Contemporary Radiation Therapy for Liver Cancer

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Miami Cancer Institute

CIO

Disclosures

Speakers Bureau, Advisory Board, Research Funding — ViewRay

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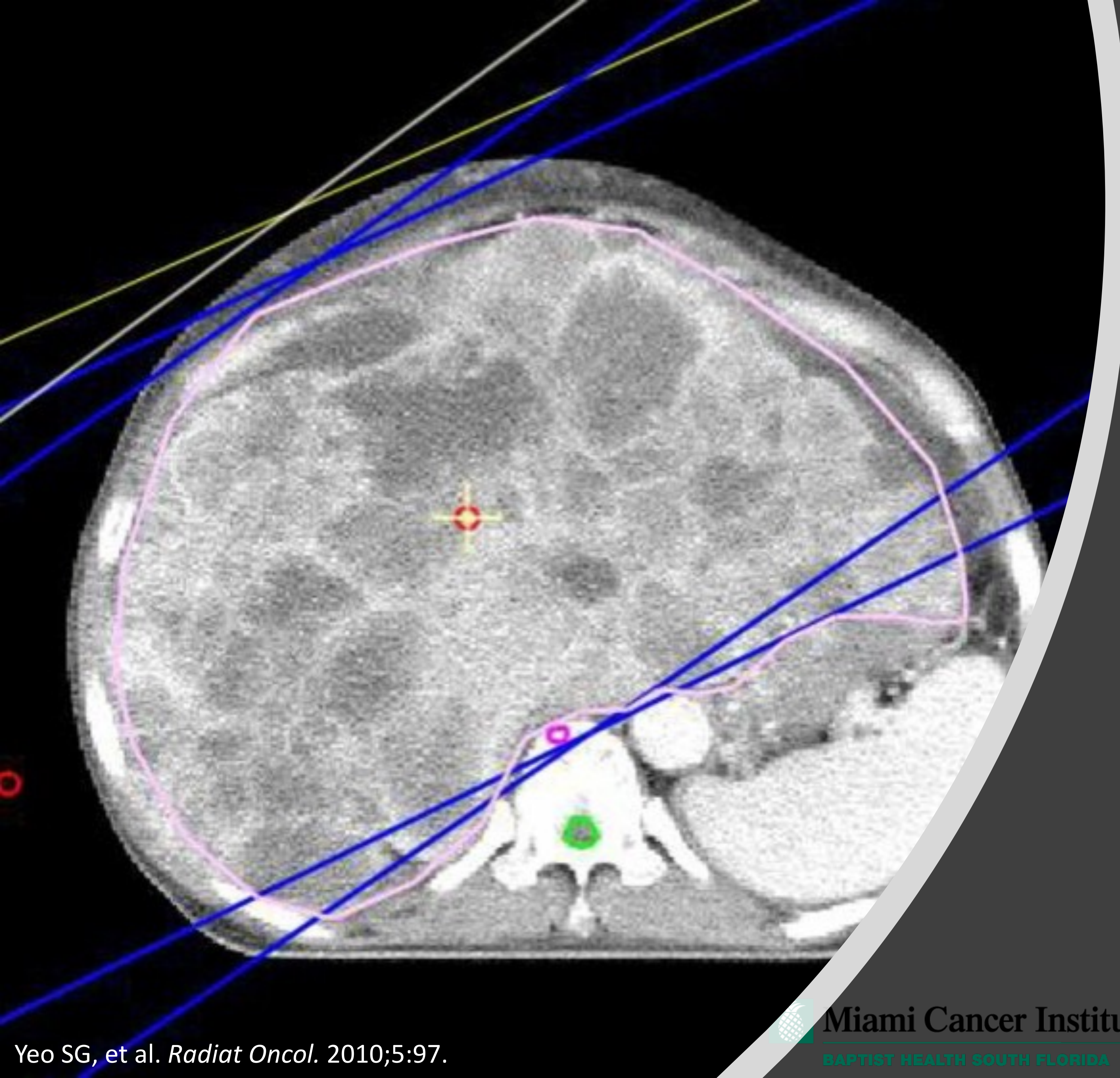
Normal Liver Tolerance

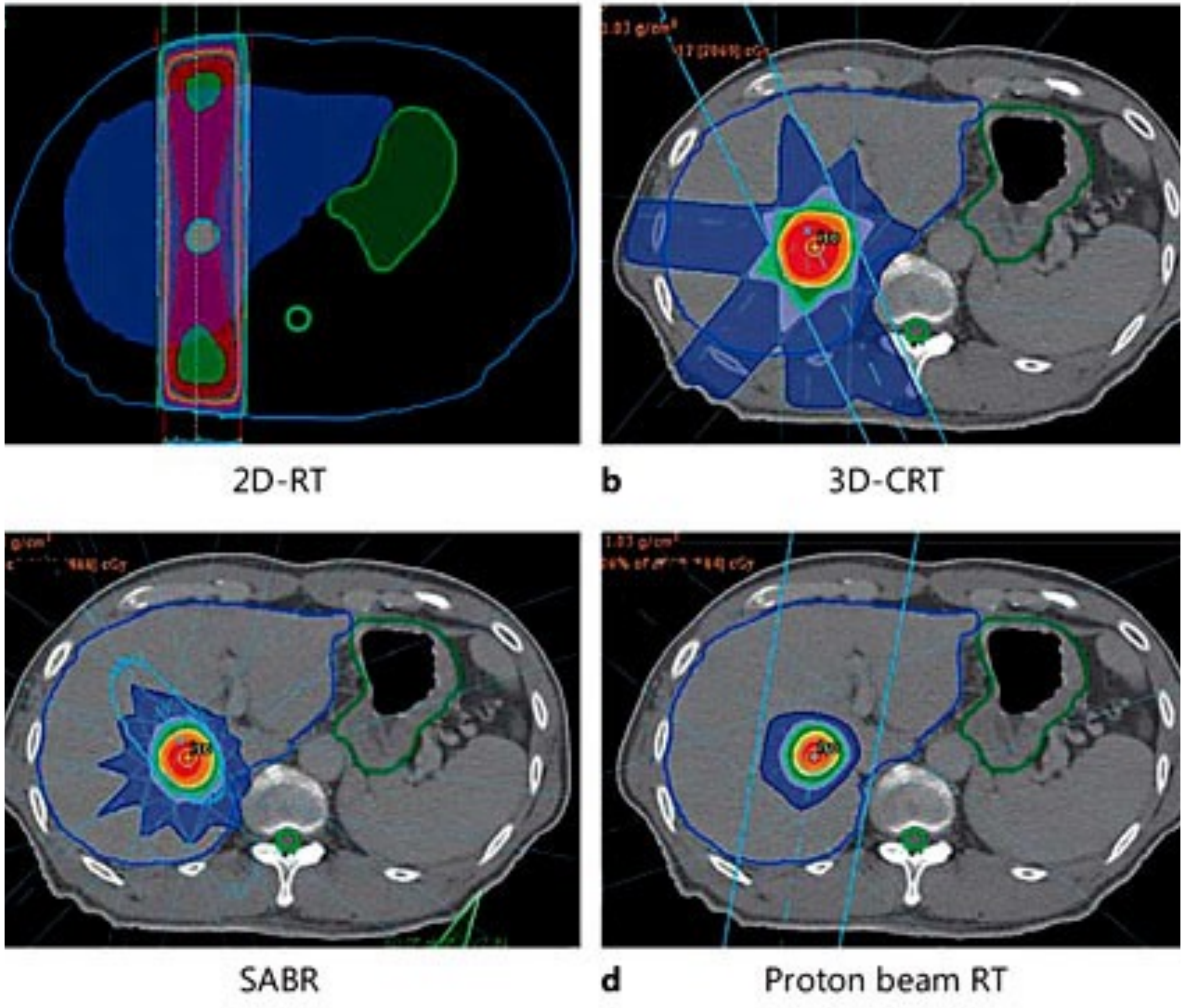
- The liver is a **parallel-functioning** organ
- **Mean liver dose** is associated with risk of RILD
  - High dose to **small liver volumes** can be well tolerated
  - **Low doses** to the liver should be minimized
- **Other factors** contribute to RILD
  - Baseline liver function
  - Volume of uninvolved liver
  - Prior therapy



Only palliative whole-liver Rt was initially possible

Yeo SG, et al. *Radiat Oncol.* 2010;5:97.

Moving the needle from palliative to curative



Yu JI, Park HC. *Dig Dis.* 2014;32(6):755-63.

International Journal of Radiation Oncology biology • physics
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Clinical Investigation

Dose-Response Relationship in Stereotactic Body Radiation Therapy for Hepatocellular Carcinoma: A Pooled Analysis of an Asian Liver Radiation Therapy Group Study

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Su *et al. Radiat Oncol* (2021) 16:79
https://doi.org/10.1186/s13014-021-01778-6

Radiation Oncology

RESEARCH Open Access

Optimal stereotactic body radiotherapy dosage for hepatocellular carcinoma: a multicenter study

Ting-Shi Su[1,2*], Qiu-Hua Liu[2], Xiao-Fei Zhu[3], Ping Liang[2], Shi-Xiong Liang[1], Lin Lai[2], Ying Zhou[2], Yong Huang[2], Tao Cheng[2] and Le-Qun Li[4*]

Abstract

Background: The optimal dose and fractionation scheme of stereotactic body radiation therapy (SBRT) for hepatocellular carcinoma (HCC) remains unclear due to different tolerated liver volumes and degrees of cirrhosis. In this study, we aimed to verify the dose-survival relationship to optimize dose selection for treatment of HCC.

Methods: This multicenter retrospective study included 602 patients with HCC, treated with SBRT between January 2011 and March 2017. The SBRT dosage was classified into high dose, moderate dose, and low dose levels: SaRT ($BED_{10} \geq 100$ Gy), SbRT ($EQD_2 > 74$ Gy to $BED_{10} < 100$ Gy), and ScRT ($EQD_2 < 74$ Gy). Overall survival (OS), progression-free survival (PFS), local control (LC), and intrahepatic control (IC) were evaluated in univariable and multivariable analyses.

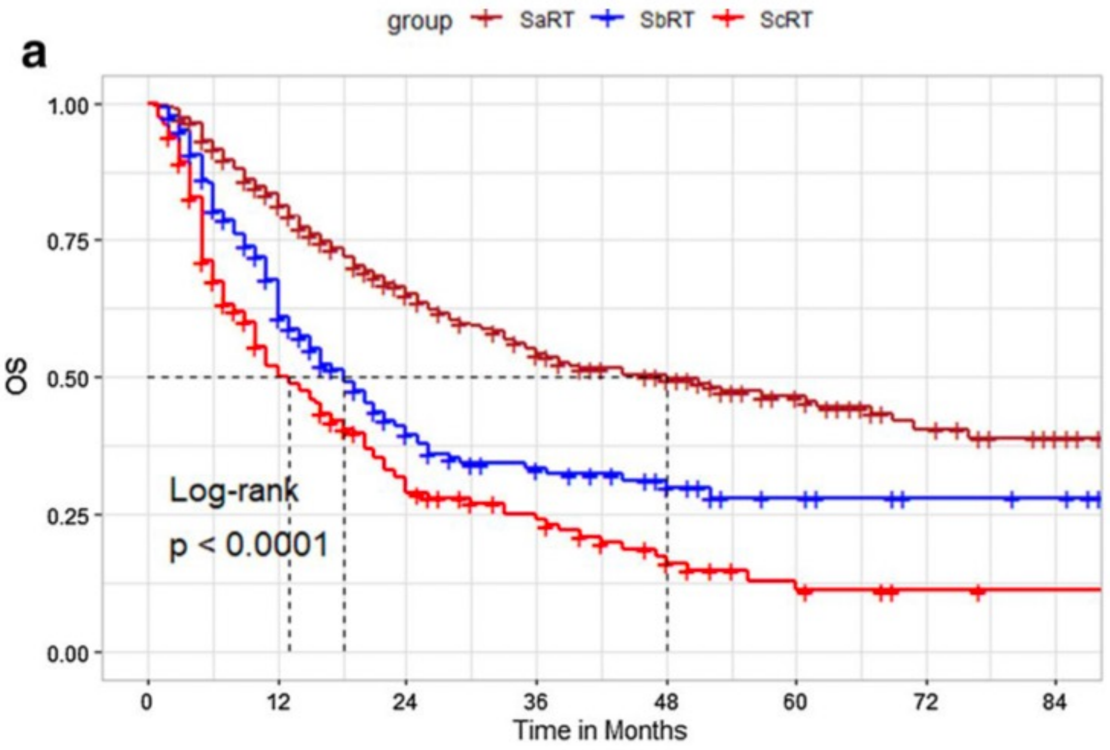
Results: The median tumor size was 5.6 cm (interquartile range [IQR] 1.1–21.0 cm). The median follow-up time was 50.0 months (IQR 6–100 months). High radiotherapy dose correlated with better outcomes. After classifying into the SaRT, SbRT, and ScRT groups, three notably different curves were obtained for long-term post-SBRT survival and intrahepatic control. On multivariate analysis, higher radiation dose was associated with improved OS, PFS, and intrahepatic control.

