MRI Guided Adaptive Radiotherapy Present and Future

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Disclosure

- Personal fees (speaking honorarium) from Viewray, Inc. outside this work

Outline

- Introduction to MRI guided radiotherapy (MRgRT)
- Rationale for adaptive radiotherapy
- Clinical workflow of MR guided adaptive radiotherapy
- Challenges in MR guided adaptive planning
- Future development

Advantages of MRI guided RT (MRgRT)

- Superior soft tissue contrast
- Functional and physiological imaging
- Real time dynamic imaging
- No radiation imaging dose

❑ Target/OAR delineation

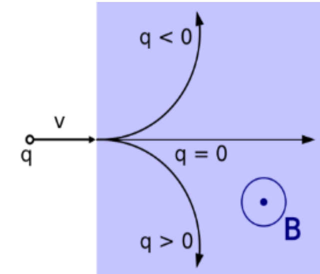
❑ Treatment setup and verification

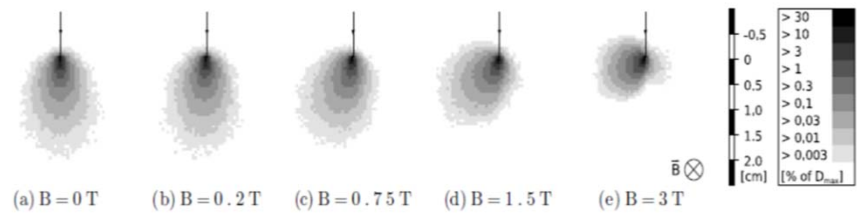
❑ Monitor treatment variations and response

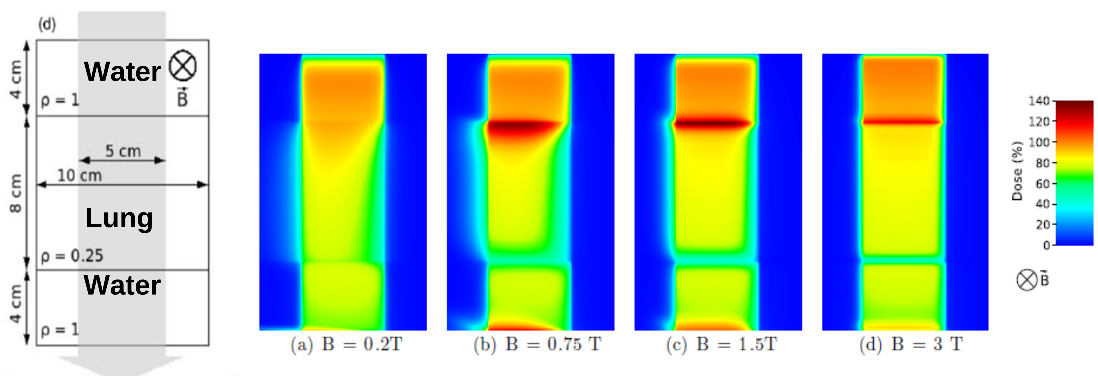
❑ Motion management

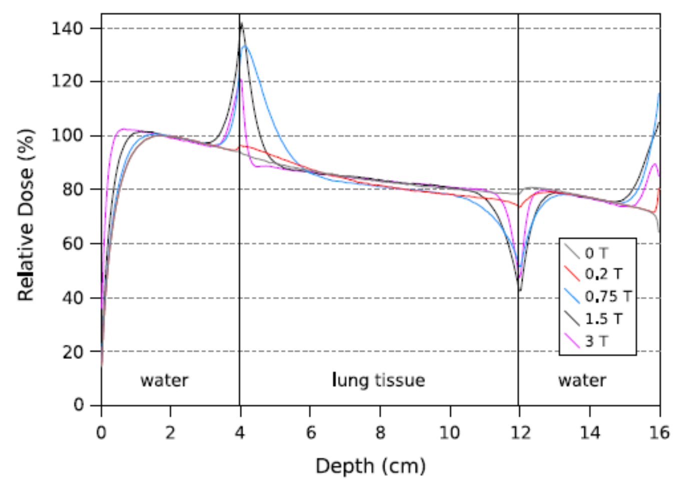
Challenges for MRgRT

- MR safety
- Patient immobilization with MR coils
- Geometric distortion
- Lack of electron density info for dose calculation
- Magnetic field interference on dose distribution

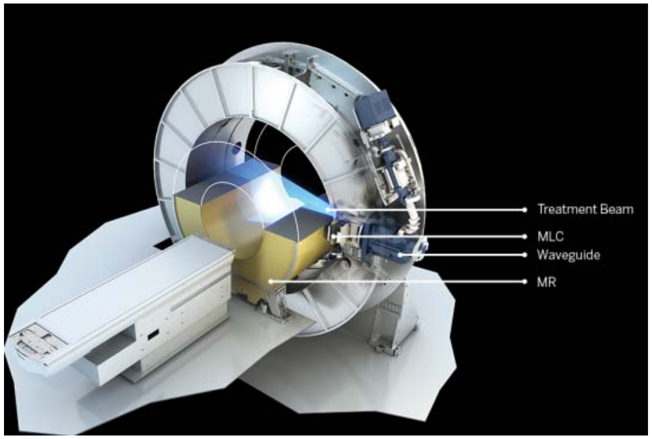




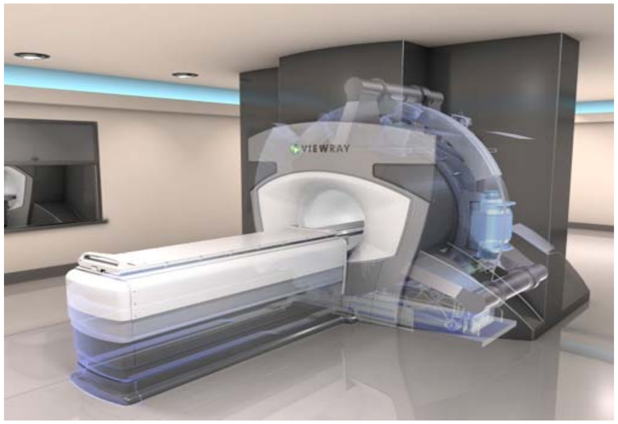




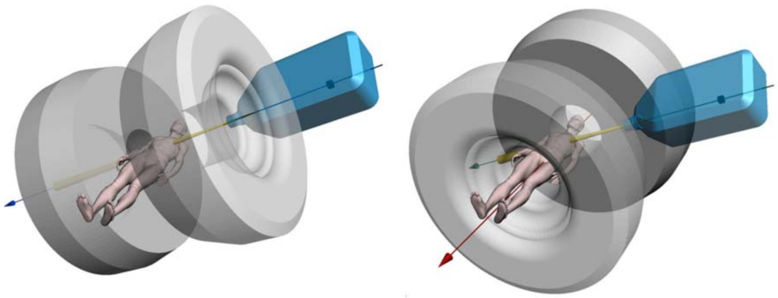
Raaijmakers et al. PMB. 53 (2008)



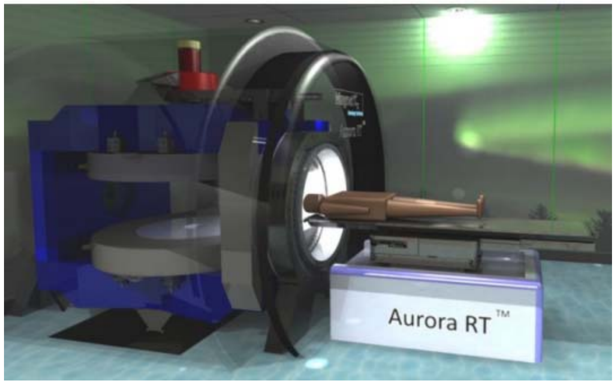
Elekta MRI-Linac Unity^{TM} (1.5T)



ViewRay MRIdian (0.35T)



The Australian MRI-Linac program (1.0T)



