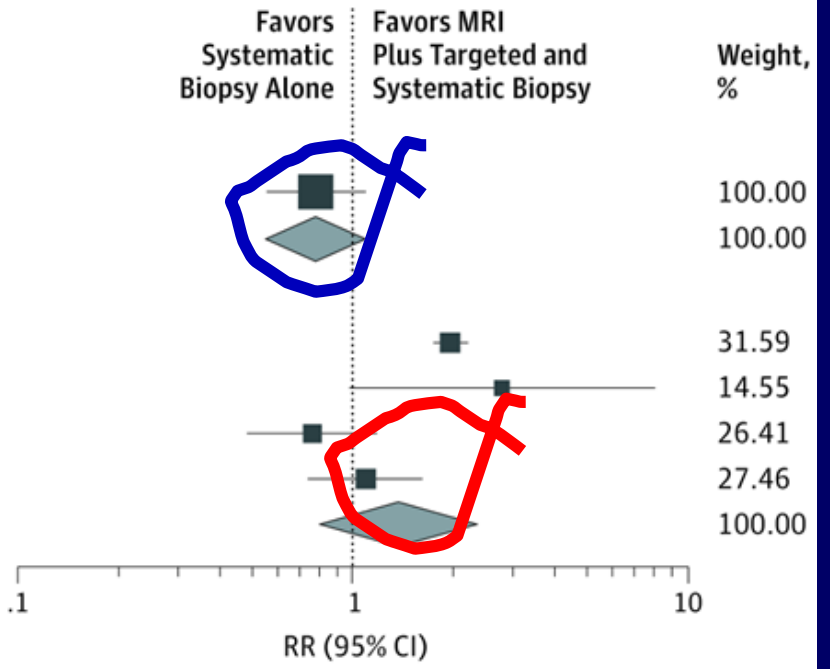
MpMRI Improves Biopsy Accuracy

- "prebiopsy mpMRI followed by a targeted biopsy into a PCa detection pathway may lead to the performance of fewer biopsies than a pathway using systematic biopsy alone. Such an approach may increase the likelihood of detecting csPCa, while reducing the detection of low-risk tumors."

Elwenspoek et al, 2019
https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2747475

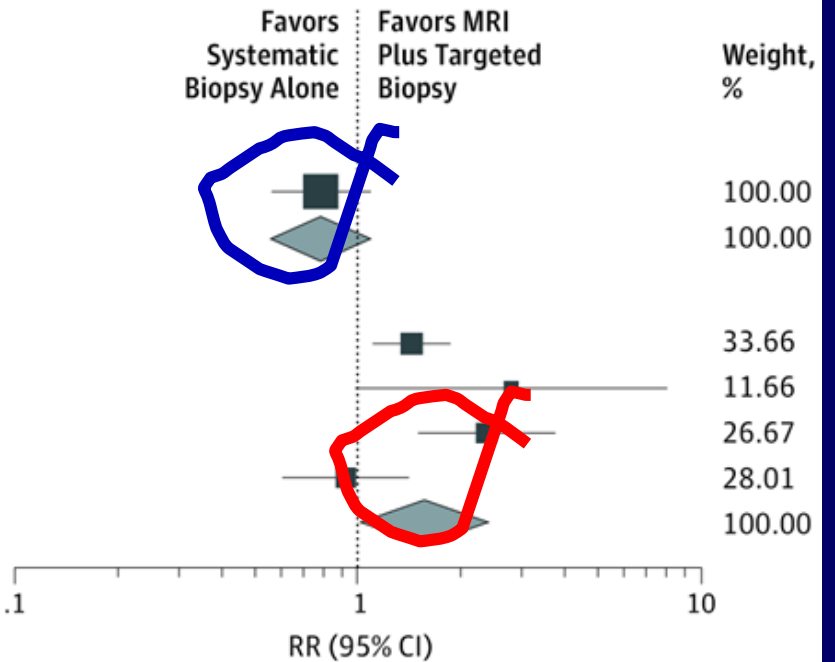
A MRI followed by targeted and systematic biopsy

Study	RR (95% CI)	Weight, %
Biparametric MRI		
Baco et al,[25] 2016	0.78 (0.55-1.09)	100.00
Subtotal	0.78 (0.55-1.09)	100.00
Multiparametric MRI		
Panebianco et al,[27] 2015	1.95 (1.73-2.20)	31.59
Park et al,[28] 2011	2.80 (0.98-7.98)	14.55
Plata-Bello et al,[31] 2018	0.76 (0.49-1.18)	26.41
Tontilla et al,[30] 2016	1.09 (0.74-1.61)	27.46
Subtotal (I^2 = 87.2%, P = .00)	1.36 (0.79-2.34)	100.00



B MRI followed by targeted biopsy

Study	RR (95% CI)	Weight, %
Biparametric MRI		
Baco et al,[25] 2016	0.78 (0.55-1.09)	100.00
Subtotal	0.78 (0.55-1.09)	100.00
Multiparametric MRI		
Kasivisvanathan et al,[26] 2018	1.43 (1.10-1.87)	33.66
Park et al,[28] 2011	2.80 (0.98-7.98)	11.66
Porpiglia et al,[29] 2017	2.38 (1.50-3.77)	26.67
Tontilla et al,[30] 2016	0.92 (0.60-1.41)	28.01
Subtotal (I^2 = 70.7%, P = .02)	1.57 (1.02-2.41)	100.00



Multiparametric MRI in Prostate Cancer

	Sensitivity	Specificity
MpMRI	**91.3%**	**66.7%**
Ratio between lesions:	84.8%	66.6%
Strain ration (SR):	78.3%	61.1%.
Enhanced Ultrosound:	40.0%	97.2%

From 82 patients with persistently high prostate specific antigen (PSA) levels after medical therapy

Drudi et al: https://pubmed.ncbi.nlm.nih.gov/31177155/

MpMRI in Lung Cancer

- MRI is not commonly used in lung cancer
- MRI is particularly good for pediatric patients or pregnant women and others have contra-indication for X-ray exposure.
- MRI provides more contrast than CT for lung nodule detection
- MRI is good for vessel invasion and lung cancer staging
- MRI provides lung function image in perfusion
- MRI provides functional assessment of heart that CT can not.

Bieder et al, Radiology. 2003;227:475–83

MpMRI for Lung Cancer Diagnosis Staging

Indications covered by MRI with advantages over CT	Complicated thoracic mass (mediastinum and chest wall invasion)[a]	Optional
	Differentiation of atelectasis and pulmonary mass[a]	Optional
	Differentiation of mediastinal masses	
	Evaluation of respiratory mechanics	
	Diagnosis of pulmonary perfusion deficits (embolism	
	Cystic fibrosis (with perfusion study)[a]	
Indications covered by MRI as effectively as with CT (if situation warrants use of MRI)	Pneumonia	
	Atelectasis	
	Cystic fibrosis (without perfusion study)[a]	
	Tuberculosis	
	Pulmonary nodules (> 3 mm)	
	Sarcoidosis	
	Acute and chronic pulmonary embolism[a]	Yes
	Abnormalities of pulmonary venous drainage	Yes
	Pulmonary arterial aneurysm	Yes
	Lung sequestration	Yes
	AV malformation (M. Osler)	Yes
	Staging of lung cancer	Yes
	Vasculitis (e.g. Wegener's)	Yes
	Pleural effusion of unclear origin	Yes
	Mesothelioma	Yes

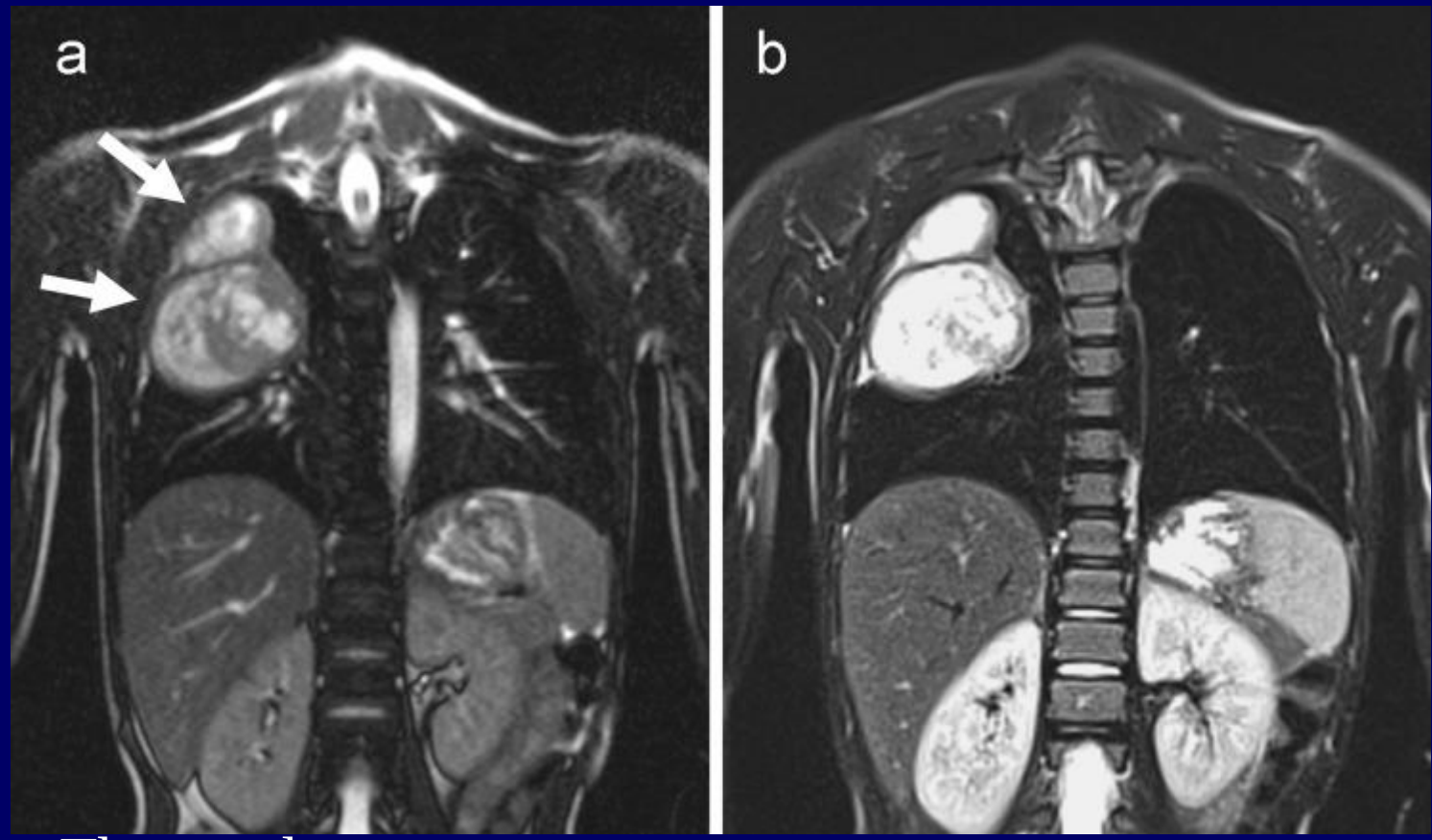
mpMRI can definitely provide functional information and better evaluation for vessels/heart that CT can not

Pediatric pregnant or radiation contraindicated patients warrant to have MRI

Bieder et al, Radiology. 2003;227:475–83

MpMRI to Diagnosis Pediatric Tumors

6 year-old with osteosarcoma

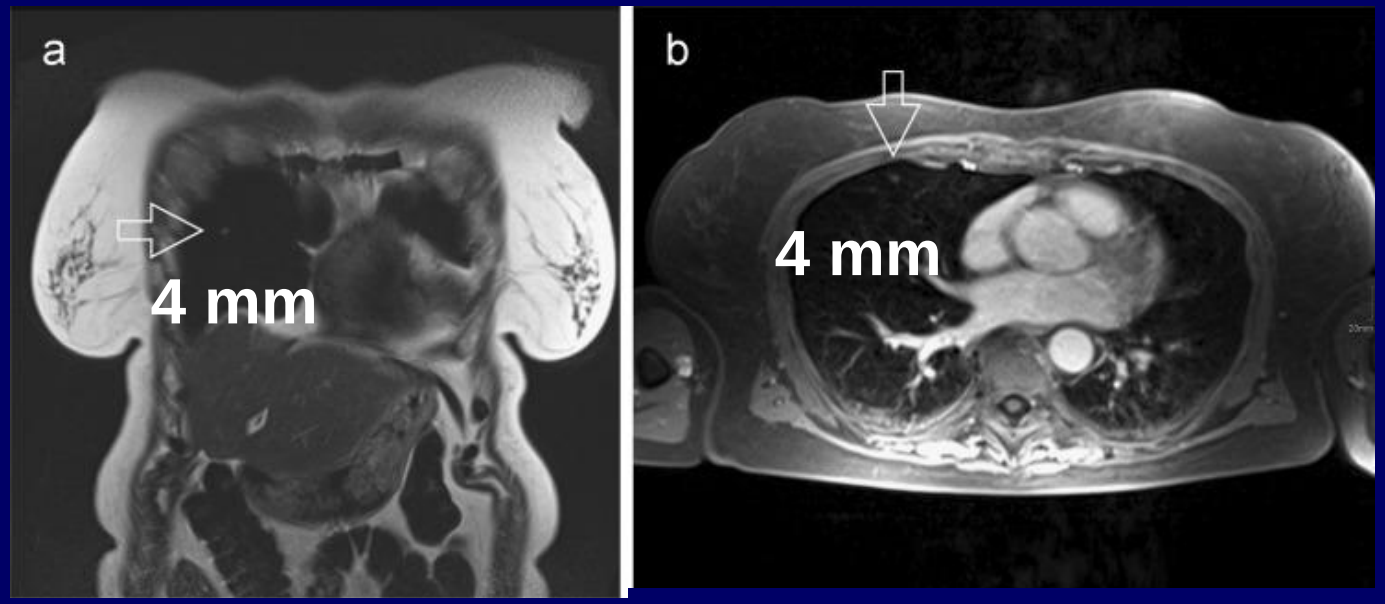


The steady state free precession study

The respiration triggered (navigator triggered) series

Bieder et al, Radiology. 2003;227:475–83

MpMRI Detects Small Lung Nodule



Multi-breath-hold T2W CE, Fat-saturated 3D GRE

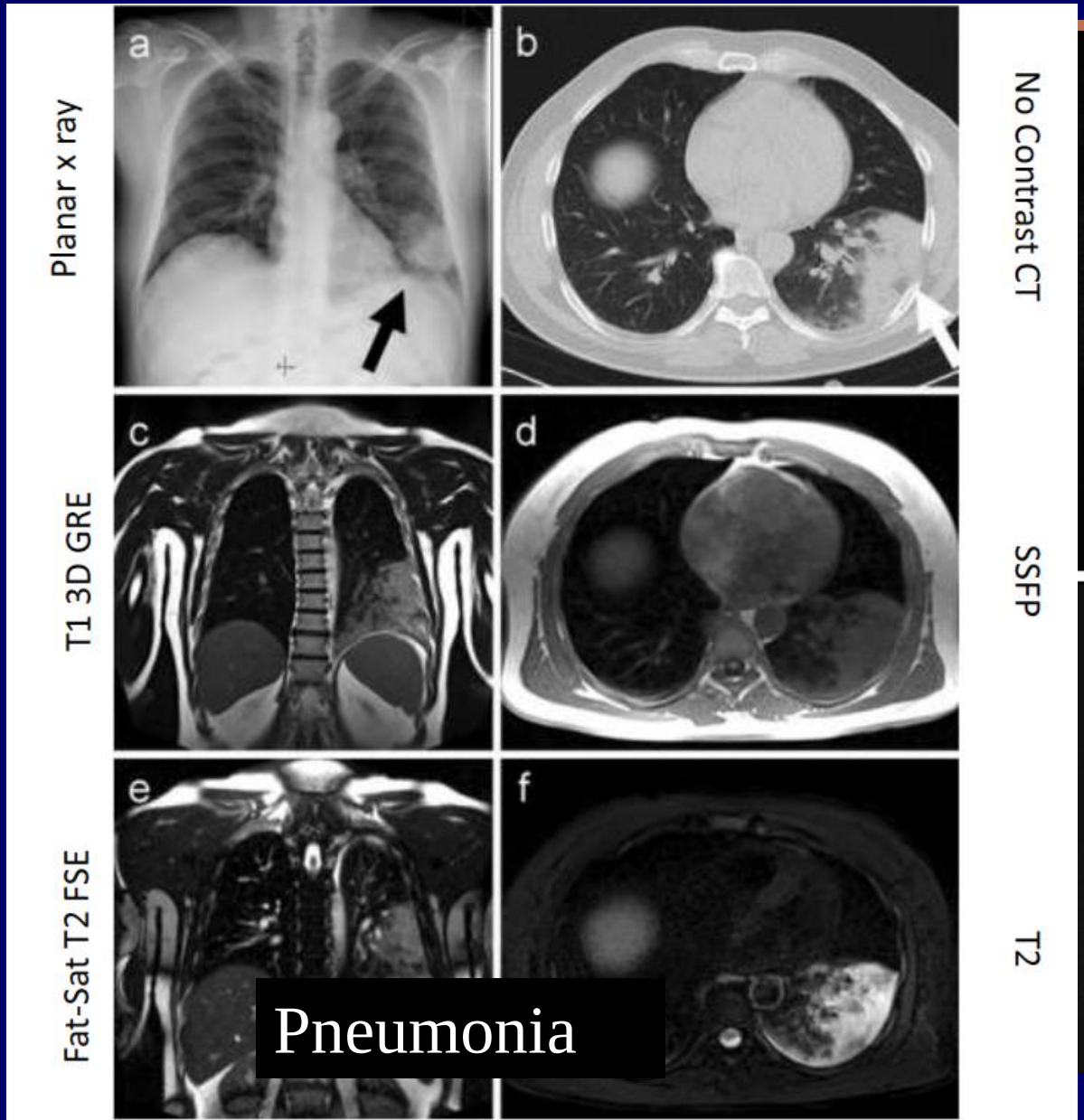
May be even faster and more efficient to read lung MRI for pulmonary nodules~bright signal against the dark background of the healthy lung tissue