Conclusions: If tolerated by normal tissue, we recommend SaRT ($BED_{10} \geq 100$ Gy) as a first-line ablative dose or SbRT ($EQD_2 \geq 74$ Gy) as a second-line radical dose. Otherwise, ScRT ($EQD_2 < 74$ Gy) is recommended as palliative irradiation.

Keywords: Hepatocellular carcinoma, Radiotherapy dosage, Stereotactic body radiotherapy, Survival rate

BED ≥100 Gy Is Ablative

Su et al, Radiat Oncol 2021



Kim et al, IJROBP 2020

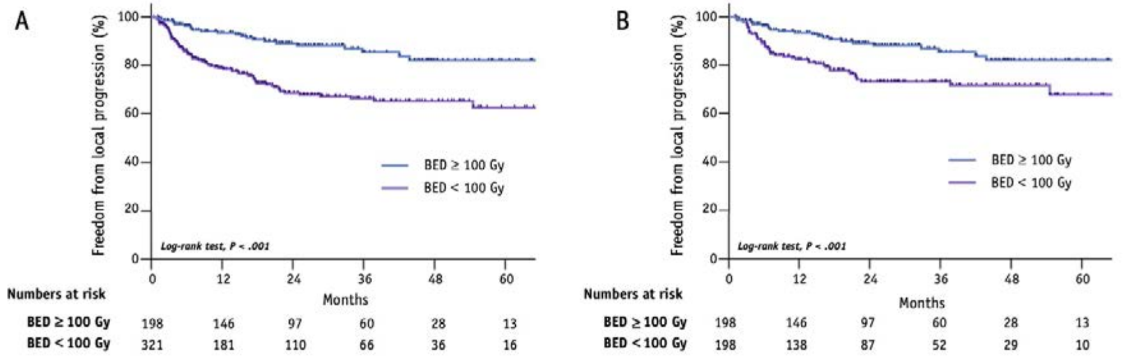


Fig. 1. Kaplan-Meier curves before (A) and after (B) propensity score matching for freedom from local progression after stereotactic body radiation therapy stratified by a biologically effective dose (BED) of 100 Gy.

Clinical and Translational Radiation Oncology 20 (2020) 45–50

Contents lists available at ScienceDirect

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journal homepage: www.elsevier.com/locate/ctro

Original Research Article

High versus low dose Stereotactic Body Radiation Therapy for hepatic metastases

Esther N.D. Kok [a,*], Edwin P.M. Jansen [b], Birthe C. Heeres [c], Niels F.M. Kok [a], Tomas Janssen [b], Erik van Werkhoven [d], Fay R.K. Sanders [e], Theodore J.M. Ruers [a,f], Marlies E. Nowee [b,1], Koert F.D. Kuhlmann [a,1]

[a] Department of Surgical Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands
[b] Department of Radiation Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands
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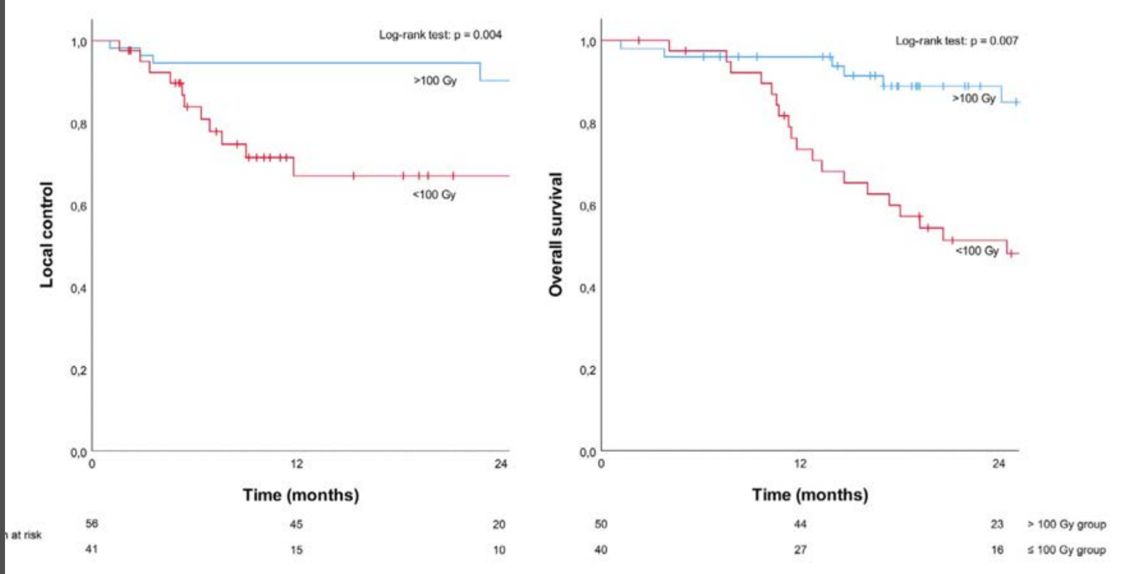
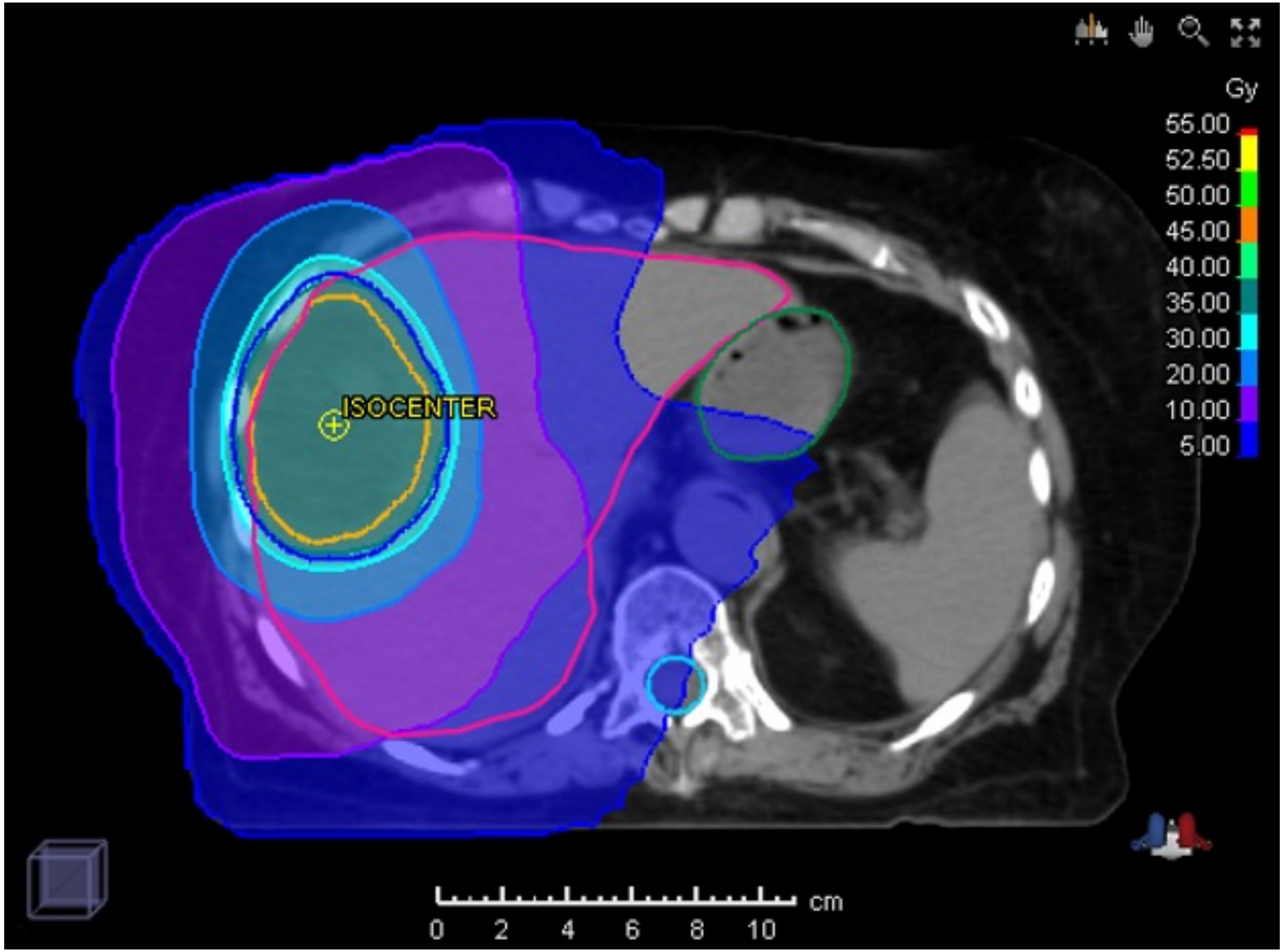
[f] Technical University of Twente, Faculty TNW, Enschede, The Netherlands

