MR Guidance and Online Adaptation of Liver and Pancreas Patients

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Miami Cancer Institute
BAPTIST HEALTH SOUTH FLORIDA

KateMRGuidance

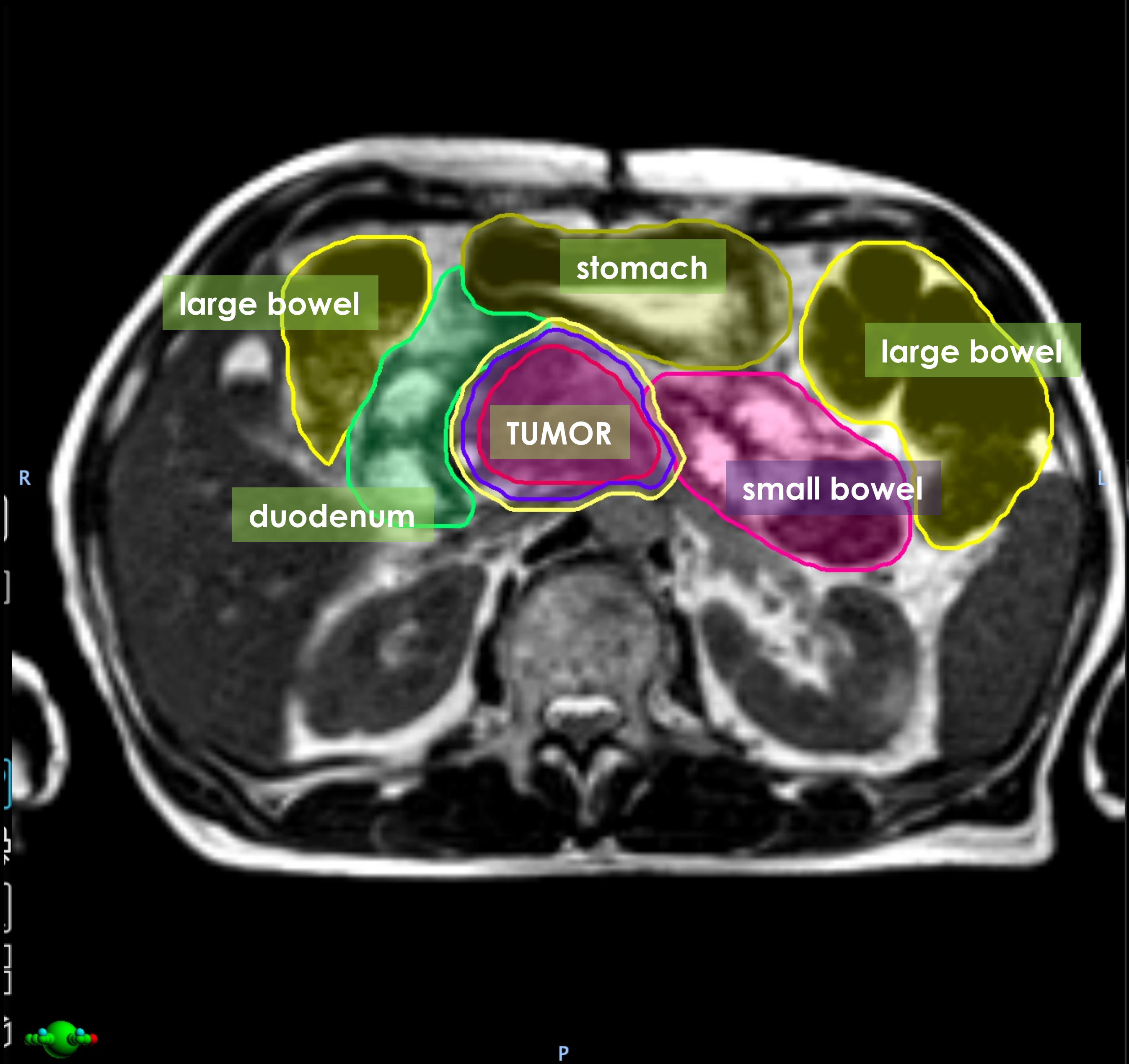
Disclosure

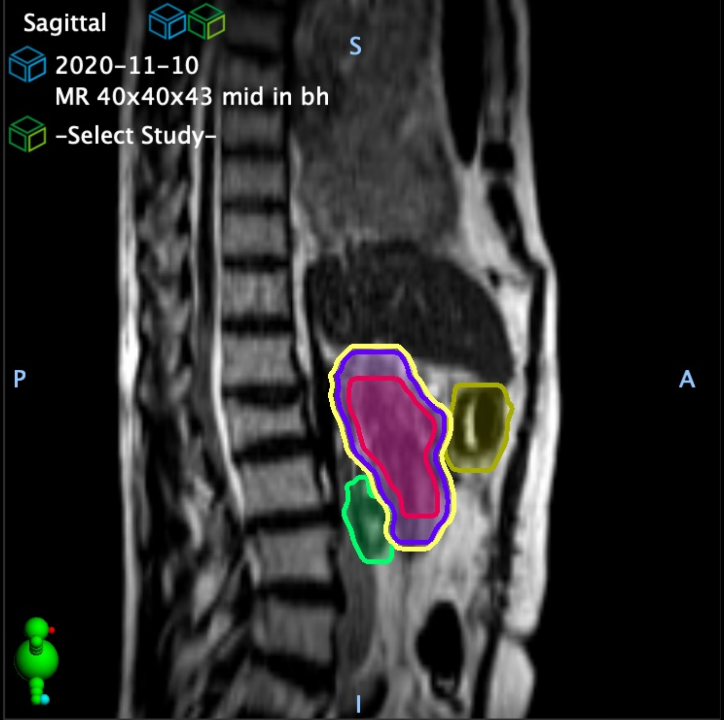
- Employer: Miami Cancer Institute, Staff Medical Physicist
- Affiliate: Florida International University, Assistant Professor
- Co-founder: MR Guidance, LLC
- Research Agreement: ViewRay Inc.

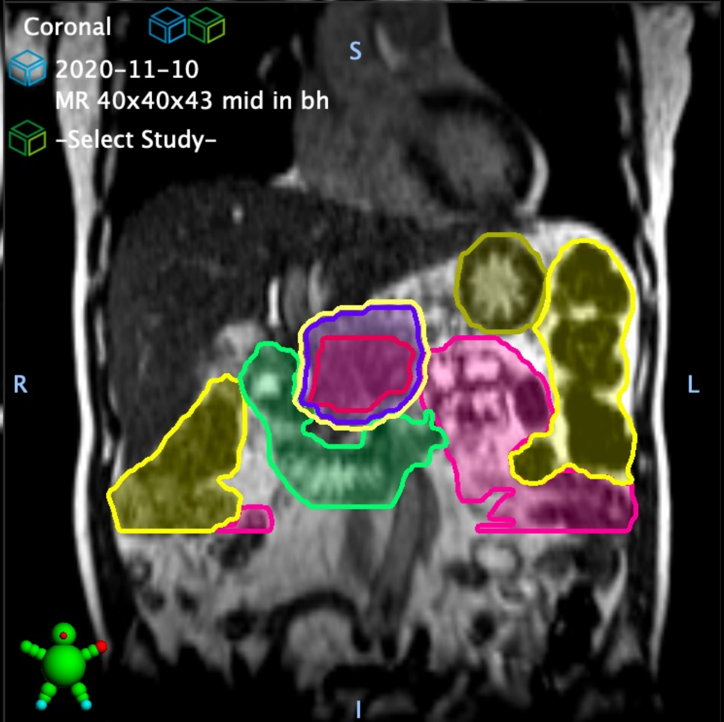
Learning objectives

- Understand the clinical rationale for MR-guided adaptive radiation therapy for pancreatic and liver cancers
- Learn importance of planning technique and robustness in online adaptation of abdominal SBRT
- Gain familiarity of current and future biological and AI initiatives in pancreas and liver ART

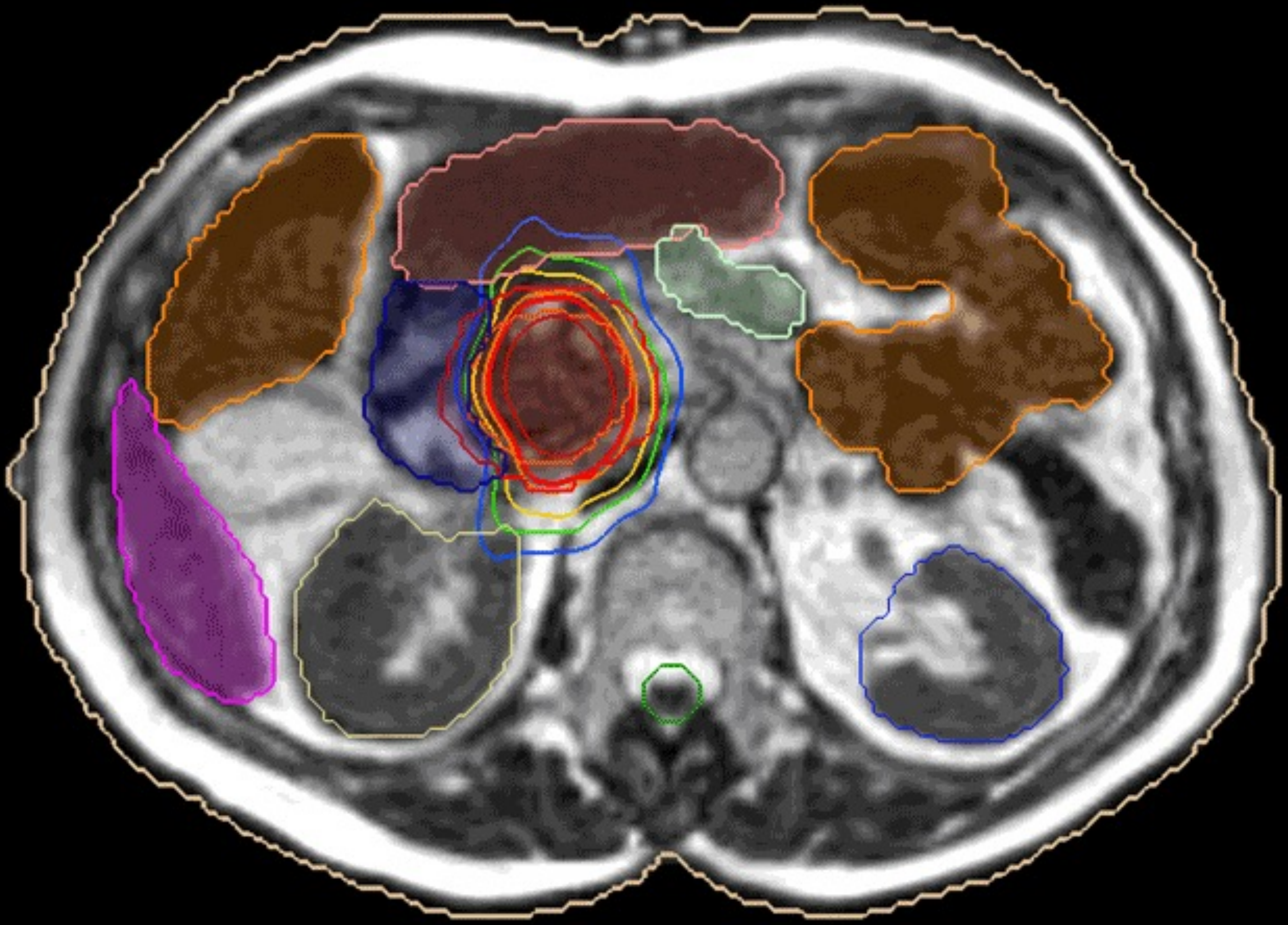
ART due to organ at risk changes







ART due to organ at risk changes



Day 1

Abdominal SMART BED 100 Gy is safe and safe

Radiotherapy & Oncology

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PHASE I TRIAL | VOLUME 126, ISSUE 3, P519-526, MARCH 01, 2018