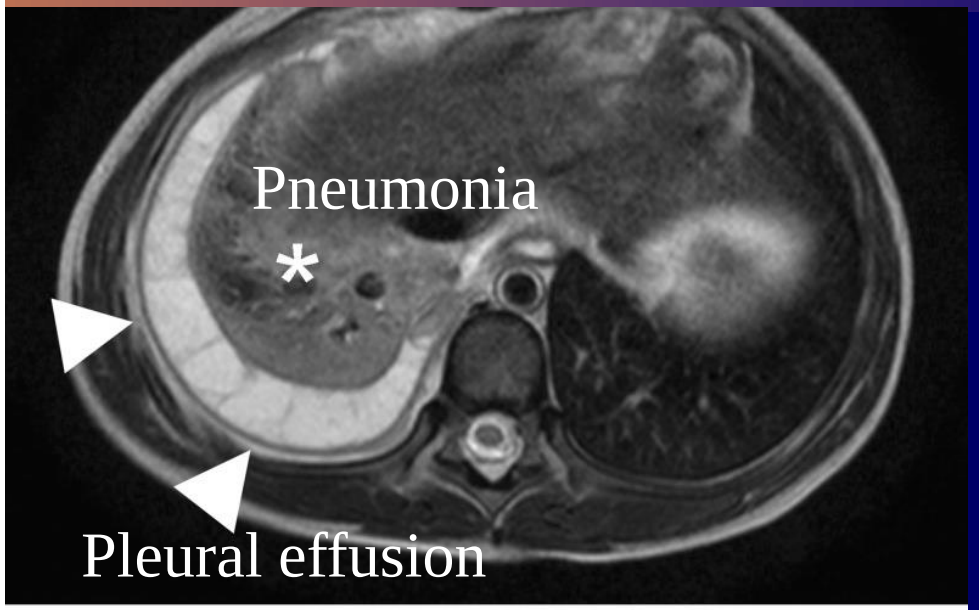
Calcified nodules tend to disappear in the lung background of T1W, as they have no inherent signal

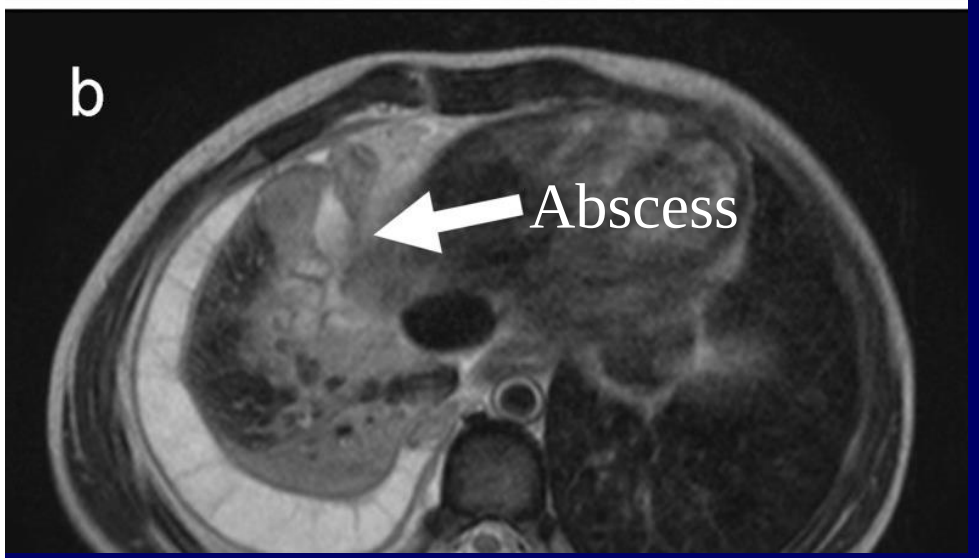
The sensitivity of MRI for lung nodules larger than 4 mm ranges between 80 and 90% and reaches 100% for lesions larger than 8 mm.

Bieder et al, Radiology. 2003;227:475–83

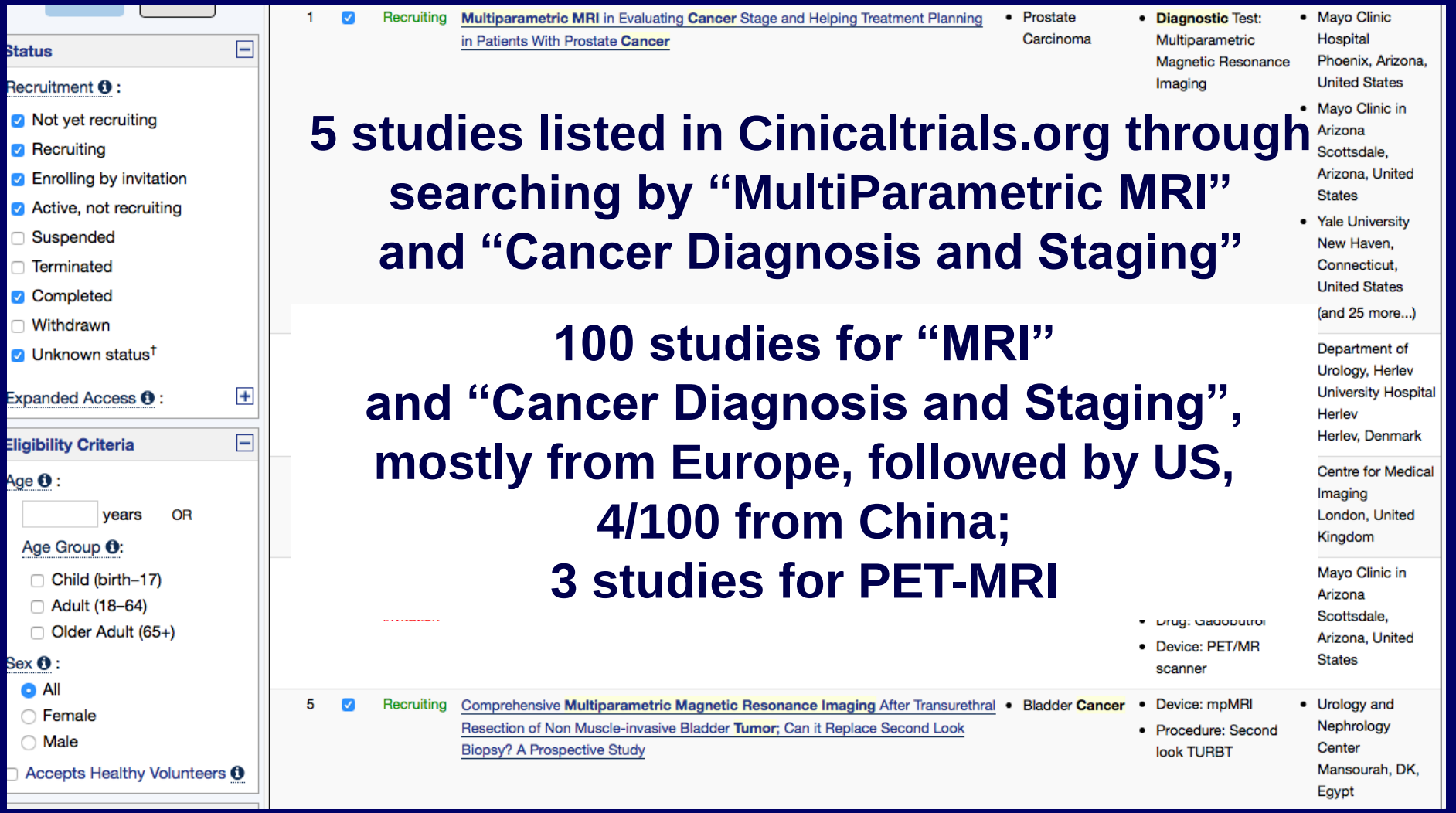
MpMRI for Non-Cancer Differentiations







Clinical Trials in mpMRI for Cancer Diagnosis and Staging



5 studies listed in Cinicaltrials.org through searching by "MultiParametric MRI" and "Cancer Diagnosis and Staging"

100 studies for "MRI" and "Cancer Diagnosis and Staging", mostly from Europe, followed by US, 4/100 from China; 3 studies for PET-MRI

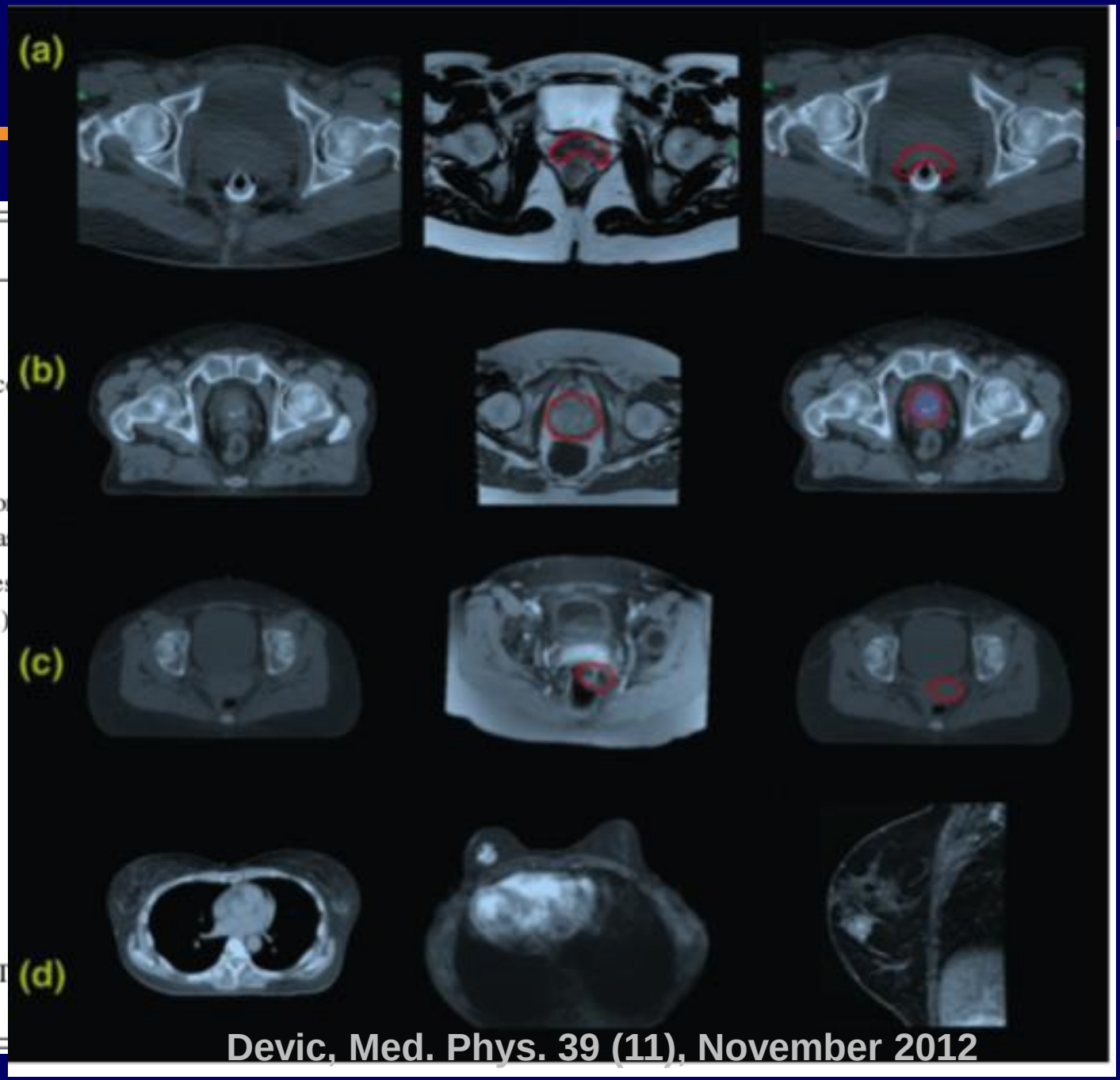
Multiparametric MRI for Precision Oncology and Radiation Oncology: A Physician's View

- Multiparametric MRI in precision oncology overview
  - Screening, diagnosis, staging, treatment response and recurrent assessment
- Multiparametric MRI in precision RT
  - Precision simulation, target delineation and RT plan
  - Precision treatment delivery
  - Precision treatment response prediction
  - Precision detection of tumor recurrence
- Multiparametric MRI future potential

MpMRI for Simulation/ target delineation/RT plan

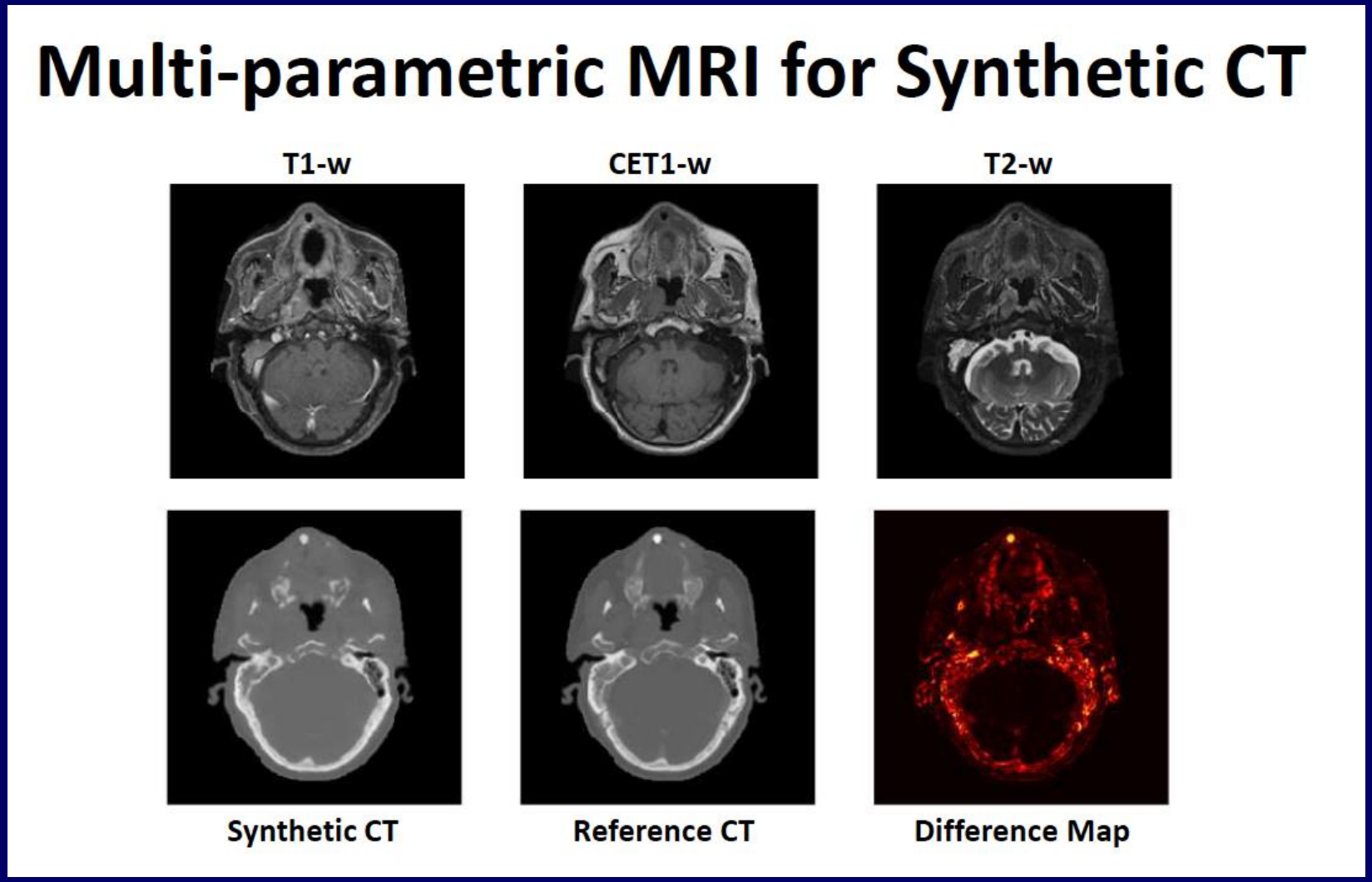
MRI Simulation for RT

Anatomical site	Acquisition sequence
Brain	T1 3D gradient echo
	Post Gd-T1 standard spin-echo
	Proton density fluid-attenuated inversion rec
	T2 FLAIR
Head and Neck	Post Gd-T1 Standard Spin-Echo
	T2-weighted sequence with fat saturatio
	T1 3D gradient echo (pre- and postcontra
Breast	T1 inversion recovery (STIR) sequence
	T2-weighted 3D fast spin echo (XETA)
	T1-weighted turbo spin echo
	T1 3D gradient echo
GYN	Turbo spin echo T2 (TSE T2)
	T2-weighted fast spin echo (FSE)
	T1 3D gradient echo
Prostate	T2-weighted fast spin echo (FSE)
	T1 3D gradient echo
Rectum	T2-weighted fast spin echo (FSE)
	T1 and T2 short tau inversion recovery (ST
	T1 3D gradient echo



Devic, Med. Phys. 39 (11), November 2012

Good Quality of Synthetic CT Make RT Possible



Slide Courtesy of Jing Cai

MRI Target Delineation

MRI Target Delineation in comparison to CT

- Nice soft tissue contrasts
- Rich presentation in detailed tissue structure
- Contains metabolic and functional information

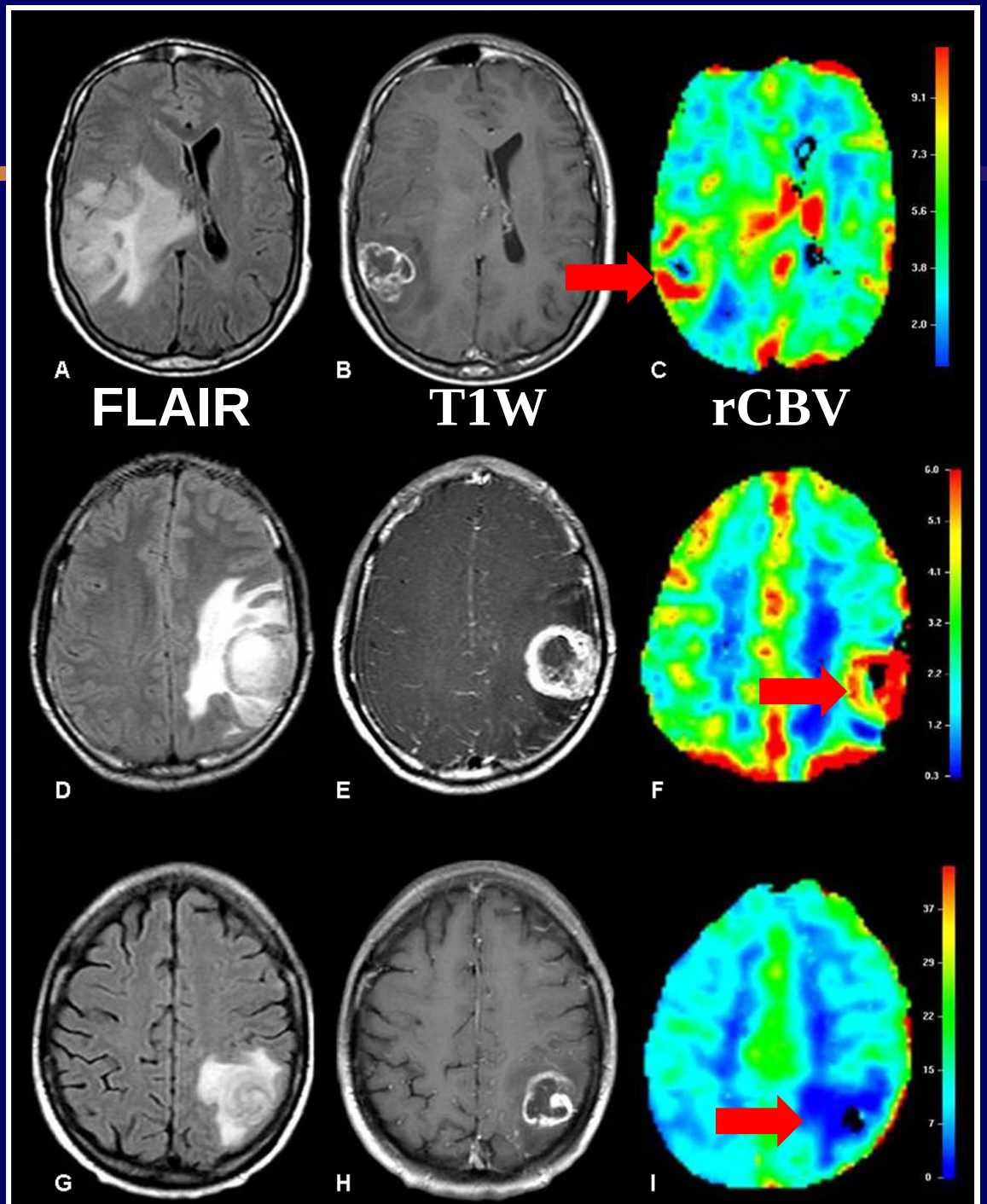
- Routinely used in RT target delineation for CNS, head/neck NPC, liver, pancreatic, cervical, prostate …and rectal cancers.