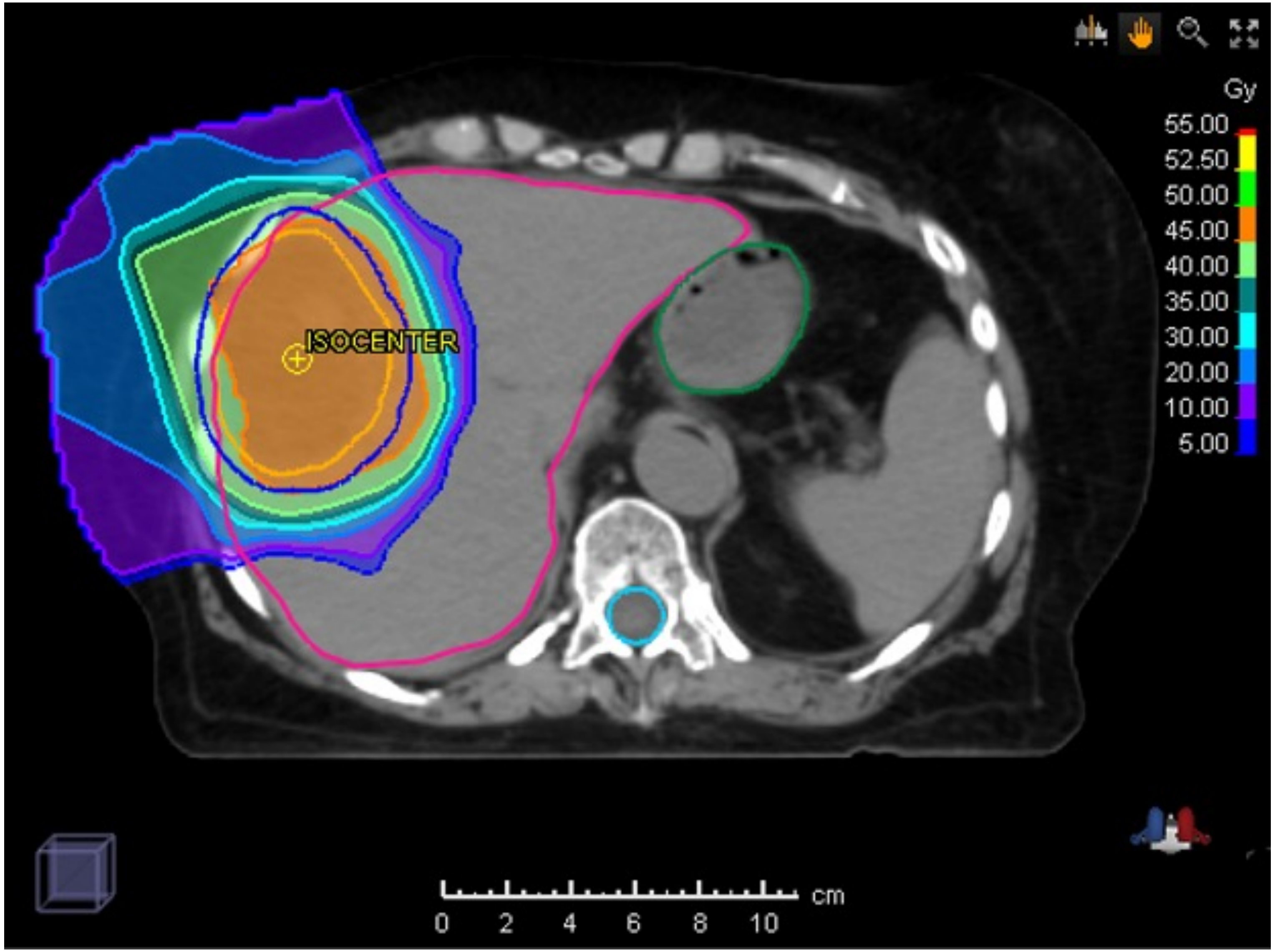


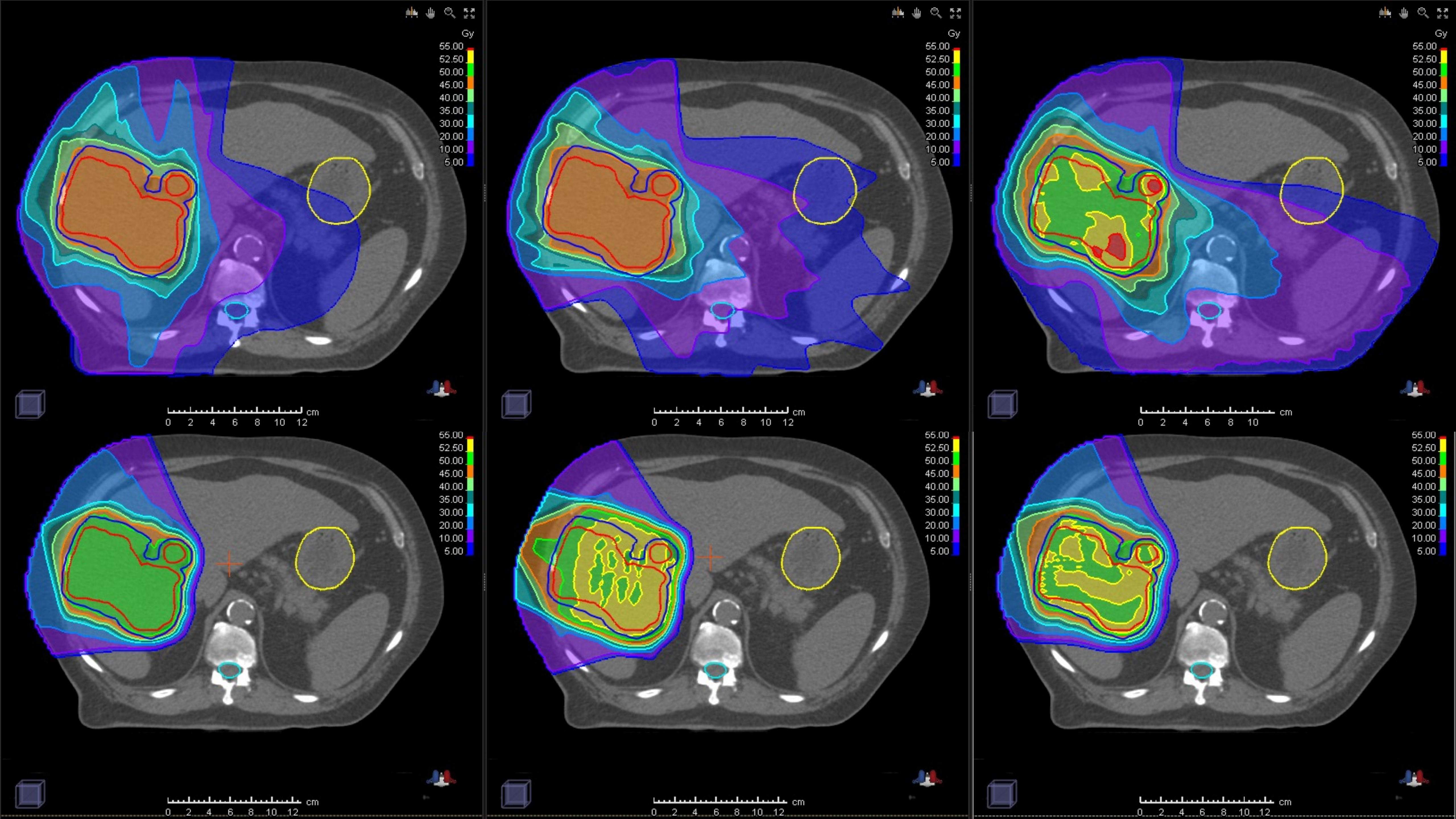

(IDEALLY ABLATIVE) TUMOR DOSE
(IDEALLY ZERO) LIVER DOSE

Large volume of liver may receive unintentional dose



Proton therapy offers dramatic liver sparing

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cm
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Gy
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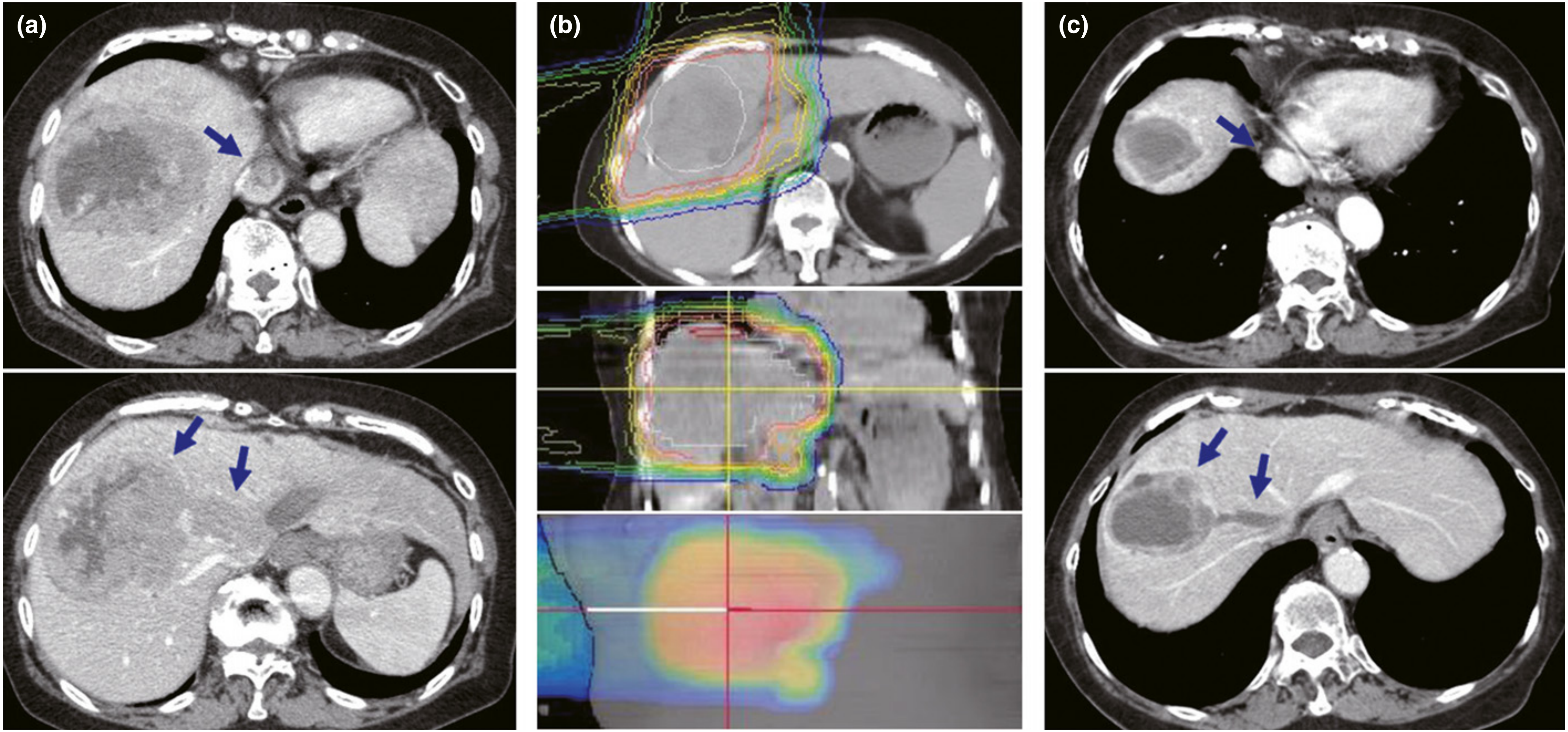


Fig. 3. Computed tomography (CT) images of an 81-year-old woman with advanced HCC involving a massive tumor thrombus in the IVC. Images were obtained before PBT (a), during isodose distribution of PBT (b), and 2 months after the completion of PBT (c). PBT demonstrated marked regression of both the main tumor and tumor thrombus (arrows). Isodose distribution is shown using contour lines (red line, 90% isodose; blue line, 10% isodose). HCC, hepatocellular carcinoma; IVC, inferior vena cava; PBT, proton beam therapy.

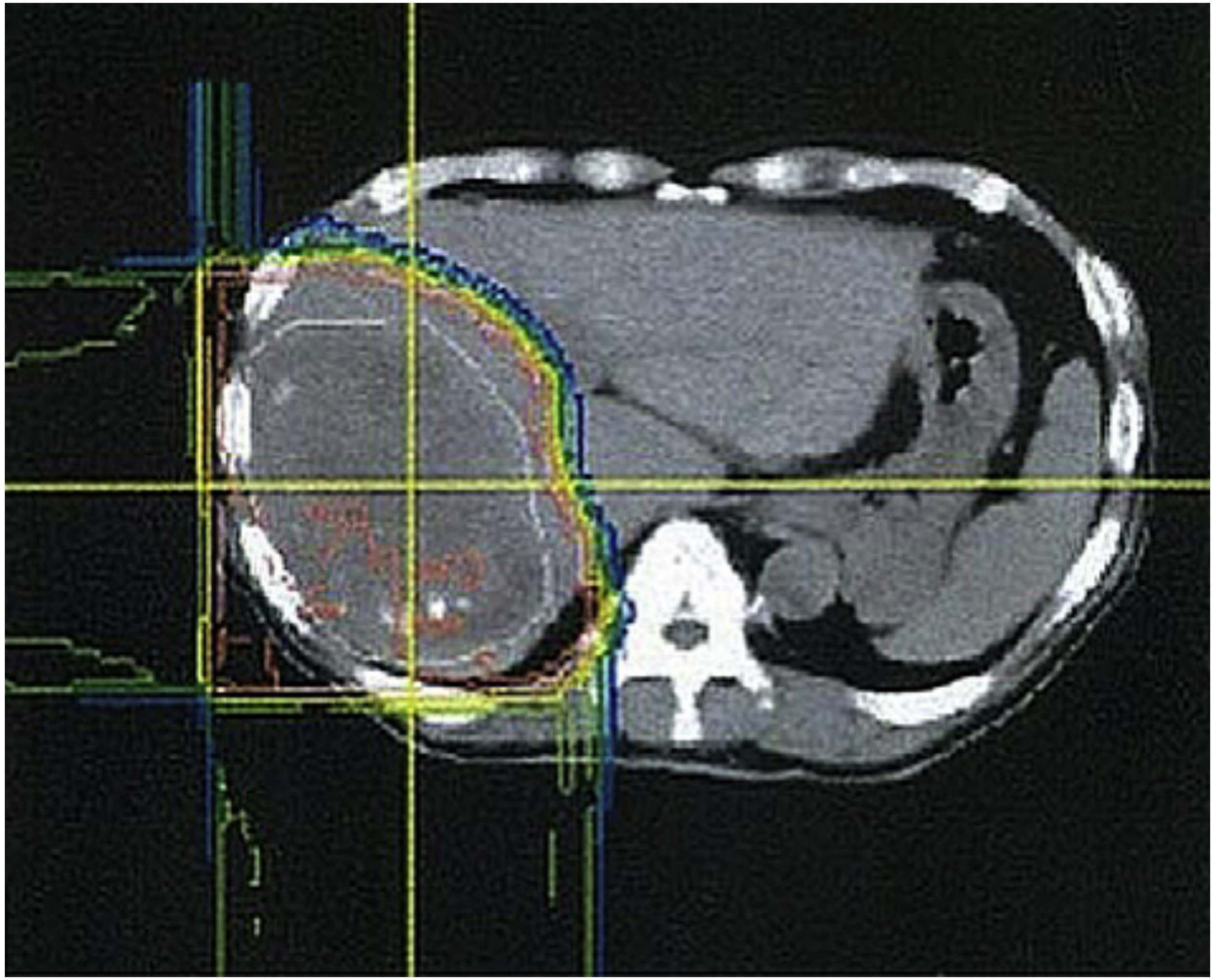
Fukuda et al. Cancer Sci 2017.