PDF [1 MB] Figures Save Share Reprints Request

Phase I trial of stereotactic MR-guided online adaptive radiation therapy (SMART) for the treatment of oligometastatic or unresectable primary malignancies of the abdomen

Lauren Henke • Rojano Kashani • Clifford Robinson • ... Sasa Mutic • Parag Parikh • Jeffrey Olsen •

Show all authors

Open Access • Published: December 22, 2017 • DOI: https://doi.org/10.

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pro practical radiation oncology ASTRO

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BASIC ORIGINAL REPORT | VOLUME 11, ISSUE 2, P134-147, MARCH 01, 2021

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Ablative 5-Fraction Stereotactic Magnetic Resonance–Guided Radiation Therapy With On-Table Adaptive Replanning and Elective Nodal Irradiation for Inoperable Pancreas Cancer

Michael D. Chuong, MD • John Bryant, BS • Kathryn E. Mittauer, PhD • ... Vivek Mishra, PhD • Gustavo Luciani, CMD • Alonso N. Gutierrez, PhD, MBA • Show all authors

Open Access • Published: September 15, 2020 • DOI: https://doi.org/10.1016/j.pro.2020.09.005 •

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advances in radiation oncology ASTRO

SCIENTIFIC ARTICLE | VOLUME 4, ISSUE 1, P142-149, JANUARY 01, 2019

A Multi-Institutional Experience of MR-Guided Liver Stereotactic Body Radiation Therapy

Stephen A. Rosenberg, MD • Lauren E. Henke, MD • Narek Shaverdian, MD • Kathryn Mittauer, PhD • Andrzej P. Wojcieszynski, MD • Craig R. Hullett, MD, PhD • Mitchell Kamrava, MD • James Lamb, PhD • Minsong Cao • Olga L. Green, PhD • Rojano Kashani, PhD • Bhudatt Paliwal, PhD • John Bayouth, PhD • Paul M. Harari, MD • Jeffrey R. Olsen, MD • Percy Lee, MD • Parag J. Parikh, MD • Michael Bassetti, MD, PhD • Show less

Open Access • Published: August 22, 2018 • DOI: https://doi.org/10.1016/j.adro.2018.08.005 •

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PlumX Metrics

Received: 5 January 2019 | Revised: 12 February 2019 | Accepted: 26 February 2019
DOI: 10.1002/cam4.2100

ORIGINAL RESEARCH

WILEY Cancer Medicine Open Access

Using adaptive magnetic resonance image-guided radiation therapy for treatment of inoperable pancreatic cancer

Soumon Rudra[1] | **Naomi Jiang**[2] | **Stephen A. Rosenberg**[3] | **Jeffrey R. Olsen**[1] | **Michael C. Roach**[1] | **Leping Wan**[1] | **Lorraine Portelance**[4] | **Eric A. Mellon**[4] | **Anna Bruynzeel**[5] | **Frank Lagerwaard**[5] | **Michael F. Bassetti**[3] | **Parag J. Parikh**[1] | **Percy P. Lee**[2]

[1]Department of Radiation Oncology, Washington University School of Medicine, St. Louis, Missouri
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[4]Department of Radiation Oncology, Sylvester Comprehensive Cancer Center, University of Miami, Miami, Florida
[5]Department of Radiation Oncology, VU University Medical Center, Amsterdam, Netherlands

Correspondence
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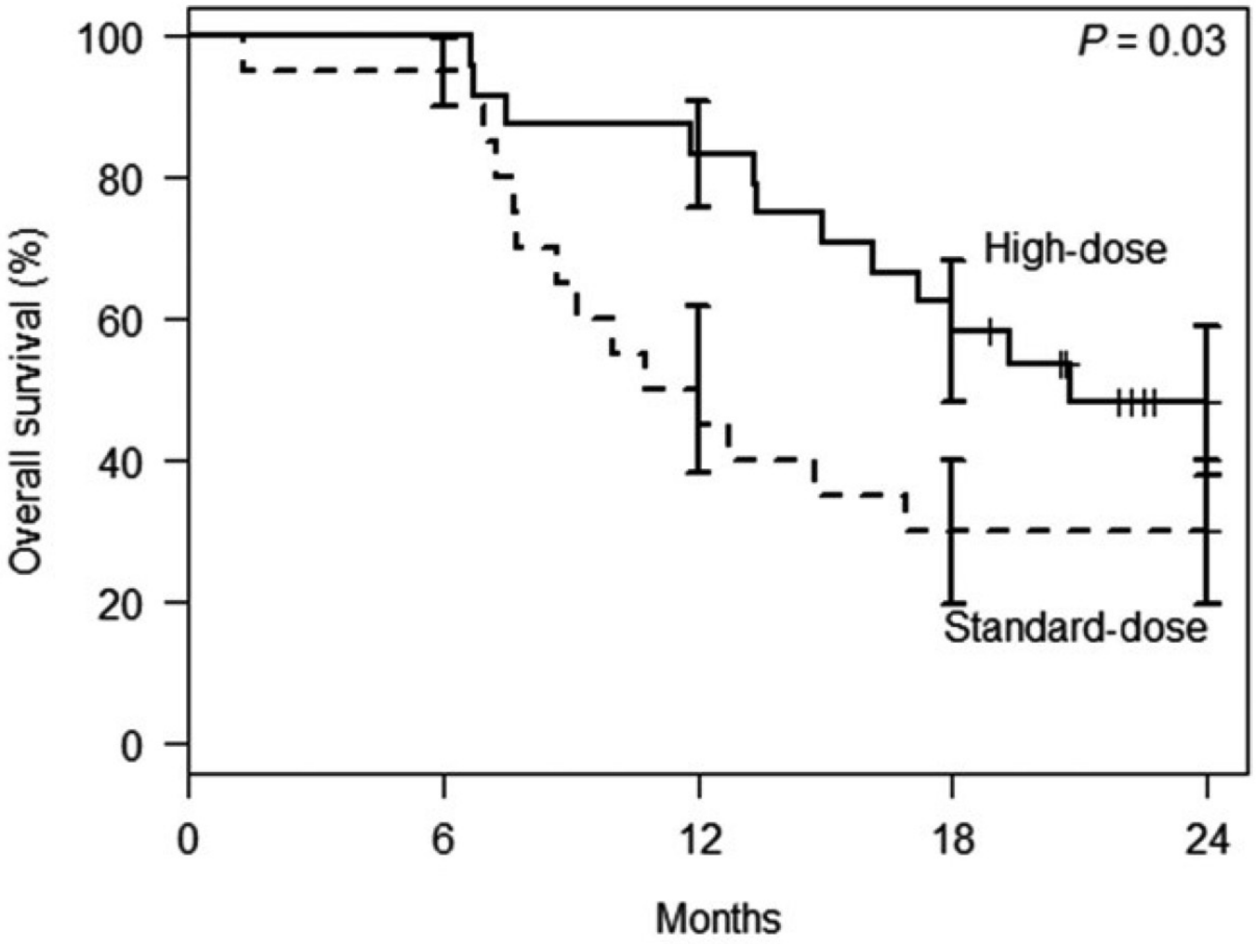
Email: pparikh2@hfhs.org

Online Adaptation: Overall Survival

2-yr OS 49% vs 30%



High-dose	24	24	20	14	5
Standard-dose	20	19	10	6	5

FIGURE 1 Overall survival from start of radiation therapy stratified by biologically effective dose (BED_{10}). Standard error bars displayed at each 6-mo timepoint

Prospective phase II Study of Stereotactic MR-guided on-table Adaptive Radiation Therapy (SMART) for Patients with Borderline or Inoperable Locally Advanced Pancreatic Cancer

Principal Investigators:

