Online Adaptive Radiation Therapy

Carri Glide-Hurst, PhD, DABR, FAAPM
Director of Translational Research, Radiation Oncology, Henry Ford Health System
Associate Professor FTA, Wayne State University

all for you @CGlideHurst

Henry Ford Cancer Institute

Disclosures

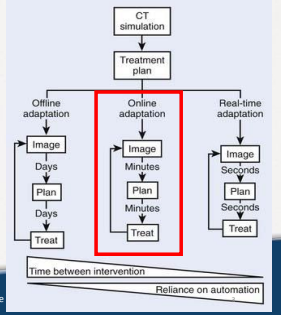
- Research funding provided by:
  - NIH R01CA204189
  - Philips Healthcare
  - HFHS A-Grant
- Research Collaborations with Modus Medical Devices, ViewRay, Inc, MedSpira
- Honorarium/Travel/Research Agreements with ViewRay, Inc
- Involvement in ViewRay, Inc sponsored clinical trial (Pancreas ART)

all for you

Henry Ford Cancer Institute

What is ART?

- Changing treatment plan based on observed changes
  - ✓ Weight loss
  - ✓ Tumor response
  - ✓ OAR variations
  - ✓ Functional changes
- Strategies based on timeframe of adaptation



all for you

Figure credit: Keall et al., Hematology, Oncology and Palliative Medicine

Evidence for Online ART in Prospective Trials

Disease Site	Study Design	ART Results	ART Clinical Benefits
Prostate[1]	Daily kV imaging + fiducials, aperture adapted if shift > 3 mm	Allowed 5 mm margins in 31/39 patients	Online ART based on prostate motion allowed for safe margin reduction
Central Lung[2]	MR-linac, 5 SBRT patients	10/25 plans adapted, 70% due to OAR violations	No grade 3 or greater toxicities, excellent local control
Oligomets[3]	MR-linac, 20 SBRT patients	Coverage increased in 20/97 Fx, OAR reduced 61/97 Fx	Reduces dose to OARs, offers potential for dose escalation

[1]Deutschmann, Red Journal, 2012, [2]Henke et al., Advances in RadOnc 2019, [3]Henke et al., Radiother Oncol, 2018

4

Low-Field MRI On-line ART Workflow

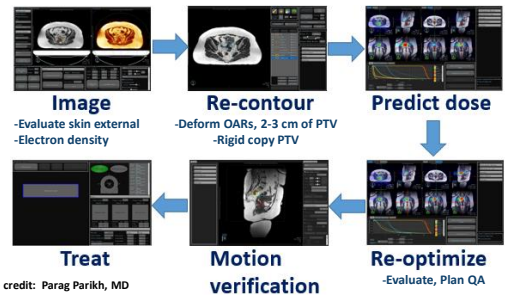


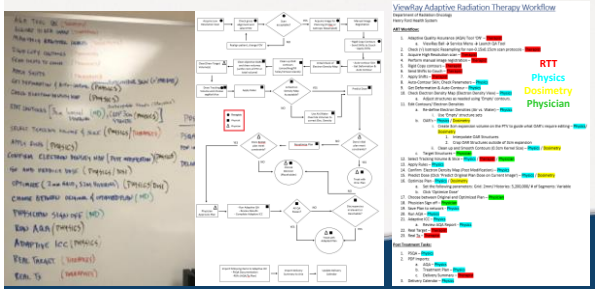
Figure credit: Parag Parikh, MD

The Move to On-line Adaptive

- **Major workflow development**
  - Rapid contouring requirements (3 cm around PTV)
  - On-the-fly electron density & plan review
  - Defining physician directives + criteria to adapt (OARs and/or Targets)
  - Safety and plan checks
  - Associated documentation
- **Major technical benchmarking**
  - MR primary planning (deformable image registration (DIR) of CT/MR, electron density mapping) for a robust patient model
  - Online optimization/planning strategies
  - Validation of vendor-provided 2ndary dose calculation tool

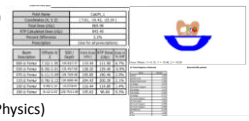
6

What MR-guided ART looks like in our clinic



MDA MRL Clinical Workflow - Online

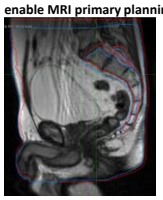
- All patients
  - Patient arrival and Daily MR assessment (RTT)
  - Patient setup (RTT)
  - MR image acquisition (RTT)
  - Online adaptation (Physics)
  - Verification of adaptation (Physician)
  - Secondary MU calculation for adapted plan (Physics)
  - Verification scan acquisition (RTT) – to verify that patient hasn't moved during plan adaptation
  - Adapted plan approval (Physician)
  - Verification of transfer of adapted plan parameters to Integrity console (Manually prior to delivery of each field using hard copy print out from secondary MU calc system) – AFS disabled (RTT)
  - Beam delivery (RTT)