Large HCC

Median, 11 cm

72.6 GyE in 22 fractions (BED_{10} 97 Gy)

No grade 3+ toxicity



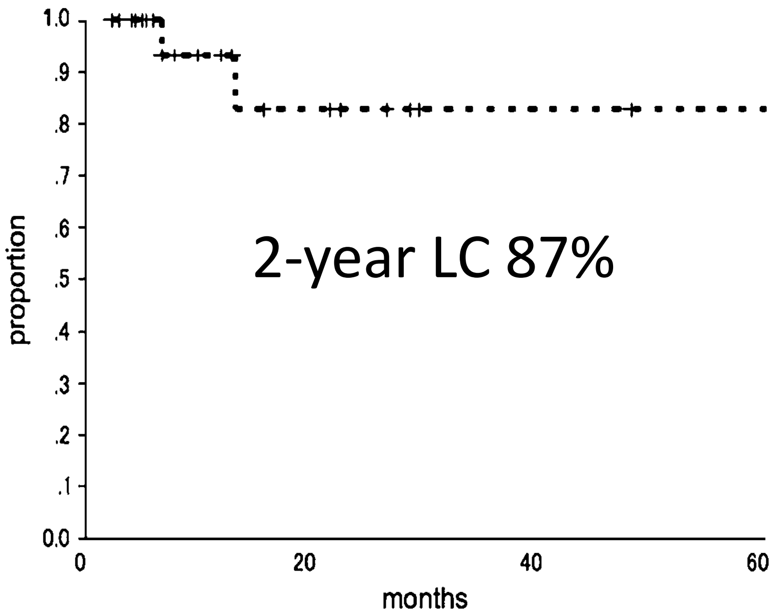
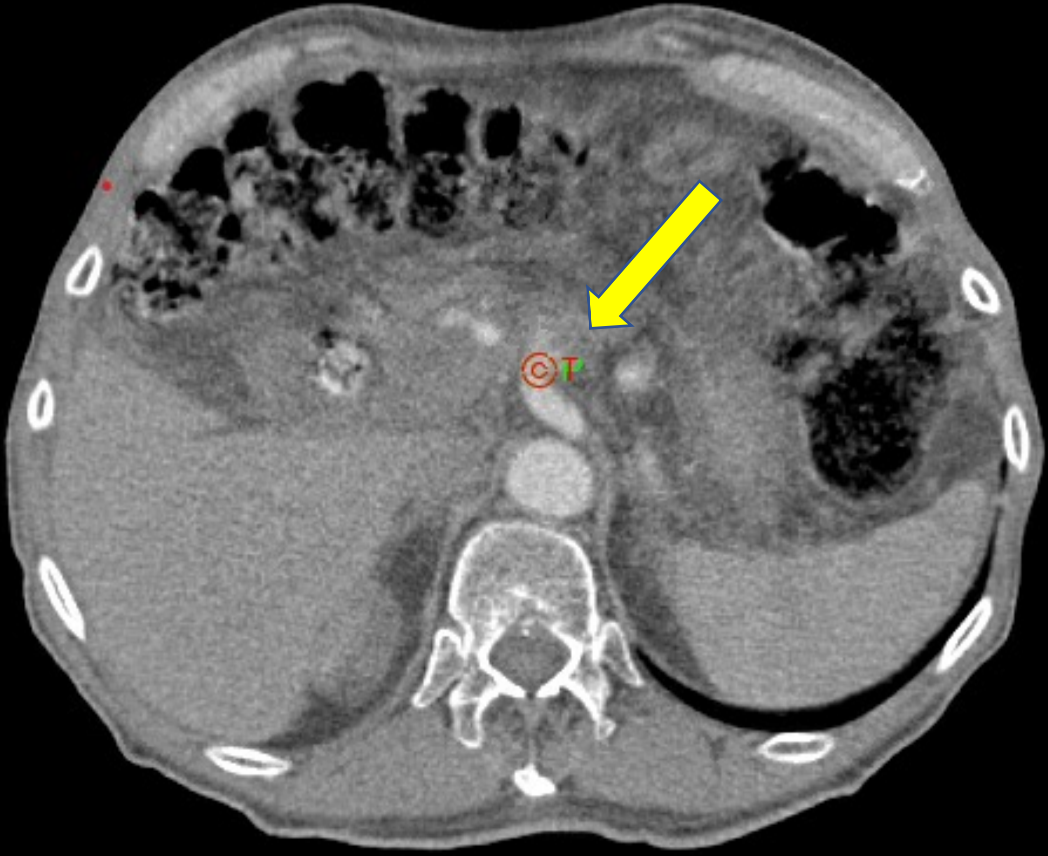


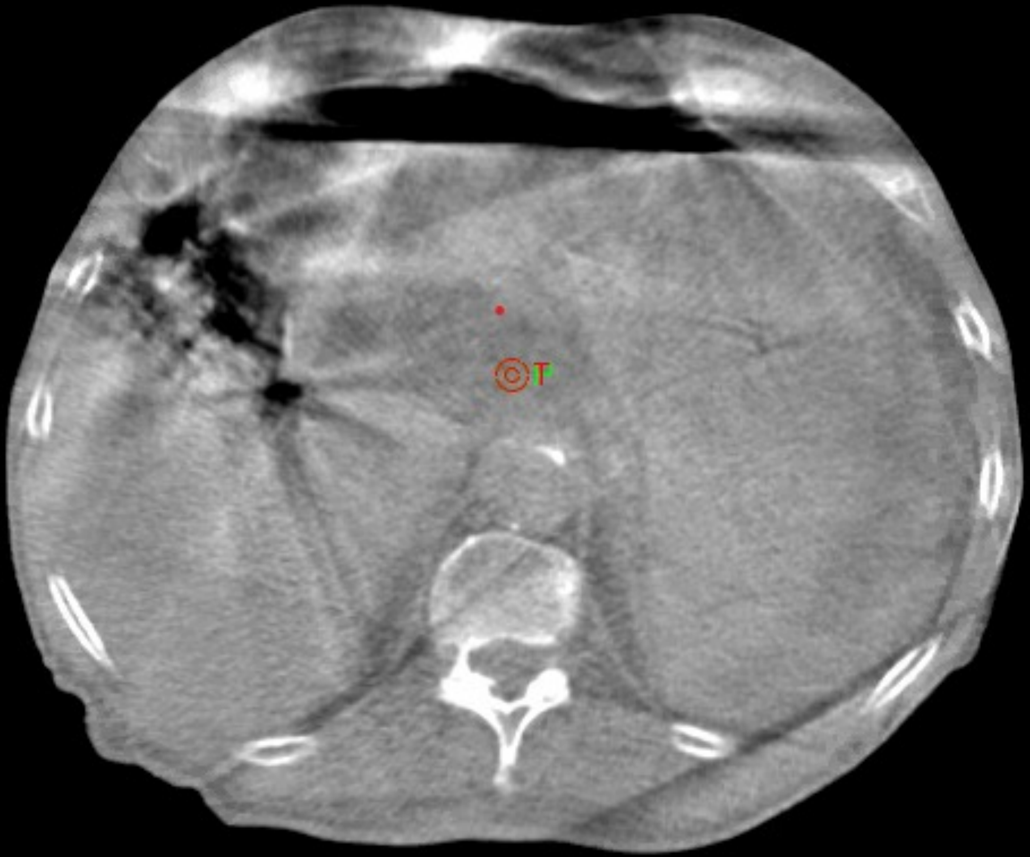
Fig. 2. Local control rates in 22 patients with hepatocellular carcinoma exceeding 10 cm treated with proton beam therapy.

Sugahara S, et al. *Int J Radiat Oncol Biol Phys*. 2010.

SIMULATION SCAN



PRETREATMENT SCAN



IMAGING DURING TREATMENT

X


Treatment
Daily QA
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Jaw Tracking
Unapp Fraction 1 of 0
Field 1 0/1500
Primary User krh
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PATIENT ORIENTATION
Head First, Supine
Privacy Shade
QA mode
WARNING: This mode is not to be used for clinical treatments, as it does not record dose.
To pause treatment, press Beam Off.
Preview
Prepare
Ready
Beam On
Record
Beam
Plan
Actual
Beam Type DYNAMIC (VMAT)
Energy Type 10xFFF
MU 1
MU 2
MU 1500
641
642
Dose Rate 2400 1228
Time 1.19 0.47
EDW None None
Int Mount No Accy No Accy
Acc Mount No Accy No Accy
e-Aperture No Accy No Accy
Comp Mount No Accy No Accy
Bolus None
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Plan
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Gantry Rtn 179.0 15.5
Gantry Stop 181.0
Coll Rtn 10.0 10.0
Y1 6.8 7.8
Y2 7.8 7.8
X1 7.7 6.0
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Lat 0.00 0.00
Rtn 0.0 0.0
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X=12.5
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MLC Arc Dynamic
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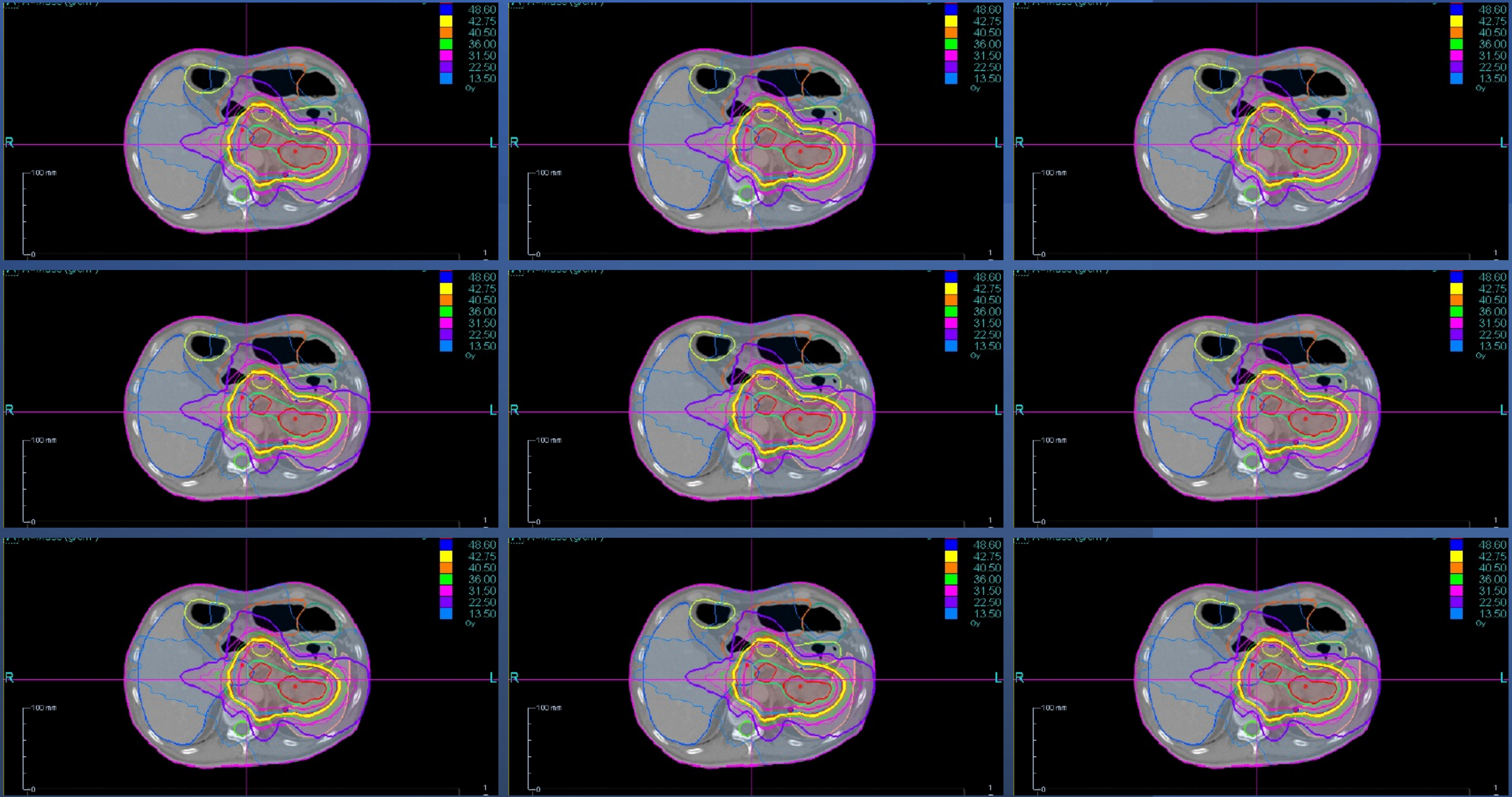
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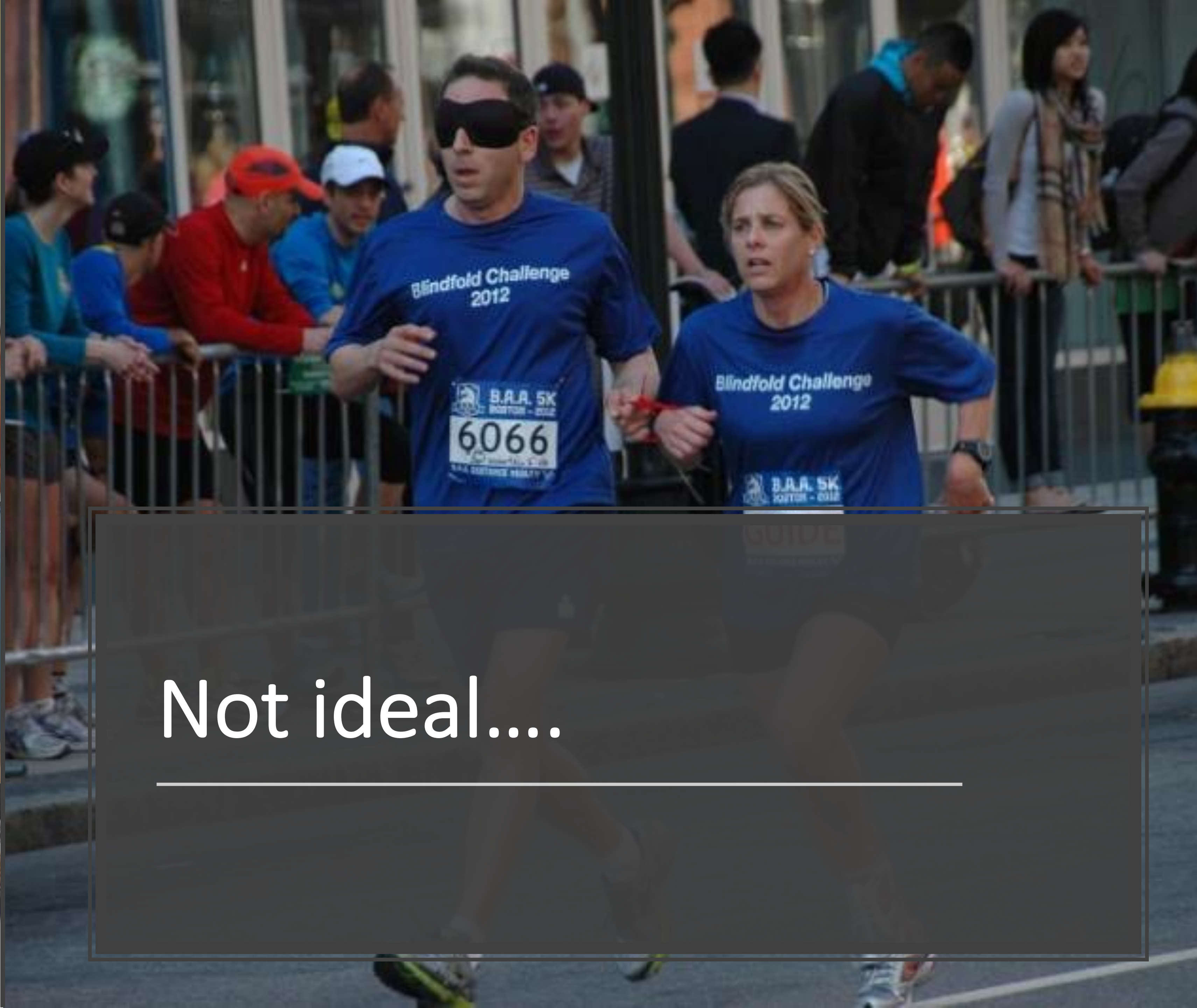
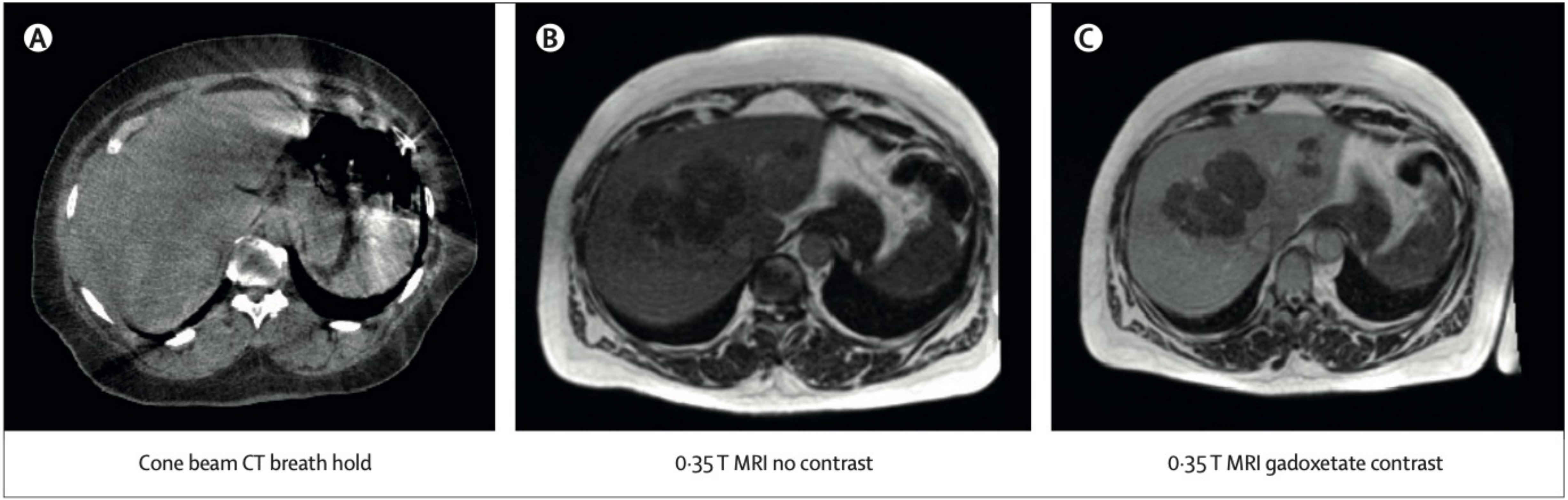