MRI and Tumor Target

Glioblastoma multiforme in a 49-year-old man

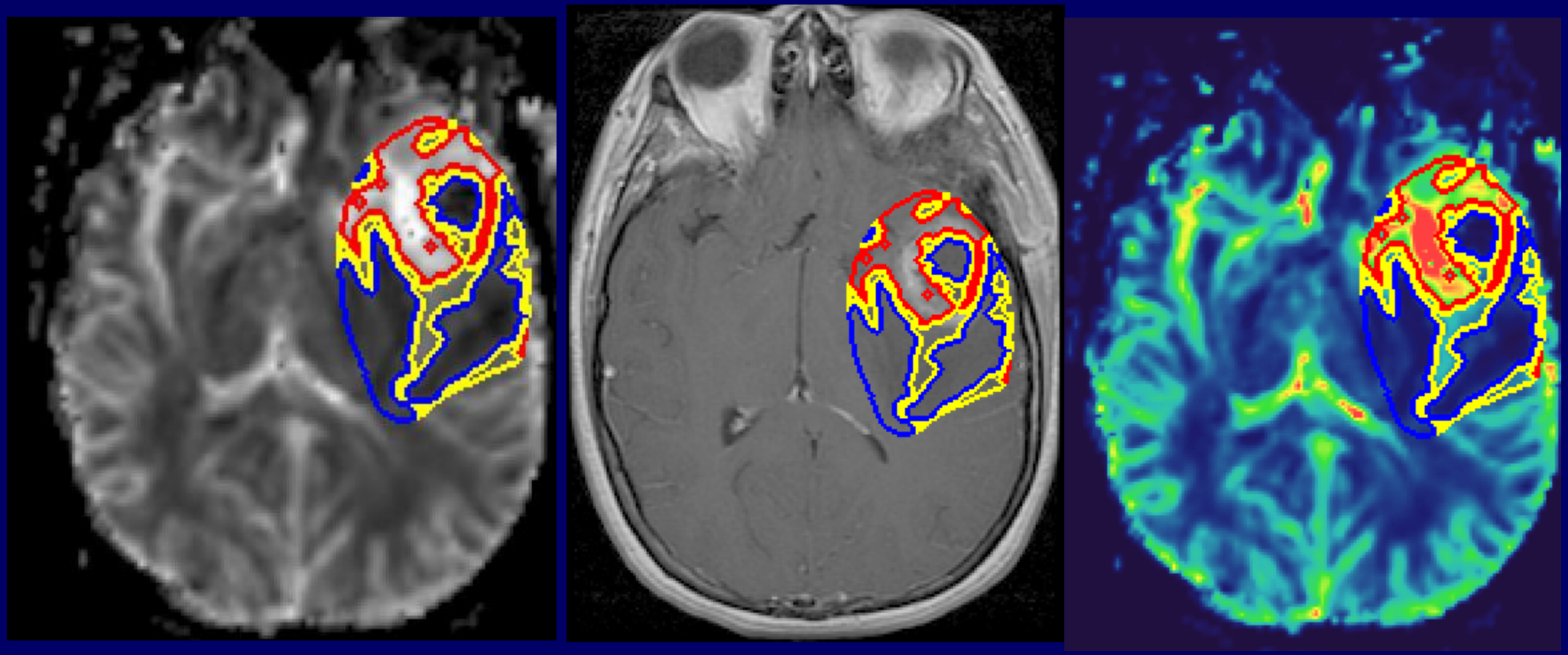
Metastatic melanoma in an 18-year-old man

Cerebral toxoplasmosis in a 54-year-old woman (Infection)



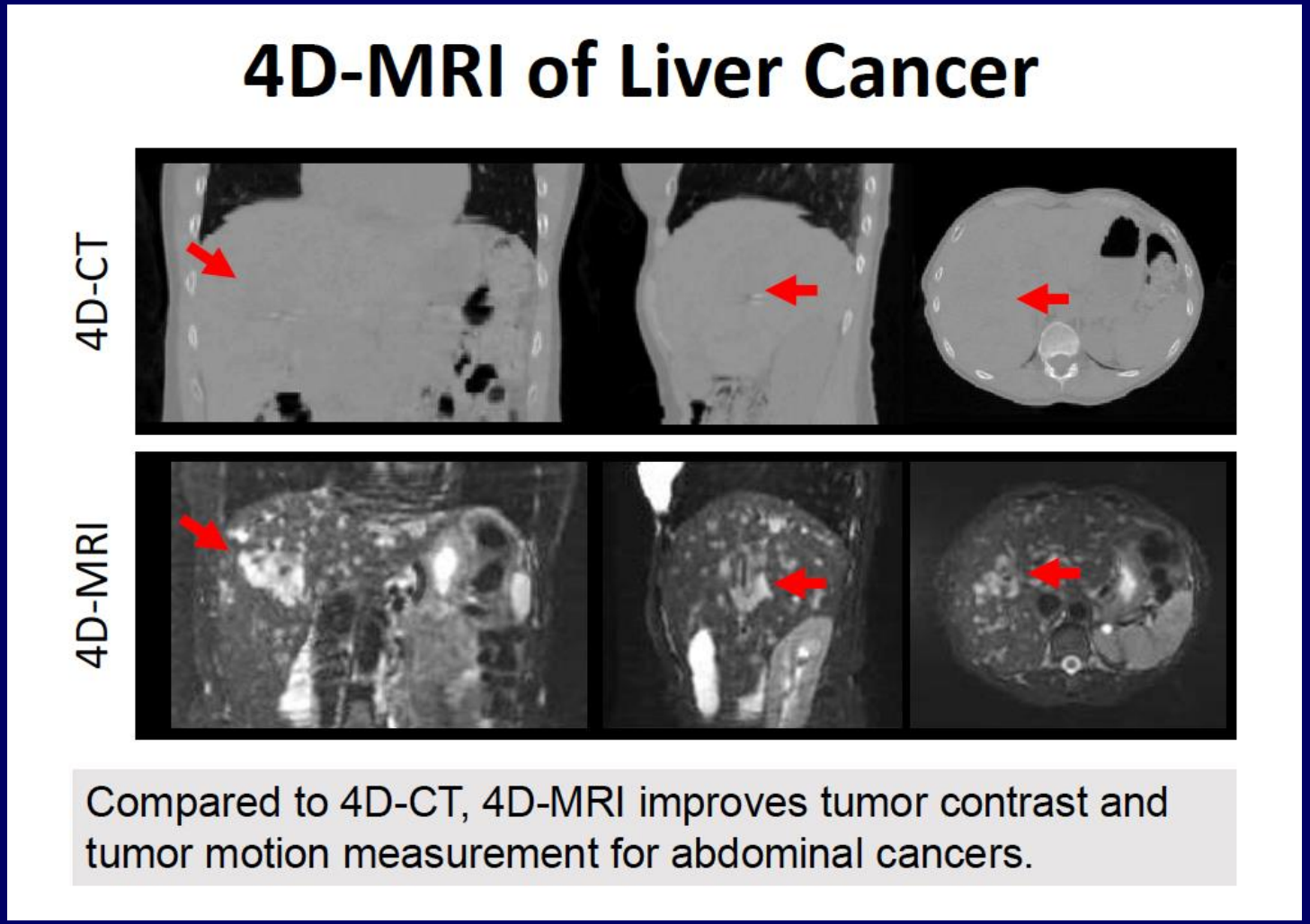
Floriano et al https://www.researchgate.net/publication/259269120

rCBV Map for Target Volume in GBM



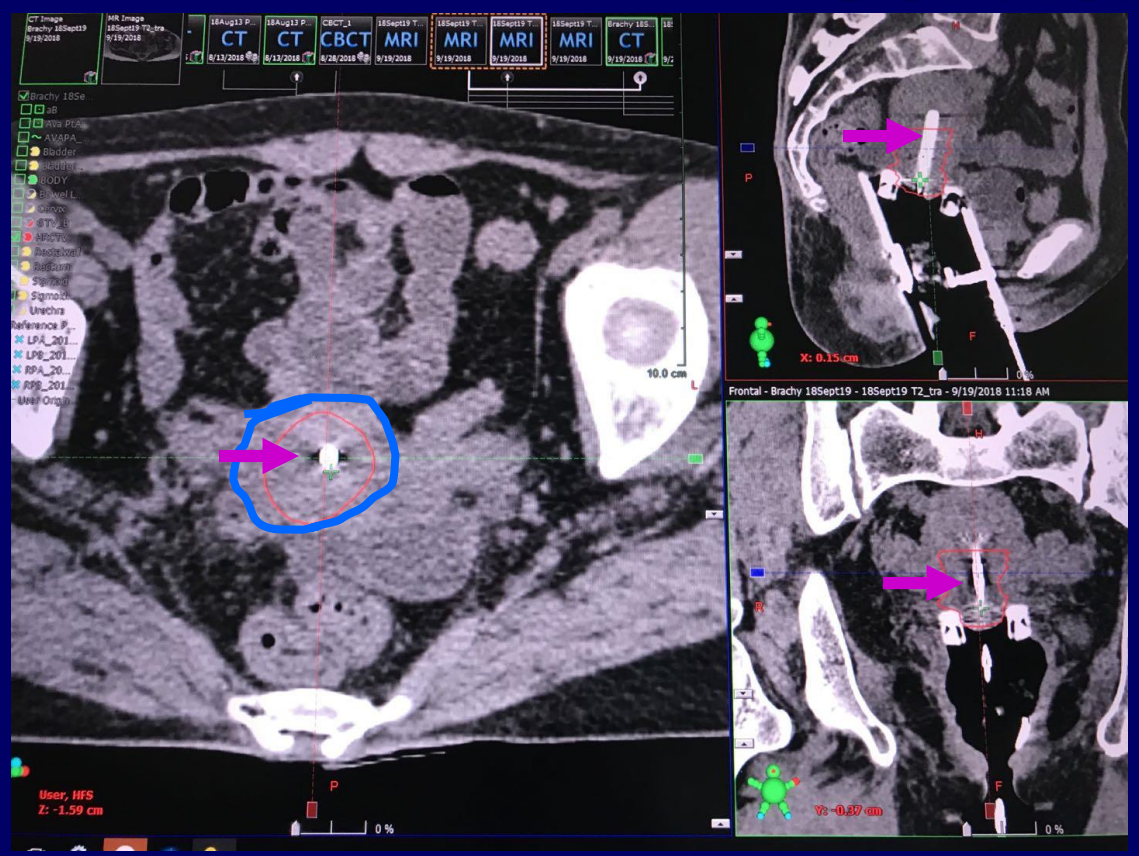
Picture from C Tsien

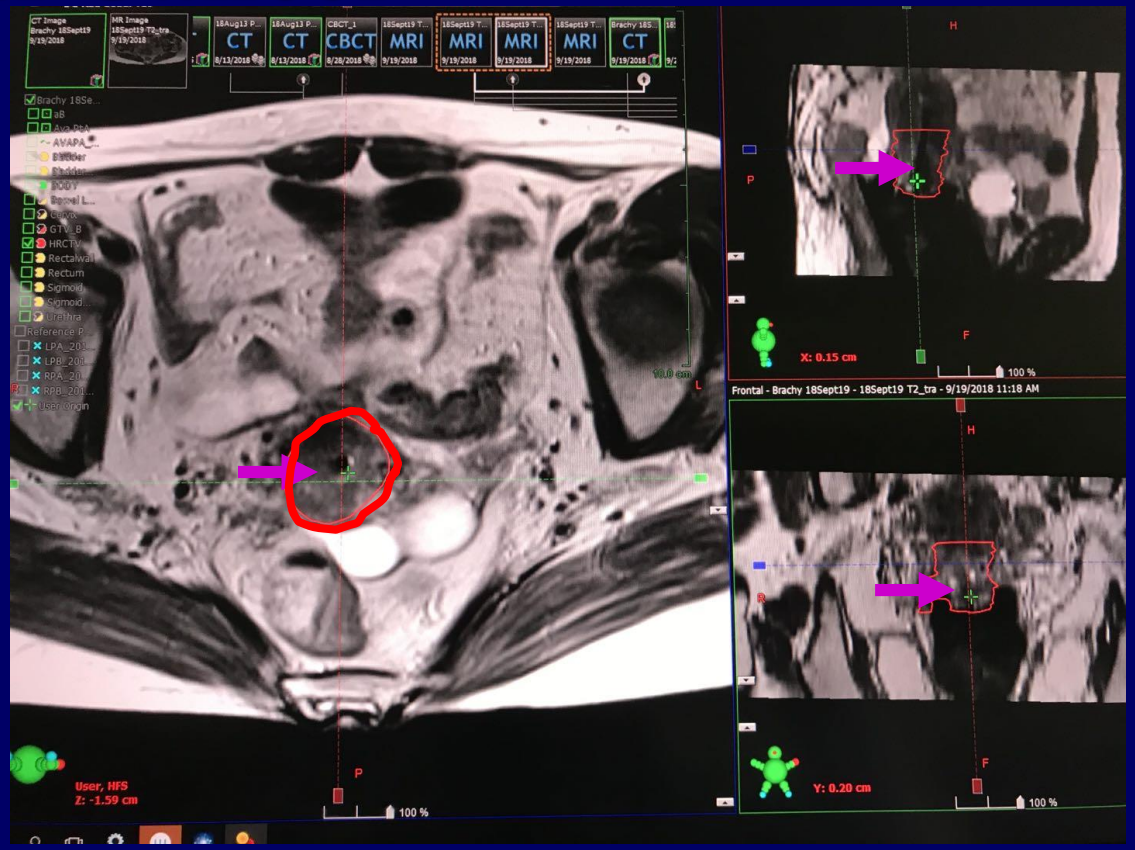
4D-MRI May Be Superior than 4D-CT in Liver



Slide courtesy of Jing Cai

MRI Target Delineation for BrachyTherapy in Cervical Cancer





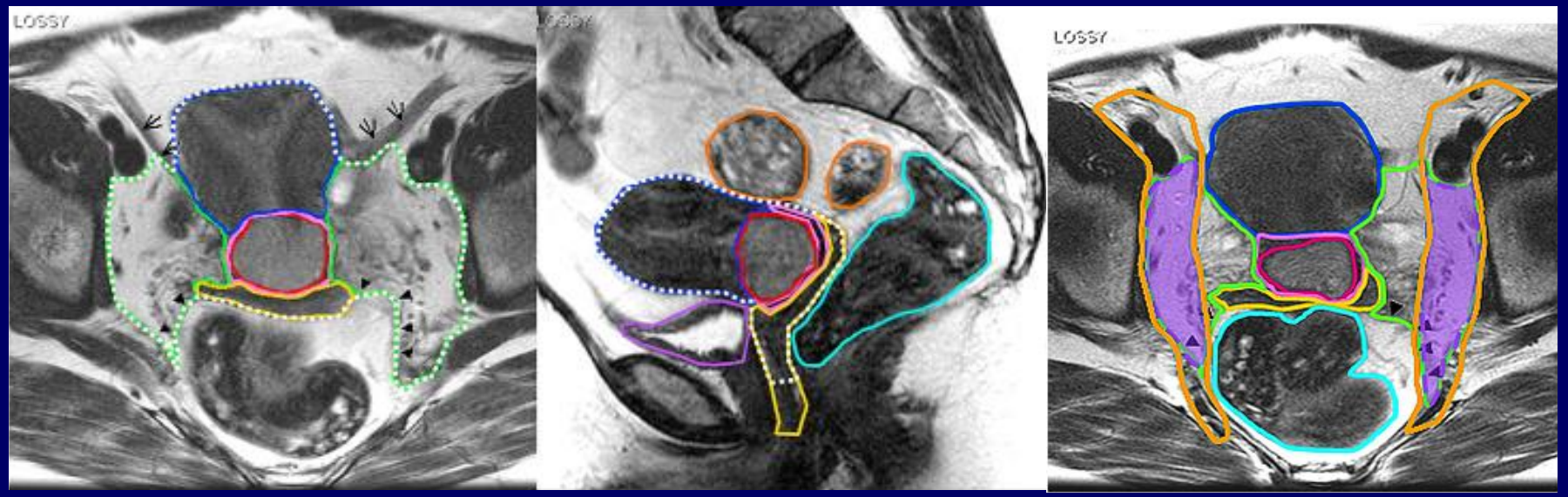
CT: Target, red or blue?

MRI: Target, clearly red!

Picture provided by Zhiyuan Xu from HKU SZH

MRI Target Delineation in Gyn Tumors

MRI/IGRT Consensus Guidelines



Tumor GTV, parametria

Lim K et *al*. IJROBP 2010; 79:348-355

http://www.rtog.org/CoreLab/ContouringAtlases/GYN.aspx

Slide Courtesy of Nina Mayr

Use of MRI Simulator Consensus Opinion

- To determine the levels at which consensus …regarding general and site-specific principles of MRI simulation for offline MRI-aided EBRT.
- A process inspired by the Delphi method to determine levels of consensus using a series of questionnaires interspersed with controlled opinion feedback.

- Full consensus was reached regarding general principles of MRI simulation.
- However, the level of consensus decreased when site-specific principles of MRI simulation were considered.