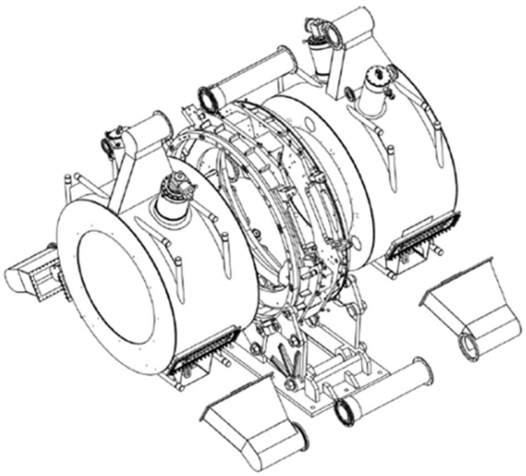
MagentTx Aurora-RT^{TM} (0.5T)

MRgRT system	Radiation	Magnet field		
		Configuration	Orientation	Strength
ViewRay MRIdian Cobalt	Cobalt-60	split superconducting close bore	Perpendicular	0.35 T
ViewRay MRIdian Linac	6 MV	split superconducting close bore	Perpendicular	0.35 T
MagnetTx Aurora RT	6 MV	superconducting rotating open bore	Parallel	0.5 T
Australian MRI-Linac	6 MV	superconducting open bore	Parallel/ Perpendicular	1.0 T
Elekta Unity	7 MV	superconducting close bore	Perpendicular	1.5 T

Introduction to ViewRay MRIdian® system

RT components:

- Cobalt system: 3 cobalt heads , 500cGy/min, 3 independent MLC system (1cm leaf width, double focus, field size 27.3cm x 27.3cm)
- MR-Linac: 6MV Flattening Filter Free Linac, 600cGy/min, 0.4cm leaf width double focus double stack MLC



MRI components:

- Split superconductor MRI (0.345 T)
- 50cm FOV with 70cm bore size
- High resolution 3D MRI images in 17-172s
- Real time cine MRI image (4 frames/s for one sagittal plane)

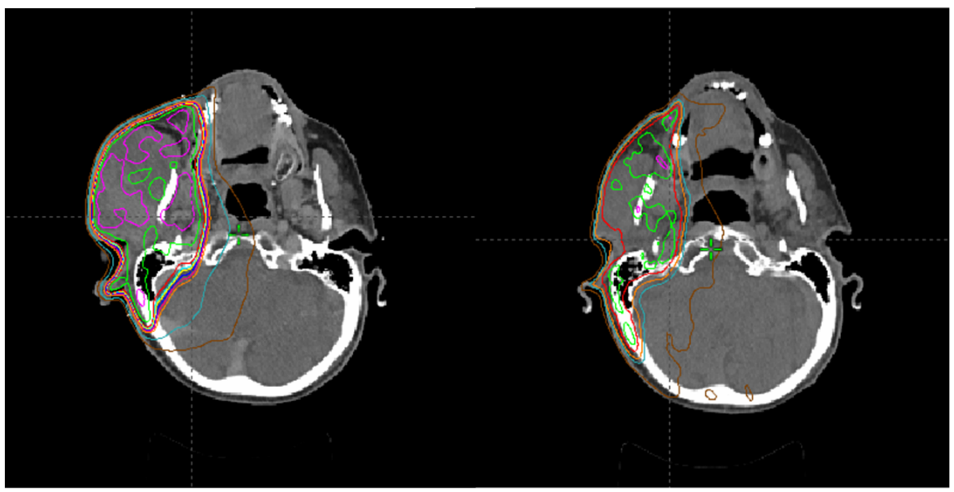
Phys. Med. Biol. **42** (1997) 123–132. Printed in the UK   PII: S0031-9155(97)67292-9

Adaptive radiation therapy

Di Yan†, Frank Vicini, John Wong and Alvaro Martinez
Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI 48073, USA

Received 11 August 1995, in final form 29 August 1996

- Adaptive radiation therapy (ART) is a close-loop process:
  - Systematic monitoring of treatment variations (e.g. IGRT)
  - Re-optimize the treatment plan to account for these variations



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Intra-treatment variations

- Tumor anatomic changes (Systematic)
  - Regression/Progression
- Weight loss (Systematic)
- Positioning and posture
- Organ at risk
  - Morphological (volume, shape etc.)
  - Position change in relative to target
- Respiratory motion

(Stochastic)

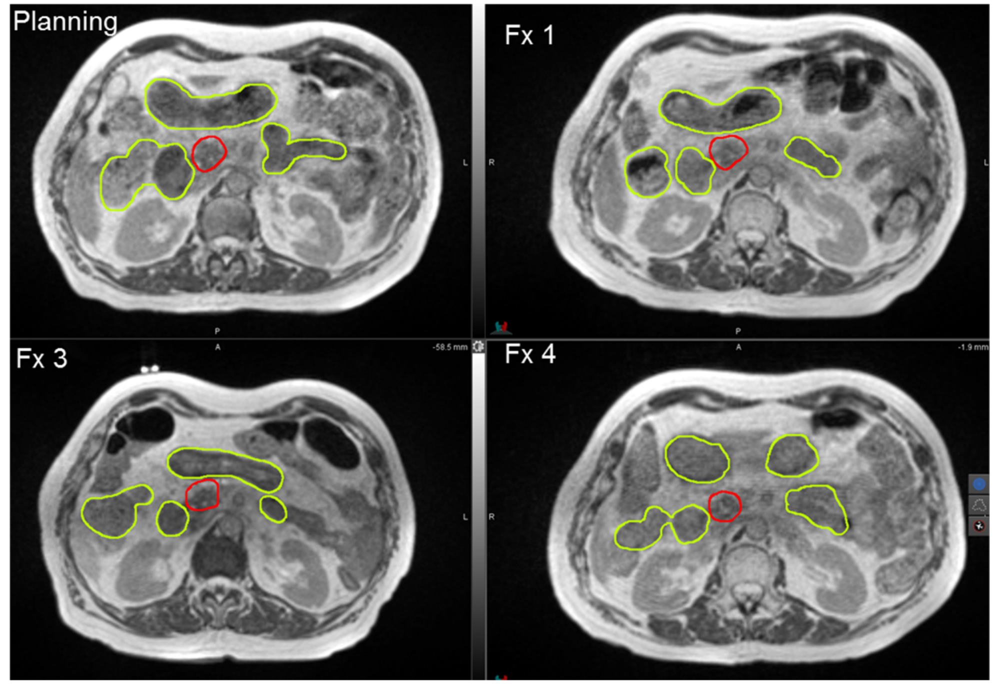
- Tumor and/or OAR biological changes (Systematic)

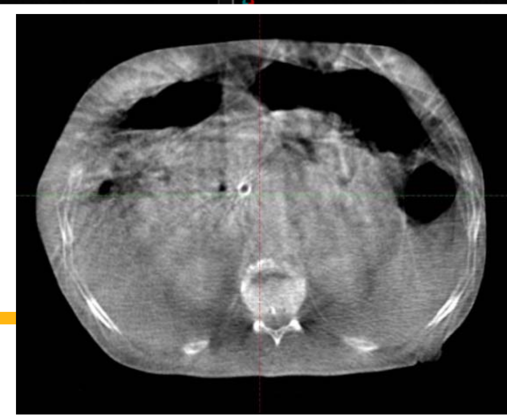
➢ Does the change lead to clinically unacceptable deviation of dose?

➢ How to account for it?