Blindfold Challenge 2012
B.A.A. 5K
6066
Blindfold Challenge 2012
B.A.A. 5K

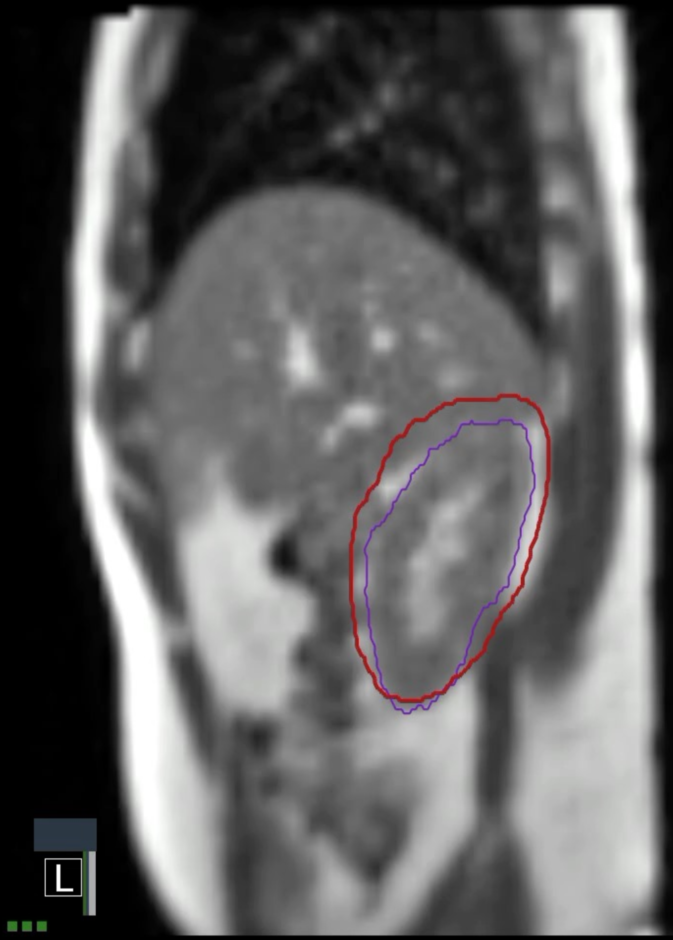
Not ideal....

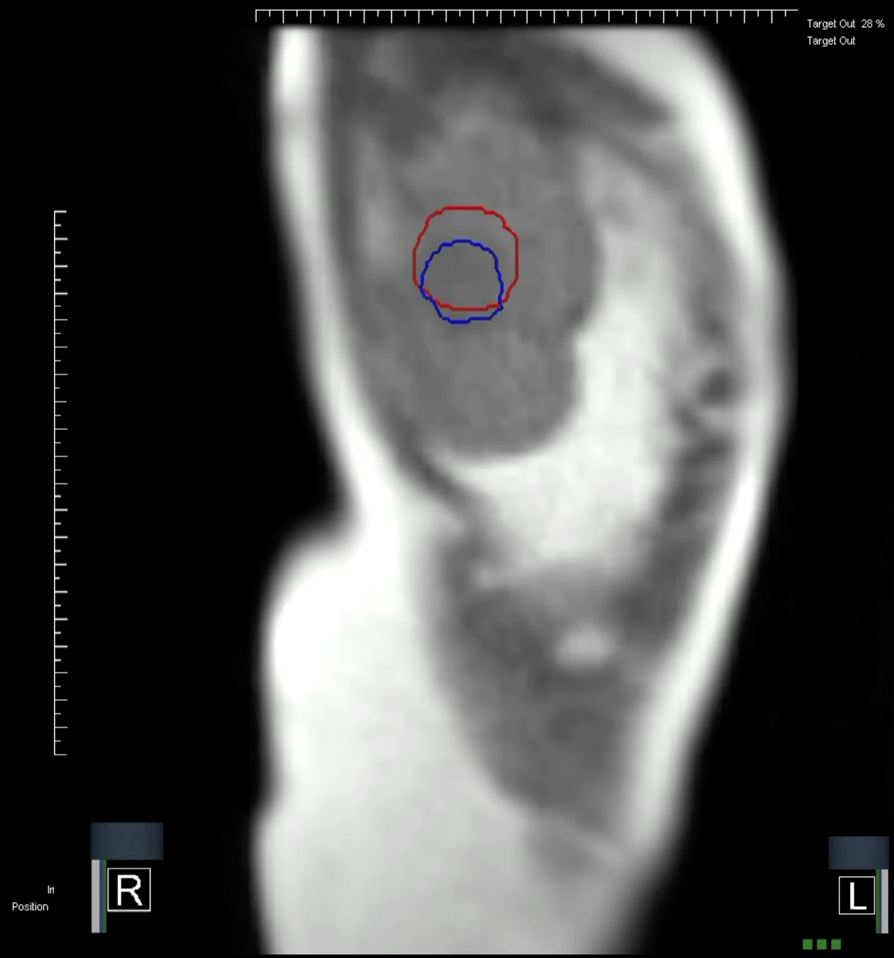


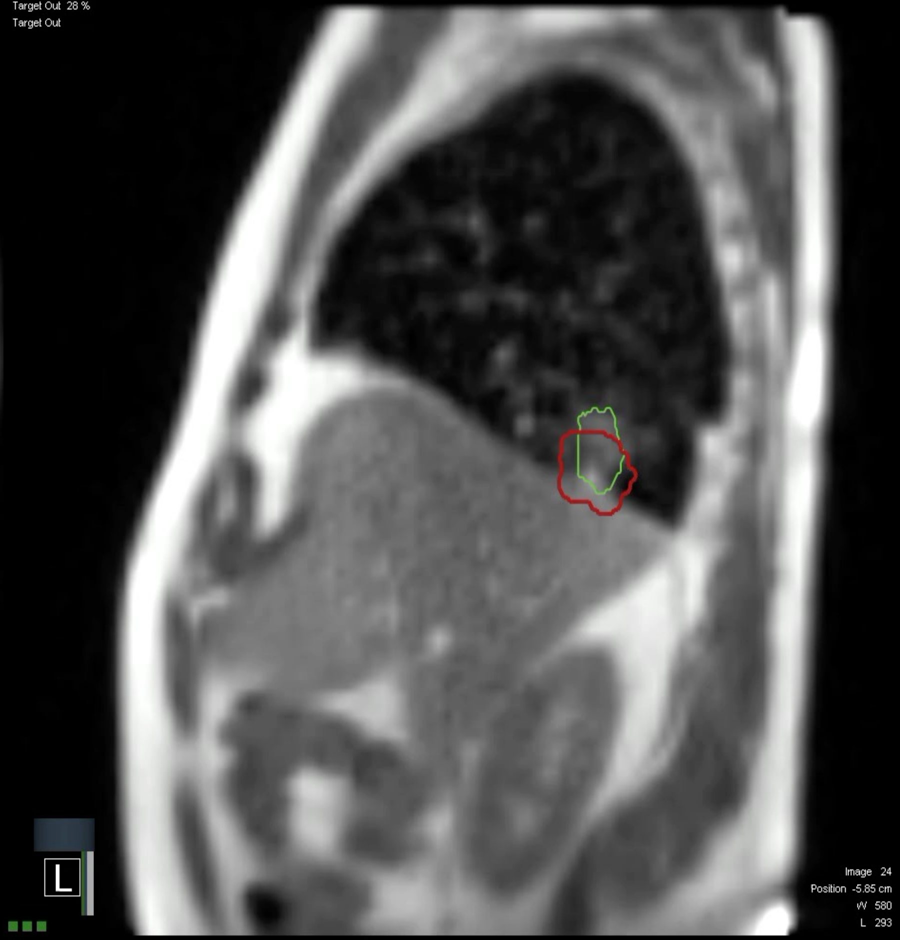
Since MRI is used for diagnosis, wouldn’t it be ideal to guide treatment?