Parag Parikh, MD, BSE
Director, MR-guided Radiation Therapy and GI Radiation Oncology
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Section Chief of Thoracic Radiation Oncology
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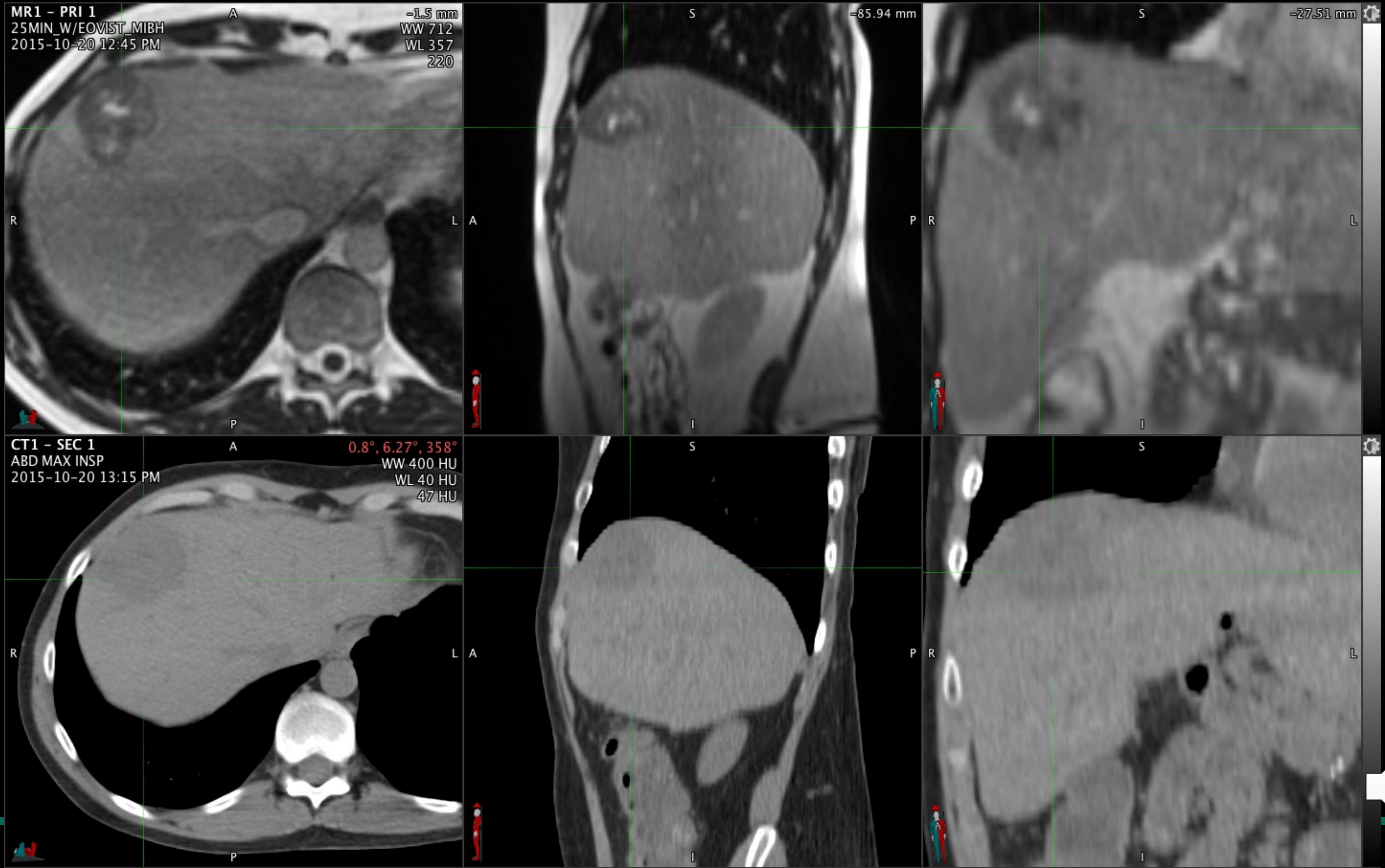
Director, Medical Physics Residency
Chief of Service, MR-IGRT
Washington University
St. Louis, MO

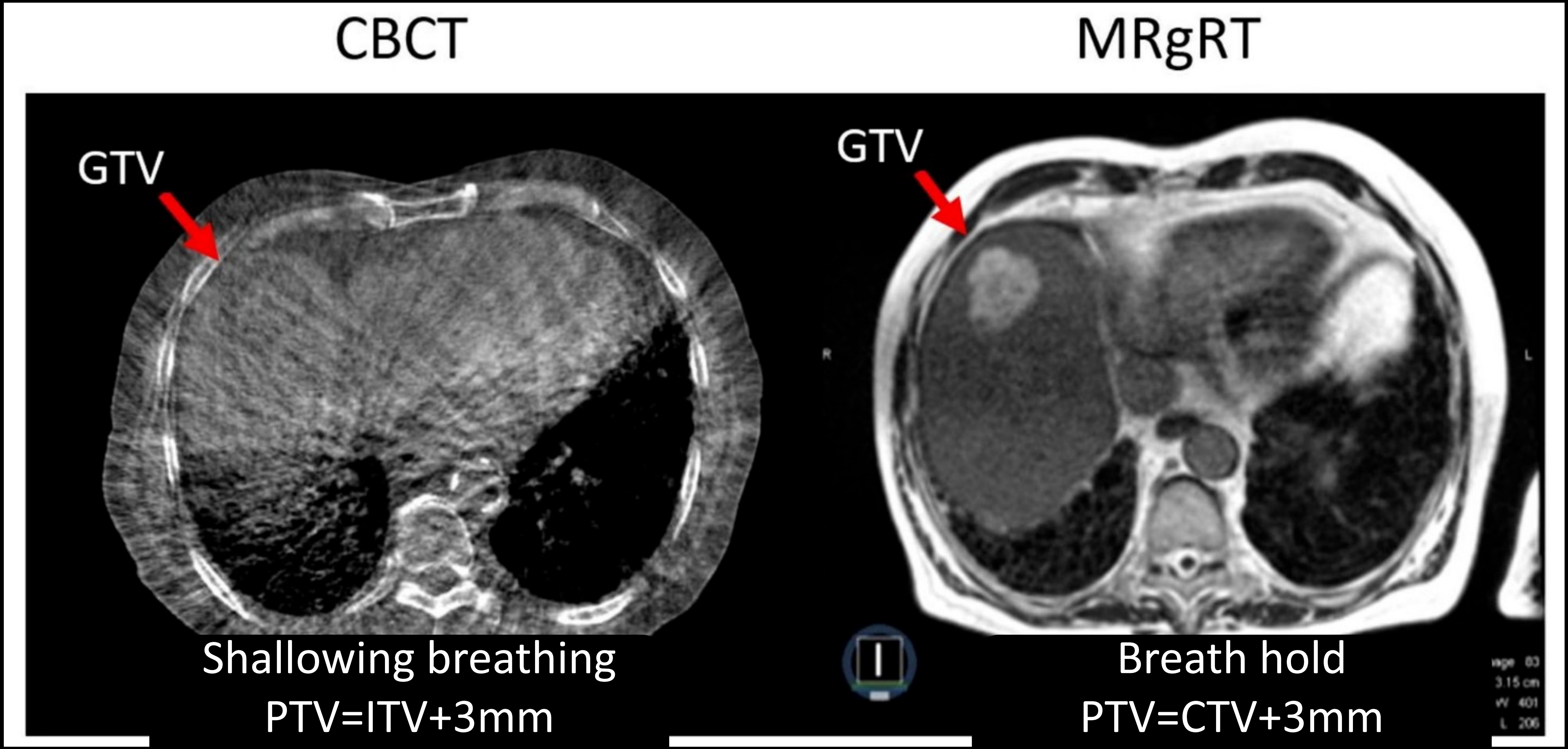
MRgRT offers superior soft tissue for simulation and each fraction

Simulation MRI

Simulation CT



MRgRT-BH may enable reduction target volume over CT-IGRT-FB and potentially reduce GI OARs dose in adaptive RT



Shallowing breathing
PTV=ITV+3mm
~140 cc

Breath hold
PTV=CTV+3mm
~120 cc

K. Mittauer, B. Paliwal, P Hill, J. E. Bayouth, M. W. Geurts, A. M. Baschnagel, K. A. Bradley, P. M. Harari, S. Rosenberg, J. V. Brower, A. P. Wojcieszynski, C. Hullett, R A. Bayliss, Z. E. Labby, M. F. Bassetti, "A New Era of Image Guidance with Magnetic Resonance-guided Radiation Therapy for Abdominal and Thoracic Malignancies," Cureus 2018.

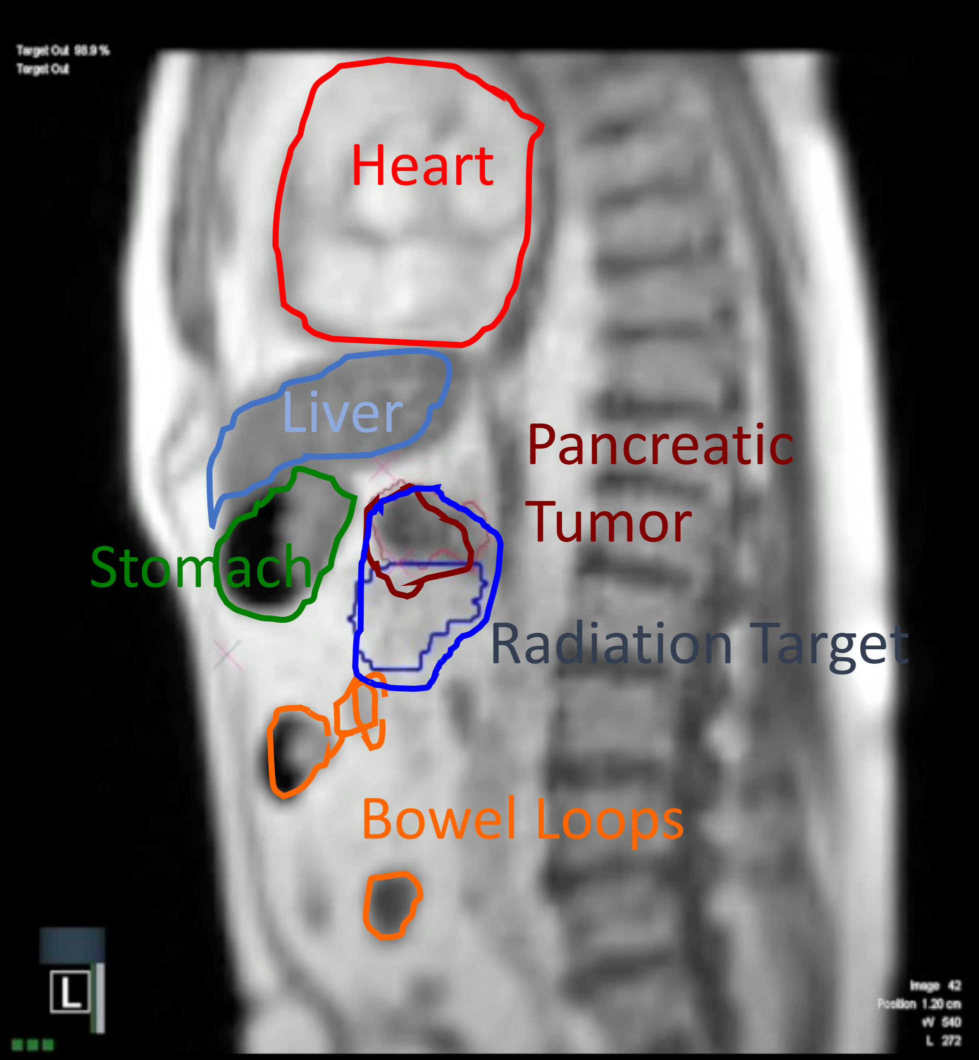
Role of real-time MR intrafraction motion management when delivering ablative dose near GI OARs