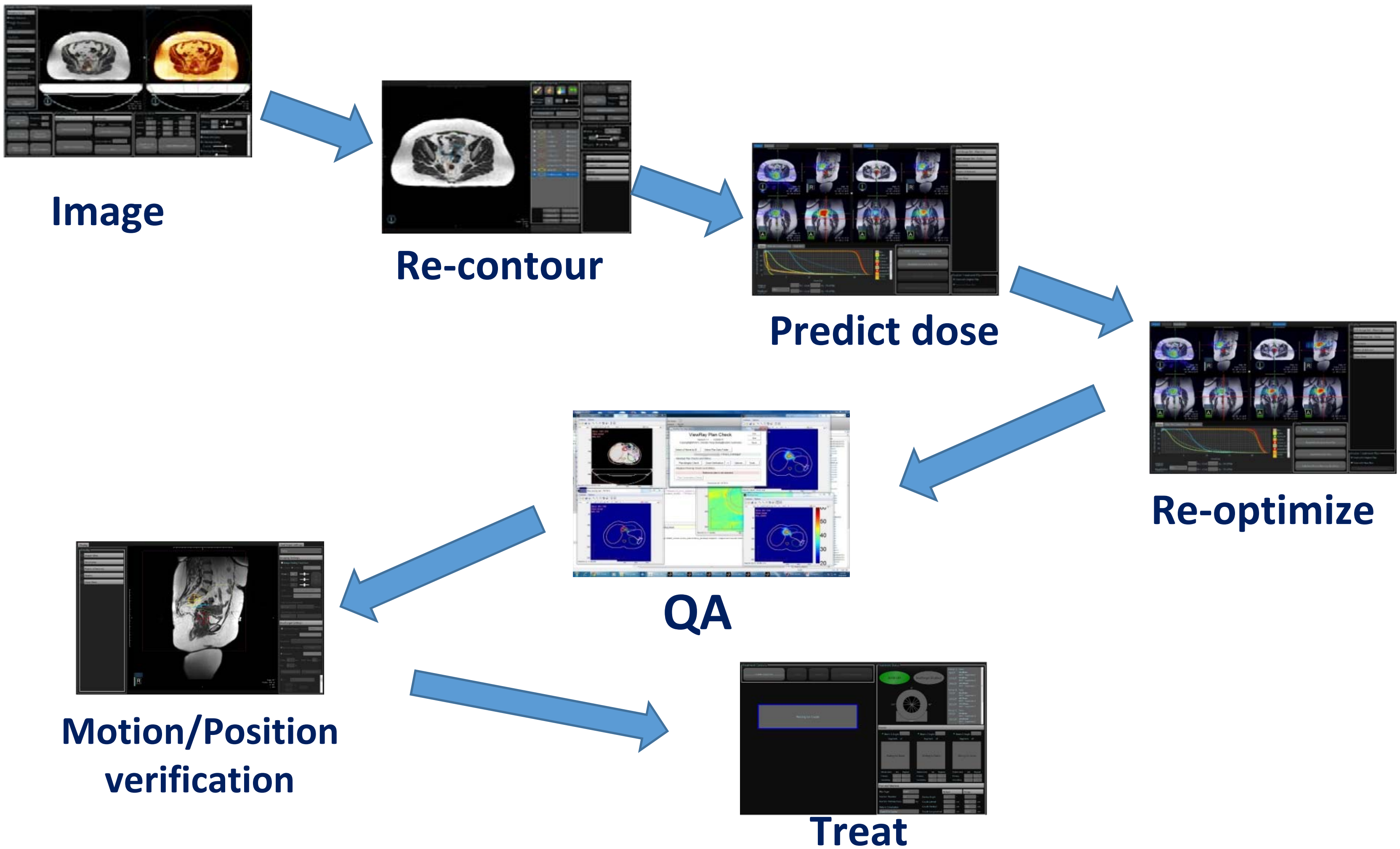
Online Adaptive Radiotherapy (On-ART)

- To account for stochastic changes of critical organs
- Potential advantages:
  - Dose escalation
  - Improve treatment tolerance
- Mandates on-board imaging guidance
- Heavily relies on image quality
- Efficient treatment planning tool is essential





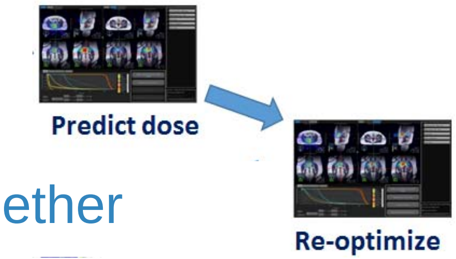
Online MR guided adaptive treatment workflow



Imaging and Contouring

- MR imaging:
  - TRUFI (true fast imaging with steady-state free precession) sequence
  - Abdomen: FOV 45x45x24cm, spatial resolution 0.15x0.3cm, acquisition time: 17s with breath hold
  - Pelvic: FOV 50x45x43cm, spatial resolution 0.15x0.15cm, acquisition time 172s with free breathing
- Contouring
  - Deformable image registration between daily MRI and the initial planning MRI
  - Initial planning contours deformed to the daily MRI
  - Reviewed and manually corrected by physician and physicist

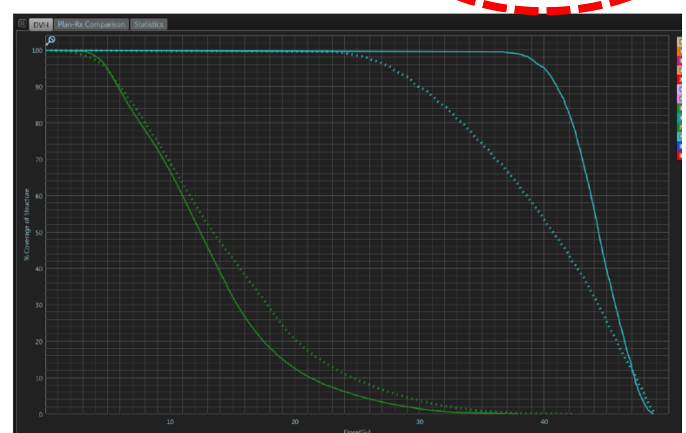
Dose prediction and re-optimization



- Initial treatment planning is re-calculated to ascertain whether treatment plan is optimal for that day's specific anatomy
  - Dosimetric metrics extracted automatically for evaluation
  - DVHs and dose distribution compared with the initial plan

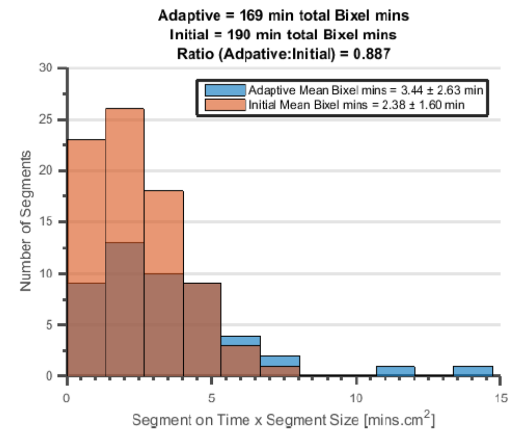
Structure/Point		Min	Mean	Max	Dose to Volume
O_Ddnm	Rx				<= 0.5 cc at 35 Gy
	Predicted	1.39	12.63	44.19	2.70 cc at 35 Gy
	Plan	1.66	11.39	38.72	0.50 cc at 35 Gy

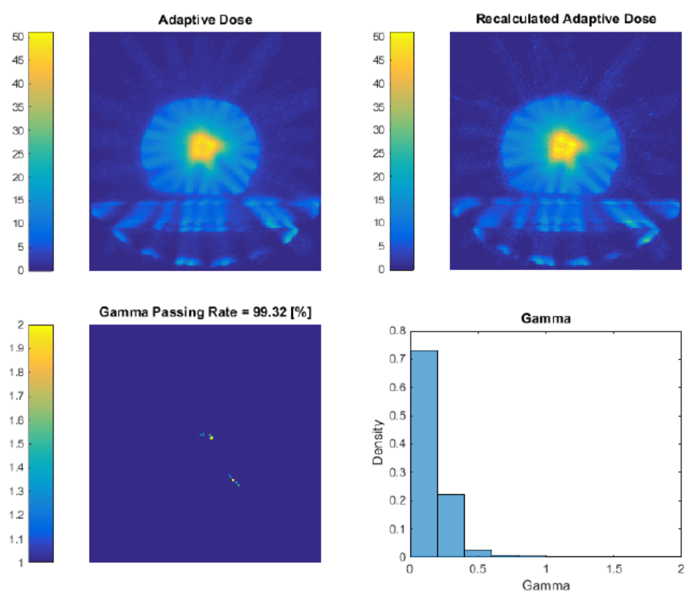
- If adaptive planning deemed necessary:
  - Re-optimization using initial planning beam angles and optimization parameters
  - Optimization parameters can be adjusted if necessary