TREATMENT PLANNING| VOLUME 121, ISSUE 2, P187-192, NOVEMBER 01, 2016

https://www.thegreenjournal.com/article/S0167-8140(16)34368-7/fulltext

Use of MRI Simulator
Clinical and Cost Effectiveness

- No tumor control outcome studies
- No cost effectiveness study
- Only one relevant clinical study MRI-CT simulation may reduce acute GU toxicity without reducing GI toxicity compared with CT simulation only.
- Recommend more research

CADTH SUMMARY WITH CRITICAL APPRAISAL
Magnetic Resonance Imaging Simulators for Simulation and Treatment for Patients Requiring Radiation Therapy

By Chantelle Lachance and Suzanne McCormack
Cite As: Magnetic resonance imaging simulators for simulation and treatment for patients requiring radiation therapy: A review of the clinical effectiveness, cost-effectiveness, and guidelines. Ottawa: CADTH; 2019 Jan. (CADTH rapid response report: summary with critical appraisal).

Clinical Trials in mpMRI for Target Delineation

1 study listed in Cinicaltrials.org through searching by "MultiParametric MRI" and "target delineation"

26 studies for "MRI" and "Target delineation", mostly from Europe, followed by US, 0/26 from China; 0 studies for PET-MRI

Clinical Trials in mpMRI for RT Plan

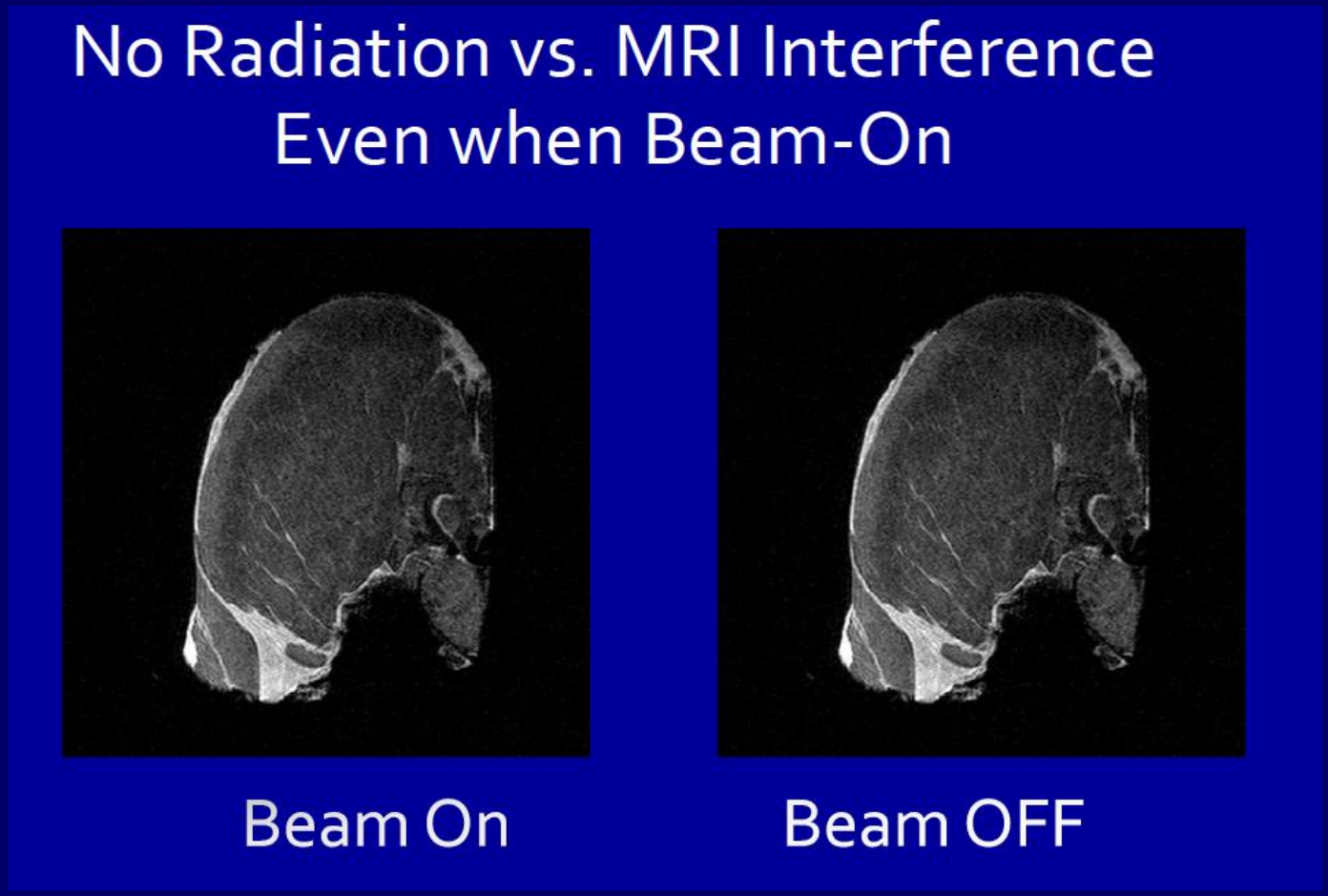
Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Unknown †	FET-PET and **Multiparametric MRI** for High-grade Glioma Patients Undergoing **Radiotherapy**	• Glioblastoma Multiforme • Anaplastic		• CHRU de Brest Brest, France
2	☐	R				y Kimmel sensive Cancer Center Hopkins , Maryland, United
3	☐	Not yet recruiting NEW	Bladder Fiducial Markers and **Multiparametric-MRI** (Mp-**MRI**) to Optimize Bladder Chemo-**radiotherapy**	• Bladder Cancer • Urinary	• Procedure: Fiducial marker placement • Diagnostic Test:	• Cedars-Sinai Medical Center (CSMC) Los Angeles, California, United of California San (UCSF) isco, California, United chool of Massachusetts General MGH) lassachusetts, United
4	☐	Recruiting	**Multi-parametric Magnetic Resonance Imaging** for Prostate Cancer Patients	• Prostate Cancer	• Device: Multiparametric MRI	• Henry Ford Health System Detroit, Michigan, United States
5	☐	Unknown †	Deformable Registration of **Multi-parametric MRI** to Intra-operative Transrectal Ultrasound for Prostate Brachytherapy	• Prostate Cancer	• Procedure: Brachytherapy	• Sheba_Medical_Center Tel Hashomer, Israel
6	☐	Unknown †	**Multi-Parametric** Brain Cancer **MRI**	• Brain Tumors	• Other: 3D MRI Scans	• Cross Cancer Institute Edmonton, Alberta, Canada
7	☐	Recruiting	Pilot Study Evaluating the Role of Histopathology Correlation	• Prostate	• Device: Uronav	• Case Comprehensive Cancer

9 study listed in Cinicaltrials.org through searching by "MultiParametric MRI" and "RT Plan"

149 studies for "MRI" and "RT plan", mostly from Europe, followed by US, 1 study for PET-MRI in recurrent GBM

MpMRI for precision RT treatment delivery

Advantages of MRI Linac is MRIgRT-1



- **No Radiation**
- **Better Quality**
- **Real time beam-on monitoring**

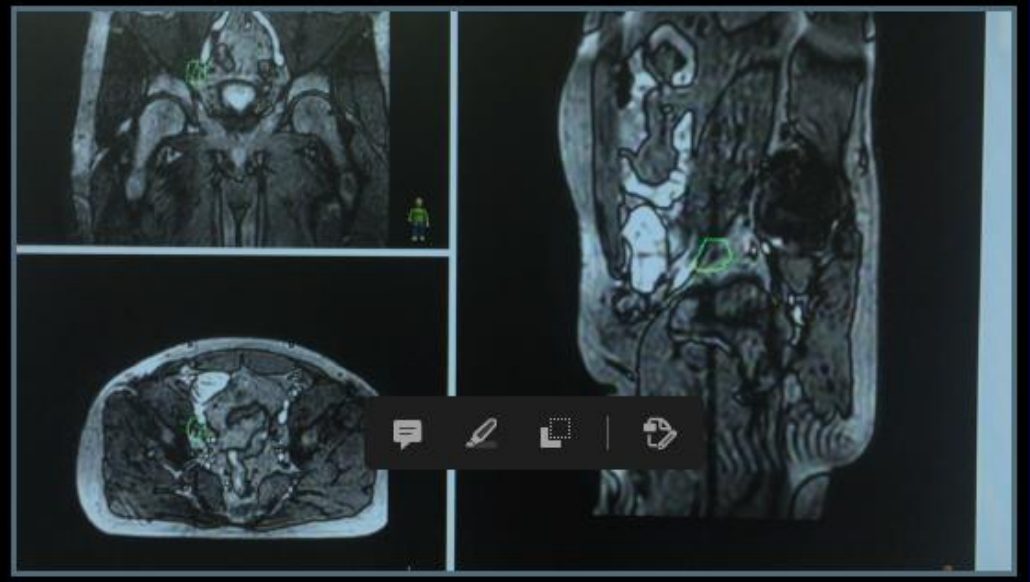
Picture Courtesy of Jihong Wang

Advantages of MRI Linac and MRgRT-2

Monitoring Patient Motion During "Beam-on"

Example of real time motion monitoring of multiple OARs

High frame-rate, multi-planar acquisition for motion monitoring



Courtesy of Jihong Wang

MRIgRT Linacs for Treatment Delivery

Does it make a difference for our patents? Evidence?

The CADTH report

- **MRIgRT Treatment Delivery: A Review of Clinical Effectiveness, Cost-Effectiveness and Guidelines**

1. What is the clinical effectiveness?
2. What is the cost-effectiveness?
3. What are the evidence-based guidelines?

1. One study of 8 matched pairs, lung SBRT, MR Linac versus Conventional Linac, no early damage
2. No evidence
3. No relevant evidence-based guidelines

CLachance and McCormack

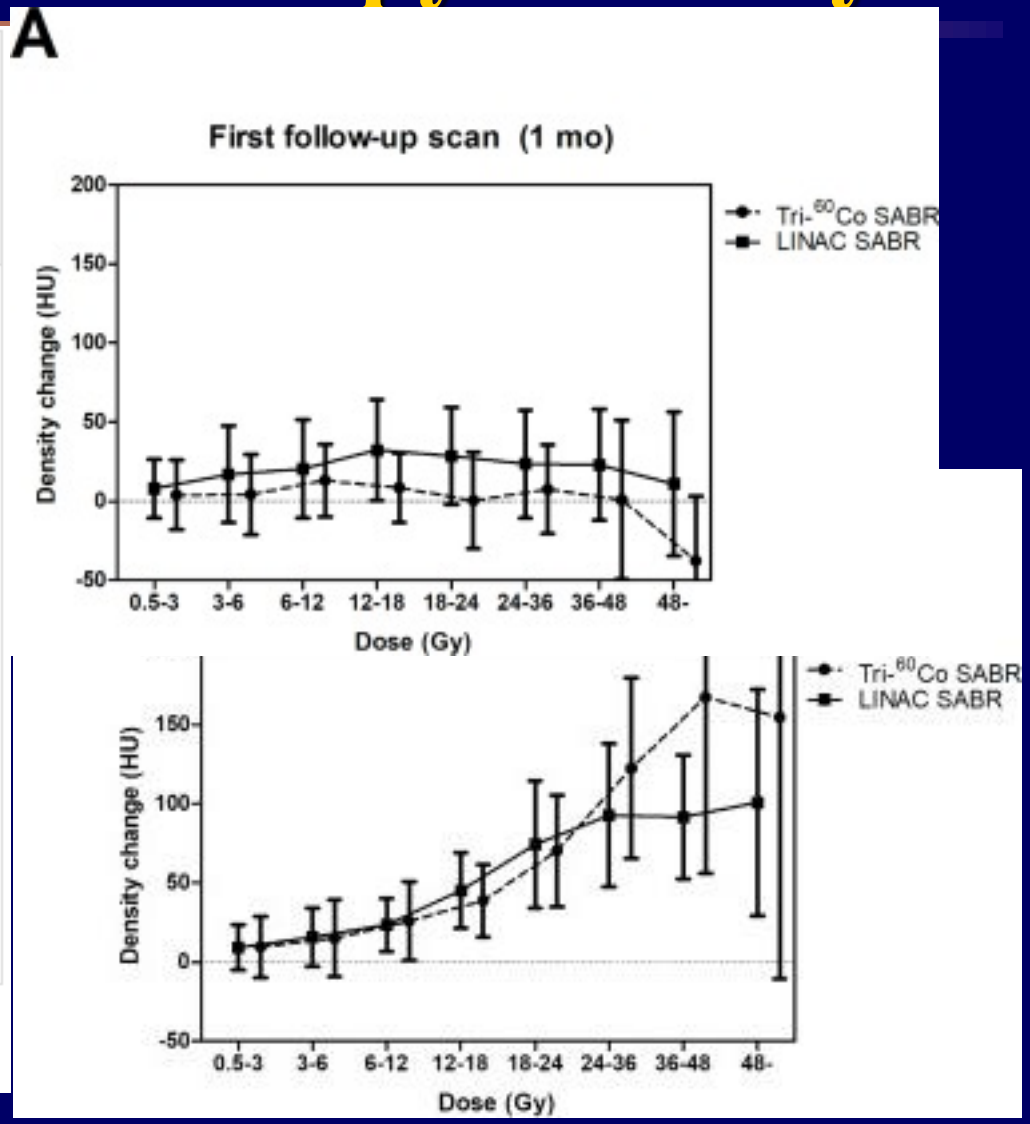
https://www.ncbi.nlm.nih.gov/books/NBK546999/

MRI Linacs for Radiation Therapy Delivery

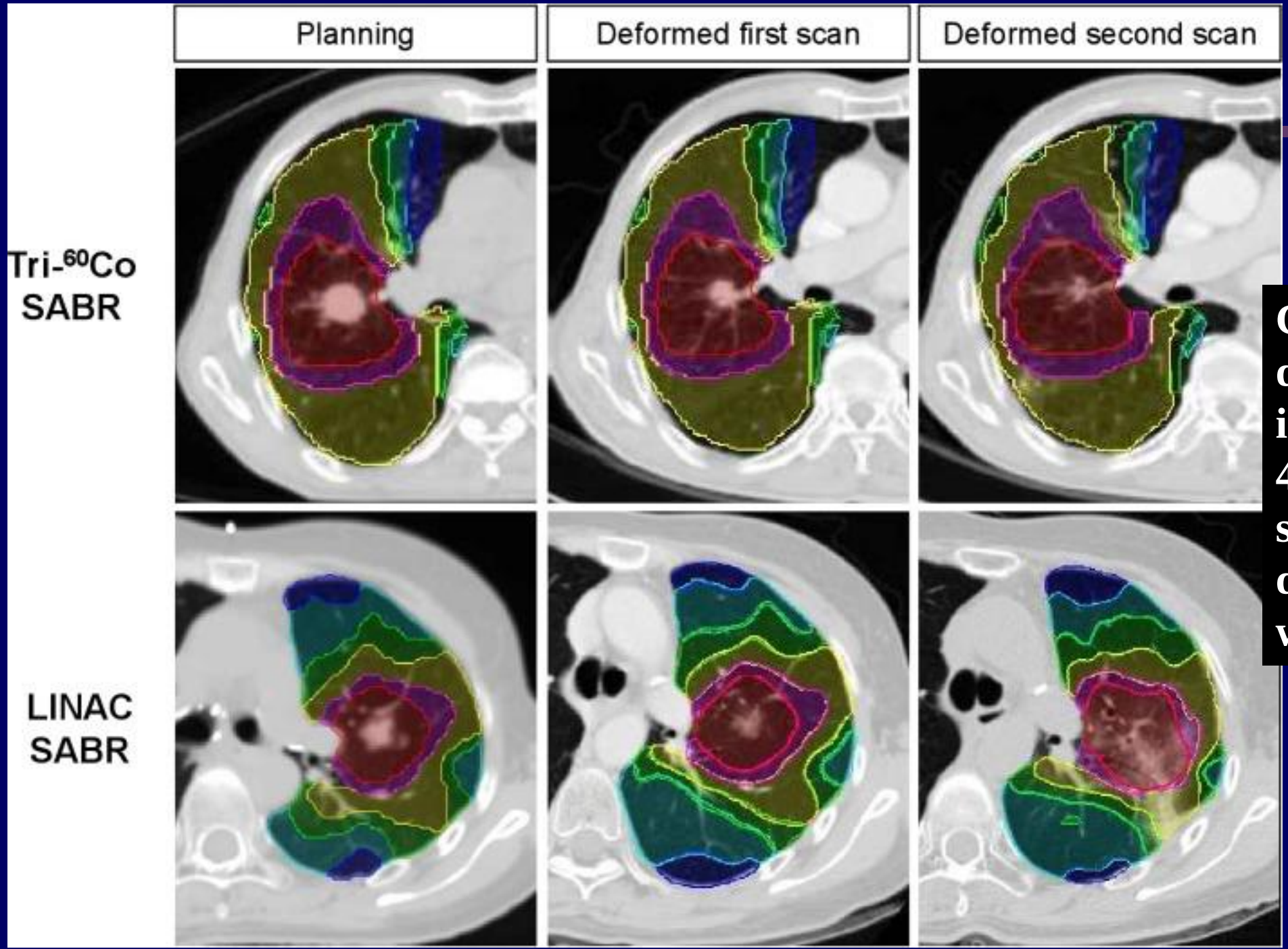
Study Design	Population Characteristics	Intervention and Comparator(s)	Clinical Outcomes, Length of Follow-Up
Non-randomized, retrospective, matched-comparison cohort study	n = 16 patients who received lung SABR for lung cancer Intervention: 8 patients, mean age 73 (SD ± 7) years; 4 men, 4 women Control: 8 patients, age 71 (S years; 6 men, 2 women	Intervention: tri-^{60}Co magnetic-resonance image guided system, MRIdian™ (tri-^{60}Co SABR; manufacturer: ViewRay Inc., Cleveland, United States) Comparator: linear accelerator (LINAC SABR; manufacturer: Varian Medical Systems, United States)	Changes in radiological lung density 2 follow-up periods: 1) after first follow-up CT scan (median interval from end date of radiotherapy to CT scan for all patients = 5.5 weeks, range 4–7 weeks) 2) after first follow-up CT scan (median interval from end date an for s, range 16–31 weeks)

ed tomography; LINAC = linear accelerator; SABR = stereotactic ablative radiotherapy; SD = standard deviation; tri-Co magnetic-resonance image guided system

MRI Linacs were not better



Kim et al, 2018 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5880382/



Comparing CT density changes in areas above 48 Gy, no significant differences were seen