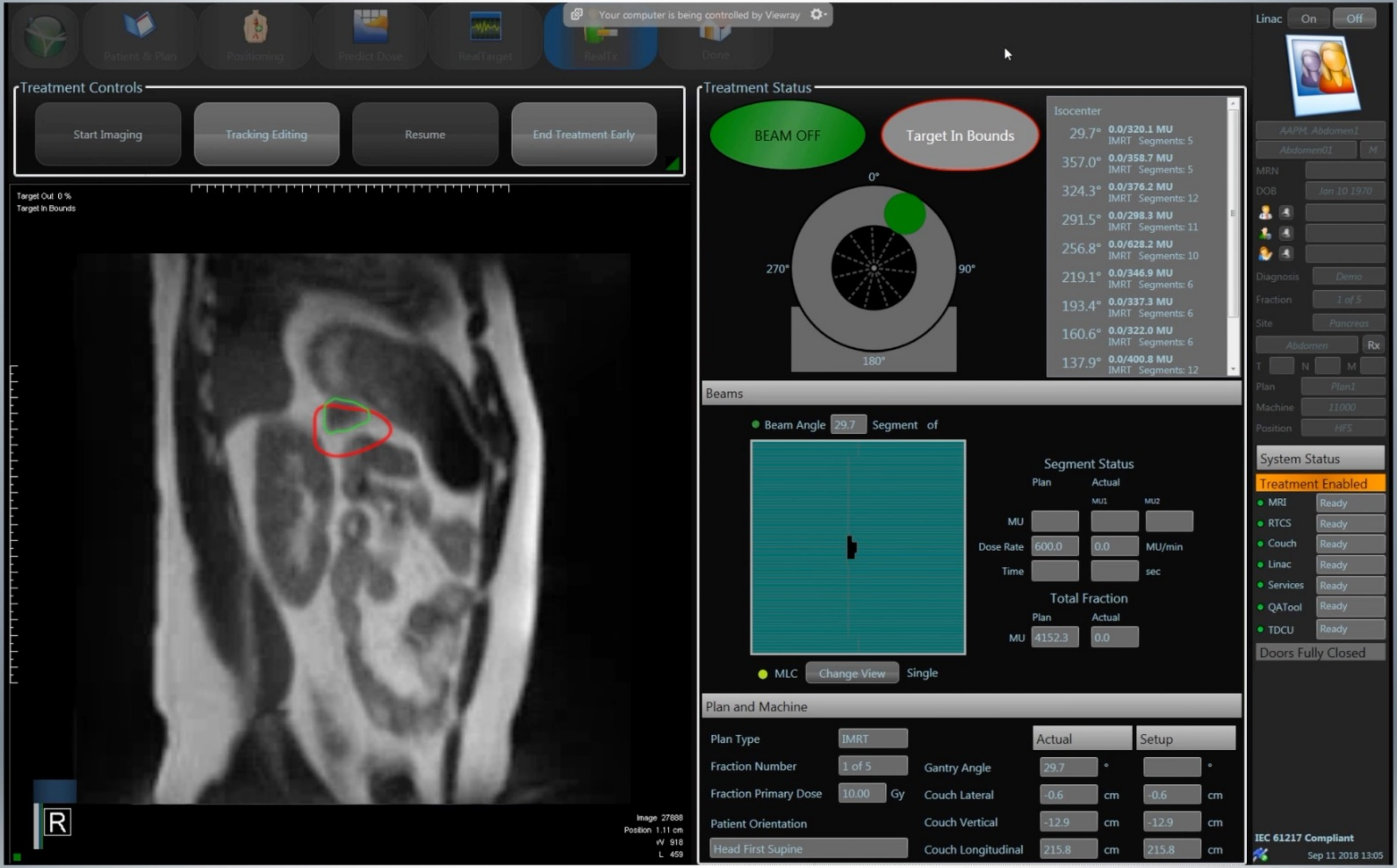
Witt et al. Lancet Oncol, 2020.

Continuous Imaging Through Treatment









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Start Imaging
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Resume
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29.7° 0.0/320.1 MU IMRT Segments: 5
357.0° 0.0/358.7 MU IMRT Segments: 5
324.3° 0.0/376.2 MU IMRT Segments: 12
291.5° 0.0/298.3 MU IMRT Segments: 11
256.8° 0.0/628.2 MU IMRT Segments: 10
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193.4° 0.0/337.3 MU IMRT Segments: 6
160.6° 0.0/322.0 MU IMRT Segments: 6
137.9° 0.0/400.8 MU IMRT Segments: 12
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Beam Angle 29.7 Segment of
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Fraction Number 1 of 5
Fraction Primary Dose 10.00 Gy
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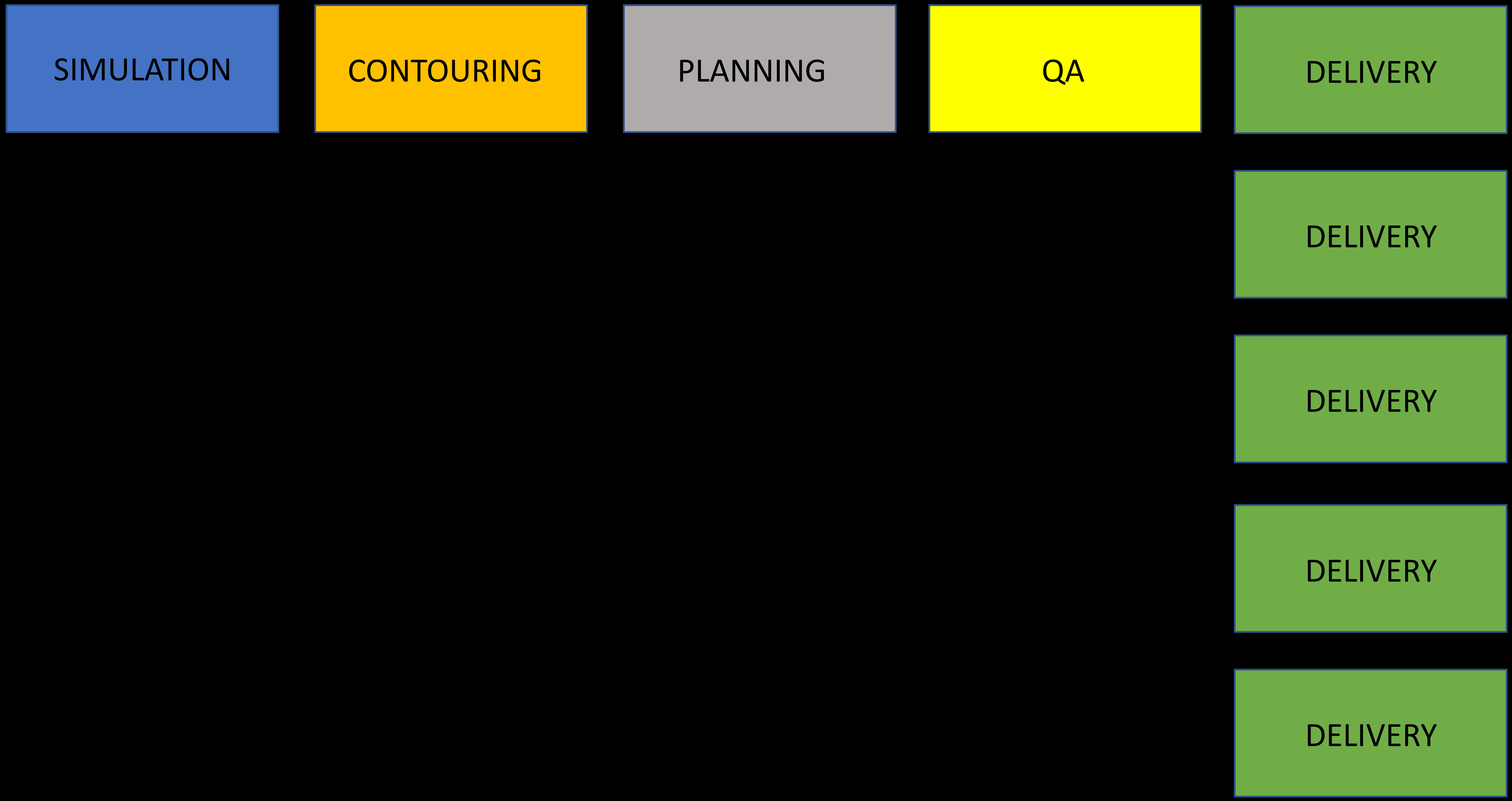
Couch Vertical -12.9 cm -12.9 cm
Couch Longitudinal 215.8 cm 215.8 cm
AAPM, Abdomen1
Abdomen01
MRN
DOB Jan 10 1970
Diagnosis Demo
Fraction 1 of 5
Site Pancreas
Abdomen
Rx
T
N
M
Plan Plan1
Machine 11000
Position HFS
System Status
Treatment Enabled
MRI Ready
RTCS Ready
Couch Ready
Linac Ready
Services Ready
QATool Ready
TDCU Ready
Doors Fully Closed
IEC 61217 Compliant
Sep 11 2018 13:05


Institute


SIMULATION
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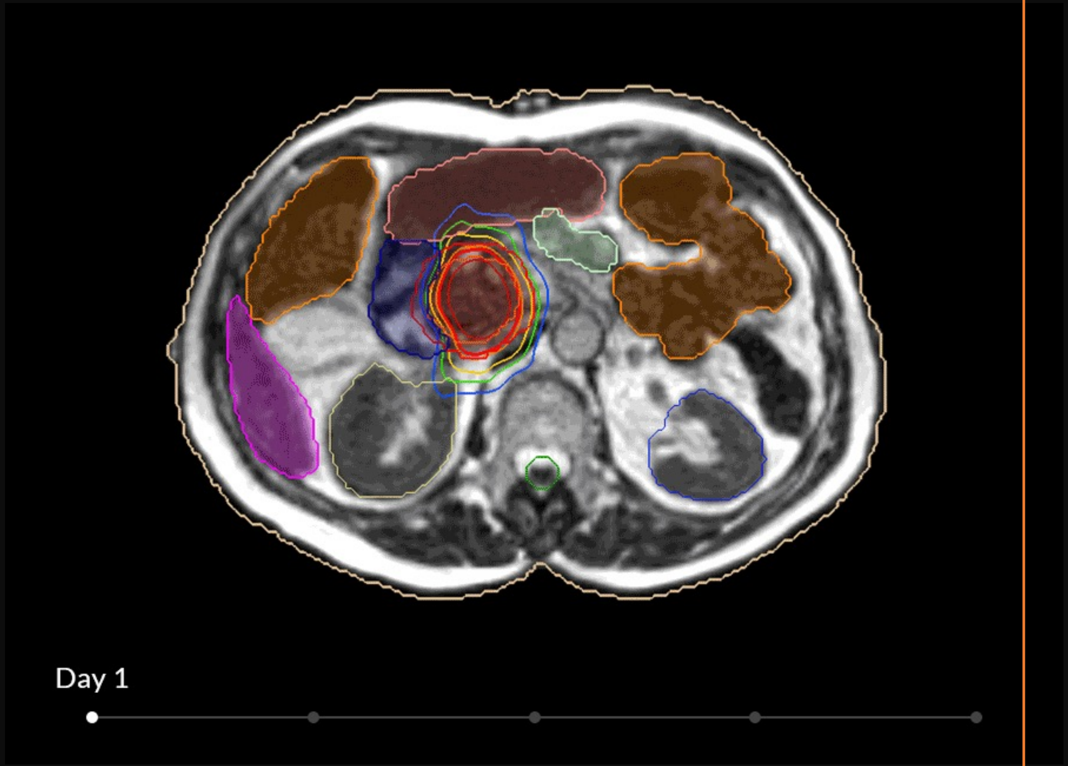
SIMULATION	CONTOURING	PLANNING	QA	DELIVERY
SIMULATION	CONTOURING	PLANNING	QA	DELIVERY
SIMULATION	CONTOURING	PLANNING	QA	DELIVERY
SIMULATION	CONTOURING	PLANNING	QA	DELIVERY
SIMULATION	CONTOURING	PLANNING	QA	DELIVERY