Plan Quality Assurance

- Online adaptive QA tools:
  - Secondary Monte Carlo dose calculation
    - DVHs, Dosimetric metric parameters
    - 3D Gamma analysis
  - Sanity check:
    - Structure volumes
    - Beam bixel-time






```
Contour Name = Adaptive Contour Volume (Initial Contour Volume) [Ratio];
Skin                 = 15687.72 (19571.35) cc [0.80]
GatingTarget         = 4.25 (4.18) cc [1.02]
O_Stomach            = 216.53 (726.59) cc [0.30]
O_Hrt                = 535.37 (450.33) cc [1.19]
O_Livr               = 1267.22 (1374.42) cc [0.92]
G_per_pancreatic     = 9.64 (11.18) cc [0.86]
O_spleen             = 81.43 (123.70) cc [0.66]
O_Kdny_Rt            = 148.54 (148.59) cc [1.00]
O_Kdny_Lt            = 205.70 (179.91) cc [1.14]
O_Bwel               = 271.40 (1845.24) cc [0.15]
O_Panc               = 3.01 (19.44) cc [0.15]
O_Cord               = 56.29 (73.70) cc [0.76]
P_peri_panreatic_40  = 26.14 (30.58) cc [0.85]
O_Esgs               = 7.08 (12.23) cc [0.58]
AVOID                = 2.52 (2.85) cc [0.88]
```

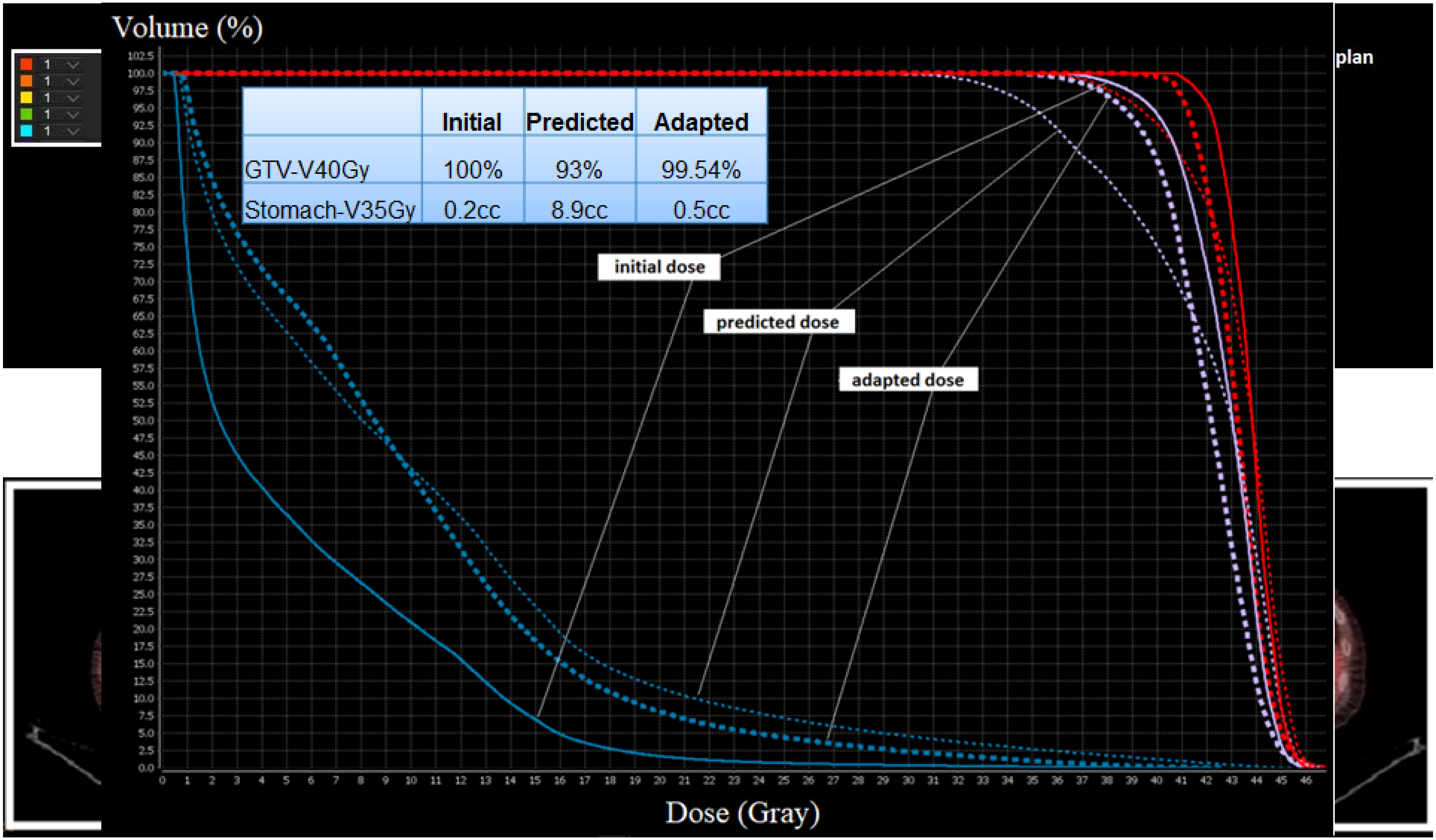
Cai et al. Z Med Phys 2017

Motion management – Soft tissue based gating

Gating based on breath hold

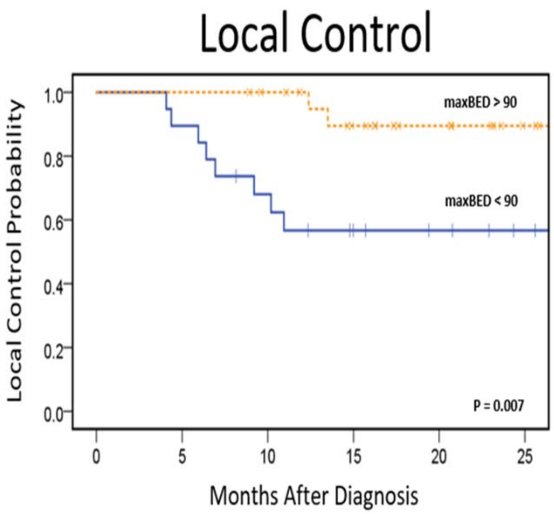
Before coaching

With coaching



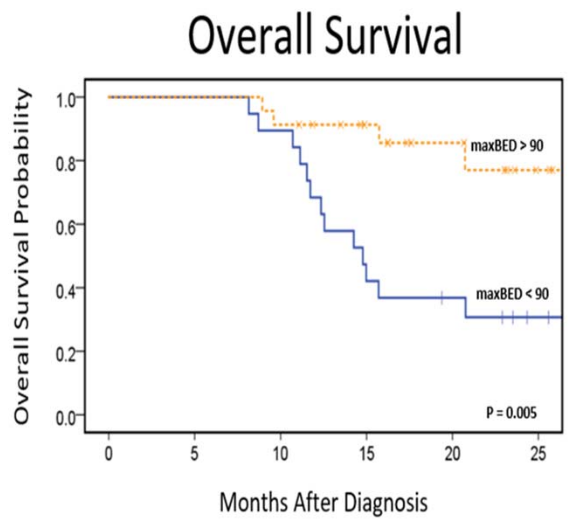
	Initial	Predicted	Adapted
GTV-V40Gy	100%	93%	99.54%
Stomach-V35Gy	0.2cc	8.9cc	0.5cc

Early Clinical Data: Efficacy and Toxicity of MRgRT for Pancreas Cancer



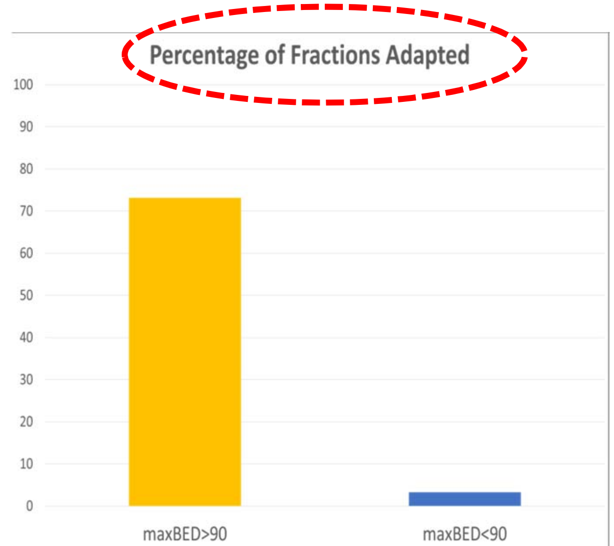
No. at Risk

	0	5	10	15	20	25
maxBED > 90	23	23	21	15	10	4
maxBED < 90	19	17	12	7	5	2



No. at Risk

	0	5	10	15	20	25
maxBED > 90	23	23	21	16	11	5
maxBED < 90	19	19	17	8	6	2



Gr 3+ GI Toxicity	
$maxBED_{10}>90$	0%
$maxBED_{10}<90$	15.8%

Challenges for online adaptive planning

- Image quality:
  - Tumor conspicuity and soft tissue contrast
  - Image artifacts (motion)
- Plan quality:
  - Contour quality
  - Electron density accuracy
  - Re-planning/optimization
  - Plan QA/QC
- Other factors:
  - Time and process management
  - Decision making
  - Staff coordination and training