Clinical Trials in mpMRI for Radiation Treatment Delivery

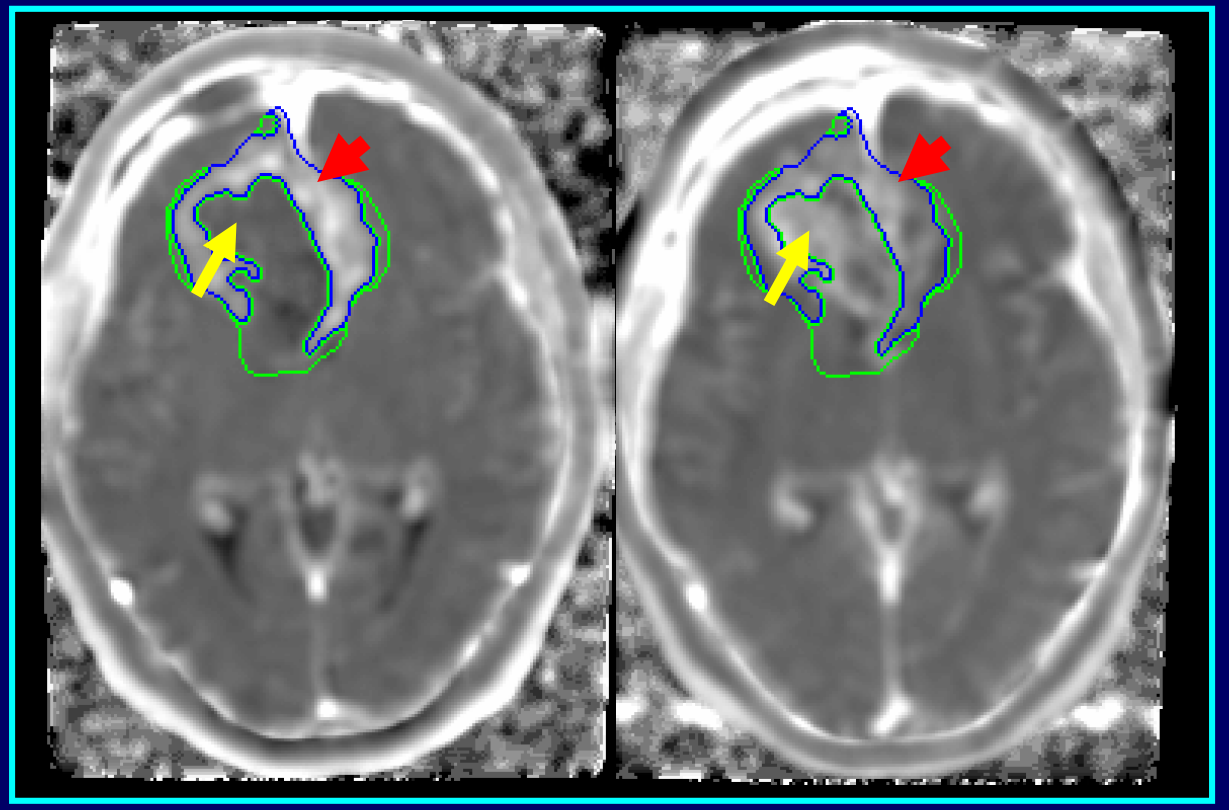
3 study listed in Cinicaltrials.org through searching by “MultiParametric MRI” and “radiation treatment delivery ”

69 studies for “MRI” and “radiation treatment delivery ”, mostly from Europe, followed by US, 1 study for PET-MRI

1		Recruiting	Stereotactic **MRI**-guided On-table Adaptive Ra… Par…	• Pancreatic Cancer	• **Radiation**: Stereotactic MRI-guided On-…	• UCLA Los Angeles, California, United States • University of Miami Miami, Florida, United States • Miami Cancer Institute Miami, Florida, United States • (and 4 more...)
2		Recruiting	Pilot Study of Same-session MR-only Simulation and **Treatment** With Stereotactic **MRI**-guided Adaptive … Oligomet…	• Oligometastases of the Spine	• Device: MRIdian Linac System from ViewRay	• Washington University School of Medicine Saint Louis, Missouri, United States
3		Completed	HCC Res…			
4		Recruiting	Optimizin… With **MRI** Guidance for Gynecologic Cancer	Cancer	• **Radiation**: Brachytherapy • Device: MRI Tracker	• Brigham and Women's Hospital Boston, Massachusetts, United States
5		Recruiting	Prostate **Radiotherapy** Integrated With Simultaneous **MRI** (The PRISM Study)	• Prostate Cancer	• Device: MR LINAC	• Royal Marsden - Surrey Sutton, England,

MpMRI for precision RT treatment response assessment

MRI Detects Early Changes During-RT: GBM



Pre RT

Week 3 during RT

Red: initially enhanced region; Yellow: initially non-enhanced tumor region

Blood-Brain/Tumor Barrier Opening During RT

Cao, Y. et al J Clin Oncol 23: 4127, 2005

rCBV MRI Demonstrates Tx Response

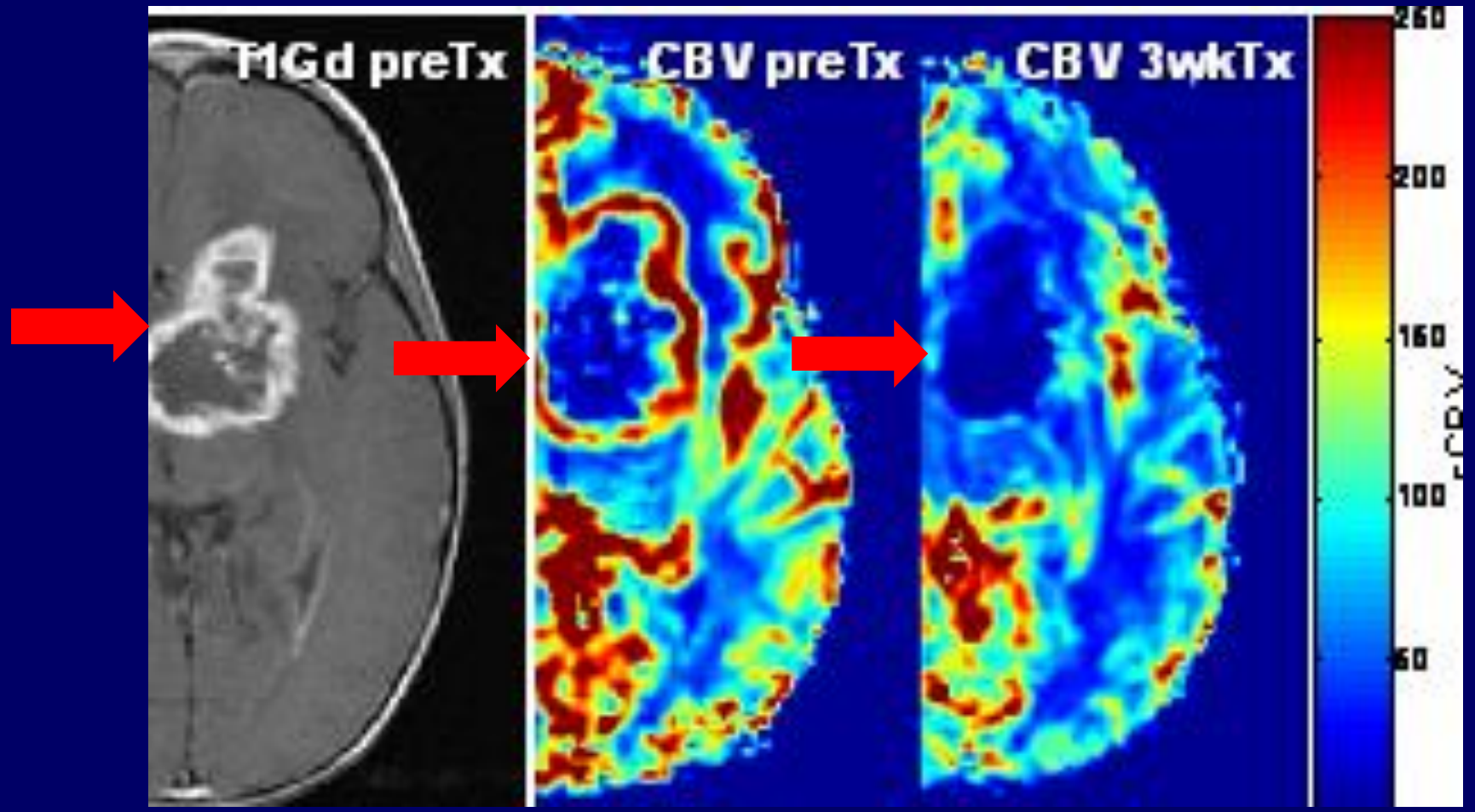
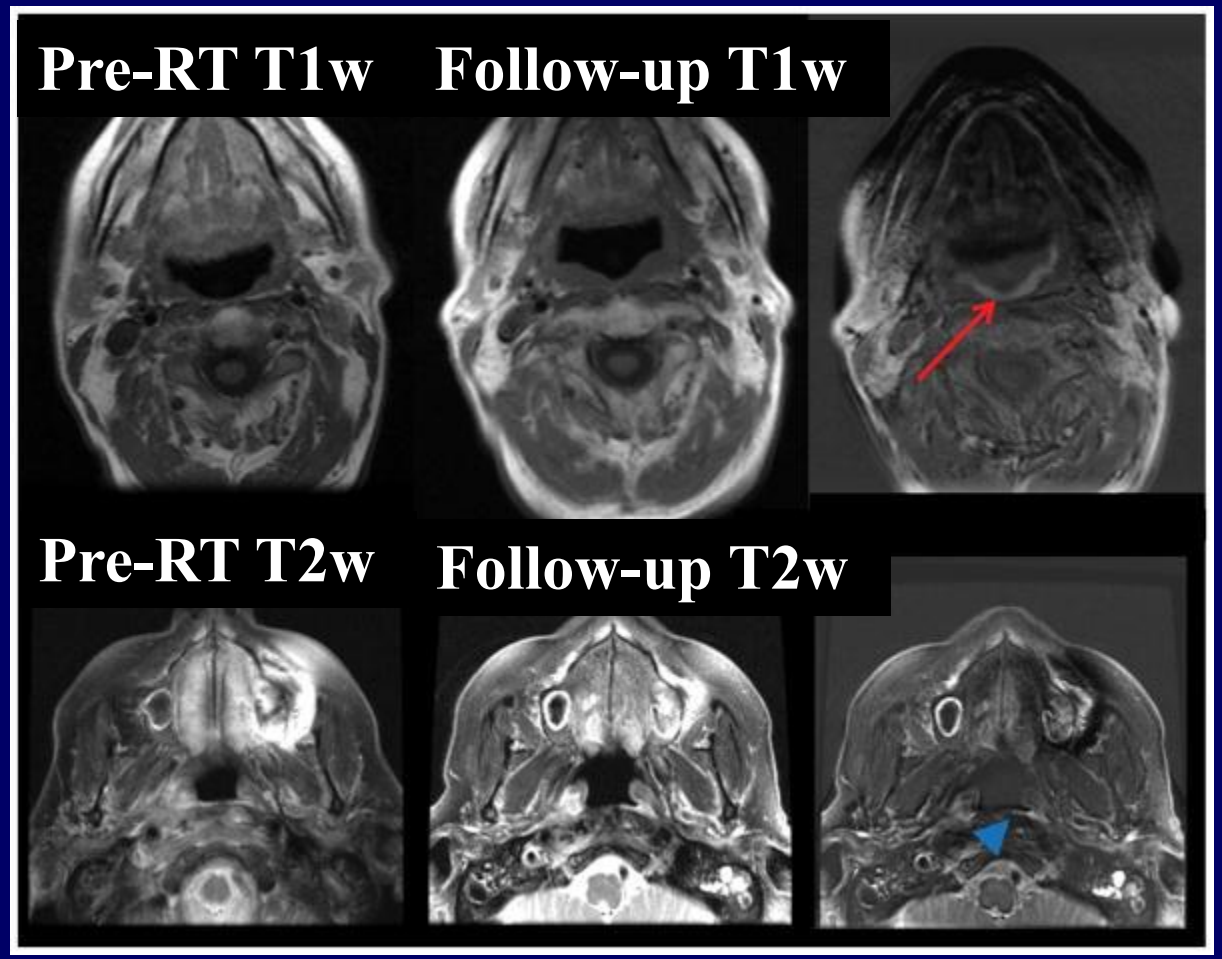
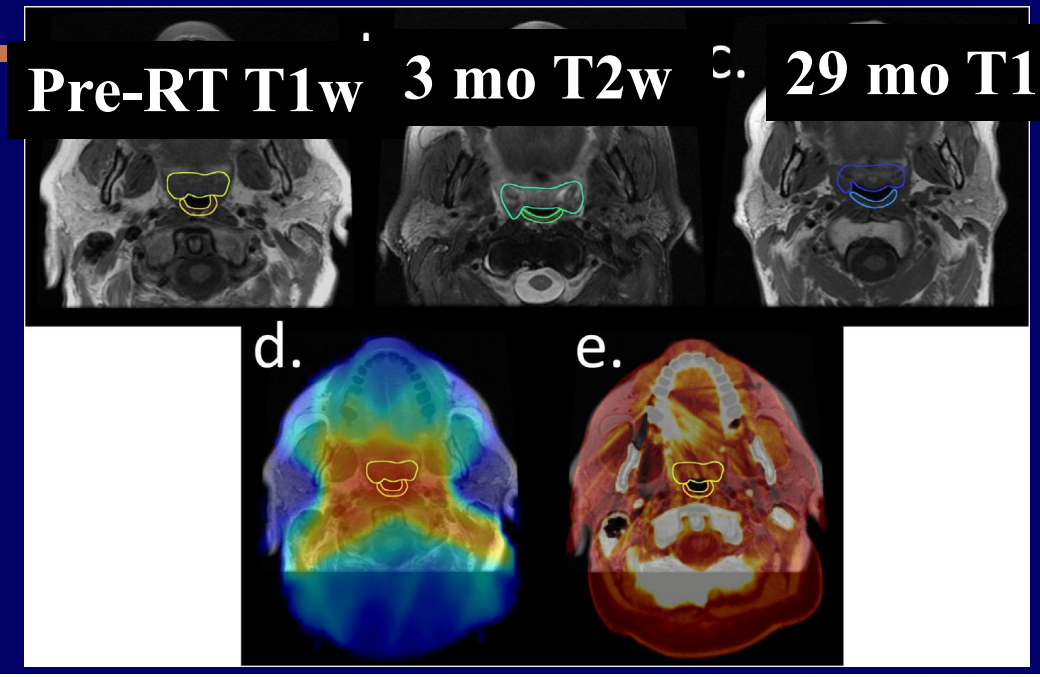
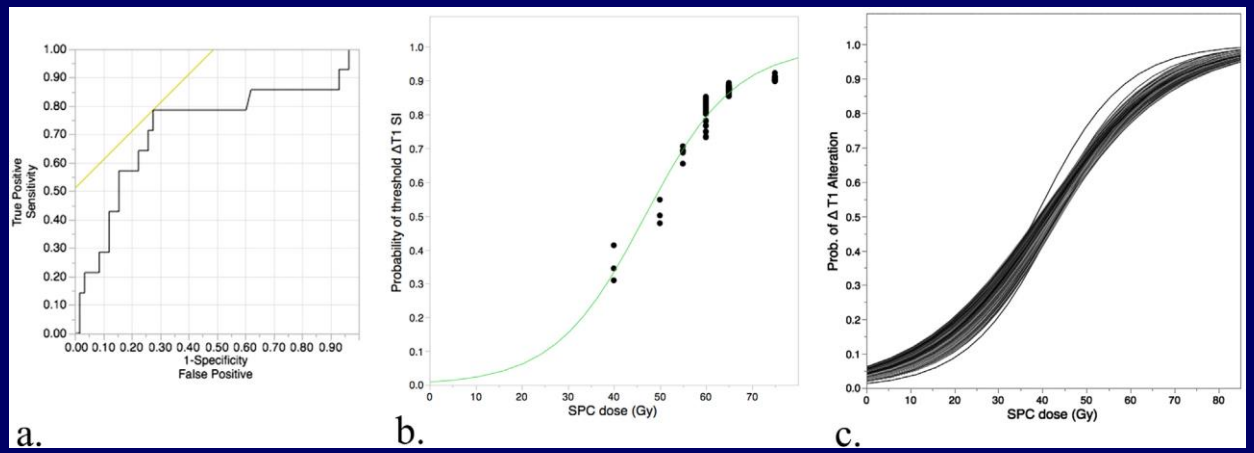


Figure provided by Chenevert T, Ph.D

Mp MRI to Assess Pharyngeal Constrictor Toxicity After Radiation







Messer J et al https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4794348/

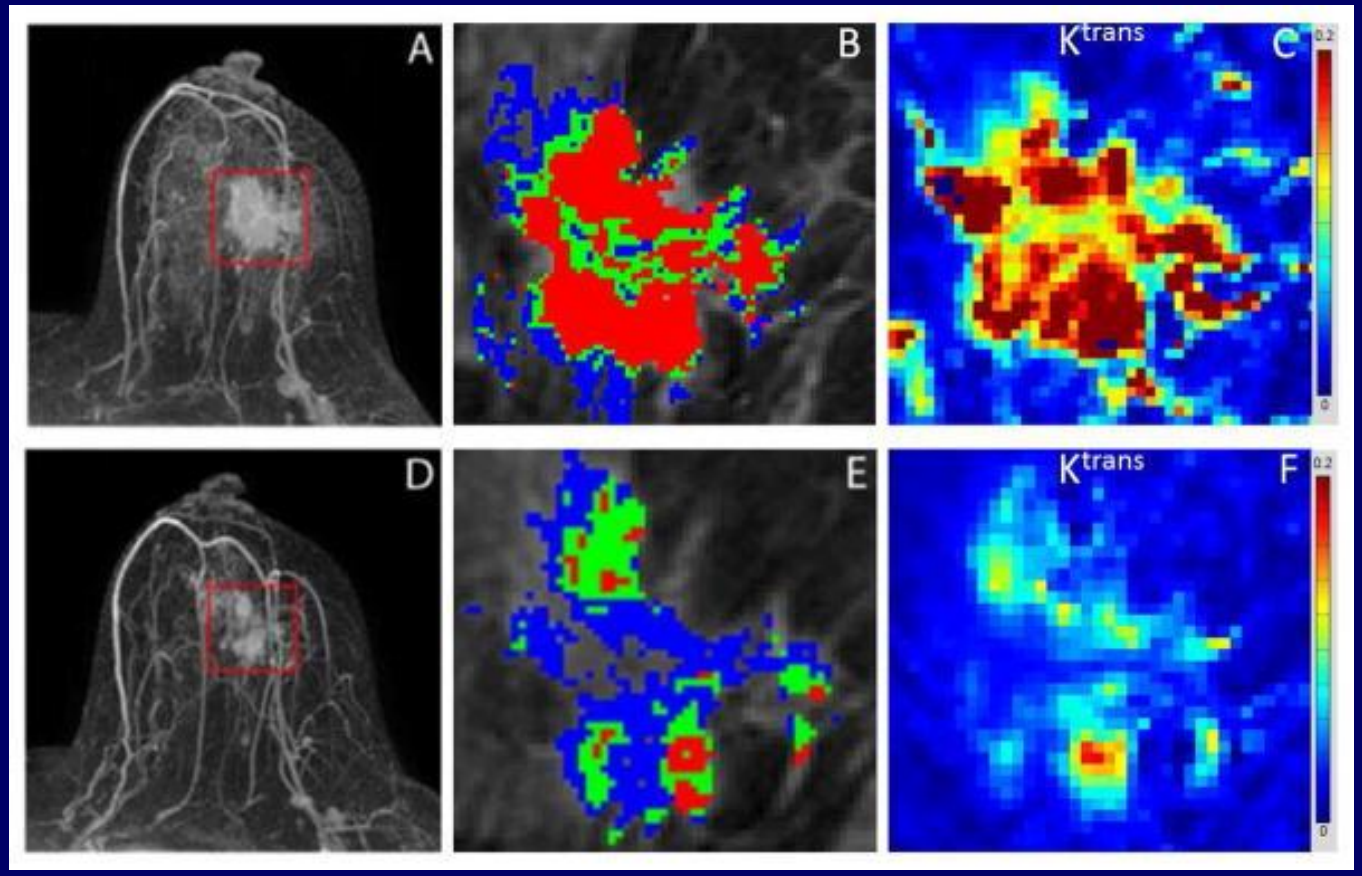
Slide courtesy of Jihong Wang

MpMRI Treatment Response for Breast Cancer

51-year-old woman invasive ductal carcinoma (Grade 3, ER+/PR+/HER2+), prior to neoadjuvant therapy