Courtesy of Jihong Wang, Seungtaek Choi, Sastry Vedam, Jinzhong Yang

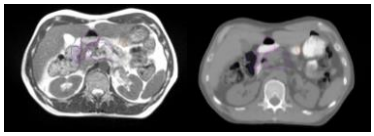
Deformable Image Registration (DIR) for Online ART

INITIAL
- **CT to MRI DIR to enable MRI primary planning**



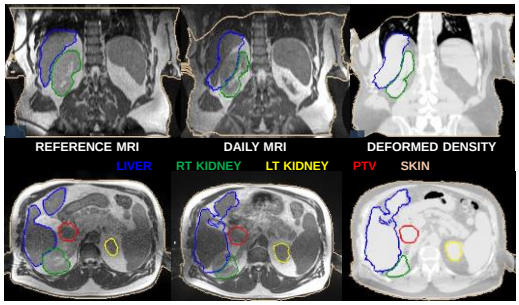
(Freeform DIR, Mutual Information)

DAILY
- **Deform electron density**
- **Contour propagation**

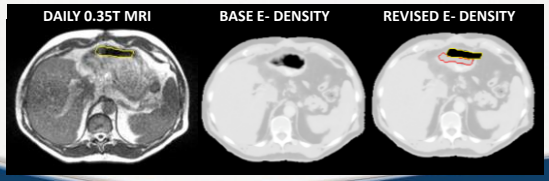


DAILY MRI **ELECTRON DENSITY MAP**

OFFLINE
- **Dose accumulation**



Daily Electron Density Validation for Accurate Dose Calculation



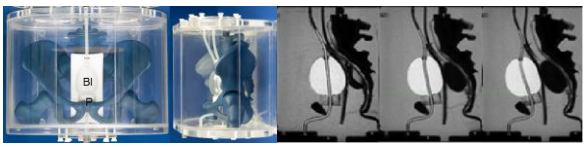
all for you

HENRY FORD CANCER INSTITUTE

11

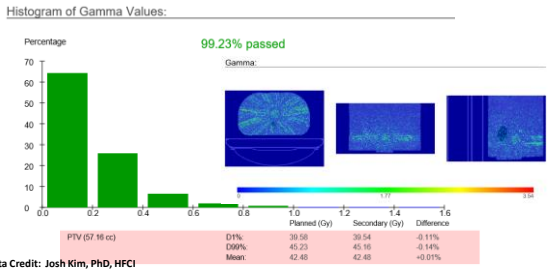
Benchmarking Adaptive with PETE

- MR-compatible Pelvic End-to-End (PETE) phantom simulated changes in rectum volumes (Empty, medium, full)
- Imaged using clinical protocol and performed ART workflow
- Generated various ART plans, evaluated 2ndary calculation, conducted PSQA on ART plan (film & point dose)



J. Cunningham et al., JACMP, 2018

Online QA: Benchmarking 2ndary Monte Carlo Dose Calculation with PETE



Data Credit: Josh Kim, PhD, HFCI

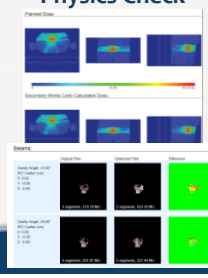
ART Benchmarking Results with PETE

	IC Measurements			Film Measurements	AQA Tool
Patients	TPS (cGy)	Measurement (cGy)	%Diff	2%/2mm Pass Rate	2%/2mm Pass Rate
Original Plan	1009.4	1011.8	0.2%	96.8%	---
Adapted Plan - Small Rectum	1015.6	1023.8	0.8%	94.1%	99.3%
Adapted Plan - Medium Rectum	981.0	999.5	1.9%	98.4%	99.2%
Adapted Plan - Medium Rectum Modified Bladder	1026.0	1035.0	0.9%	95.4%	98.6%
		MEAN	0.9%	96.2%	99.1%
		STDEV	0.6%	1.6%	0.3%