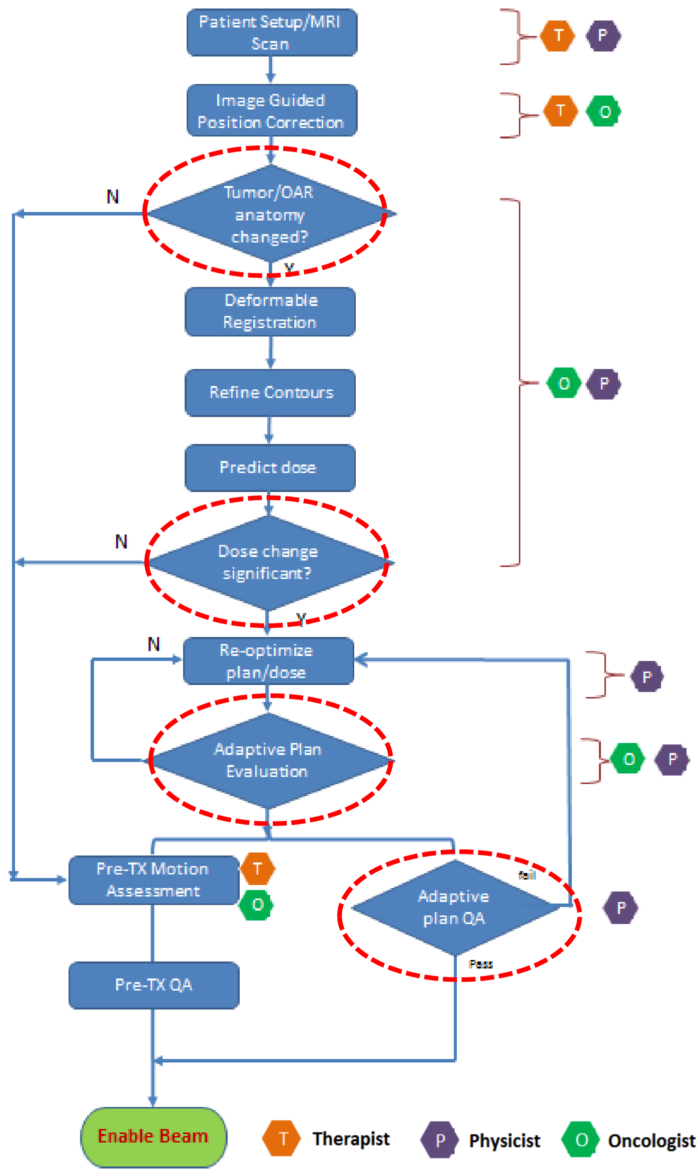
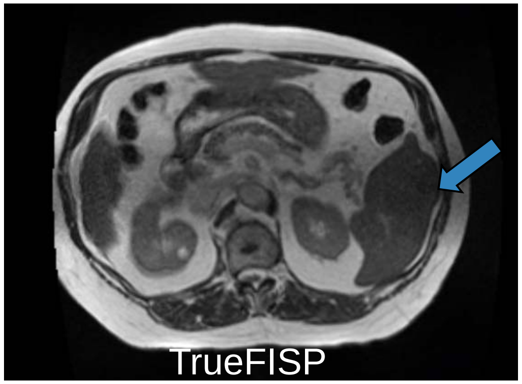
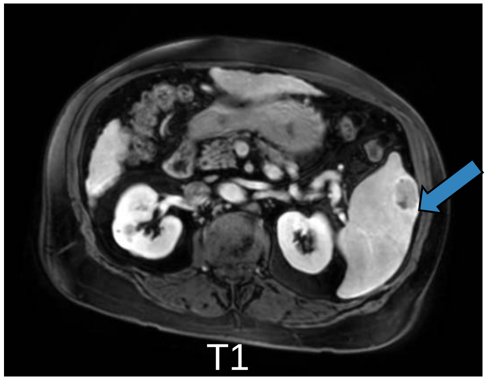


Image quality

- Sub-optimal soft tissue contrast with TrueFISP sequence

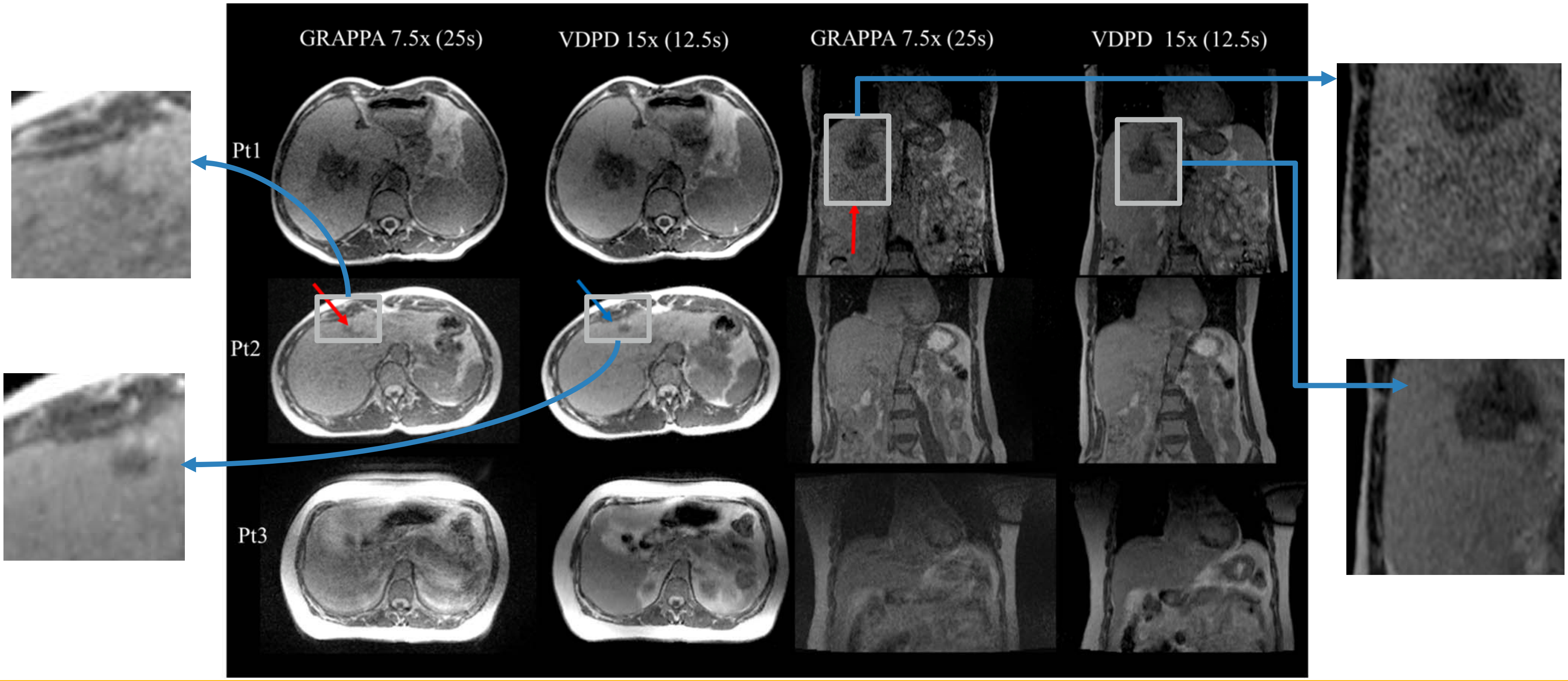




- MRI is prone to motion artifacts due to volumetric acquisition with slow K space sampling