14 days after starting treatment with paclitaxel and trastuzumab

DCE MRI DCE MRI-MIP **K-Trans**



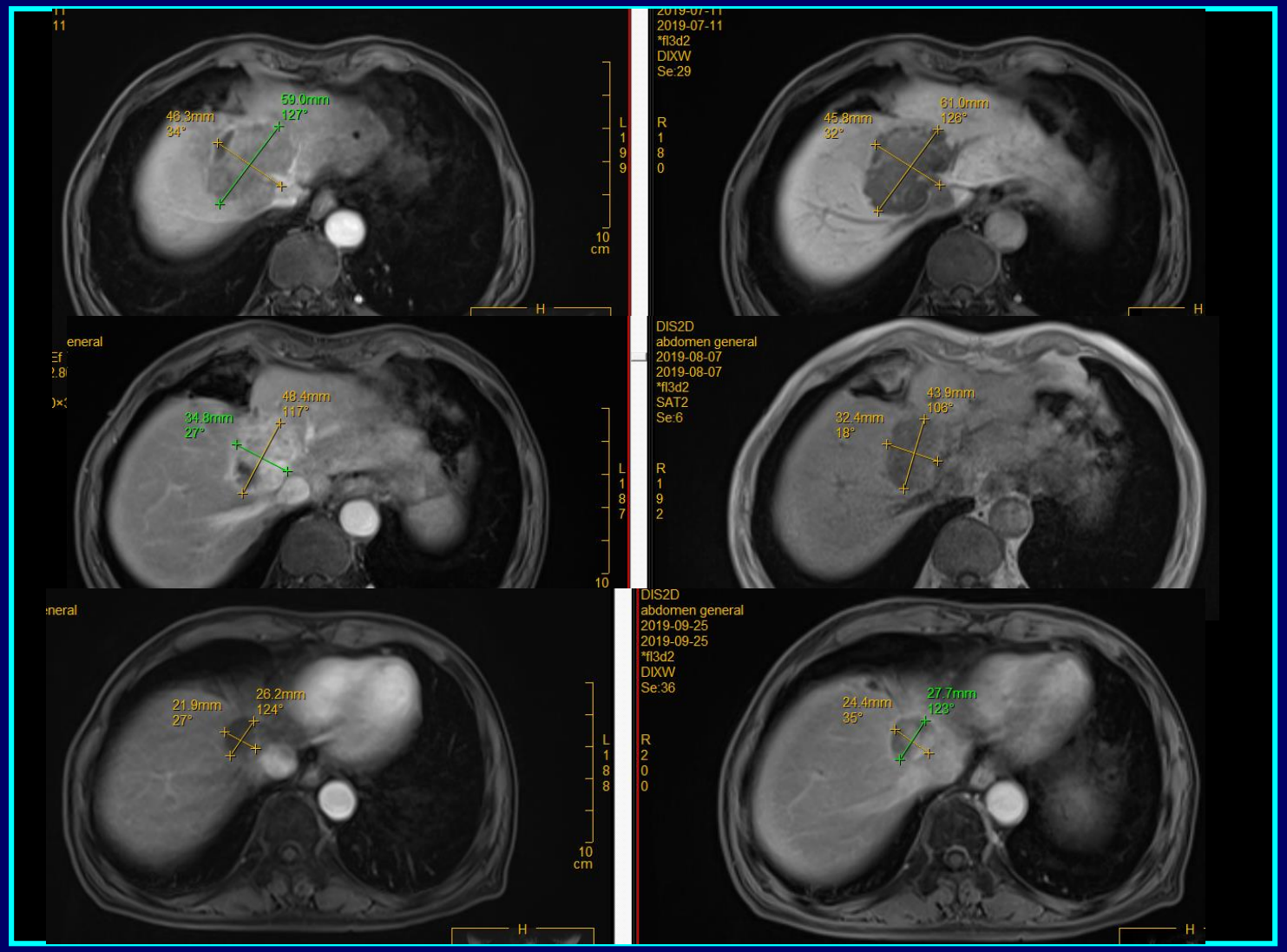
Rahbar et al, Magn Reson Imaging Clin N Am. 2016 Feb; 24(1): 223–238.

MRI Detects Early Changes During-SBRT: HCC

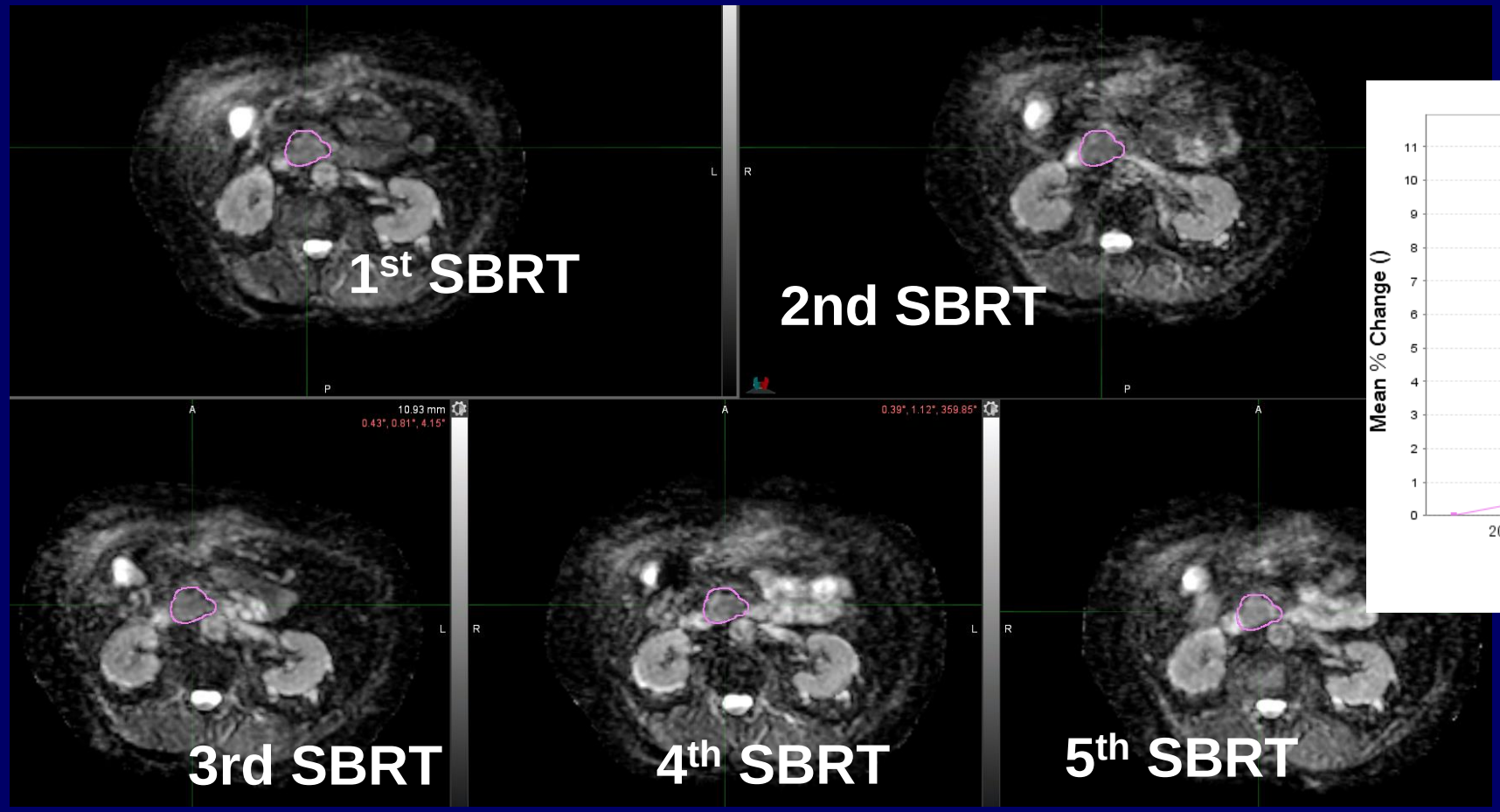
Pre SBRT
Unresectable

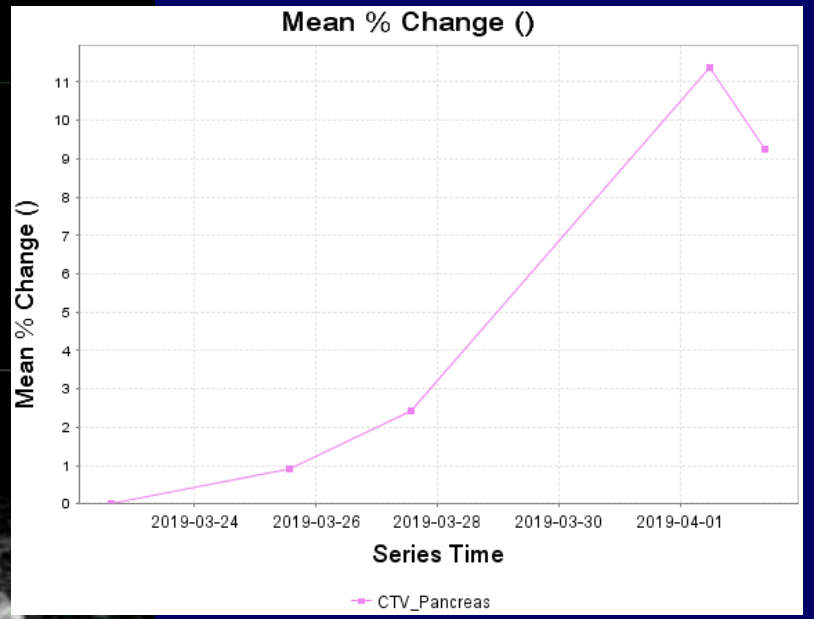
During SBRT
s/p 2/5 Tx

One month
Post-SBRT



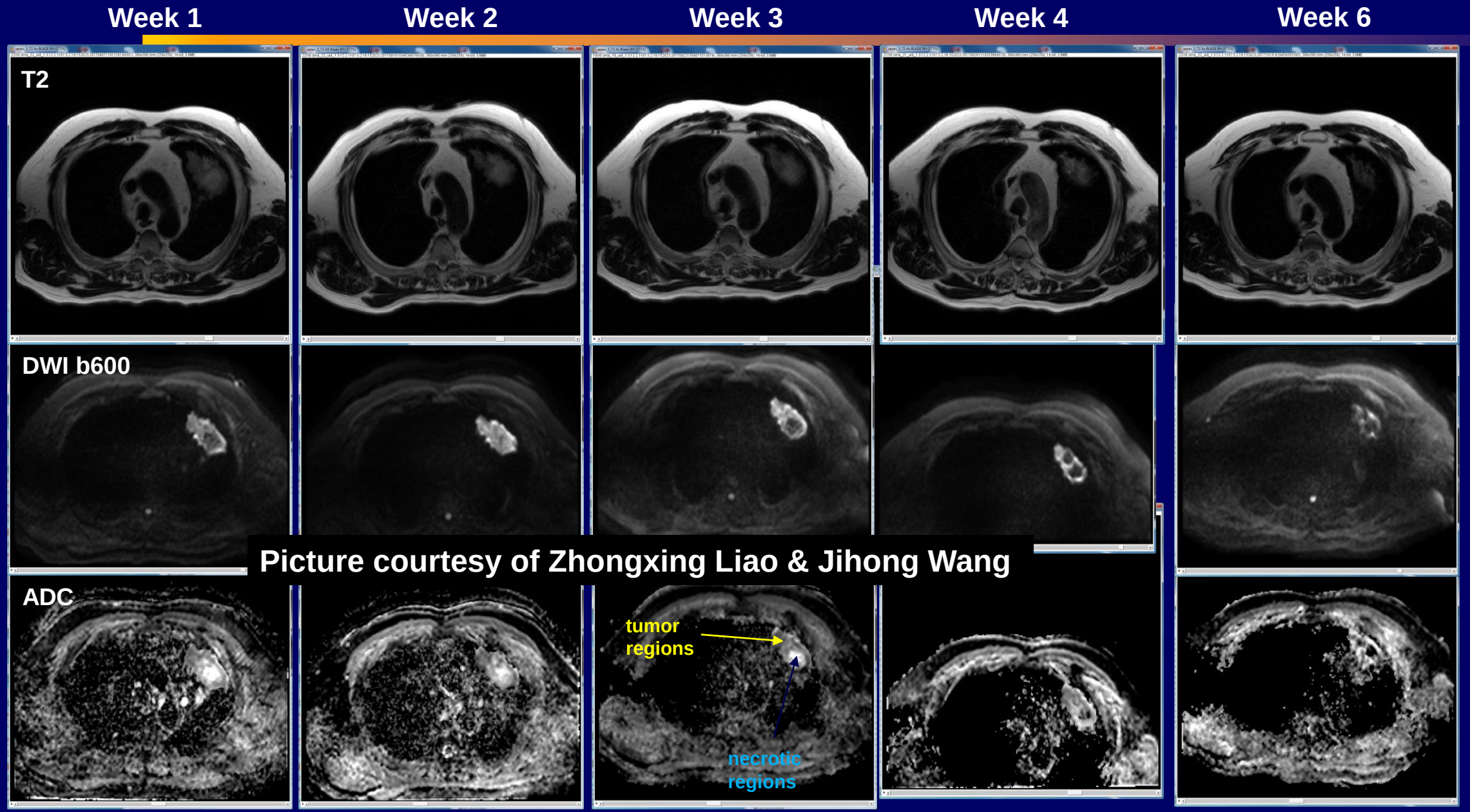
Changes of ADC in Pancreatic Cancer during RT





Slide Courtesy of Allen Li

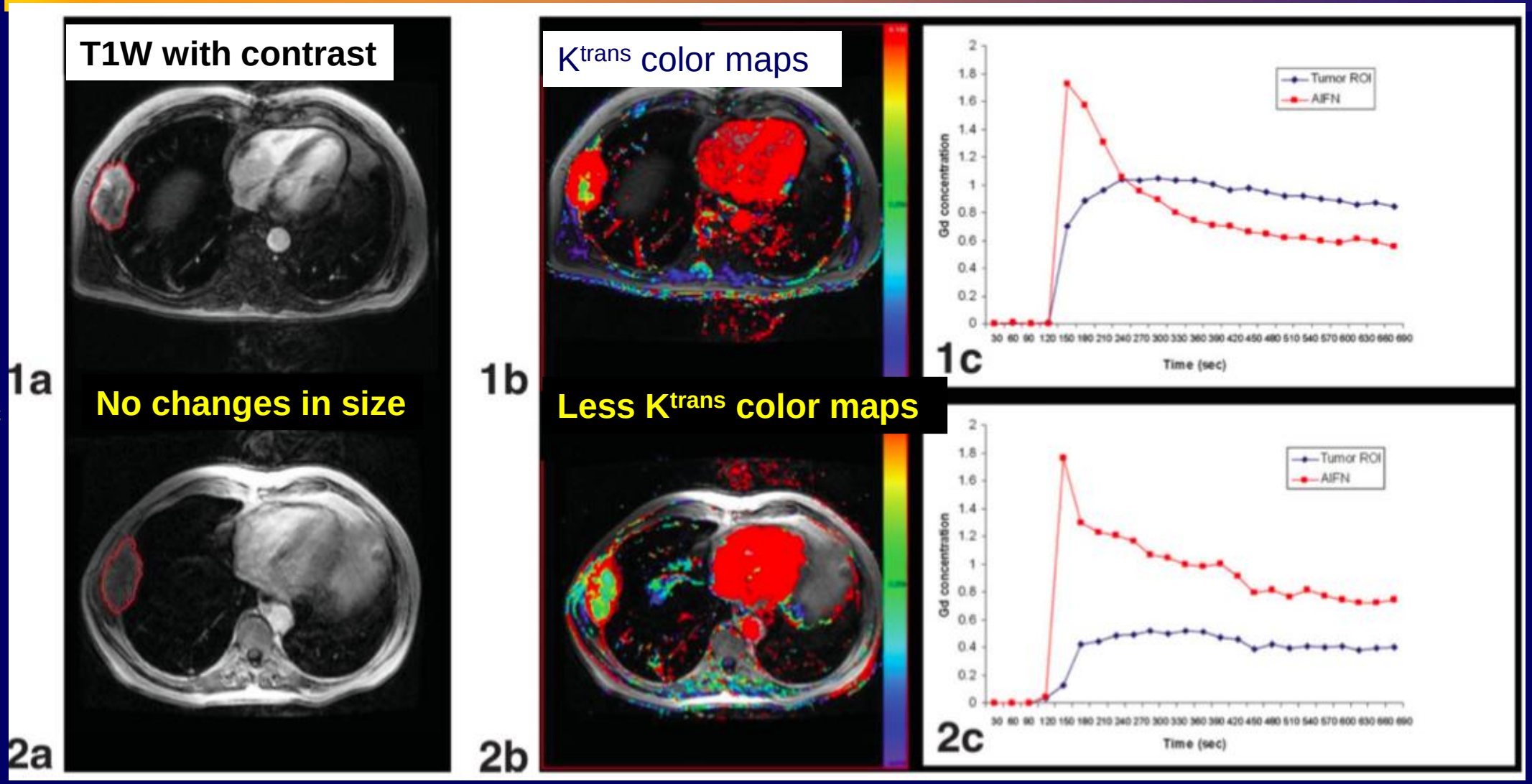
Weekly DWI During Lung Treatment



K^{-trans} MRI Detects Early Changes in Metastatic Melanoma

Pre-RT

2weeks into anti-angiogenic treatment



Barret et al, J. Magn. Reson. Imaging 2007;26:235–249.

