ANNUAL

Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

Precision Power: Advanced GI Cancer Treatment with Precision Radiotherapy

Sameer Keole, MD

Consultant, Department of Radiation Oncology Mayo Clinic Arizona

Disclosures

• I do not have any relevant financial relationships.

This presentation and/or comments will provide a balanced, non-promotional, and evidence-based approach to all diagnostic, therapeutic and/or research related content

Cultural Linguistic Competency (CLC) & Implicit Bias (IB)

STATE LAW:

The California legislature has passed <u>Assembly Bill (AB) 1195</u>, which states that as of July 1, 2006, all Category 1 CME activities that relate to patient care must include a cultural diversity/linguistics component. It has also passed <u>AB 241</u>, which states that as of January 1, 2022, all continuing education courses for a physician and surgeon **must** contain curriculum that includes specified instruction in the understanding of implicit bias in medical treatment.

The cultural and linguistic competency (CLC) and implicit bias (IB) definitions reiterate how patients' diverse backgrounds may impact their access to care.

EXEMPTION:

Business and Professions Code 2190.1 exempts activities which are dedicated solely to research or other issues that do not contain a direct patient care component.

The following CLC & IB components will be addressed in this presentation:

- Will review how RT advances are independent of race, gender, and sexual orientation.
- Will address possible barriers in communication.

2025 Annual Advances and Innovations in Endoscopic Oncology and Multidisciplinary Gastrointestinal Cancer Care

ASTRO Annual Meeting



Sep 27 to Oct 1, 2025 San Francisco



RT for GI tumors: Key Approaches and Innovations

- 1. Image-Guided Radiation Therapy (IGRT)
- 2. Intensity-Modulated Radiation Therapy (IMRT)
- 3. Stereotactic Body Radiation Therapy (SBRT)
- 4. Adaptive Radiation Therapy (ART)
- 5. Proton Beam Therapy (PBT)
- 6. Biologically Targeted and Molecular-Guided Radiation
- 7. Theranostics and Radiopharmaceuticals
- 8. Artificial Intelligence (AI) and Big Data Integration

Image-Guided Radiation Therapy (IGRT)

- Uses advanced imaging techniques (e.g., cone-beam CT, MRI) to enhance tumor localization and track changes during treatment.
- Precision Advantage: Ensures accurate delivery to GI tumors despite organ motion (e.g., bowel peristalsis, respiratory motion).
- Applications: Pancreatic cancer, rectal cancer, and esophageal cancer benefit from improved targeting and reduced treatment margins.

Intensity-Modulated Radiation Therapy (IMRT)

- Includes commercial terms including "VMAT" and "Rapid Arc"
- Inversely planned
- Beamlets used to modulate beam intensity
- Improves dose conformality
- May increase integral dose
- Becoming SOC for complex GI cases to reduce GI toxicity

Stereotactic Body Radiation Therapy (SBRT)

- Overview: Delivers high-dose radiation in a few fractions with submillimeter accuracy.
- Precision Advantage: Enables ablative doses to tumors while minimizing exposure to healthy tissues.
- Applications: Common in treating unresectable pancreatic cancer, liver metastases, and oligometastatic disease.

Adaptive Radiation Therapy (ART)

- Overview: Adjusts treatment plans in real-time or between sessions based on anatomical and biological changes.
- Precision Advantage: Adapts to tumor shrinkage, organ movement, and patient weight changes.
- Applications: Particularly useful for GI cancers where organ motion and tumor regression are common.

Proton Beam Therapy (PBT)

- Overview: Uses protons rather than photons to deliver radiation with a sharp dose fall-off (Bragg peak).
- Precision Advantage: Reduces dose to surrounding organs, lowering toxicity.
- Applications: Ideal for treating GI tumors near critical structures, such as esophageal cancer and liver tumors.

Biologically Targeted and Molecular-Guided Radiation

- Overview: Integrates genomic and molecular profiling to guide radiation dose and volume.
- Precision Advantage: Allows for individualized treatment plans based on tumor biology and radiosensitivity.
- Applications: Trials are exploring radiosensitizers, biomarkers for response prediction, and personalized treatment intensification.