Accelerated 3D Balanced SSFP imaging

- Variable-density Poisson-Disk (VDPD) technique with 15x under-sampling (12.5s)



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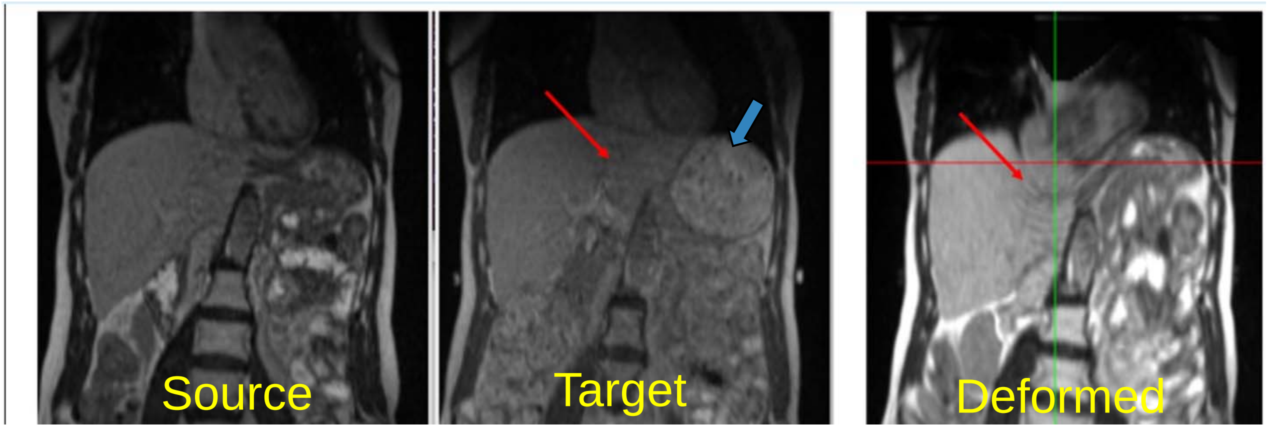
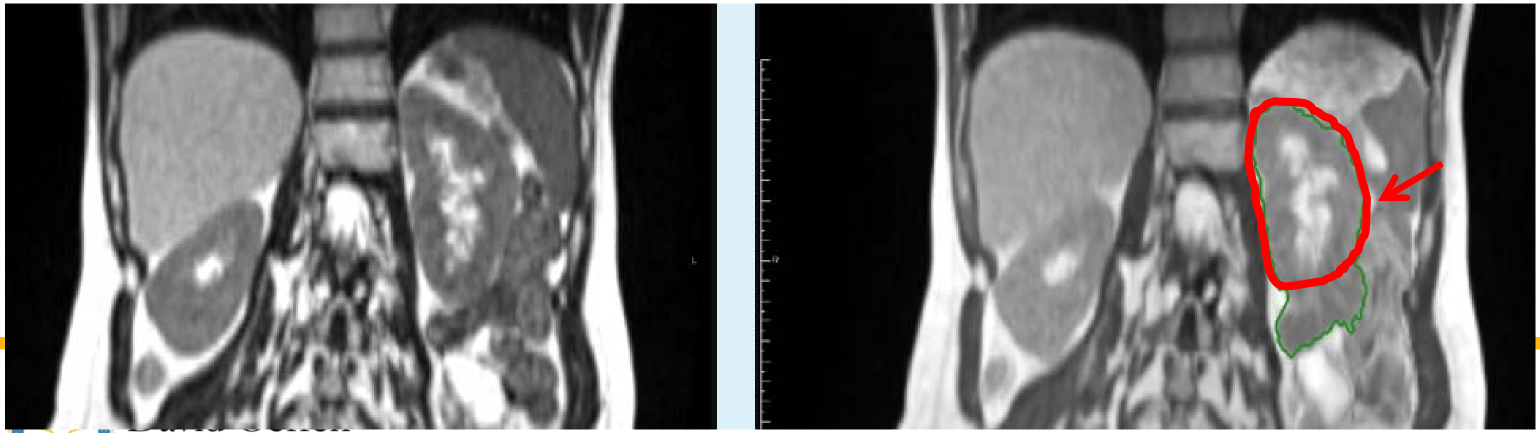
Courtesy of Dr. Yingli Yang

Quality and Efficiency of Contouring

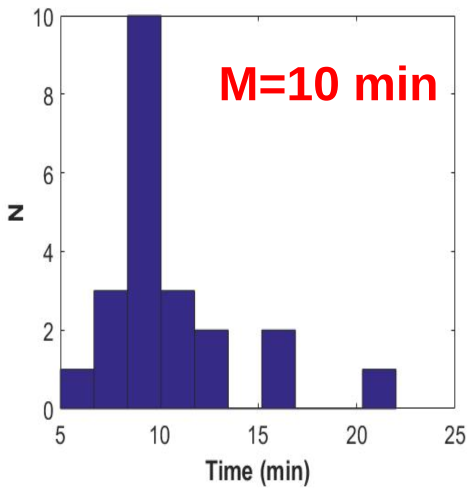
- Heavily replies on deformable image registration
- Usually requires labor-intensive manual correction



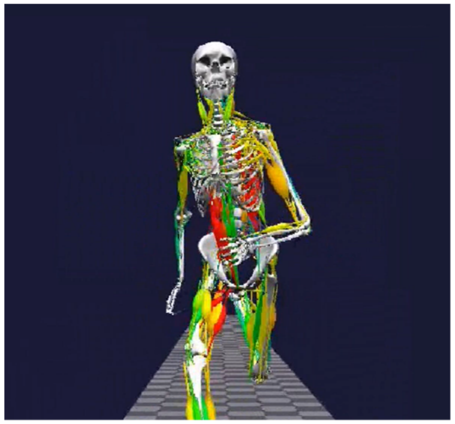


Automated contour segmentation

- Advanced auto-segmentation approaches:
  - Statistical shape model
  - Statistical appearance model
  - Machine learning based model
  - Biomechanical model
    - Rigidity of bones
    - Elasticity of organs
    - Boundary conditions between tissues



Time for adaptive re-contour

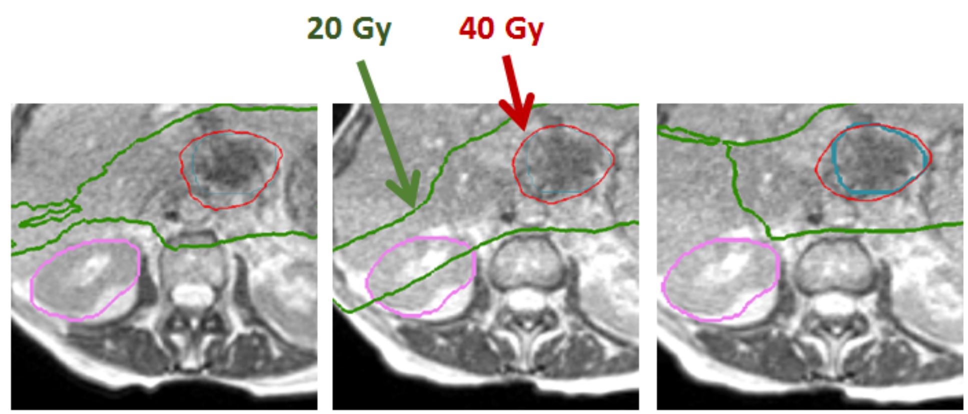


Sharp et al. Medical Physics, Vol. 41, No. 5, 2014

Biomechanics Of Bodies: bob-biomechanics.com

Re-planning/optimization

- With limited time, how to achieve the best possible plan dosimetry?
  - Quality of the initial plan is important
  - Improvement of optimization algorithm
  - Beam angle optimization
  - Knowledge based planning



Original plan | 1st adaptive plan | 2nd adaptive plan

Planning algorithms doesn’t know to avoid the kidney if minimal priority is not given – human judgement crucial

Process management and improvement

- Compressing many days of work in one setting with patient on table
- Median time of the adaptive process is about 24 minutes
- Room for improvement
    - Improve image acquisition speed and quality
    - Contouring accuracy and efficiency
    - Re-planning and QA efficiency
    - Staff training, coordination and communication