Beam off

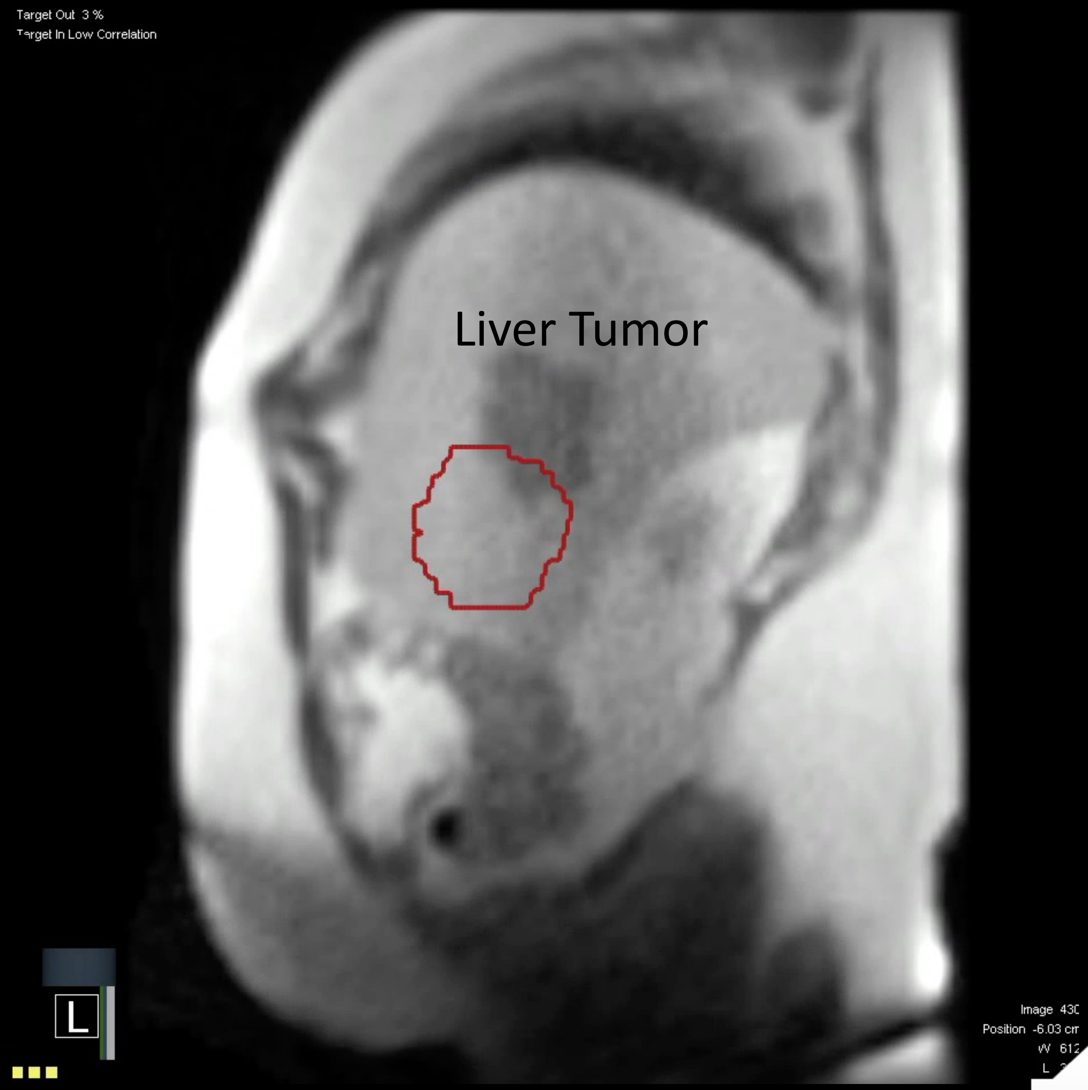
Beam on

K. Mittauer, B. Paliwal, P Hill, J. E. Bayouth, M. W. Geurts, A. M. Baschnagel, K. A. Bradley, P. M. Harari, S. Rosenberg, J. V. Brower, A. P. Wojcieszynski, C. Hullett, R A. Bayli … E. Labby, M. F. Bassetti, “A New Era of Image Guidance with Magnetic Resonance-guided Radiation Therapy for Abdominal and Thoracic Malignancies,“ Cureus 2018.

Ablative dose near critical GI likely benefit from real-time intrafraction management



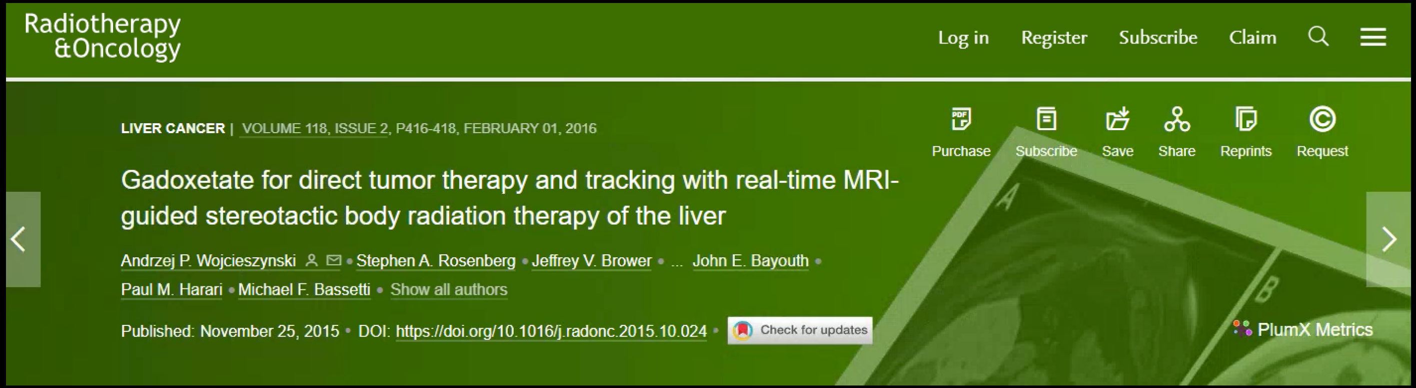
MR sagittal plane real-time tracking in pancreas SBRT



MR sagittal plane real-time tracking in liver SBRT

Gadoxetic acid for target delineation in liver SMART

- Gadobenate dimeglumine (Gd-BOPTA; Eovist™/Primovist™) and gadoxetate disodium (Gd-EOB-DTPA; MultiHance™) are liver-specific gadolinium-based MR contrast agents.
- Mechanism: Gadoxetic acid distributes into hepatocytes and the biliary tract system in a late, hepatobiliary phase. This allows for a differentiation of hepatocytes from neoplastic cells, which do not show a gadoxetic acid uptake
- **Visualization for metastases as well as some primary HCC and CC**
- **Heptaobiliary phase targeted for MRgRT localization and real-time tracking—Wojcieszynski et al, 2016**



Five phases:

1. T1W precontrast
2. late arterial (30-35 sec)
3. portal venous (~75 sec)
4. "transitional" (~3 min)
5. **Hepatobiliary (~20 min to 1 hour with Gadoxetate disodium and 1-3 hours for Gadobenate dimeglumine)**

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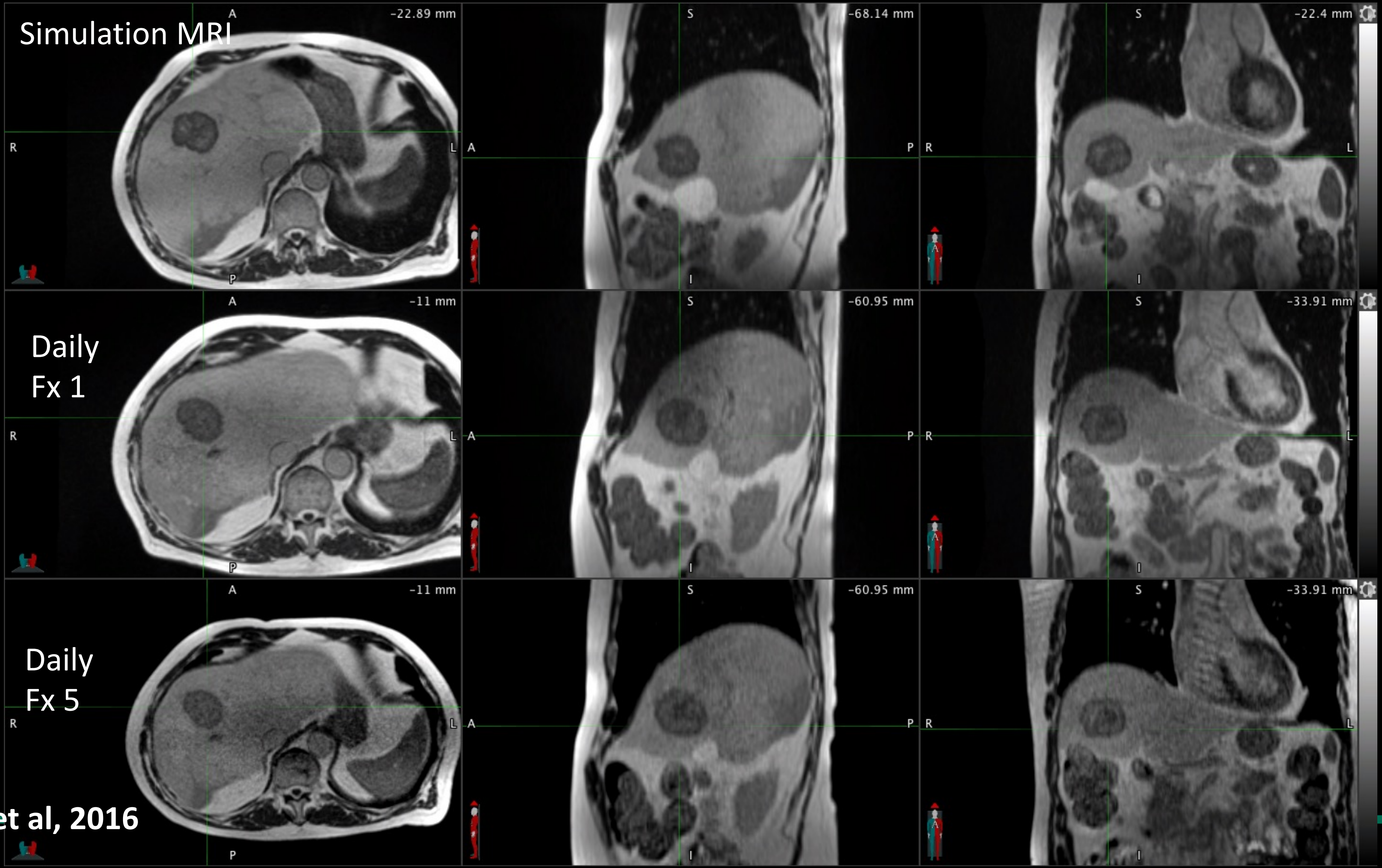
https://cortex.acr.org/RadsPreview