Clinical Trials in mpMRI for Treatment Response Assessment

13 study listed in Cinicaltrials.org through searching by "MultiParametric MRI" and "treatment response assessment"

455 studies for "MRI" and "tx response assessment", mostly from Europe, followed by US, 4 studies for PET-MRI

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	☐	Unk				
2	☐	Rec				el Cancer Center at Johns Hopkins Baltimore, Maryland, United States
3	☐	Not yet recruiting NEW	Bladder Fiducial Markers and **Multiparametric-MRI** (Mp-**MRI**) to Optimize Bladder Chemo-**radiotherapy**	• Bladder Cancer	• Procedure: Fiducial marker placement	• Cedars-Sinai Medical Center (CSMC) eles, California, United y of California San o (UCSF) ncisco, California, United School of e/Massachusetts General (MGH) Massachusetts, United
4	☐	Recruiting	**Multi-parametric Magnetic Resonance Imaging** for Prostate Cancer Patients	• Prostate Cancer	• Device: Multiparametric MRI	• Henry Ford Health System Detroit, Michigan, United States
5	☐	Unknown †	Deformable Registration of **Multi-parametric MRI** to Intra-operative Transrectal Ultrasound for Prostate Brachytherapy	• Prostate Cancer	• Procedure: Brachytherapy	• Sheba_Medical_Center Tel Hashomer, Israel
6	☐	Unknown †	**Multi-Parametric** Brain Cancer **MRI**	• Brain Tumors	• Other: 3D MRI Scans	• Cross Cancer Institute Edmonton, Alberta, Canada
7	☐	Recruiting	Pilot Study Evaluating the Role of Histopathology Correlation	• Prostate	• Device: Uronav	• Case Comprehensive Cancer

MpMRI for precision ART treatment

Essential Components for Precision ART

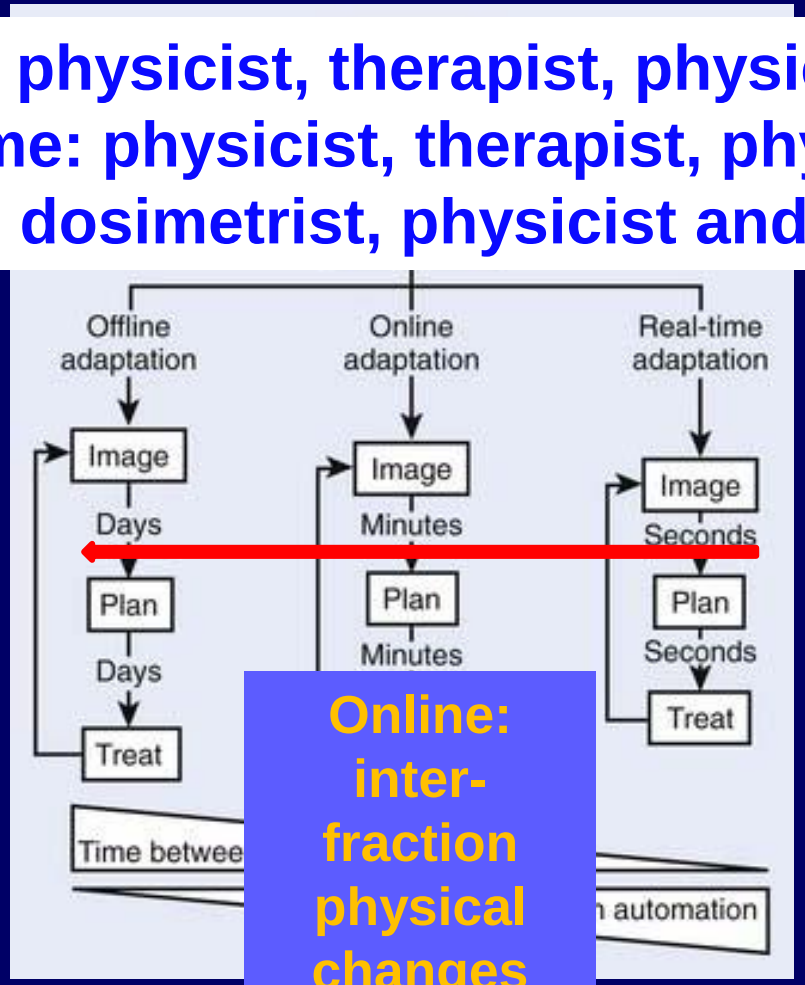
- Modern pretreatment imaging
- Real time imaging to detect the changes
- Evaluation the changes in tumor and OARs
- Precise image registration (deformable)
- Model based segmentation, automatic re-contouring (ideally)
- Accurate dose computation (deformable)
- Rapid automatic treatment planning (ideally)

MRI Linac holds almost all of these essential needs for ART.
MRI Can also use function imaging to guide Biology Guided Adaptive Radiation Therapy (BigART).

MRI Can Guide ART, Online or Offline

Online: physicist, therapist, physician
Real time: physicist, therapist, physician
Offline: dosimetrist, physicist and physician

Offline: Suitable for progressive change such as tumor response to RT

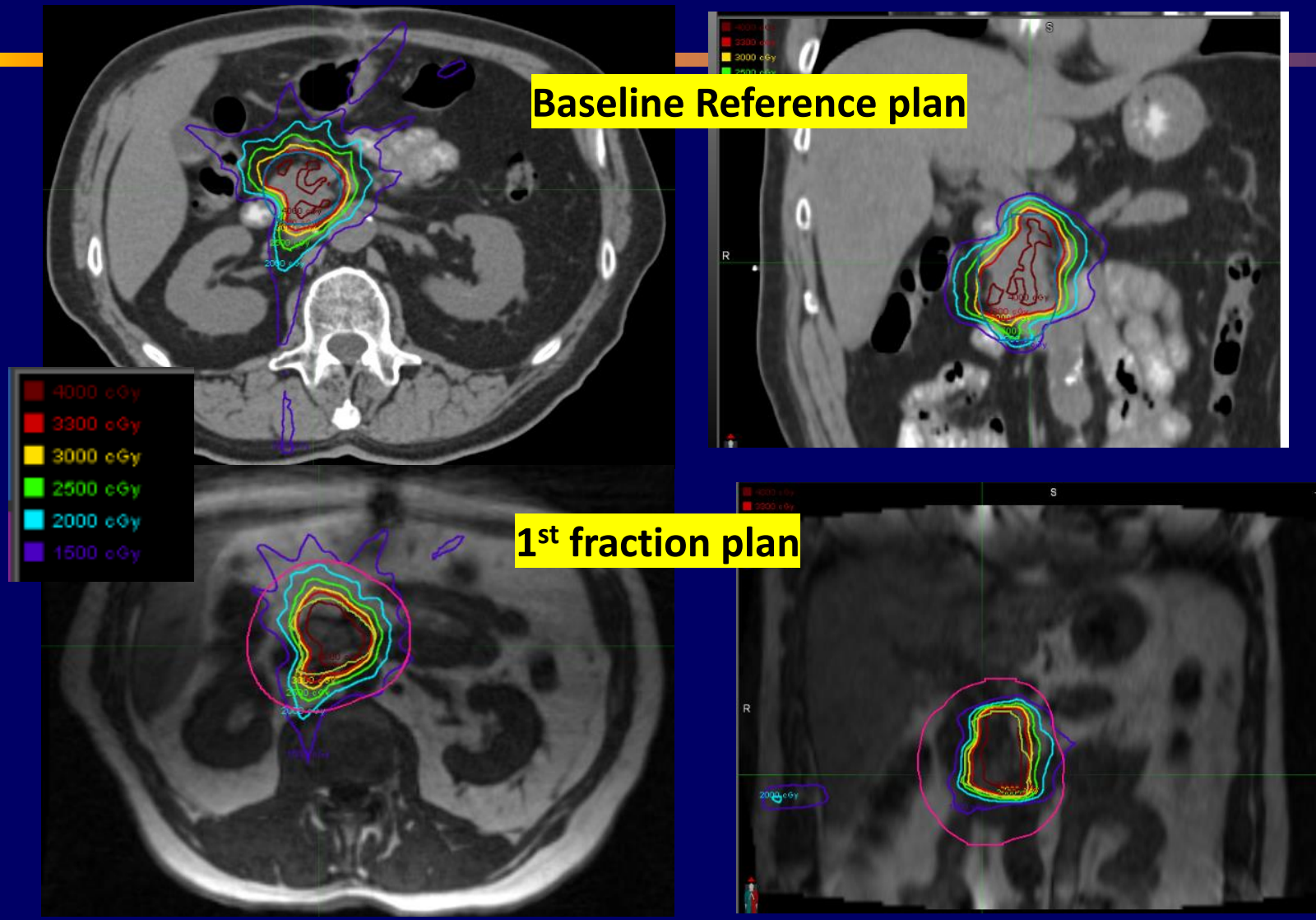


Online: inter-fraction physical changes

intra-fraction physical changes

Keall, Shu and Xing: http://clinicalgate.com/image-guided-adaptive-radiotherapy/, 2015

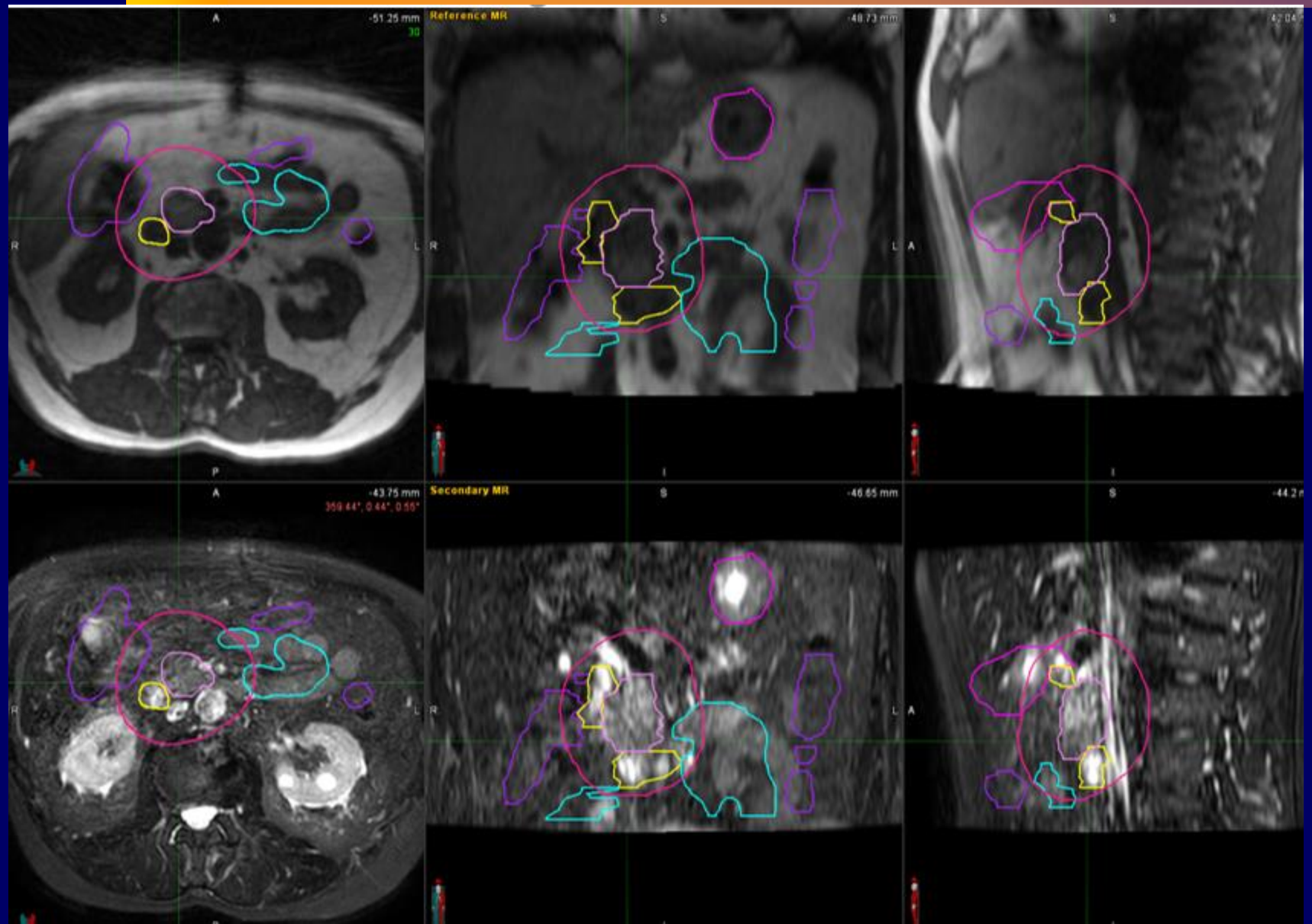
Pancreatic SBRT Using Online Daily Adaptive Plans



Slide Courtesy of Allen Li

Froedtert & Medical College of Wisconsin

Online Adaptation: Contour Editing



Motion Averaged 4D

Respiration triggered 3D T2

Slide Courtesy of Allen Li

Online Parallel Contour Editing \

MR Philips control

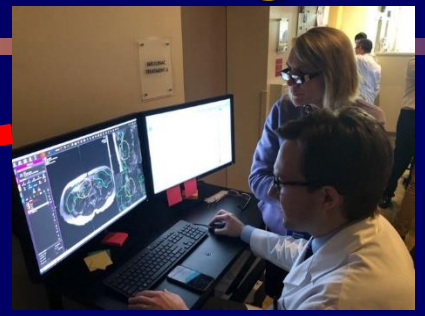
MIM

- Image Reg
- Contour population
- Contour distribution
- Contour combination

Online Monaco

MD MIM

- Editing GTV/CTV
- Editing OAR inside ring



Phys MIM

- Editing bone
- External contour
- Identifying air
- Checking Syn CT

RTT MIM

- Editing OARs

Technical Note: Acceleration of online adaptive replanning with automation and parallel operations.
Zhang J, Ahunbay E, **Li XA**.
Med Phys. 2018 Oct;45(10):4370-4376. doi: 10.1002/mp.13106. Epub 2018 Sep 24.

Time reduction >50%

Slide Courtesy of Allen Li, MCW

Paulson E, Ahunbay E, Chen X, Erickson B, Hall W, Li XA, presenting at ASTRO 2019.

Patient Name: RT#:

MR Linac Treatment Checklist

		RTT	PHY	MD	Time
Setup	Confirm no interrupts, interlocks on Integrity	x	x		09:03:20
	Confirm gantry at 0 degrees	x	x		09:03:24
	Clean Online and Offline Monaco Import Directories		x		09:03:26
	Confirm patient is closed on Offline Monaco		x		09:03:41
	Open and configure Moniqa, ArtQA, Online Monaco, Offline Monaco, Shadows	x	x	x	09:04:35
	Launch MIM and set search date to TODAY	x	x	x	09:04:58
	Daily MR Assessment (no bra with metal underwire or clasps)	x			09:05:01
	Ear plugs, headphones with music, no loops	x			09:21:33
Pre-Beam	Confirm auto-push to Online Monaco is off on Philips Host	x			09:05:26
	Adjust shim volume; confirm FOV contains anatomy	x			09:21:36
	Manually push daily MR to <Online Monaco, Offline Monaco, MIM>				
	Confirm all daily MR slices transferred (100% in Job Queue on Philips Host)	x			09:27:49
	Acquire B0 map, qMRI sequences during registration and plan adaptation				
Workflow Decision	If AP shift > +/-1cm tolerance, use Adapt to Shape				
	If target rotation or deformation, use Adapt to Shape				
	If target close to air cavity, use Adapt to Shape				
	If changes in radiological depth (external contour), use Adapt to Shape				
Adapt to Position	3D plans use Adapt Segments only				
	If small shifts Optimize Weights; otherwise Optimize Shapes				
Adapt to Shape	Run "FH MRL Setup Parallel Contouring" workflow in MIM		x		09:35:26
	Confirm patient (external) contour is correct (use sagittal or coronal views)		x		09:42:47
	OAR contour approval within edit ring			x	09:42:44
	Target contour approval			x	09:42:50
	Run "FH MRL Post Parallel Contouring" workflow in MIM		x		09:42:54
	View Synthetic CT; confirm electron density assignment (feces or air?)		x		09:47:51
	If small shifts Optimize Weights; otherwise Optimize Shapes		x		09:48:28
	Start from Segments (small anatomy change); otherwise Start from Fluence		x		09:46:54
	Scale adaptive plan for PTV coverage		x		09:54:12
Plan Evaluation	Optional: Acquire verification image; push to Online Monaco	x			09:54:09
	Adaptive plan review (compare DVHs, etc)		x		09:53:56
	Evaluate plan with traffic lights (green = ideal; yellow = acceptable)		x		09:53:52
	Save plan; run Moniqa (plan quality and MR-MV check mode)		x		09:54:01
	Run ArtQA secondary dose check		x		09:54:04
	Optional: Perform Adapt to Position on verification image		x		09:54:31
	Adaptive plan approval		x		09:57:16
	Run Moniqa (Mosaiq integrity check mode)		x		09:58:59
	Visual beam parameter verification cross-check		x		09:58:54
	Initiate motion monitoring	x			09:56:25
Beam-On		x			10:00:10
Post-Beam	Optional: Acquire post-beam verification image	x			10:11:02
	DICOM export qMRI and B0 images to MIM Clinical	x			09:55:37
	Run Moniqa (treatment delivery check mode)		x		10:11:14
	Reconstruct dose on post-beam verification MR				
	Export daily MR, structures, plan, and dose to MIM; generate DVH summary				
	Scale and accumulate daily dose on first fraction MR; generate report				
	Post-process quantitative imaging				
	Add QA session in Treatment Calendar				
	Add plan document, ArtQA, DVH summary, SPC, IMRTQA report to Mosaiq				
1/31/19	Date/Initials:				