→ ***Automation to maximize efficiency, quality and safety***

Minimizing errors through application of risk analysis

Lamb J, Cao M, Kishan A, et al. Cureus 9(8): e1618

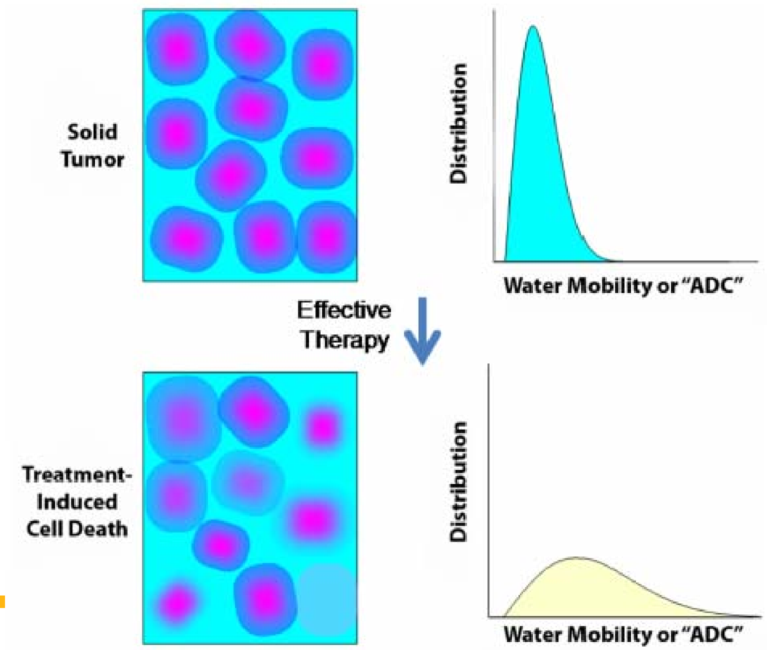
Functional imaging as biomarker

- Tumor exhibits complex and heterogeneous microenvironment
- Biological changes may occur before detectable morphological changes
- Functional MRI imaging as a biomarker to assess radiation treatment response:

Biological Processes	Modalities
Metabolism	1H -13C- MR Spectroscopic imaging (MRSI)
Hypoxia	Blood Oxygenation Level-Dependent (BOLD) MRI
Proliferation/Apoptosis	Diffusion Weighted MRI
Angiogenesis	Dynamic Contrast Enhanced (DEC) MRI

Diffusion weighted MRI (DWI)

- A technique to measure the movement of water molecules at cellular level through MR gradients
- Water perfusion and diffusion are influenced by **tissue cellularity**, tissue organization and extracellular space tortuosity and cell membrane function etc.
- Non-invasive and quantitative
- Dose not require any exogenous contrast agent
- Biomarker to assess treatment response



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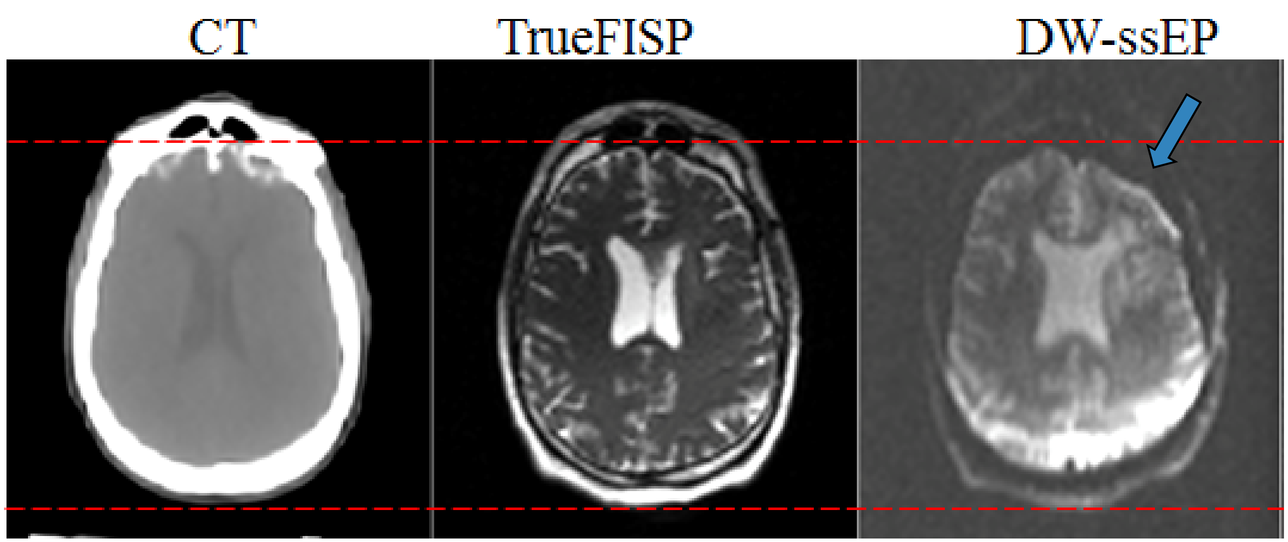
Thoeny et al. J Magn Reson Imaging. 2010 32(1): 2–16.

Sequence for DWI

- Standard diagnostic sequence: single-shot echo-planar-imaging (ssEPI)

+ Rapid acquisition
+ Less susceptible to ghosting

- Low SNR
- Low spatial resolution
- **Severe geometric distortion**



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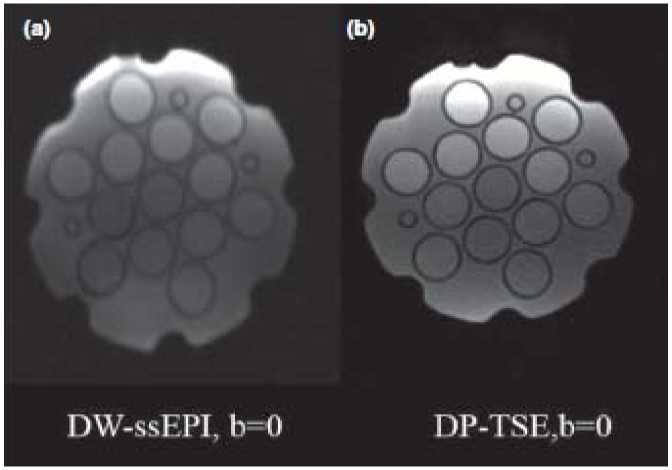
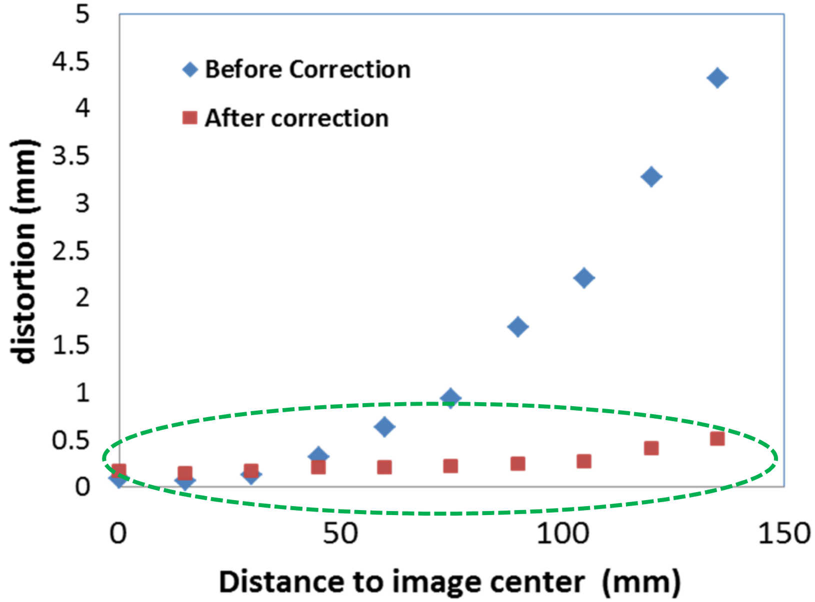
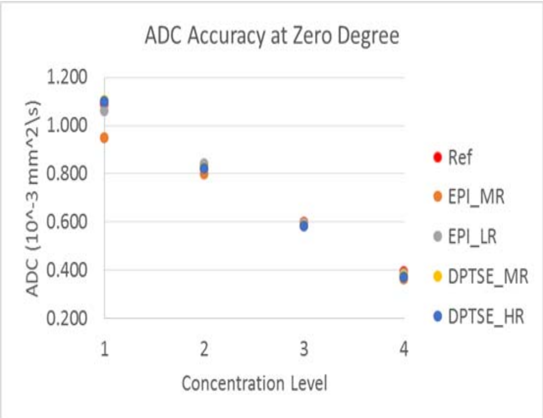
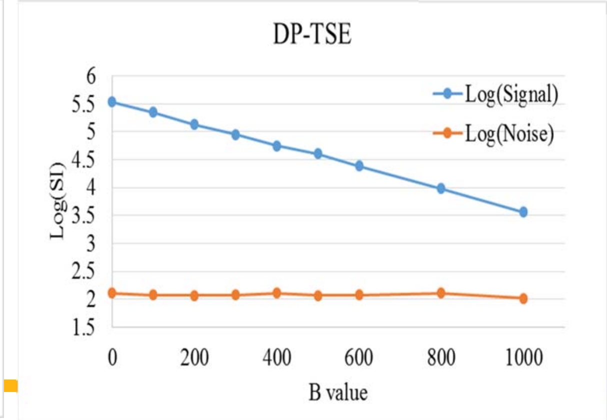
Gao et al. Medical Physics, 44 (10), 2017