Daily Gadoxetic contrast for liver SMART to enable accurate liver tumor delineation/localization/tracking



Wojcieszynski et al, 2016

On-table MR-guided ART clinical workflow

Positioning → Deformation → Contouring → Plan re-optimization → Plan quality evaluation → Treatment

Positioning

THERAPIST: Image and registration of scan of the day to initial to simulation scan

PHYSICIAN: Verify localization for SBRT

Contouring

PHYSICIAN: Edit deformed contours

PHYSICIST: Evaluate deformed electron density; edit deformed contours; apply contour Boolean operations and margin expansion

Plan re-optimization

PHYSICIST: Plan generation; Compare adaptive plan to initial plan recalculated on anatomy of the day

Plan quality evaluation

PHYSICIAN: Plan quality review

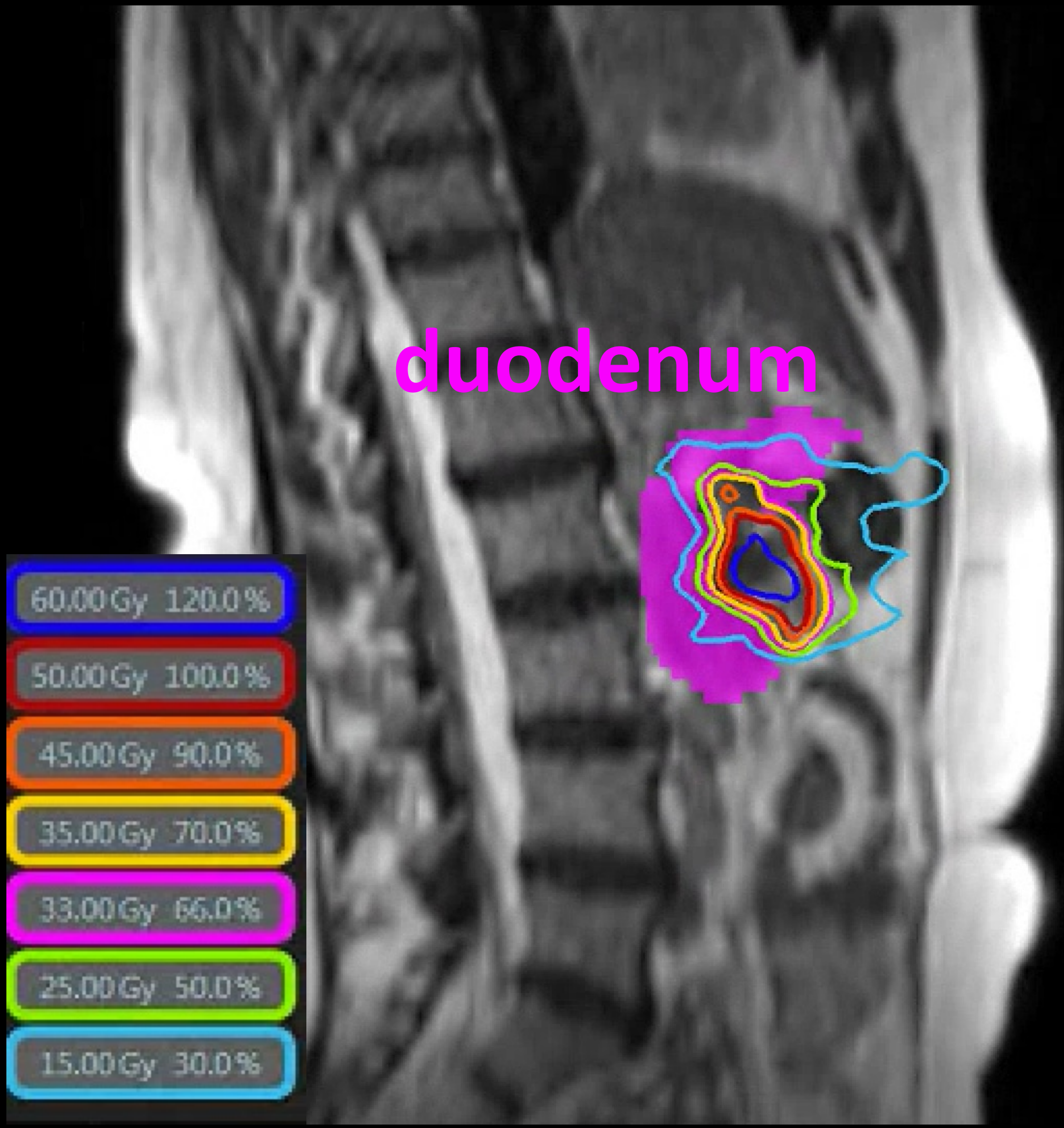
PHYSICIST: Plan QA through secondary dose calculation

Treatment

THERAPIST: Treatment delivery

Hill P and Mittauer K, "MR-guidance in radiation therapy, " AAPM Summer School, 2018

Intrafraction gastroduodenal peristalsis can result in overdose of GI OAR



Video speed x4

Potential sources of error in MR-guided online ART

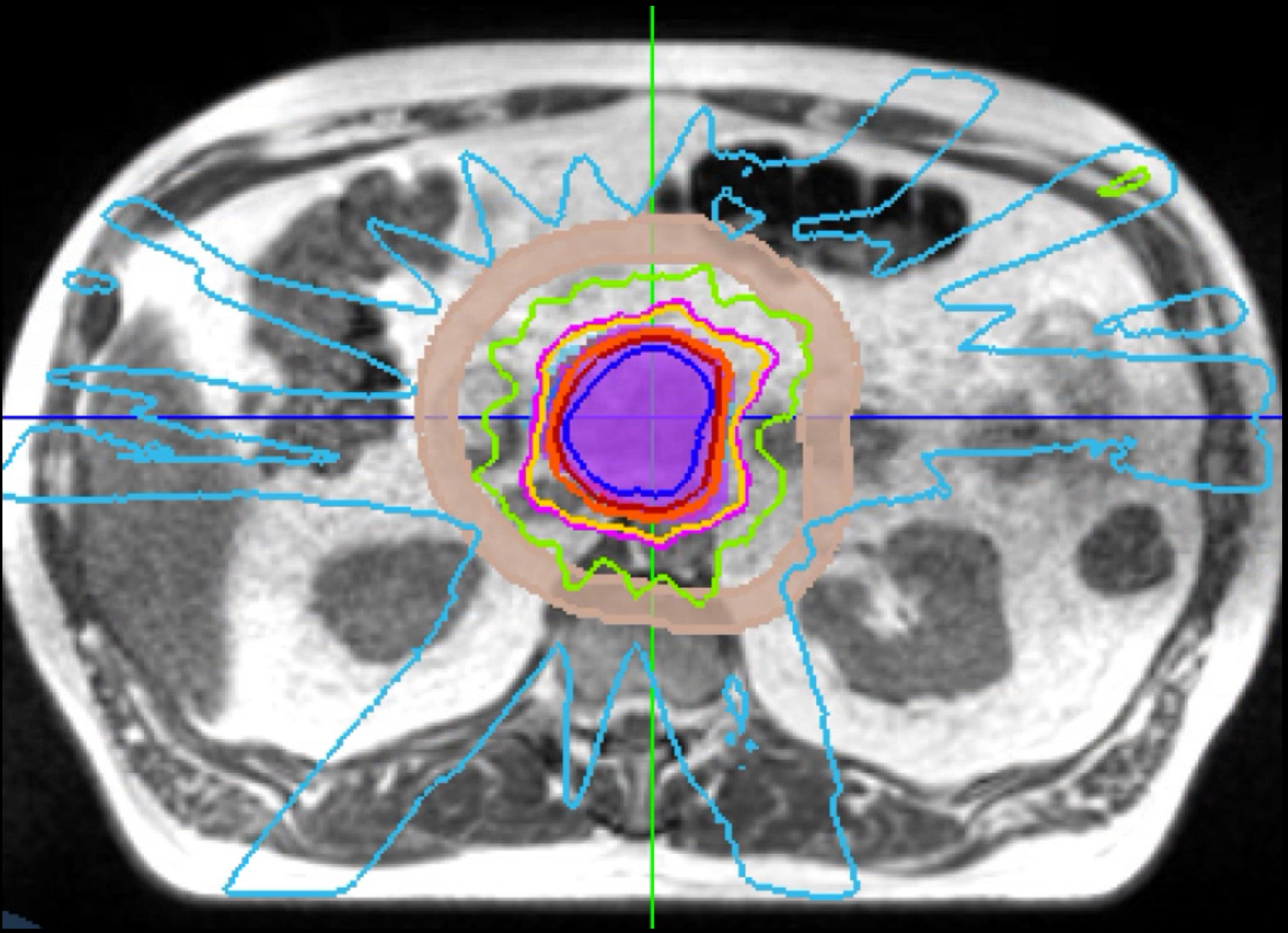
1. Scan FOV
2. Electron density
3. Segmentation
4. IMRT plan fidelity (non-measured based IMRT QA)
5. Out of date anatomy during ART replanning (i.e., intrafraction GI peristalsis)
6. Cumulative dose from summed ART fractions

Positioning → Deformation and electron density → Contouring → Predict dose and plan re-optimization → Plan quality evaluation → Post-treatment

- Overcome with checklists, workflow checks/hard stops, secondary observer

Positioning → Deformation and electron density → Contouring → Predict dose and plan re-optimization → Plan quality evaluation → Post-treatment

How to adapt robustly with large GI interfractional anatomical changes?



Rx Dose = 50.00 Gy

Dose (Gy)	Rx (%)
60.00	120.0
50.00	100.0
45.00	90.0
35.00	70.0
33.00	66.0
25.00	50.0
15.00	30.0

Table 1 Organ at risk constraints for 5-fraction pancreas stereotactic magnetic resonance image guided adaptive radiation therapy

Organ at risk	Dose constraint
Stomach, duodenum, small bowel	V35 <0.5 mL V40 <0.03 mL
Large bowel	V38 <0.5 mL V43 <0.03 mL
Kidneys	Mean <10 Gy
Liver	Mean <15 Gy
Spinal cord	V25 <0.03 mL

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How to adapt robustly?