Theranostics and Radiopharmaceuticals

- Overview: Combines diagnostic imaging with targeted radiotherapy using radiopharmaceuticals.
- Precision Advantage: Offers systemic radiation delivery tailored to molecular targets.
- Applications: Lutetium-177 and Yttrium-90 are being used for liver metastases and neuroendocrine tumors.

Artificial Intelligence (AI) and Big Data Integration

- Overview: Uses machine learning to optimize treatment planning and predict patient outcomes.
- Precision Advantage: Improves efficiency in contouring, adaptive planning, and toxicity prediction.
- Applications: AI is being integrated into GI radiation oncology for patient selection and personalized treatment pathways.

MR linear accelerator technology (MRL)

The following slides are courtesy of Michael Chuong, MD at Miami Baptist Cancer Institute. MCI was an early adopter of MR linear accelerator tech

We do NOT have an MR linear accelerator at Mayo Clinic

Causes of death

VOLUME 27 · NUMBER 11 · APRIL 10 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

DPC4 Gene Status of the Primary Carcinoma Correlates With Patterns of Failure in Patients With Pancreatic Cancer

Christine A. Iacobuzio-Donahue, Baojin Fu, Shinichi Yachida, Mingde Luo, Hisashi Abe, Clark M. Henderson, Felip Vilardell, Zheng Wang, Jesse W. Keller, Priya Banerjee, Joseph M. Herman, John L. Cameron, Charles J. Yeo, Marc K. Halushka, James R. Eshleman, Marian Raben, Alison P. Klein, Ralph H. Hruban, Manuel Hidalgo, and Daniel Laheru

A B S T R A C T

Purpose

From the Departments of Pathology,

Surgery, and Oncology, The Sol Gold-

Center, Johns Hopkins Medical Institu-

tions. Baltimore MD: and the Depart-

ment of Epidemiology, Johns Hopkins

Bloomberg School of Public Health, and Department of Surgery and the Jeffer-

man Pancreatic Cancer Research

son Pancreas, Biliary and Related

Cancer Center, Thomas Jefferson

Submitted April 24, 2008; accepted

ahead of print at www.jco.org on

-file-bb (CID) The level C

November 24, 2008; published online

Supported by grants No. CA62924 and

CA106610 from the National Institutes

University, Philadelphia PA.

March 9, 2009.

Contrary to the extensive data accumulated regarding pancreatic carcinogenesis, the clinical and molecular features characteristic of advanced stage (stage III and IV) disease are unknown. A comprehensive study of pancreatic cancers from patients who have succumbed to their disease has the potential to greatly expand our understanding of the most lethal stage of this disease and identify novel areas for intervention.

Materials and Methods

Rapid autopsies were performed on 76 patients with documented pancreatic cancer. The histologic features of end stage disease were determined and correlated to the stage at initial diagnosis, patterns of failure (locally destructive v metastatic disease) and the status of the *KRAS2*, *TP53*, and *DPC4* genes.

Results

At autopsy, 30% of patients died with locally destructive pancreatic cancer, and 70% died with

Rapid autopsy study 2003-2007 Stage: I/II: 29%, III: 24%, IV: 47% Metastatic disease at autopsy: 88%

"30% died from locally destructive pancreatic cancer"

"contrary to common belief, not all patients die of widespread metastatic disease"