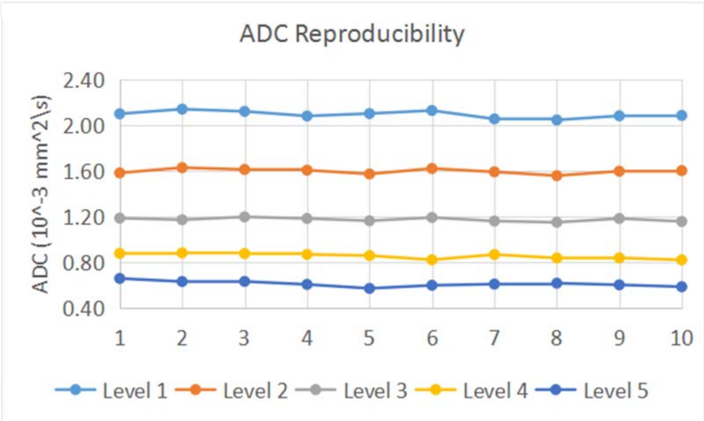
Turbo spin echo (TSE) based DWI sequence











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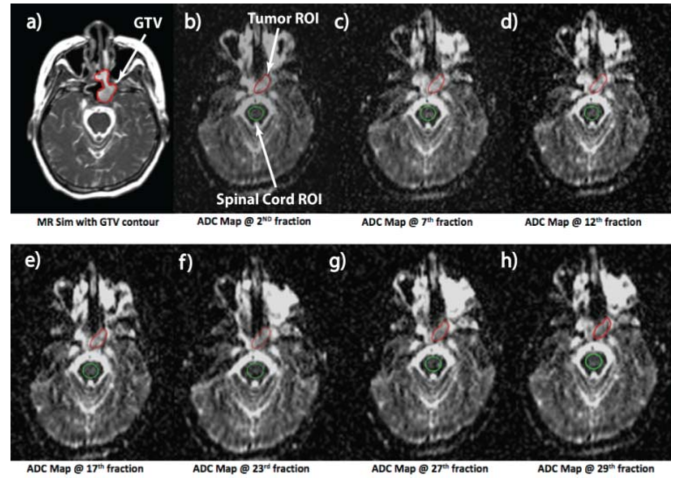
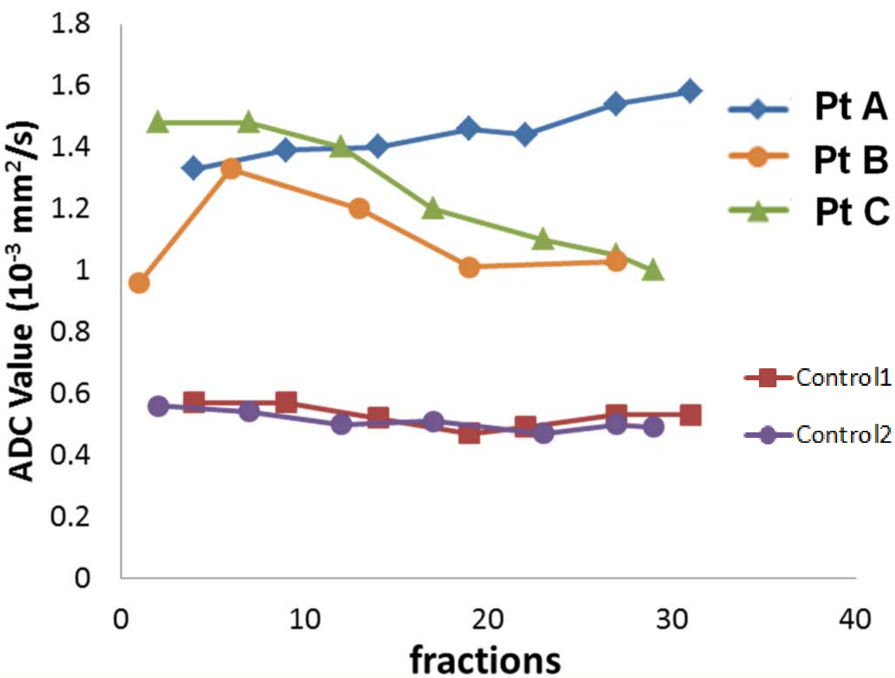
GAO et al. Medical Physics, 44 (10), 2017

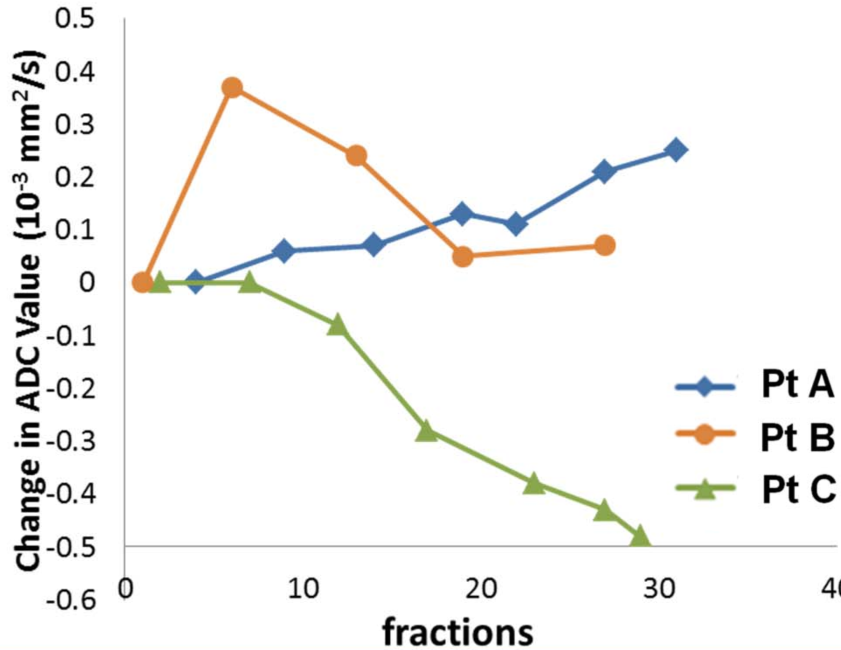
Medical Physics
The International Journal of Medical Physics Research and Practice

Longitudinal diffusion MRI for treatment response assessment: Preliminary experience using an MRI-guided tri-cobalt 60 radiotherapy system

Yingli Yang, Minsong Cao, Ke Sheng, Yu Gao, Allen Chen, Mitch Kamrava, Percy Lee, Nzhde Agazaryan, James Lamb, David Thomas, Daniel Low, and Peng Hu







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Summary

- MRIgRT has tremendous potential in personalized precision-guided radiotherapy
- MRI-guided adaptive radiotherapy may become a new RT paradigm that allows us to offer high quality and personalized patient care
- Opportunities for improvement include high quality and fidelity imaging, better motion management and efficient adaptive workflow as well as biological and functional based adaption

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