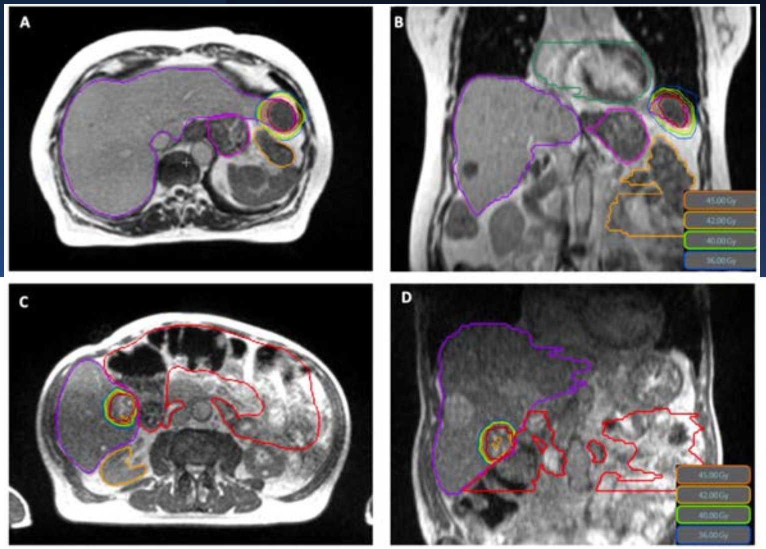
Daily adaptive replanning

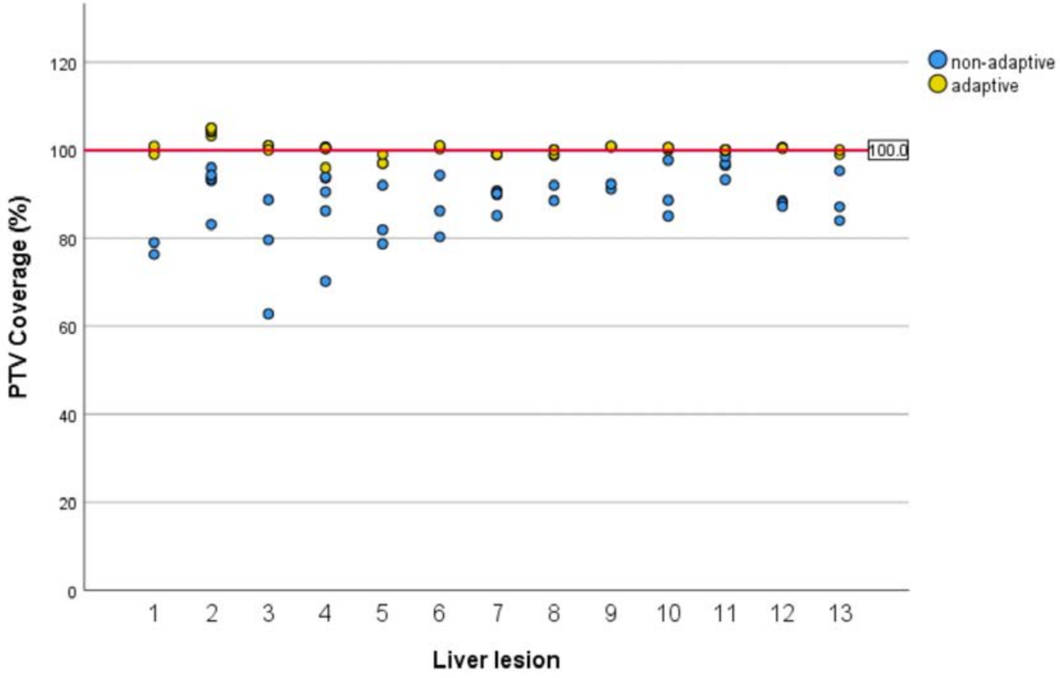
- CT-guided: completed over **days**
- MR-guided: completed in **minutes**

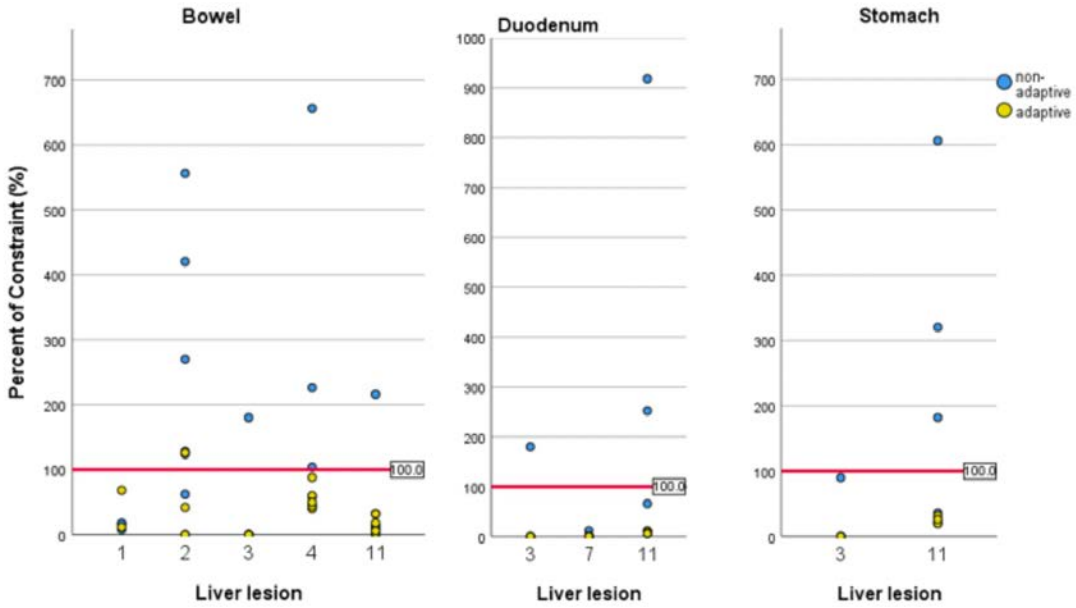


University Hospital LMU Munich

Rogowski, Corradini et al. Cancers, 2021.

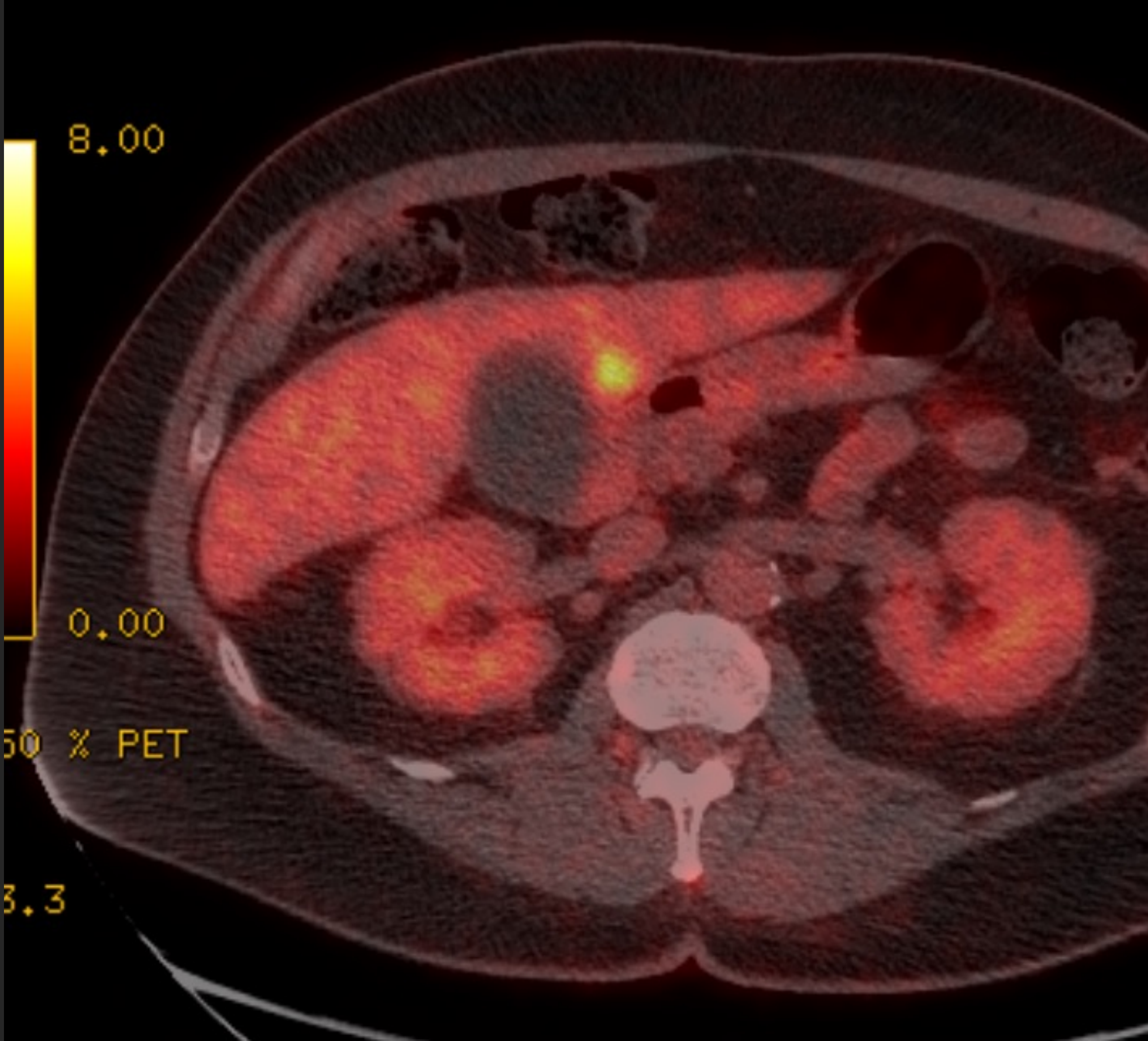




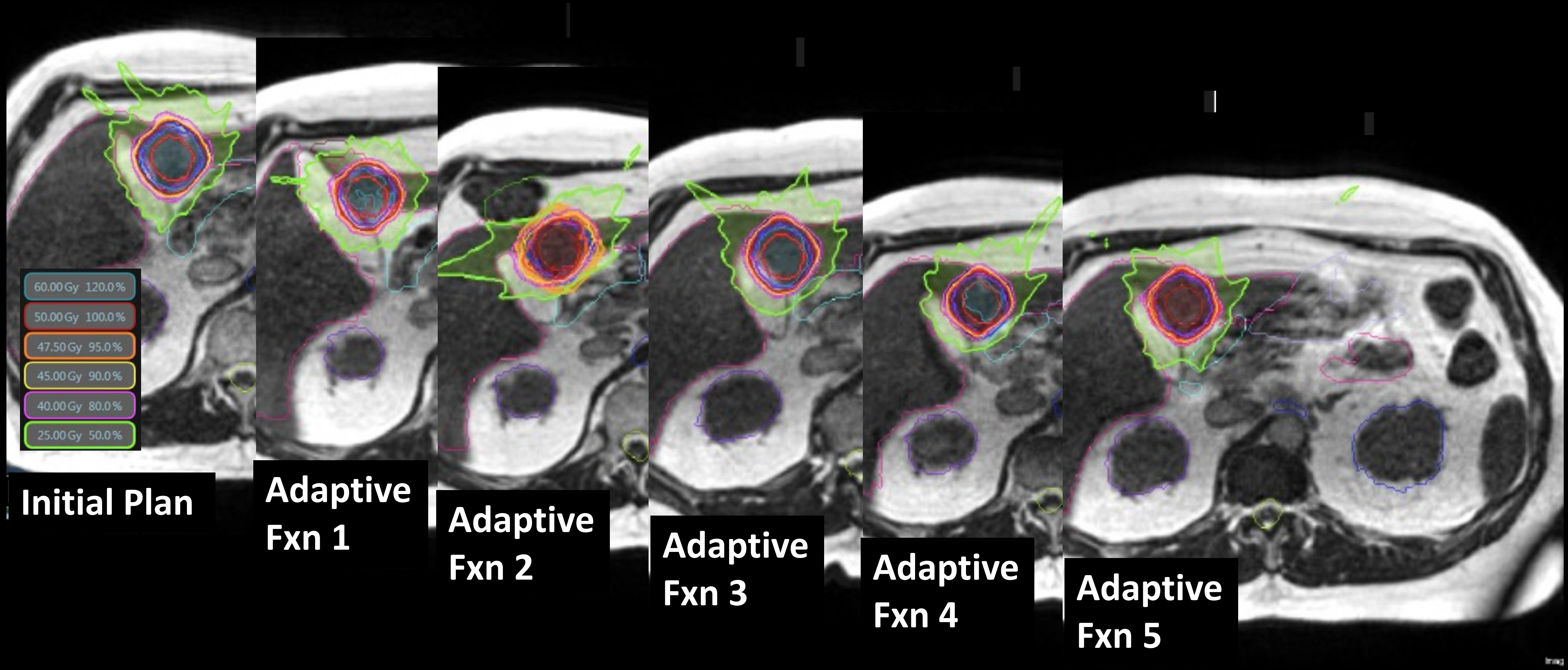


Colorectal liver metastasis near duodenum

Standard SBRT approach for this case would be <u>non-ablative</u>



10 Gy x 5 (BED_{10} = 100 Gy)



Advances in Radiation Oncology (2020) **5**, 761-773

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in radiation oncology

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Critical Review

Single-Fraction Stereotactic Body Radiation Therapy: A Paradigm During the Coronavirus Disease 2019 (COVID-19) Pandemic and Beyond?

Sylvia S.W. Ng, MD, PhD,[a] Matthew S. Ning, MD, MPH,[a] Percy Lee, MD,[a] Ryan A. McMahon, MD,[b] Shankar Siva, MBBS, PhD,[b] and Michael D. Chuong, MD[c,]*

[a]Department of Radiation Oncology, The University of Texas MD Anderson Cancer Center, Houston, Texas; [b]Department of Radiation Oncology, Peter MacCallum Cancer Center, University of Melbourne, Victoria, Australia; and [c]Department of Radiation Oncology, Miami Cancer Institute, Miami, Florida

Received 11 May 2020; revised 9 June 2020; accepted 10 June 2020

Abstract

Purpose: Owing to the coronavirus disease 2019 (COVID-19) pandemic, radiation oncology departments have adopted various strategies to deliver radiation therapy safely and efficiently while minimizing the risk of severe acute respiratory syndrome coronavirus—2 transmission among patients and health care providers. One practical strategy is to deliver stereotactic body radiation therapy (SBRT) in a single fraction, which has been well established for treating bone metastases, although it has been infrequently used for other extracranial sites.

Methods and Materials: A PubMed search of published articles in English related to single-fraction SBRT was performed. A critical review was performed of the articles that described clinical outcomes of single-fraction SBRT for treatment of primary extracranial cancers and oligometastatic extraspinal disease.