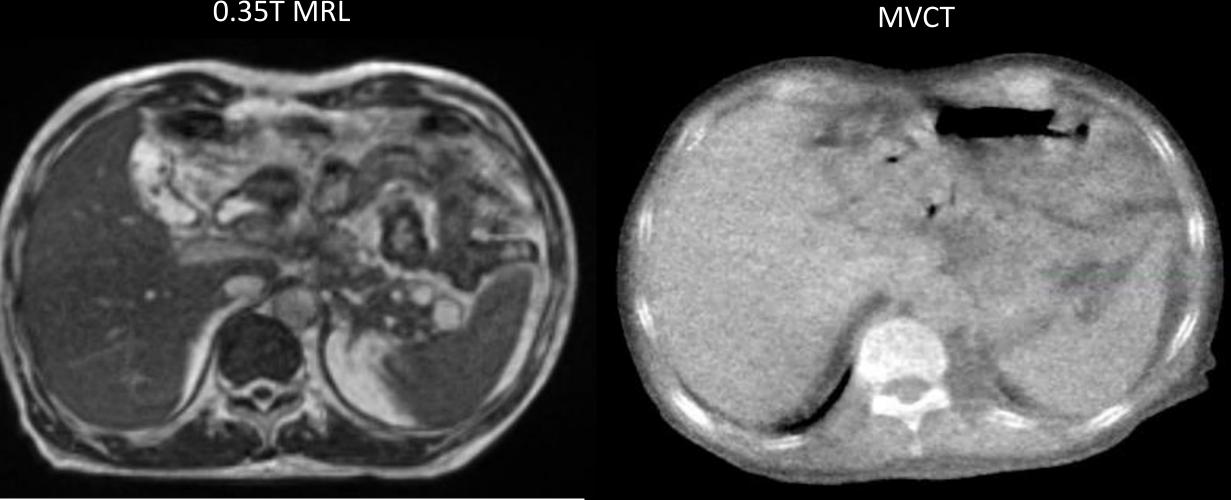
X



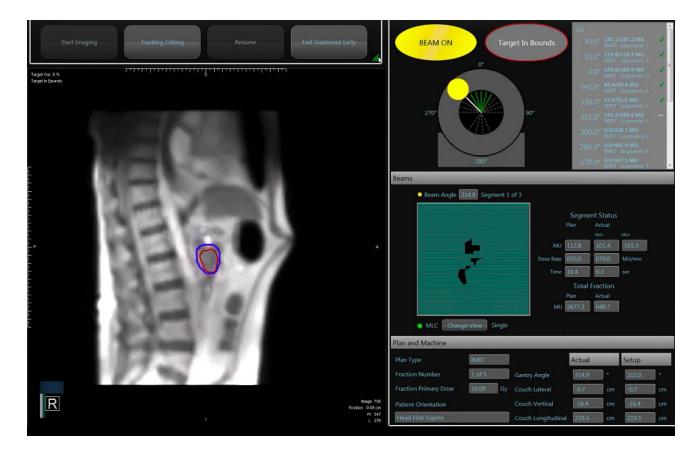
Slide courtesy of Michael Chuong, MD

Superior soft tissue contrast of MRI

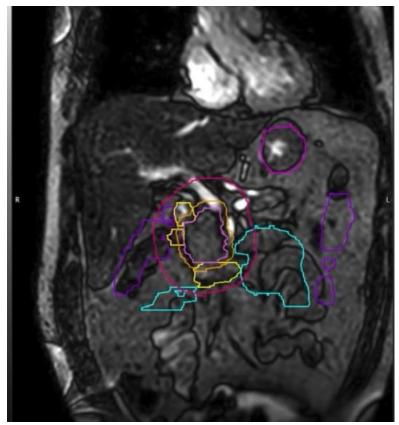




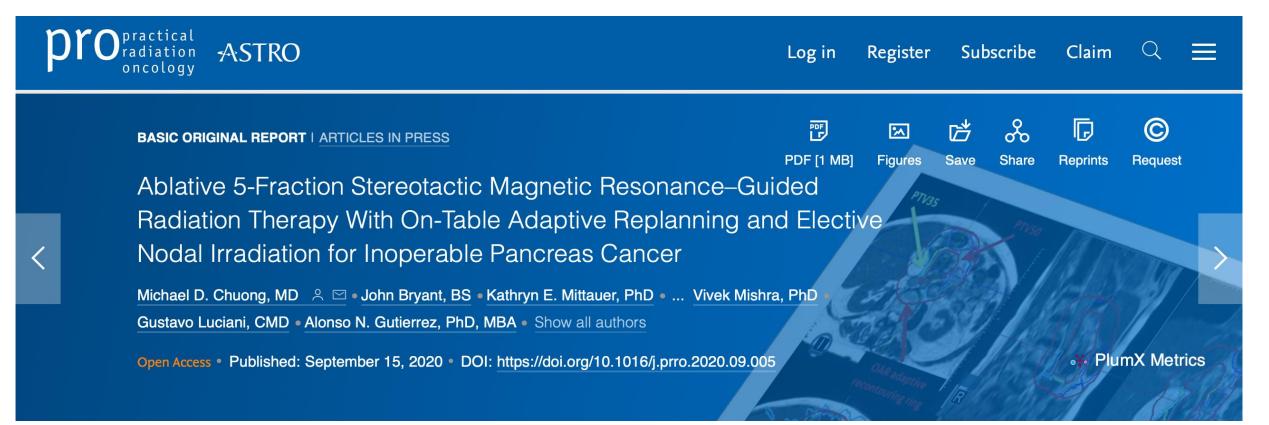
0.35T MR Linac







First 5-fraction MR-Linac outcomes (MCI)



Daily treatment No prophylactic PPI Acute/late grade 3+ toxicity: 2.9% 1-yr LC: 88%, 1-yr OS: 59%

Favorable LC and OS



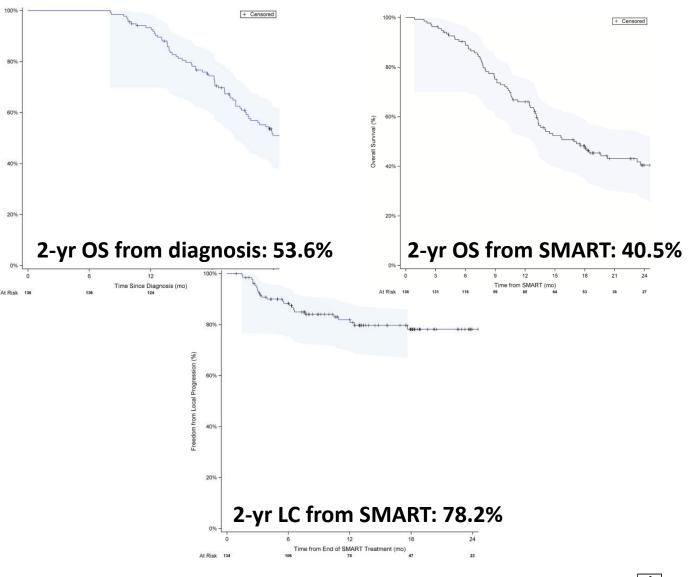
Radiotherapy and Oncology Available online 20 December 2023, 110064 In Press, Journal Pre-proof (?) What's this? 7

Original Article

Stereotactic MR-guided on-table adaptive radiation therapy (SMART) for borderline resectable and locally advanced pancreatic cancer: a multi-center, openlabel phase 2 study