- Adequate # of beam angles. Enables degrees of freedom for dynamic changes to fluence based on anatomical geometry of the day
- Optimization structures that auto-populate, particularly in regions of target and OAR overlap
- Optimization objectives based on these overlapped regions with differential gradients based on spatial position
- Conformality is king. Rings can eliminate dose spillage
- A hotspot driver away from overlap region of the OAR. Eliminates hotspot being in unsafe location on anatomy of the day
- Simple is better. Elimination of potential conflicting objectives for future adaptive anatomical geometries.
- Standardization is key. Allows for ease and feasibility for cross-coverage of users and ability to apply manual updates to optimization objectives without a priori plan knowledge
- A class solution is ideal. A set of optimization objectives and geometric beam arrangements that are sufficiently robust to produce a clinically acceptable dose distribution regardless of the patient anatomy, target volume or organs at risk

Chow et al 2021, O. Bohoudi et al 2017, J.E. van Timmeren 2020, Clark et al 2017

Defining the gradient with OAR intersection of rings and ANN-based optimization objectives —the AUMC approach

Bohoudi O, Bruynzeel AME, Senan S, Cuijpers JP, Slotman BJ, Lagerwaard FJ, Palacios MA. Radiother Oncol. 2017 Dec;125(3):439-444

Plan quality: baseline plan versus adaptive plan —AUMC approach

	Baseline plans				Plans Fx			
	SMART $_{3CM}$-baseline		FULLOAR-baseline		SMART $_{3CM}$ -adaptive		FULLOAR-adaptive	
	mean	(range)	mean	(range)	mean	(range)	mean	(range)
PTV V $_{95\%}$ (Gy)	89.4	(74.0–95.1)	89.4	(74.0–95.1)	89.6	(66.5–99.0)	89.6	(66.5–99.0)
PTV D $_{mean}$ (Gy)	43.7	(42.4–44.8)	43.1	(41.7–43.9)	44.0	(40.9–45.9)	43.0	(40.4–44.6)
PTV D $_{1cc}$ (Gy)	50.6	(49.4–53.2)	50.0	(48.6–51.3)	50.9	(46.7–53.6)	49.9	(46.0–53.4)
HI	1.28	(1.24–1.34)	1.26	(1.22–1.31)	1.28	(1.17–1.34)	1.26	(1.16–1.35)
CI	1.18	(0.91–1.34)	1.17	(0.91–1.32)	1.19	(0.81–1.41)	1.17	(0.75–1.40)
Beam-on time *	9.16	(7.85–11.3)	9.20	(8.48–10.5)	9.24	(7.11–12.9)	8.89	(7.07–11.1)
Segments	52	(36–79)	50	(31–80)	51	(33–76)	45	(30–73)
Optimizations **	4	(2–6)	18	(12–22)	1	(1–1)	1	(1–1)

Bohoudi O, Bruynzeel AME, Senan S, Cuijpers JP, Slotman BJ, Lagerwaard FJ, Palacios MA. Radiother Oncol. 2017 Dec;125(3):439-444

ART robustness and stability—the MCI approach

AAPM 2021
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Session: Imaging in Treatment Planning [Return to Session]

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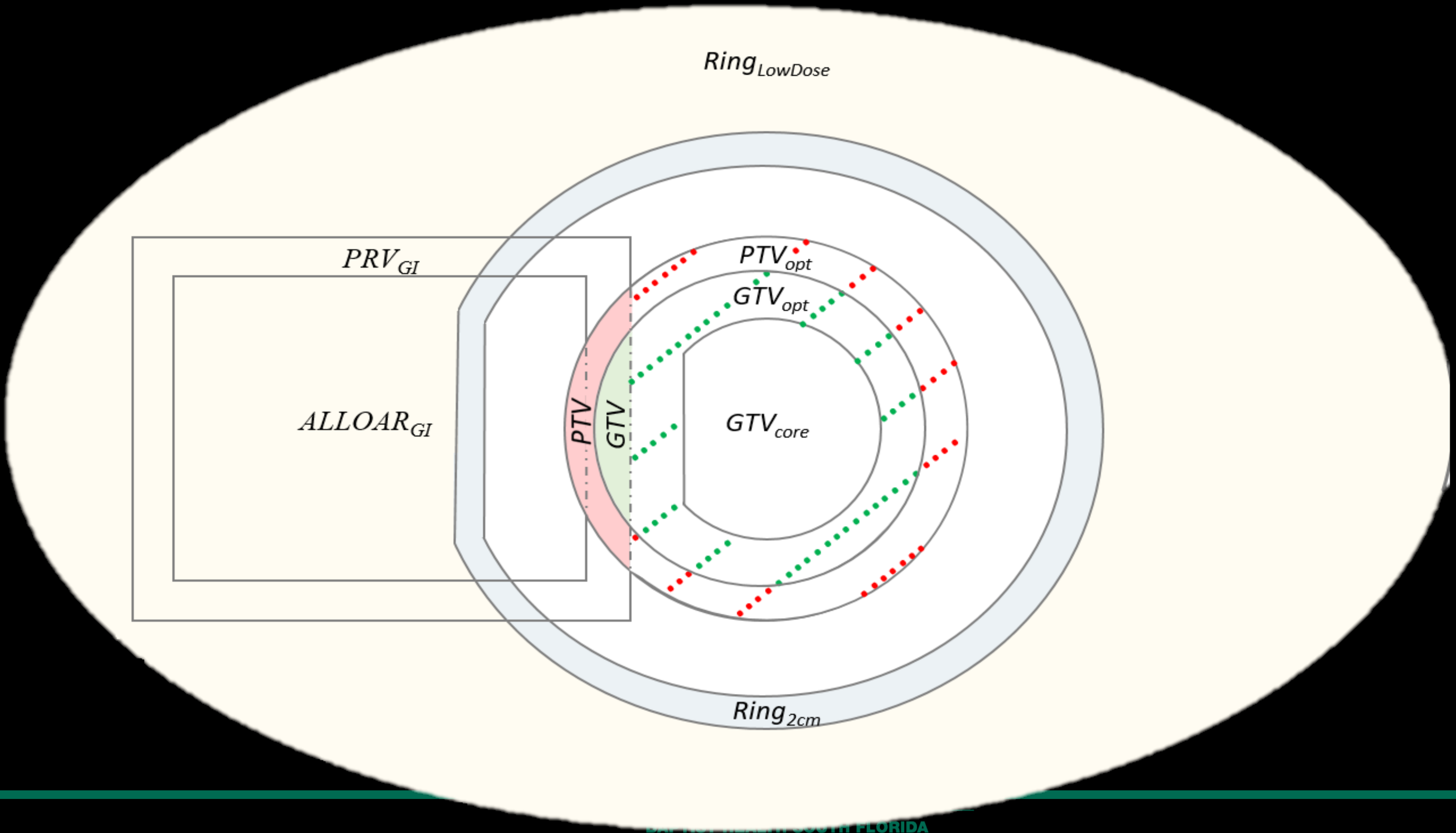
Online Adaptive Radiotherapy: Assessment of Planning Technique and On-Table Adaptive Plan Quality

K Mittauer[1,2]*, J Bryant[1], A Gomez[1], T Romaguera[1,2], D Alvarez[1,2], J McCulloch[1,2], R Herrera[1], D Doty[1], M Mehta[1,2], A Gutierrez[1,2], M Chuong[1,2], (1) Miami Cancer Institute, Baptist Health South Florida, Miami, FL, (2) Florida International University, Herbert Wertheim College of Medicine, Miami, FL