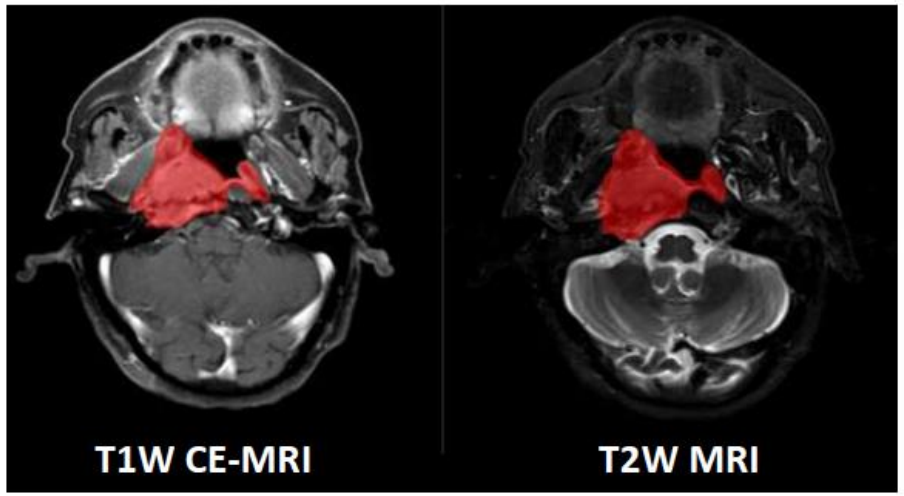
Average times for Adapt to Shape

	Duration
Patient setup	5 min
Pre-beam 4DMRI (acqui + recon + trans)	6 min
Reg + Contour editing	13 min
Plan adaptation	11 min
ArtQA + double checks	1 min
Beam-on time	10 min
Post-tx 4DMRI	3 min
Total on-table time	50 min

Off Line MpMRI Radiomic Based BigART

Multi-parametric MRI Radiomics

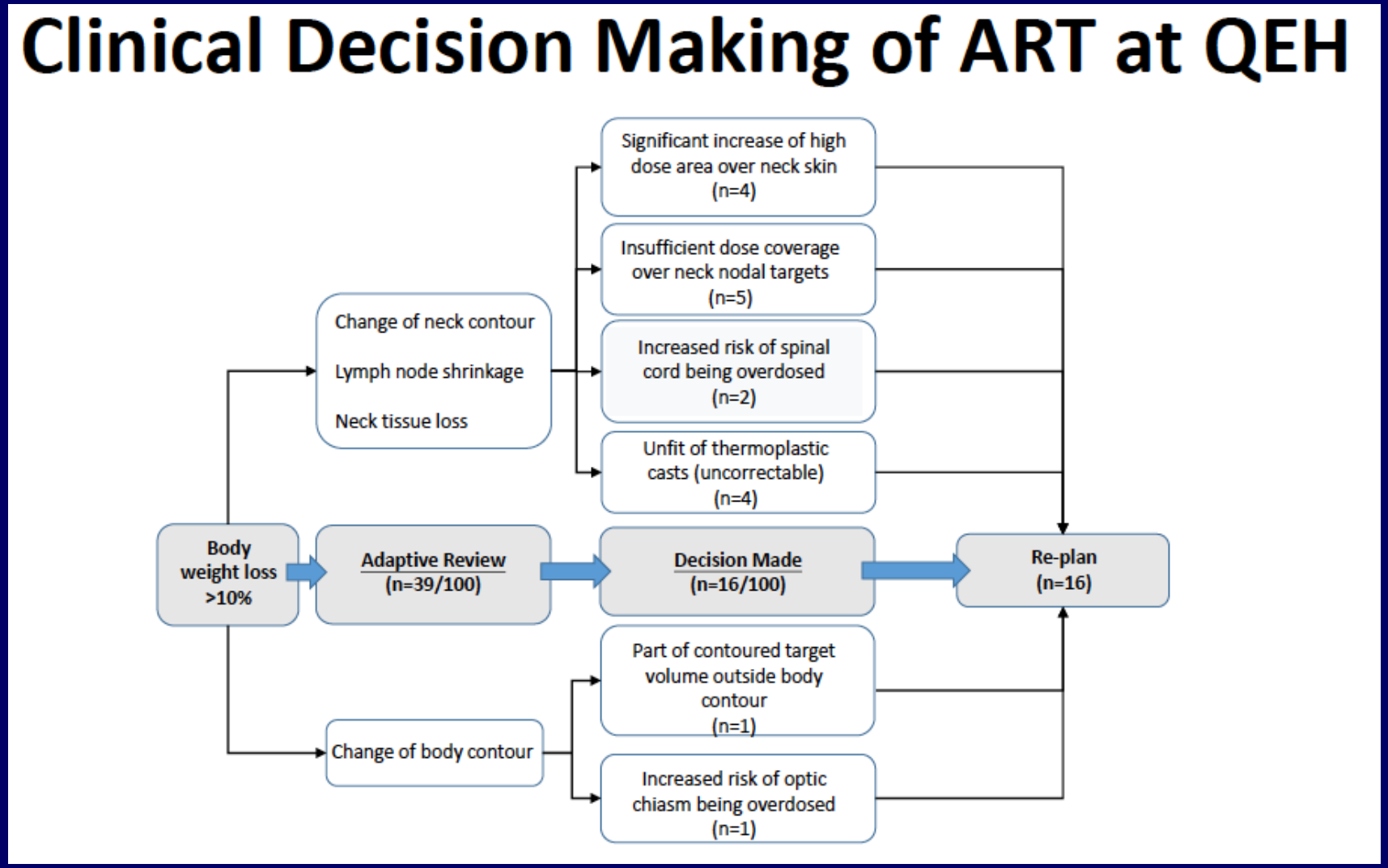
Pretreatment Prediction of Adaptive Radiation Therapy Eligibility using MRI-based Radiomics for Advanced Nasopharyngeal Carcinoma Patients



Baseline mpMRI radiomic can be used for prediction

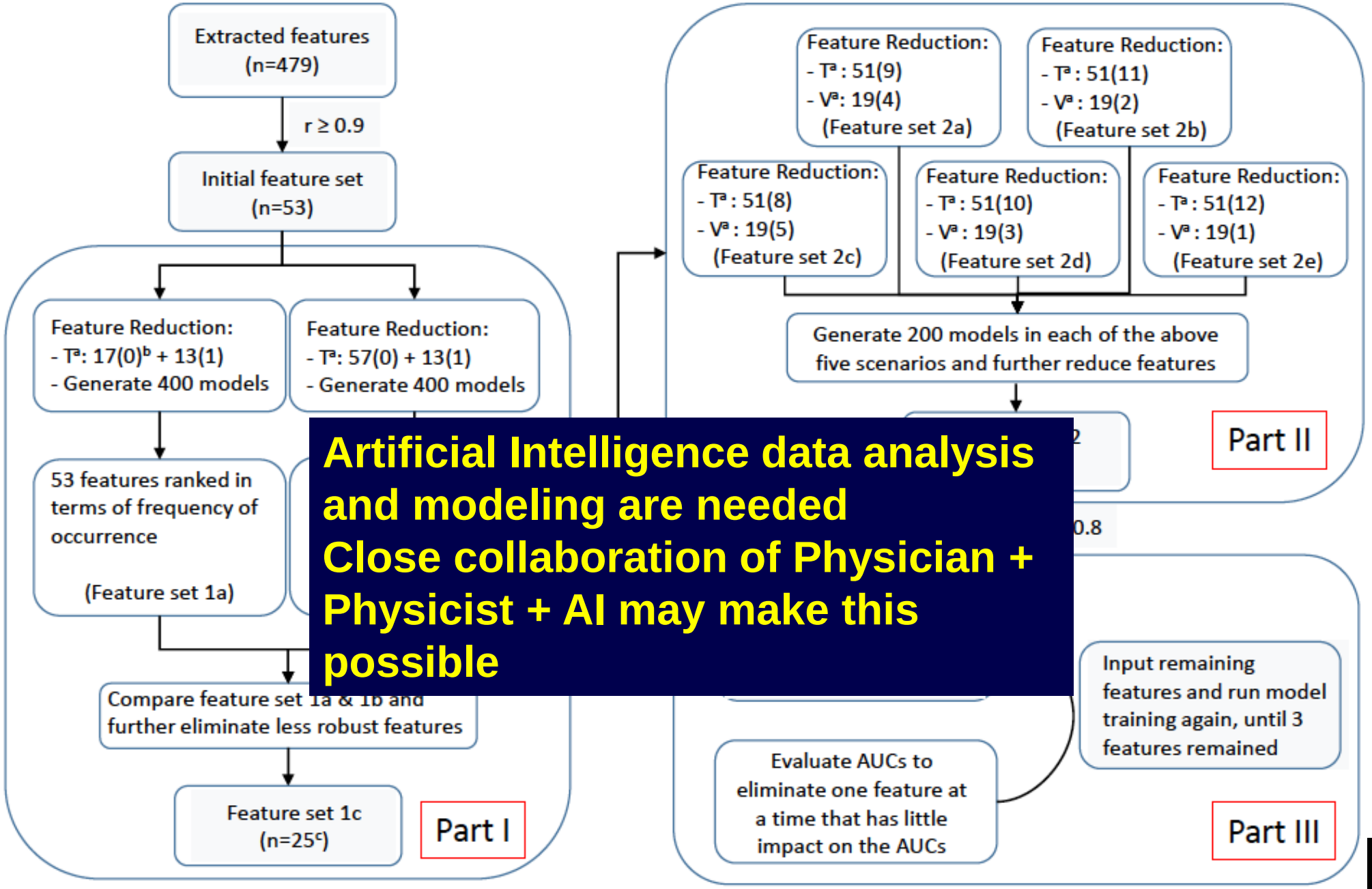
Slide Courtesy of Jing Cai

MpMRI plus Clinical Knowledge for BigART



Slide Courtesy of Jing Cai

Clinical trial ongoing in HongKong, Jing Cai et al



From Jing Cai, 2020

MpMRI Radiomic Model Guided ART Decision

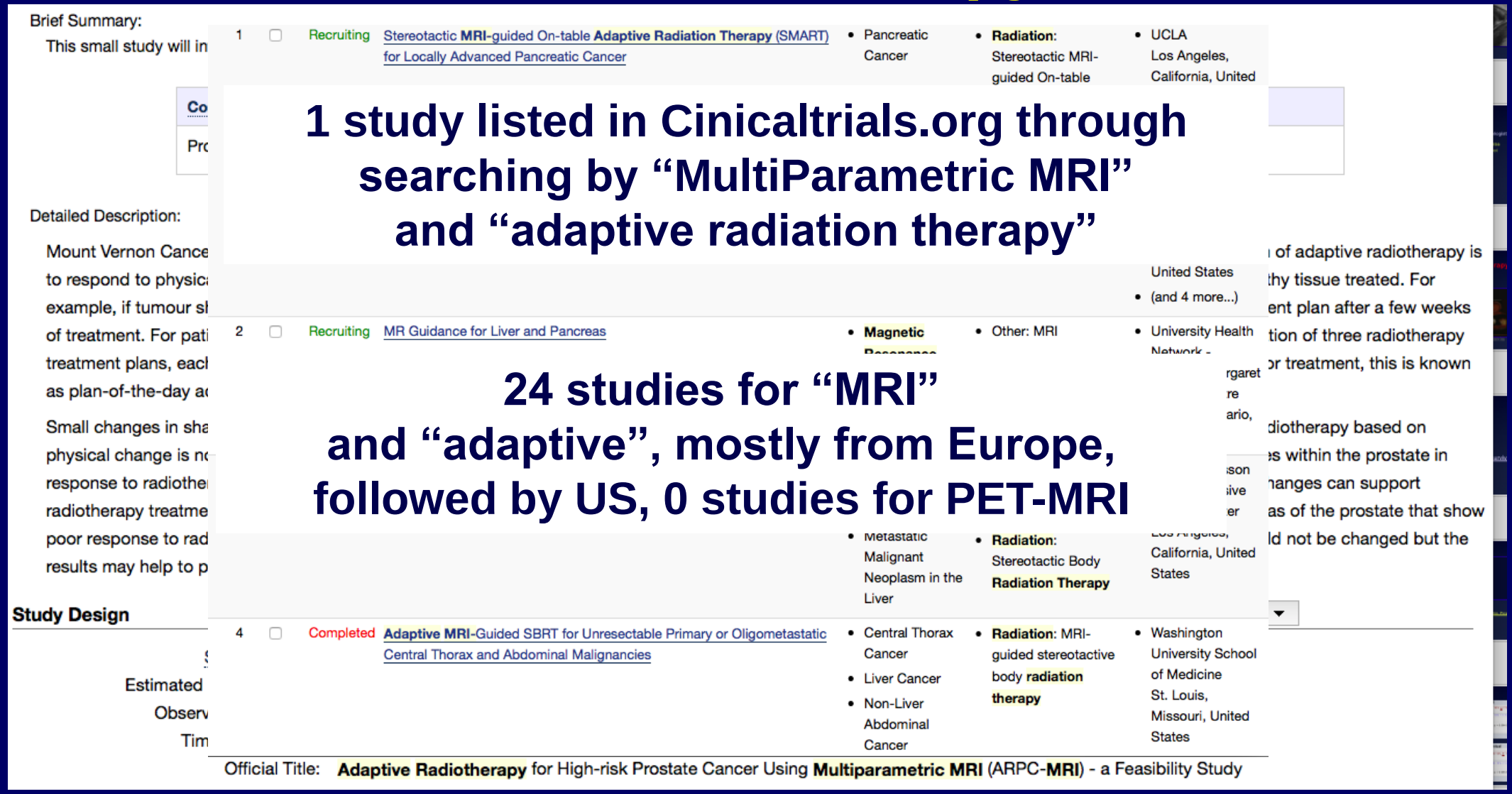
Radiomics-based Prediction Model for Adaptive Radiation Therapy (ART)		
Images sequences	MR Images – T2W-STIR	
No. of Selected Features	8	
Individual Feature	Feature Value	Weight
1. Original shape Elongation	a	0.5697537
2. Original shape SurfaceArea	b	1.2716523
3. Original firstorder Kurtosis		
4. Log-sigma-2.0-mm-3D gldm LargeDependenceHighGrayLevel Emphasis		
5. Log-sigma-2.0-mm-3D glcm Imc1		
6. Log-sigma-2.0-mm-3D firstorder Median	f	0.6391367
7. Log-sigma-3.0-mm-3D glcm Idn	g	-1.9804444
8. Log-sigma-3.0-mm-3D ngtdm Strength	h	-0.1232414
The best-performance feature	Log-sigma-3.0-mm-3D glcm Idn	-1.9804444
Rad-score formula	-2.012202747 + 0.5697537a + 1.2716523b - 0.3969821c + 1.4055497d + 0.2008964e + 0.6391367f - 1.9804444g - 0.1232414h	

MpMRI will lift the level of precision oncology and radiation oncology to generate clinical benefit!

Radiomics-based Prediction Model for Adaptive Radiation Therapy (ART)		
Images sequences	MR Images - CET1	
No. of Selected Features	8	
Individual Feature	Feature Value	Weight
1. Original glcm Imc2	a	3.146997
2. Original first order skewness	b	0.102094
3. Log sigma 20mm 3D glcm MCC	c	-4.303517
		1.088471
		5.247539
		1.711327
7. Log sigma 40mm 3D gldm Small Dependence Low Gray Level Emphasis	g	-6.345265
8. Log sigma 40mm 3D firstorder Kurtosis	h	-1.015541
The best-performance feature	Log sigma 40mm 3D gldm Small Dependence Low Gray Level Emphasis	-6.345265
Rad-score formula	-3.066949 + 3.146997a + 0.102094b - 4.303517c +1.088471d + 5.247539e + 1.711327f - 6.345265g - 1.015541h	

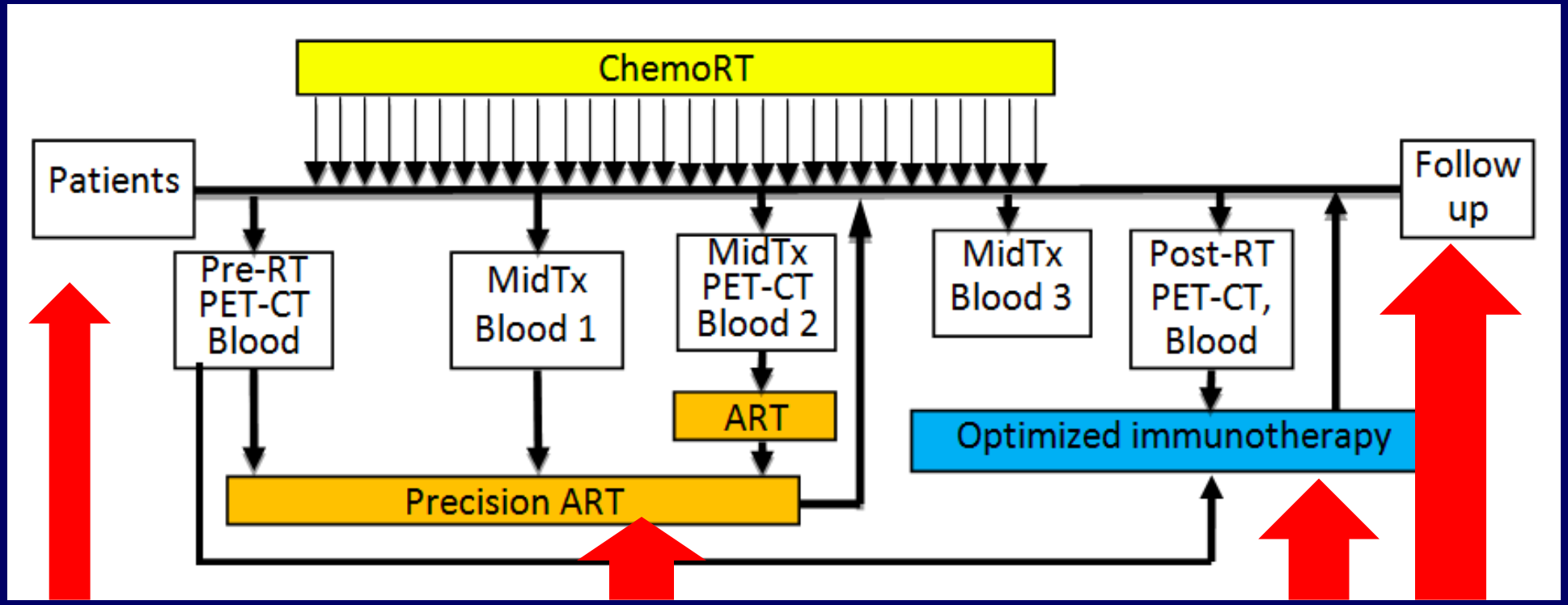
From Jing Cai, 2020

Clinical Trials in mpMRI for Adaptive Radiation Therapy



Future of MpMRI in Precision Oncology & Radiation Oncology

Stage III NSCLC for example



MRI Precision Oncology to Make the Best Decision

MRI Precision BigART to Optimize Treatment

MRI Precision Adjuvant Therapy and Follow-up to Improve Survival

Thank You!!!

Slide Courtesy

- Jing Cai, PhD
- Allen Li, PhD
- Jihong Wang, PhD
- Nina Mayr, MD, PhD

Kong's Collaborative lab on imaging and Blood Biomarkers