<u>Michael D. Chuong</u>^a *Q* ⊠, <u>Percy Lee</u>^b, <u>Daniel A. Low</u>^c, <u>Joshua Kim</u>^d, <u>Kathryn E. Mittauer</u>^a, <u>Michael F Bassetti</u>^e, <u>Carri K. Glide-Hurst</u>^e, <u>Ann C. Raldow</u>^f, <u>Yingli Yang</u>^f, <u>Lorraine Portelance</u>^g, <u>Kyle R. Padgett</u>^g, <u>Bassem Zaki</u>^h, <u>Rongxiao Zhang</u>^h, <u>Hyun Kim</u>ⁱ, <u>Lauren E. Henke</u>ⁱ, <u>Alex T. Price</u>ⁱ, <u>Joseph D. Mancias</u>^j, <u>Christopher L. Williams</u>^j, John Ng^k, <u>Ryan Pennell</u>^k, <u>M. Raphael Pfeffer</u>^l, <u>Daphne Levin</u>^l, <u>Adam C. Mueller</u>^m, <u>Karen E. Mooney</u>^m, <u>Patrick Kelly</u>ⁿ, <u>Amish P. Shah</u>ⁿ, <u>Luca Boldrini</u>^o, <u>Lorenzo Placidi</u>^o, <u>Martin Fuss</u>^p, <u>Parag Jitendra Parikh</u>^d