Results: Single-fraction SBRT for peripheral early-stage non-small cell lung cancer is supported by randomized data and is strongly endorsed during the COVID-19 pandemic by the European Society for Radiotherapy and Oncology-American Society for Radiation Oncology practice guidelines. Prospective and retrospective studies supporting a single-fraction regimen are limited, although outcomes

Miami Cancer Institute Enrolls First Patients in Single-Fraction Stereotactic MRI-Guided Adaptive Radiation Therapy for Inoperable Primary or Metastatic Cancer Trial

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Investigator-Led Study Explores Feasibility and Tolerability of Single-fraction Stereotactic Ablative Body Radiotherapy Using MRIdian's Daily MRI-Guidance with On-Table Adaptive Replanning

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ViewRay, Inc. →
Jul 07, 2021, 06:30 ET

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CLEVELAND, July 7, 2021 /PRNewswire/ -- ViewRay, Inc. (NASDAQ: VRAY) today announced that the Miami Cancer Institute, part of Baptist Health South Florida, has enrolled the first patients in its "Stereotactic MRI-guided Adaptive Radiation Therapy (SMART) in One Fraction for Inoperable Primary or Metastatic Carcinoma" clinical study – referred to as the SMART ONE trial (NCT#04939246). This single-arm prospective study that was developed and led by Dr. Michael Chuong, MD, FACRO, radiation oncologist and Medical Director of Proton Therapy and MR-guided Therapy at Miami Cancer Institute, is exploring the feasibility and tolerability of single-fraction stereotactic ablative body radiation therapy (SABR) for primary or metastatic carcinoma involving the lung, liver, adrenal gland, abdominal/pelvic lymph node, pancreas, and kidney.*

Single-Fraction SABR

- Treatment delivery in breath hold: 17 minutes
- Total in-room time: 40 minutes
- No anesthesia, no contrast, no patient downtime

International Journal of
Radiation Oncology
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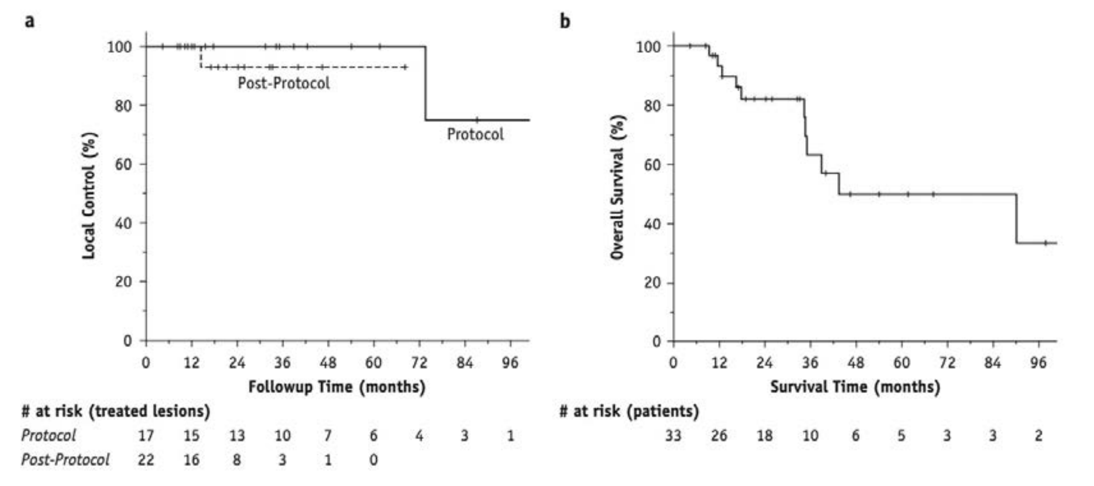
Clinical Investigation

Long-Term Results of a Phase 1 Dose-Escalation Trial and Subsequent Institutional Experience of Single-Fraction Stereotactic Ablative Radiation Therapy for Liver Metastases

Michael R. Folkert, MD, PhD,* Jeffrey J. Meyer, MD, MS,† Todd A. Aguilera, MD, PhD,* Takeshi Yokoo, MD, PhD,‡ Nina N. Sanford, MD,* William G. Rule, MD,§ John Mansour, MD,‖ Adam Yopp, MD,‖ Patricio Polanco, MD,‖ Raquibul Hannan, MD, PhD,* Lucien A. Nedzi, MD,* and Robert D. Timmerman, MD*

*Department of Radiation Oncology, UT Southwestern Medical Center, Dallas, Texas; †Department of Radiation Oncology and Molecular Radiation Sciences, Johns Hopkins University School of Medicine, Baltimore, Maryland; ‡Department of Radiology, UT Southwestern Medical Center, Dallas, Texas; §Department of Radiation Oncology, Mayo Clinic, Phoenix, Arizona; and ‖Department of Surgery, UT Southwestern Medical Center, Dallas, Texas

Received May 27, 2020, and in revised form Nov 21, 2020. Accepted for publication Dec 10, 2020.



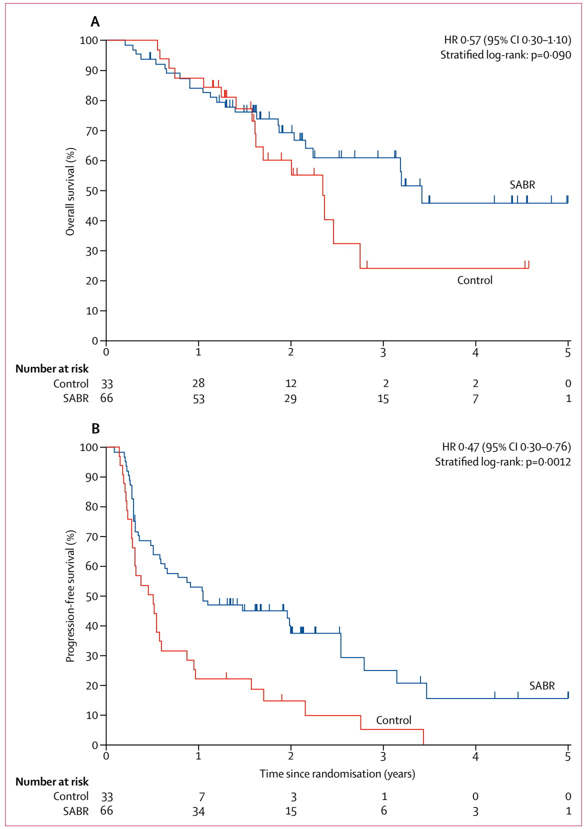
- 35-40 Gy in 1 fraction (BED_{10} = 157.5-200 Gy)
- 4-yr LC 96.4%
- No G3+ toxicity

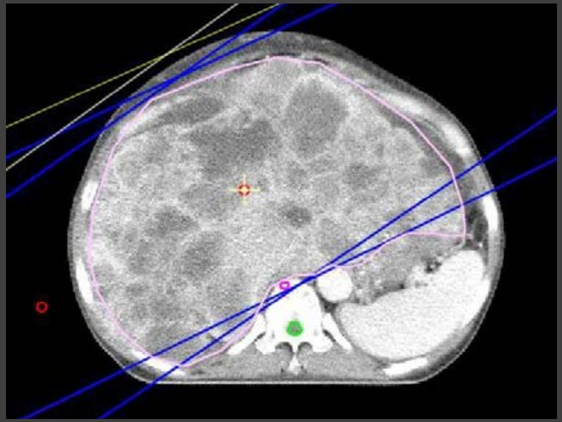
SBRT Improves OS for Oligometastatic Disease

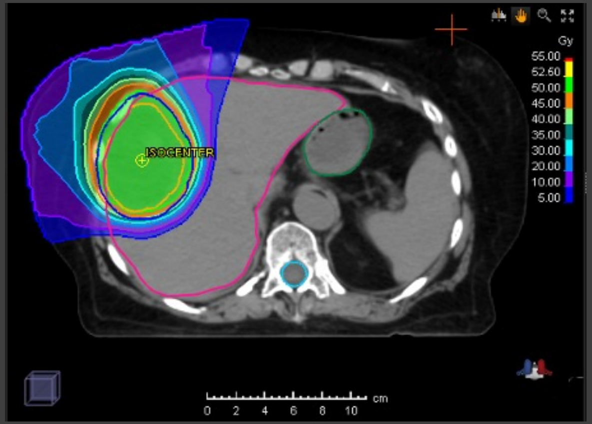
Stereotactic ablative radiotherapy versus standard of care palliative treatment in patients with oligometastatic cancers (SABR-COMET): a randomised, phase 2, open-label trial

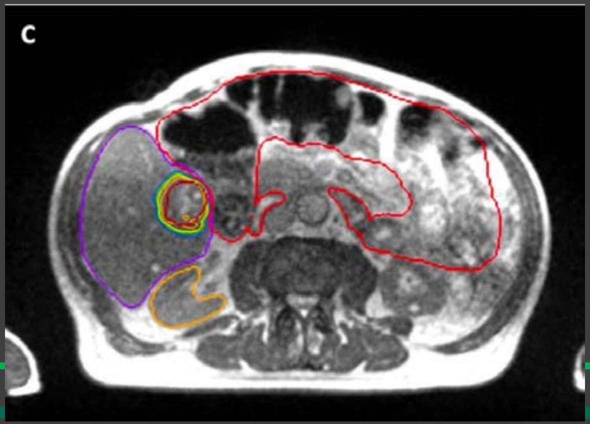
David A Palma, Robert Olson, Stephen Harrow, Stewart Gaede, Alexander V Louie, Cornelis Haasbeek, Liam Mulroy, Michael Lock, George B Rodrigues, Brian P Yaremko, Devin Schellenberg, Belal Ahmad, Gwendolyn Griffioen, Sashendra Senthi, Anand Swaminath, Neil Kopek, Mitchell Liu, Karen Moore, Suzanne Currie, Glenn S Bauman, Andrew Warner, Suresh Senan

Palma DA, et al. *Lancet*. 2019;393(10185):2051-2058.









We Have Come a Long Way

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Radiation Oncology

REVIEW **Open Access**

MR-guided proton therapy: a review and a preview

Check for updates

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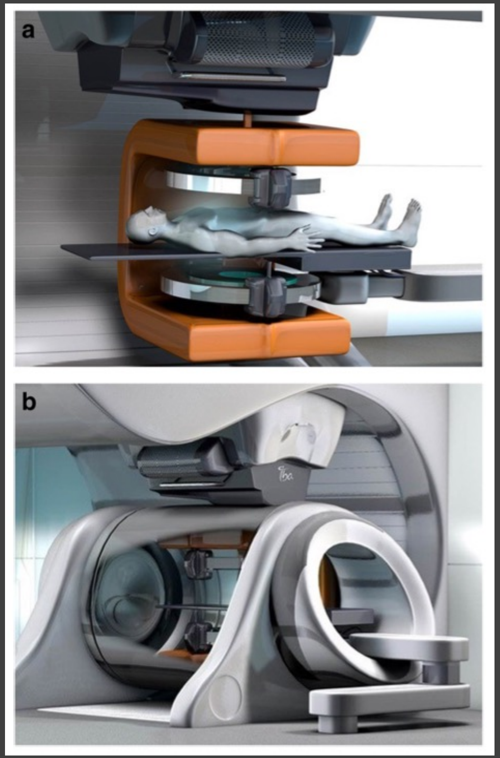
Abstract

Background: The targeting accuracy of proton therapy (PT) for moving soft-tissue tumours is expected to greatly improve by real-time magnetic resonance imaging (MRI) guidance. The integration of MRI and PT at the treatment isocenter would offer the opportunity of combining the unparalleled soft-tissue contrast and real-time imaging capabilities of MRI with the most conformal dose distribution and best dose steering capability provided by modern PT. However, hybrid systems for MR-integrated PT (MRiPT) have not been realized so far due to a number of hitherto open technological challenges. In recent years, various research groups have started addressing these challenges and exploring the technical feasibility and clinical potential of MRiPT. The aim of this contribution is to review the different aspects of MRiPT, to report on the *status quo* and to identify important future research topics.

Methods: Four aspects currently under study and their future directions are discussed: modelling and experimental investigations of electromagnetic interactions between the MRI and PT systems, integration of MRiPT workflows in clinical facilities, proton dose calculation algorithms in magnetic fields, and MRI-only based proton treatment planning approaches.

Conclusions: Although MRiPT is still in its infancy, significant progress on all four aspects has been made, showing promising results that justify further efforts for research and development to be undertaken. First non-clinical research solutions have recently been realized and are being thoroughly characterized. The prospect that first prototype MRiPT systems for clinical use will likely exist within the next 5 to 10 years seems realistic, but requires significant work to be performed by collaborative efforts of research groups and industrial partners.

Keywords: Proton therapy, Magnetic resonance imaging, Image guidance



Conclusions

- Radiation therapy technology has improved dramatically over the past decade
- Much ability to spare the uninvolved liver, deliver ablative tumor dose, and shorten fractionation
- Ablative radiation therapy is especially beneficial for larger tumors and those in challenging anatomic locations
- Combining ablative radiation therapy with other liver-directed therapies can benefit some patients


THANK YOU