Data Credit: Josh Kim, PhD, HFCI

Electron Density/Contouring
Verify high resolution image or isotropic resampling in use
Verify skin contour accuracy in clinically relevant area
Clean/review deformed contours (3D/MPR)
Visually verify electron density map
Verify density overrides (assigned value/priority)
Verify margin expansion
Plan Quality
Verify 2 mm dose grid resolution, 5.2M histories
Verify Plan-Rx Comparison criteria are met
Verify location/magnitude of D_{max}
Verify isodose lines on each slice
Plan quality reviewed
Verify relevant OARs implemented in optimization
AQA Report
Verify gamma analysis >97% (2%/2mm local)
Verify total segment number/MU change <10%
Visually verify gamma map
Visually verify fluence maps
Documentation
Physician approval of ART Plan

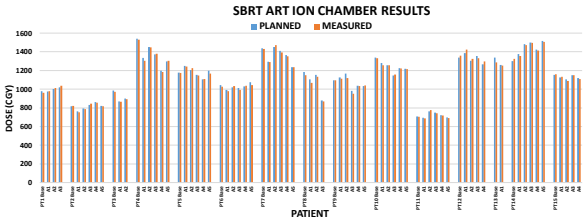
Example Online ART Physics Check



Post-Treatment ART PSQA Benchmarking

- SBRT: A26MR micro-ion chamber and gafchromic EBT3 film measured in a 15cm Solid Water stack
- Conventional: A26MR micro-ion chamber and ArcCheck measurements
- Both: Evaluated AQA results, conducted PSQA on ART plan (film & point dose)

Results: SBRT ART PSQA, Initial & ART Fx (15 Patients)

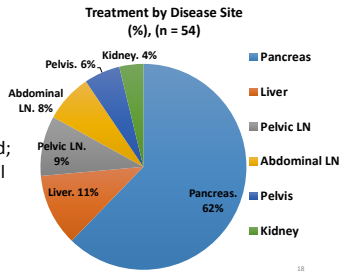


-IC Results: -0.5 ± 0.1% (MR-compatible A26)
-Gafchromic EBT3 Film: 95.3% [90.7, 99.6] (3%/1mm global)
-Vendor-supplied AQA Tool: 99.5% [97.5, 100.0] (2%/2mm local)

Data Credit: Josh Kim, Dongsu Du, HFCI

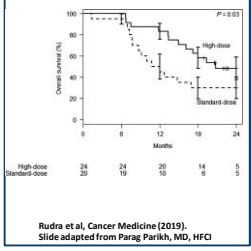
MR-Guided Adaptive Cases (10/2018-present)

- 54 Patients (50 SBRT, 4 Conventional)
- 290 total treatments
- 81% of treatments adapted; others did not meet clinical ART criteria



Clinical Case: MR-guided Pancreas ART

Retrospective Data



Rudra et al, Cancer Medicine (2019).
Slide adapted from Parag Parikh, MD, HFCI

Prospective Trial

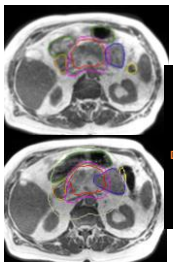
Inoperable Pancreas Cancer after >= 3 months of chemotherapy → 50 Gy / 5 fractions MR guided, adapted and tracked

Primary endpoint: Toxicity at 90 days
Secondary endpoints: Disease-related outcomes
Goal: 100 patients

Actionable limits:

- ✓ Constraints violated for OARs (or)
- ✓ GTV/CTV coverage <85% by 47.5 Gy (or)
- ✓ Favorable shift GTV/OARS where ART increases coverage by 10% or more