- ^a Miami Cancer Institute, Baptist Health South Florida, Miami, FL
- ^b City of Hope National Medical Center, Los Angeles, CA
- $^{\rm c}$ $\,$ UCLA Department of Radiation Oncology, Los Angeles, CA $\,$
- ^d Henry Ford Health Cancer, Detroit, MI
- ^e University of Wisconsin—Madison, Department of Human Oncology, Madison, WI
- $^{\rm f}~$ Department of Radiation Oncology, UCLA David Geffen School of Medicine, Los Angeles,



Proton Beam Therapy – Whole Pelvic RT

Indications for Proton Therapy

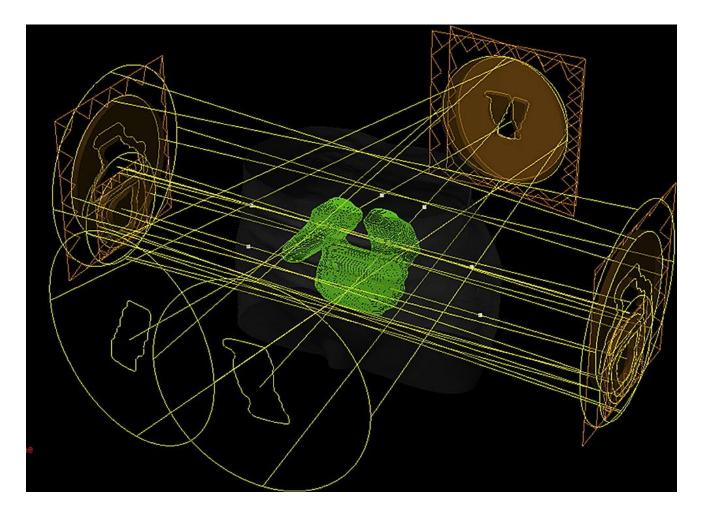
"Classic"

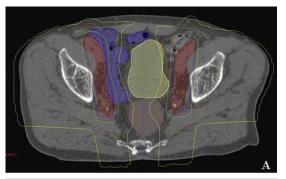
- Pediatric tumors
- Brain tumors
- Base of skull tumors
- Spinal tumors
- Paraspinal tumors
- Prostate cancers
- Uveal melanomas
- Intracranial radiosurgery

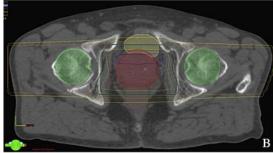
"Emerging"

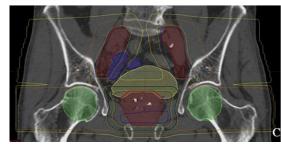
- Lung
- Esophagus
- Breast
- Head and neck (PNS, NPC,
- Whole pelvic RT
 - Examples: Rectal & Anal Canal
- Large sarcomas
- Liver
- Mediastinal tumors
 - Example: Lymphoma & Thymoma