Additional Links

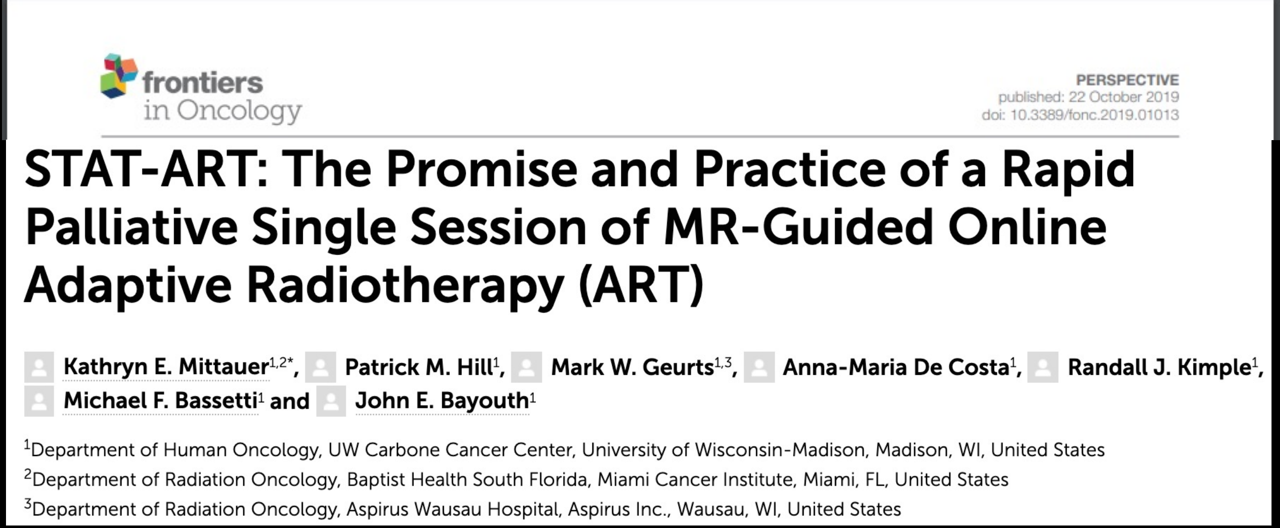
Meeting Program

Automation of spatial gradient based on GI OAR of the day—the MCI approach



Future direction in MR-guided ART including biological and AI opportunities

Simulation-free workflow in MR-guided adaptive RT is feasible



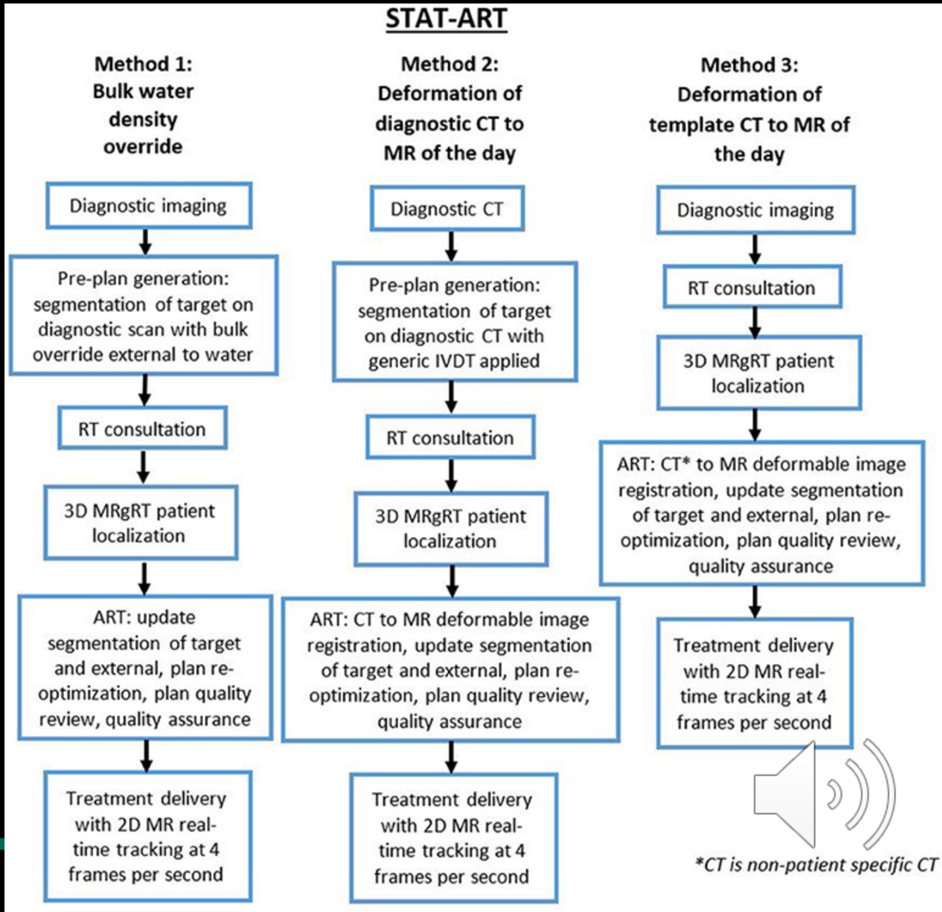
frontiers in Oncology
PERSPECTIVE
published: 22 October 2019
doi: 10.3389/fonc.2019.01013

STAT-ART: The Promise and Practice of a Rapid Palliative Single Session of MR-Guided Online Adaptive Radiotherapy (ART)

Kathryn E. Mittauer[1,2*], Patrick M. Hill[1], Mark W. Geurts[1,3], Anna-Maria De Costa[1], Randall J. Kimple[1], Michael F. Bassetti[1] and John E. Bayouth[1]

[1]Department of Human Oncology, UW Carbone Cancer Center, University of Wisconsin-Madison, Madison, WI, United States
[2]Department of Radiation Oncology, Baptist Health South Florida, Miami Cancer Institute, Miami, FL, United States
[3]Department of Radiation Oncology, Aspirus Wausau Hospital, Aspirus Inc., Wausau, WI, United States

- Our prior study showed ART can be collapsed down to same day consult-to-treat for palliative RT for a simulation-free workflow
- Eliminating initial plan creation may improve start time, simulation and planning resources, and clinical efficacy for pancreas SBRT
- In abdominal sites, the anatomy at the time of simulation is likely out of date by the first fraction.
- Can we do this for complex adaptive sites e.g., 50Gy/5 fraction SBRT pancreas?



Planning-free workflow in MR-guided adaptive RT is feasible

International Journal of
Radiation Oncology • Biology • Physics
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QUICK PITCH ORAL ABSTRACT | VOLUME 108, ISSUE 3, SUPPLEMENT , S187-S188, NOVEMBER 01, 2020

A Novel Pre-plan Technique for On-table Adaptation of Pancreatic Stereotactic MR-guided Online Adaptive Radiotherapy

K.E. Mittauer • R. Herrera • M.D. Chuong • ... M.D. Hall • M.P. Mehta • A. Gutierrez • Show all authors

DOI: https://doi.org/10.1016/j.ijrobp.2020.07.982 • Check for updates

- "SMART ART"= a class solution of a pre-plan template for pancreas SBRT built on sim anatomy of 38 pancreas SMART patients and evaluated on 66 pancreas SMART patients.
- We demonstrated adapting a generic pre-plan to the anatomy-of-the-day is equivalent to the plan quality of adapting a patient-specific initial plan to the anatomy-of-the-day in pancreas SBRT.

~~Sim~~ | ~~Planning~~ | 1st fraction: Adaptive RT

Radiotherapy &Oncology

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ORIGINAL ARTICLE | VOLUME 159, P197-201, JUNE 01, 2021

PDF [1 MB]

First experience of autonomous, un-supervised treatment planning integrated in adaptive MR-guided radiotherapy and delivered to a patient with prostate cancer

Luise A. Künzel • Marcel Nachbar • Markus Hagmüller • ... Simon Boeke • Daniel Zips • Daniela Thorwarth • Show all authors

Open Access • Published: April 01, 2021 • DOI: https://doi.org/10.1016/j.radonc.2021.03.032 •

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Highlights

- First-in-human: Integration and delivery of autonomous planning as basis for online adaptive MRgRT.
- Autonomous plan generation, including OAR segmentation, target generation and optimization.
- First checkpoint for human interaction at the time of clinical online adaptation at the MR-Linac.

The overall time from simulation to MR-Linac treatment was reduced to less than six hours, where no human interaction was required. Consequently, such an

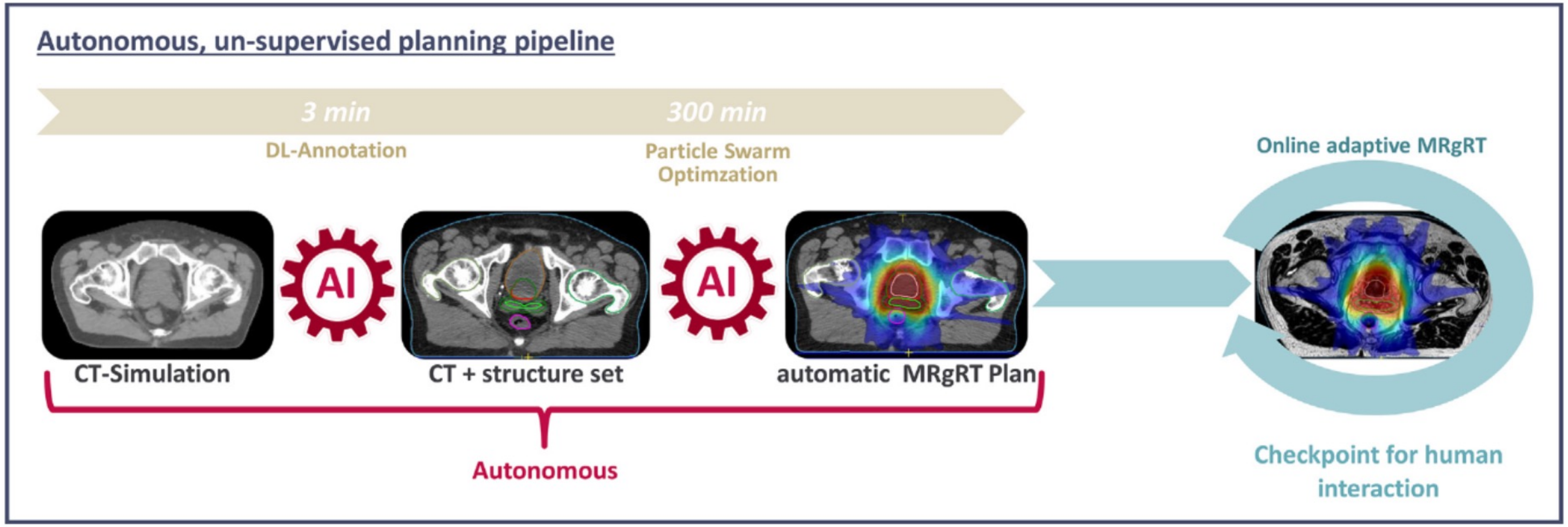

Fig. 1. Flowchart of the autonomous planning workflow and daily adaptation for online adaptive MRgRT (AI: artificial intelligence, CT: computed tomography, DL: deep learning, MRgRT: magnetic resonance image guided radiotherapy).

Physica Medica European Journal of Medical Physics

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FULL LENGTH ARTICLE | VOLUME 85, P175-191, MAY 01, 2021

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Artificial Intelligence in magnetic Resonance guided Radiotherapy: Medical and physical considerations on state of art and future perspectives

Davide Cusumano • Luca Boldrini • Jennifer Dhont • ... Vincenzo Valentini • Dirk Verellen • Luca Indovina •
Show all authors • Show footnotes

Published: May 19, 2021 • DOI: https://doi.org/10.1016/j.ejmp.2021.05.010 • Check for updates

- Current barriers in ART
  - Manual steps
  - Human error
  - Checklist and real-time observer required

Physica Medica 85 (2021) 175–191

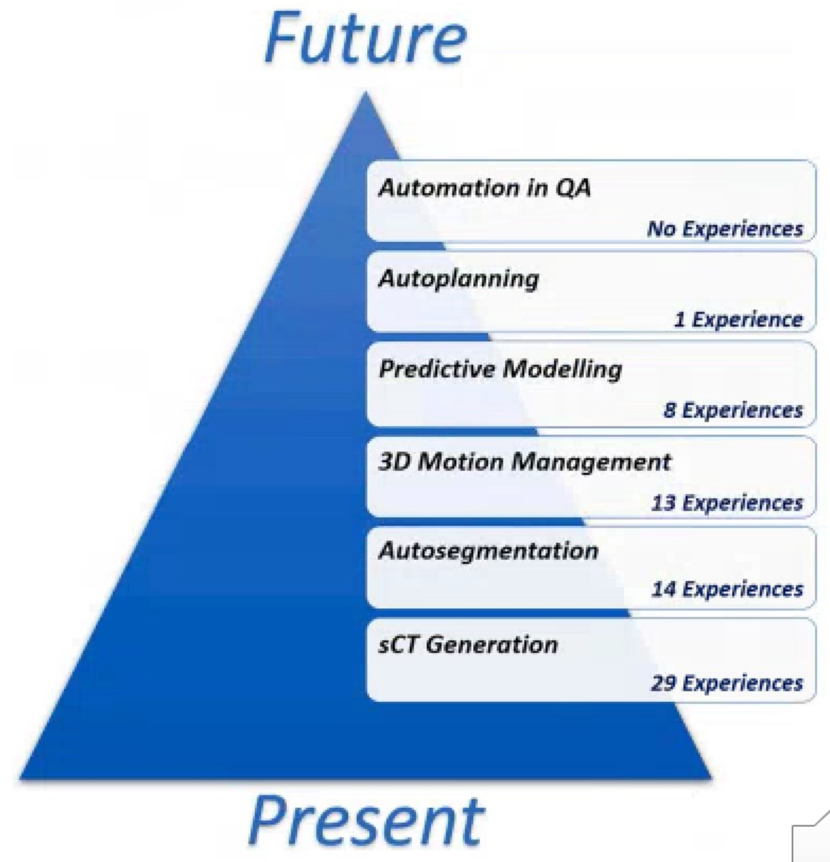

Fig. 3. Number of AI-based experiences in MRgRT field according to Scopus database in December 2020.