Benefit of ART: Resolve Small Bowel Dose Violation

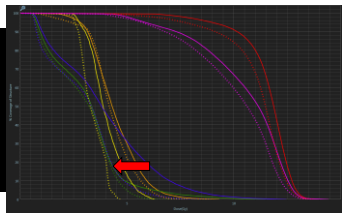


INITIAL

CTV
PTV
STOMACH
DUODENUM
SM BOWEL
COLON

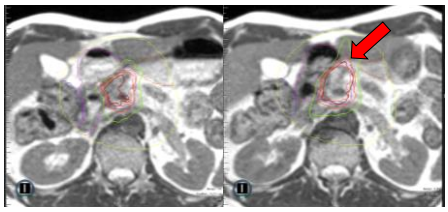
FX 1

SOLID = PREDICTED, DASHED = ART DELIVERED

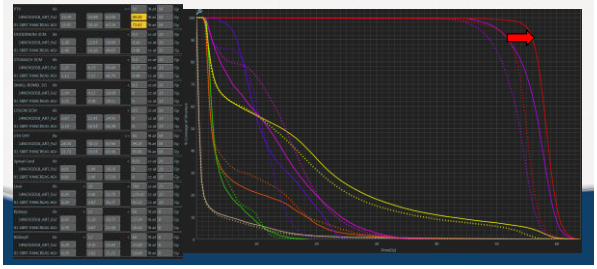


ART Scenario: More Favorable Geometry for Isotoxic Approach

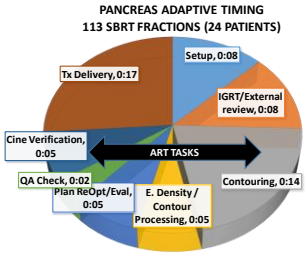
INITIAL PLAN | ART FRACTION



Target Dose Improvement: Solid = ART, Dashed = Base Plan



On-Line Adaptive Treatment Times



PANCREAS TOTAL TIME = 71 ± 14 MIN

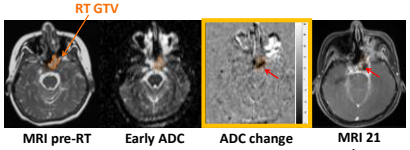
ART TIME = 25 ± 6 MIN

ART CRITERIA:

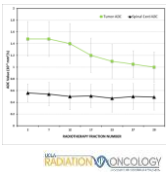
- Normal tissue out of tolerance
- Increase CTV/PTV >10% to OAR tolerance

MRgRT for Response Prediction

- H&N cancer patient, decreased ADC observed in GTV
- Longitudinal DWI is feasible with the 0.35T ViewRay MRI

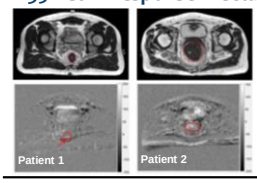


MRI pre-RT | Early ADC map during RT | ADC change slope map throughout RT | MRI 21 months post-RT – confirm recurrence



Slide courtesy of Yingli Yang, PhD

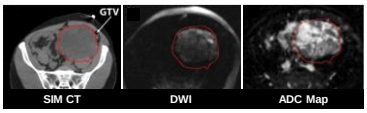
0.35T Co^{60} Response: Rectal Cancer & Sarcoma



Functional diffusion map: Darkened areas suggest treatment-resistant subregions

Shaverdian et al, BJR, 2017

Yang *et al.*, Med Phys, 2016



Imaging Innovations: 0.35T MR-linac Resolution of Fluid, Changes in T1/R2* Maps

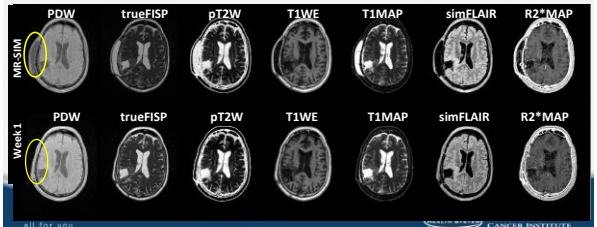
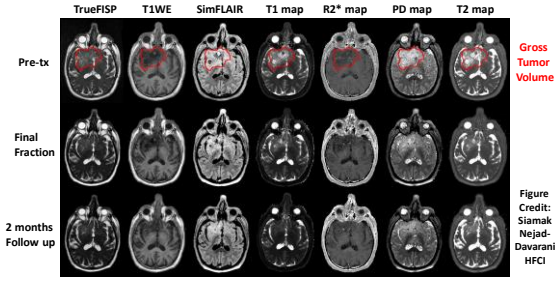


Figure Credit: Siamak Nejad-Davarani, HFCI

Patient 3, Serial STAGE Imaging: Bifrontal Oligodendroglioma



- Improvement in FLAIR abnormalities, mass effect, resolved 5 mm node

Conclusions & Future Directions

- Establishing MRgART introduces new technical and workflow challenges
- Offers strong potential to improve targeting/accuracy for patient populations expected to benefit
- Despite added complexity, online ART offers significant potential for toxicity reduction or dose escalation when anatomy is favorable
- Next steps: to begin well-curated clinical trials to fully capture benefits of online MRI/MR-guided ART→NRG currently preparing for multi-institutional trial work.

28

Acknowledgements

Clinicians: Parag Parikh (Program Director); Jadranka Dragovic; Newton Hurst; Ben Movsas (Dept. Chairman)

Physicists: Indrin Chetty (Physics Division Head); Anthony Doemer; Joshua Kim; Dongsu Du; Ning (Winston) Wen

Dosimetrist: Kate Aldridge

Therapists: Robert Rusnac (lead); Emily Moats; Paul Jackson; Jacob Arch; Eileen Monark

Collaborators: Mark Haacke, Yongsheng Chen

all for you

HENRY FORD CANCER INSTITUTE