Whole Pelvis RT using Double Scatter Protons

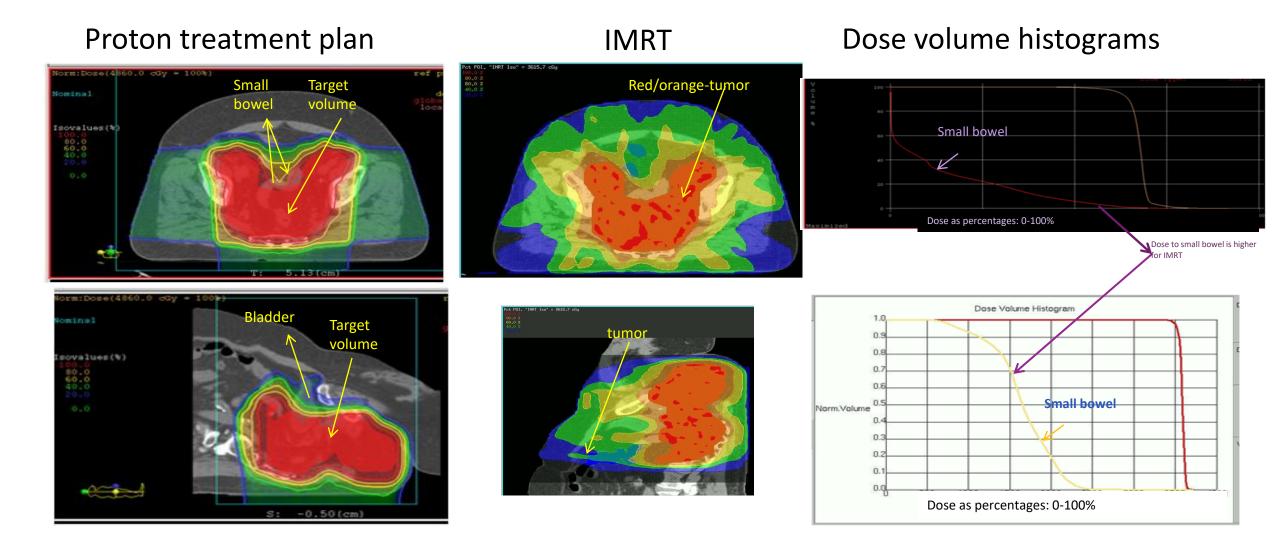




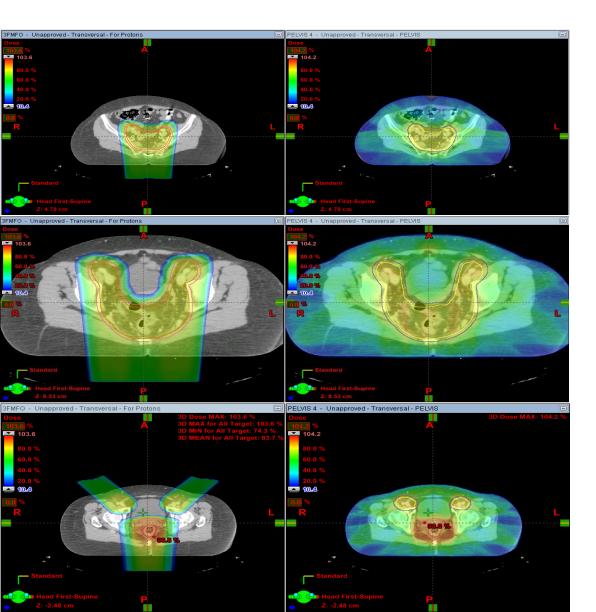


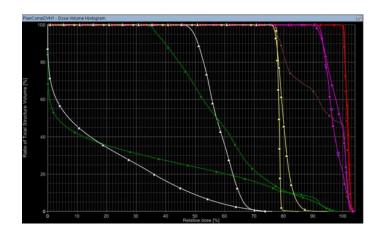


Whole Pelvis RT using Uniform Scanning Protons

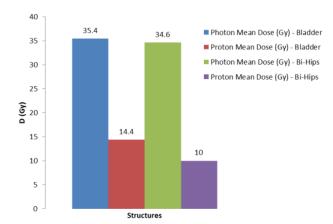


Whole Pelvis RT using Pencil Beam Scanning Protons





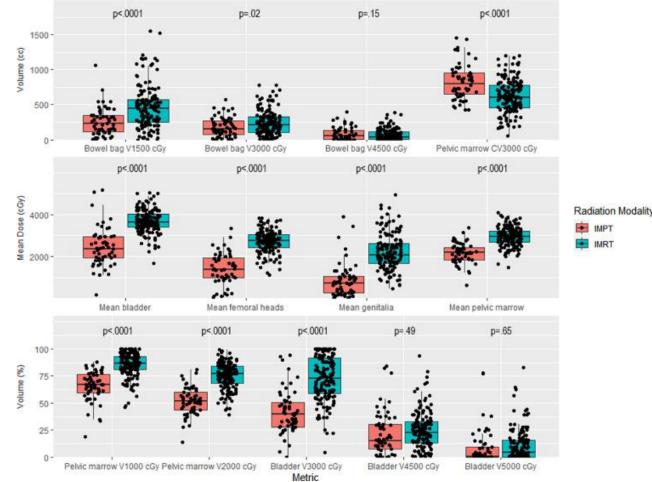
Legend: IDL : White -- BI- Hips; Green -- Bladder; Yellow – CTV 45; Magenta – CTV 54; Red -- GTV 60



Whole Pelvis RT – The Proton Evolution

- Fewer treatment fields
 - 6 fields \rightarrow 3/4 fields \rightarrow 2/3 fields
 - 60 min \rightarrow 40 min \rightarrow 25 min
- Improved sparing of non-target tissues
 - Bladder
 - Rectum
 - Bone marrow
- More practical & feasible

Initial data does NOT support reduced acute toxicity with protons vs. IMRT for anal canal cancer, however

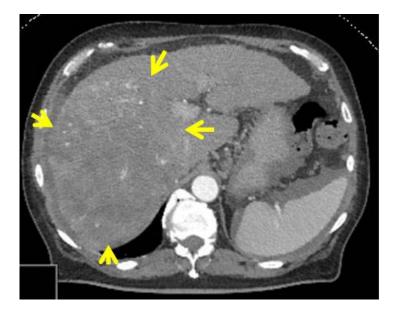


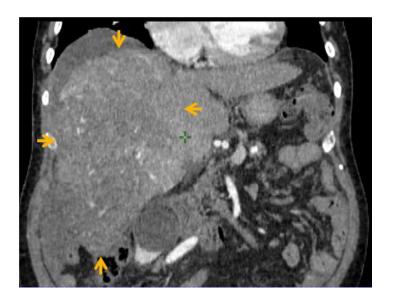