ASTRO ANNUAL 2021 MEETING

ASTRO'S 63RD ANNUAL MEETING
October 24 – 27, 2021

Presentation #: 1095
Abstract Title: Establishing the Gastroduodenal Maximum Tolerated Dose for Ablative 5-Fraction Stereotactic MR-guided Online Adaptive Radiation Therapy (SMART) in a Novel Swine Model
Presenter: Kathryn Mittauer
Author Block: Kathryn Mittauer, Michael Bassetti, Jennifer Meudt, Melissa Graham, Michael Wood, Jessica Miller, MIchael Lawless, Jennifer Frank, Russ Ward, Albert Van Der Kogel, Dhanansayan Shanmuganayagam, John Bayouth
Scientific Session Title: Phys 7 - Dose Response Analysis and Novel Treatment Technology
Session Date/Time: TBD

RSNA® Radiological Society of North America

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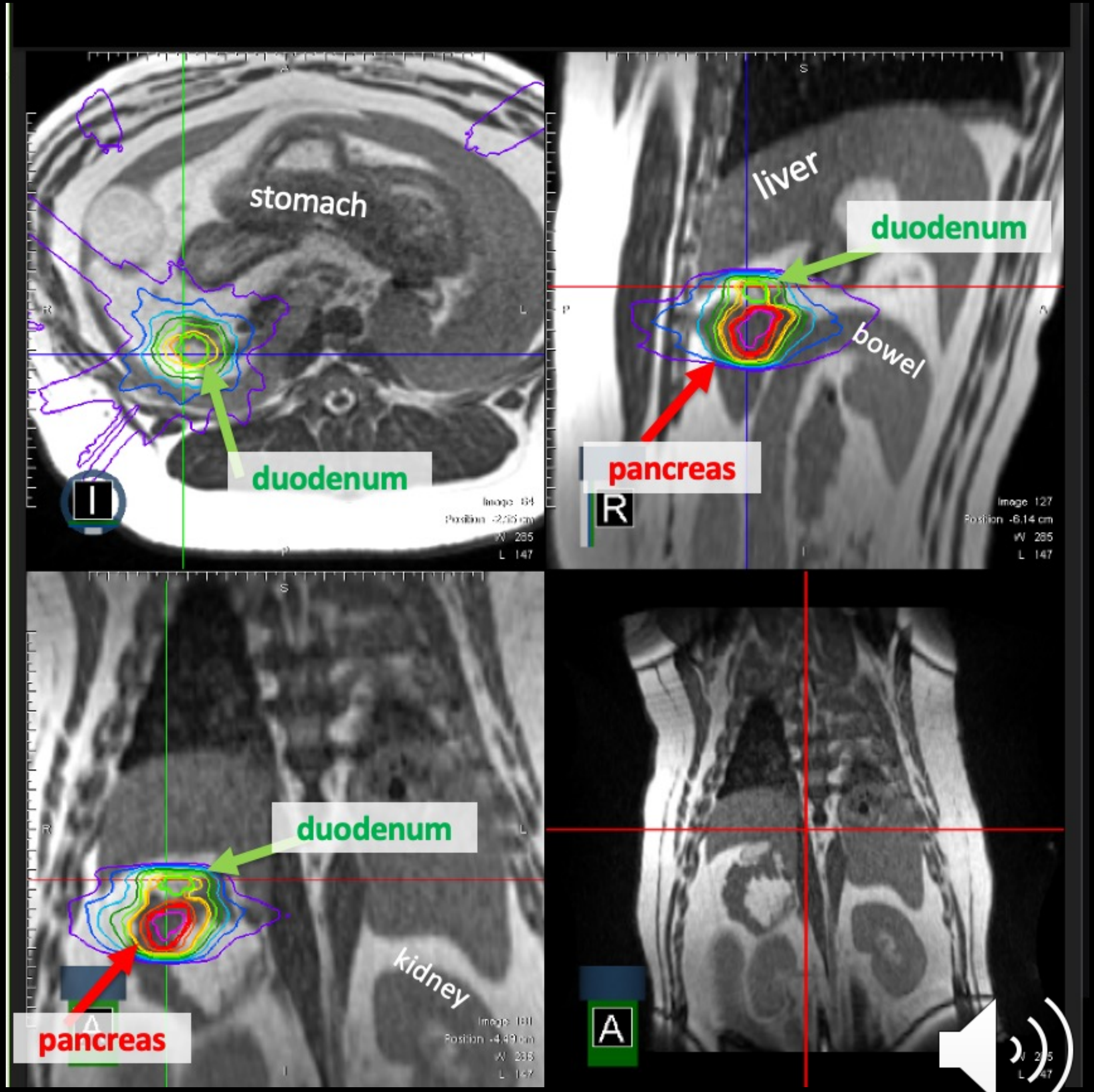

MRgRT adaptive dose escalation liver trial to assess **maximum tolerated dose** bowel $D_{0.5cc}$ and liver D_{700cc}

THE LANCET
Oncology

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REVIEW | VOLUME 21, ISSUE 2, E74-E82, FEBRUARY 01, 2020

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MRI-guided adaptive radiotherapy for liver tumours: visualising the future

Jacob S Witt, MD • Stephen A Rosenberg, MD • Michael F Bassetti

Published: February, 2020 • DOI: https://doi.org/10.1016/S1470-2045(20)30034-6 • Check for updates

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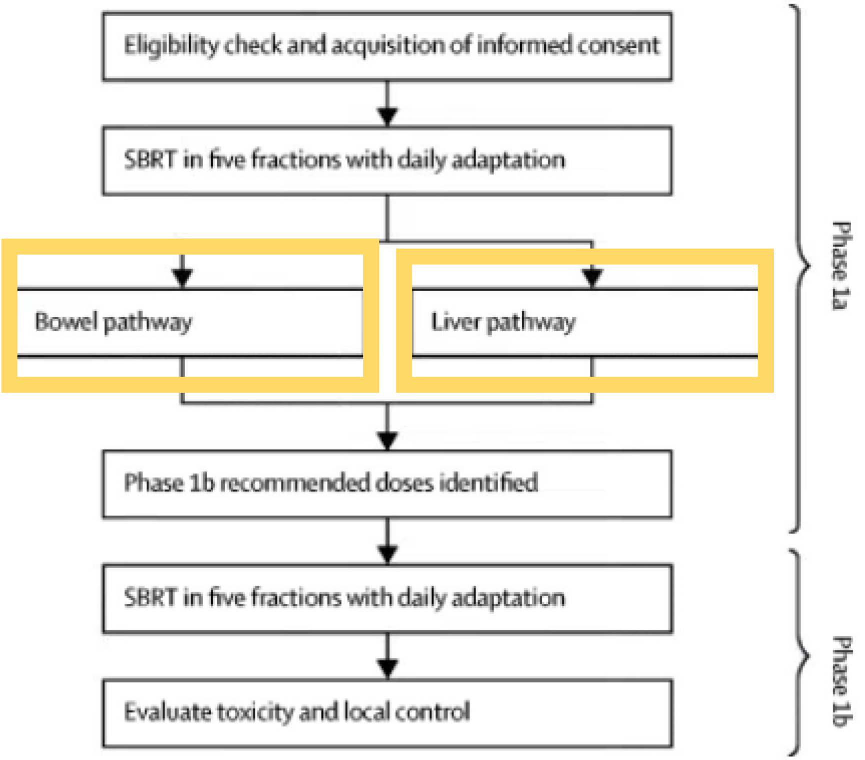

Figure 3

Trial schematic for our organs at risk-based dose escalation liver SI

Patients will be dose-escalated on the basis of increasing doses to the liver or bowel, followed by a subsequent phase 1b expansion cohort. SBRT=stereotactic body radiotherapy.

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ClinicalTrials.gov

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Experimental: MRI-Guided SBRT Dose Escalation

Treatment on MRI Linac with SBRT in 5 fractions with adaptive planning, maximum dose 80 Gy

Dose Escalation Bowel Pathway, V34 < 0.5cc Dose Escalation Liver Pathway, 700 cc < 16 Gy

Subsequent Phase 1B: CRC only for Safety and Local Control, dosage informed by Phase 1A

SMART ultra-hypofractionation: single fraction SMART in pancreas/liver

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Stereotactic MRI-guided Adaptive Radiation Therapy (SMART) in One Fraction (SMART ONE)

ClinicalTrials.gov Identifier: NCT04939246

Study Description Go to

Brief Summary:

This is a single arm feasibility study of single-fraction Stereotactic MRI-guided Adaptive Radiation Therapy (SMART) for primary or metastatic carcinoma involving the lung, liver, adrenal gland, abdominal/pelvic lymph node, pancreas, and/or kidney. Stereotactic ablative body radiation therapy (SABR) is a highly-focused radiation treatment that gives an intense dose of radiation concentrated on a tumor, while limiting the dose to the surrounding organs.

Condition or disease	Intervention/treatment	Phase
Metastatic Carcinoma	Radiation: Stereotactic ablative body radiation therapy	Not Applicable

Study Design Go to

Study Type : Interventional (Clinical Trial)

Estimated Enrollment : 30 participants

- Delivery time
- Potential for > GI peristalsis
- BH reproducibility/stability
  - Supplemental O2
  - In-room monitor--visual real-time feedback on BH position
- Patient tolerability/stamina for 90 min
  - screening for compliance (i.e., performance status, claustrophobia, etc.)
  - Establish patient education and expectations

BIGART (biological image-guided adaptive radiotherapy): role of MRI for predictor of tumor response and normal tissue toxicities

MINI REVIEW ARTICLE

Front. Oncol., 29 January 2021 | https://doi.org/10.3389/fonc.2020.615643

Check for updates

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Quantitative Magnetic Resonance Imaging for Biological Image-Guided Adaptive Radiotherapy

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Summary: Needs/future direction of MR-guided ART

1. Planning approach is critical for robust online adaptive RT in which interfraction OAR to target motion is anticipated
2. Users should be cautious of on-table adaptation time due to GI peristalsis (i.e., MR anatomy “decaying away”)
3. Simulation and initial planning may no longer be necessary with the integration of AI solutions into adaptive RT workflow
4. Prospective multi-institutional studies with daily on-treatment qMRI is needed for assessment of biomarkers for future integration


THANK YOU
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