	IMPT, No. (%)	IMRT, No. (%)	<i>P</i> value
Hospitalized during radiation therapy	23 (40)	49 (33)	.34
Febrile neutropenia	16 (28)	22 (15)	.03
Median treatment time, d	41	42	.33
Grade 2 or greater acute toxicity			
GI or GU	39 (67)	91 (61)	.38
GI	38 (65)	88 (59)	.37
GU	4 (7)	14 (9)	.58
Skin	50 (86)	117 (78)	.19
Pain	31 (53)	80 (53)	.99
Hematologic	40 (69)	87 (69)	.99
Overall	57 (98)	141 (95)	.34
Grade 3 or greater acute toxicity			
GI or GU	14 (24)	31 (21)	.59
GI	13 (22)	30 (20)	.70
GU	1 (2)	1 (1)	.50
Skin	12 (21)	43 (29)	.24
Pain	7 (12)	20 (13)	.81
Hematologic	32 (55)	59 (47)	.29
Overall	39 (67)	92 (68)	.96

Protons for Liver Tumors

- Significantly reduced dose to non-target liver
- Less RILD with excellent OS
 - Sanford NN, Hong TS IJROBP 2019
- Supported in payer guidelines

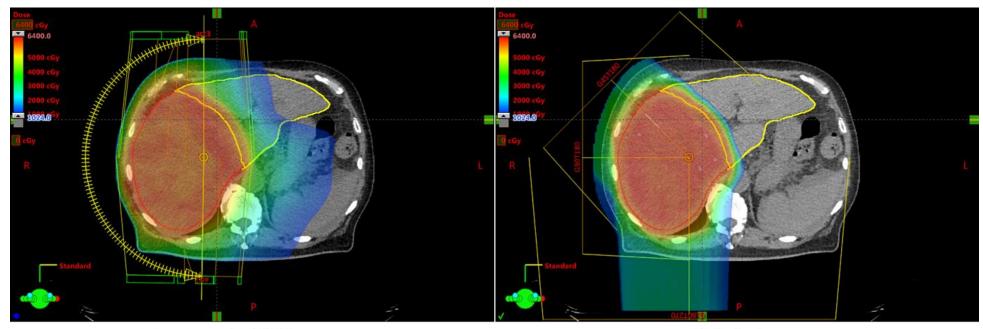
• CT: cirrhosis, 20 cm HCC, right branch portal vein tumor thrombus





• Plan: PBT 58.5 Gy/15 fx

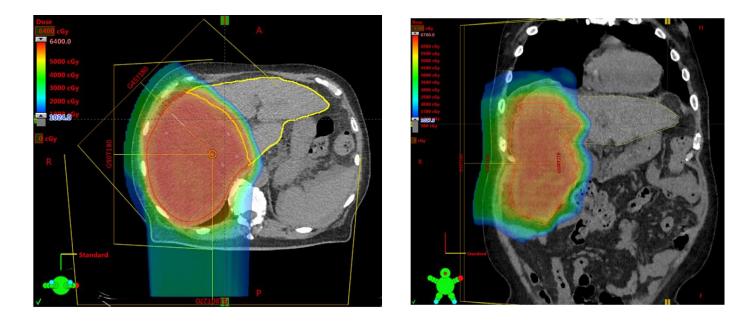
- Fiducials, breath hold
- GTV: 2721 cc
- Protons: significant liver sparing



Photon MR

Courtesy of C. Hallemeier, MD

- G180T270: 86 energy layers, 38,199 spots
- G90T180: 71 energy layers, 44,114 spots
- G45T180: 73 energy layers, 48,880 spots

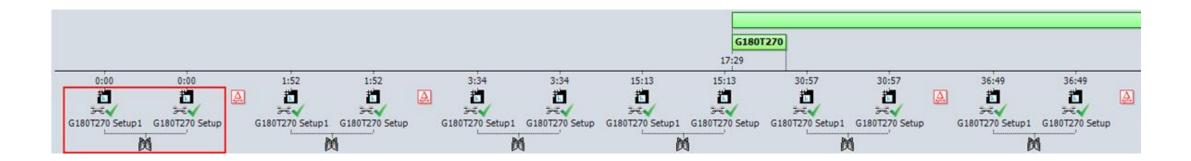


Courtesy of C. Hallemeier, MD

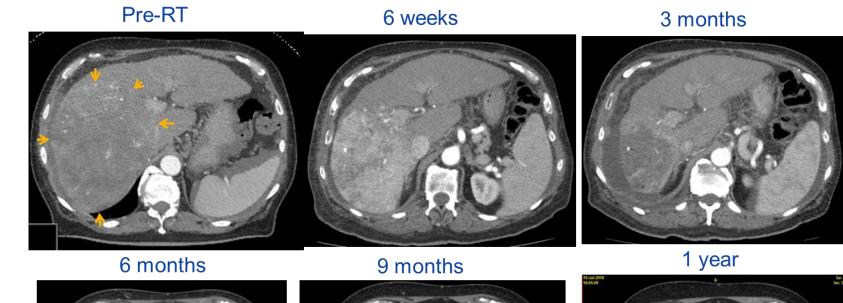
• Fx 1, 10:30 am \rightarrow 120 minutes



• Fx 2, 10:00 pm \rightarrow 90 minutes

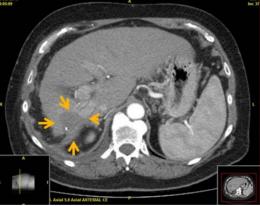


Courtesy of C. Hallemeier, MD









Courtesy of C. Hallemeier, MD

Future Directions

- Personalized Dose Escalation: Using biomarkers and imaging to identify patients who benefit from higher radiation doses.
- Combination Therapies: Integrating radiation with immunotherapy (e.g., checkpoint inhibitors) for improved efficacy.
- Liquid Biopsies: Monitoring circulating tumor DNA (ctDNA) to guide adaptive therapy and detect minimal residual disease.

Thank you!