The Future of SBRT

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Disclosures

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- Varian Medical
- Viewray Inc.
- VisionTree

Future SBRT

"We've found a mass. The good news is we have weapons of mass destruction."

SBRT Context : Advances in RT

- **Diagnostics / Prognostics**

- **Planning:**
  Target identification / Imaging
  Knowledge based planning / Automated planning

- **Delivery:**
  Dose conformality / compactness: 3DRT, IMRT, Brachy, Protons
  Guidance: Stereo / Surface / Imaging / Electromagnetic
  Adaptation: Dose monitoring and adaptation
  Combination with Drugs

- **Safety:**
  Standardization / Automation / Redundance / Monitoring
  Training, Retraining, and Testing
  Quality QA / Accreditation

SBRT Context : Future practice of RT

- Efficacy
- Toxicity (late)

} Dose Equivalence;
Biologic dose-escalation:
Can we rely on BEDs?

- Economics: Cost versus Revenue
- Patient convenience / Provider convenience
- Fear
- Ignorance
- Blind faith
- Zeal

CONVENTIONAL FRACTIONATION
versus
HYPOFRACTIONATION
versus
STEREOTACTIC BODY RADIOSURGERY (SBRT) or SABR

Number of fractions	1	5	~35	45
Fraction Size	>7 Gy		1.8-2.0 Gy	
Total Dose	~35-50 Gy	~50-75 Gy	~75-85 Gy	
Biological Rationale	Ablative??	Normal tissue sparing		

CONVENTIONAL FRACTIONATION
versus
HYPOFRACTIONATION
versus
STEREOTACTIC BODY RADIOSURGERY (SBRT) or SABR

What is considered SBRT?

6-7 fractions image-guided IMRT?

5 fractions, 5 Gy per fx, large field image-guided IMRT?

Future SBRT: New Knowledge

- **Biology of (very) large fractions:** **New science**
  Understanding of underlying mechanisms
  Vasculature, Immune response, DNA damage, etc…

- **Technical delivery** **New approach**
  Perfection of the individual fraction compact delivery:
  Imaging, Planning, On-line and off-line assessments, Adaptation
  Safety considerations
  Standardization / Automation / (Real Time) Monitoring

- **Clinical impact of large fractions:** **New perspectives**
  Clinical Trials
  Registries
  Case Reviews

Future SBRT

Technical delivery:

Perfection of the individual fraction delivery

- *Compactness* — *Delivery machine*
- *Localization*
- *Functional information*
- *Adaptation*

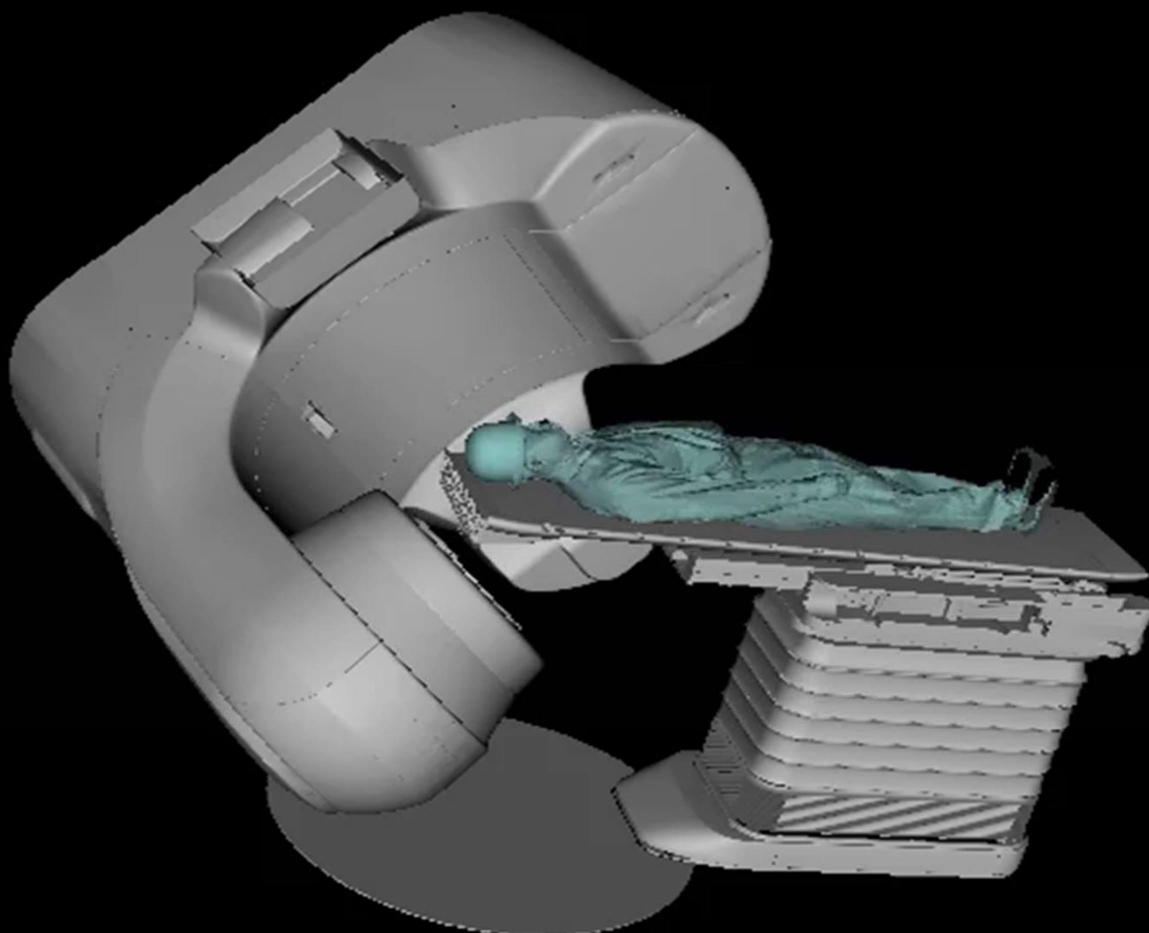
Imaging

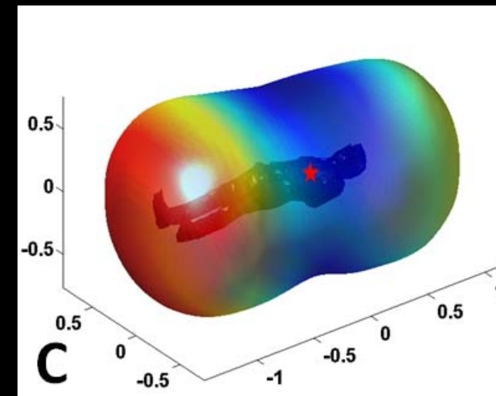
Future SBRT

Evolution of
Dose Conformality / Compactness:

- 3DRT
- IMRT
- Brachytherapy
- Protons / IMPT
- **? 4pi**

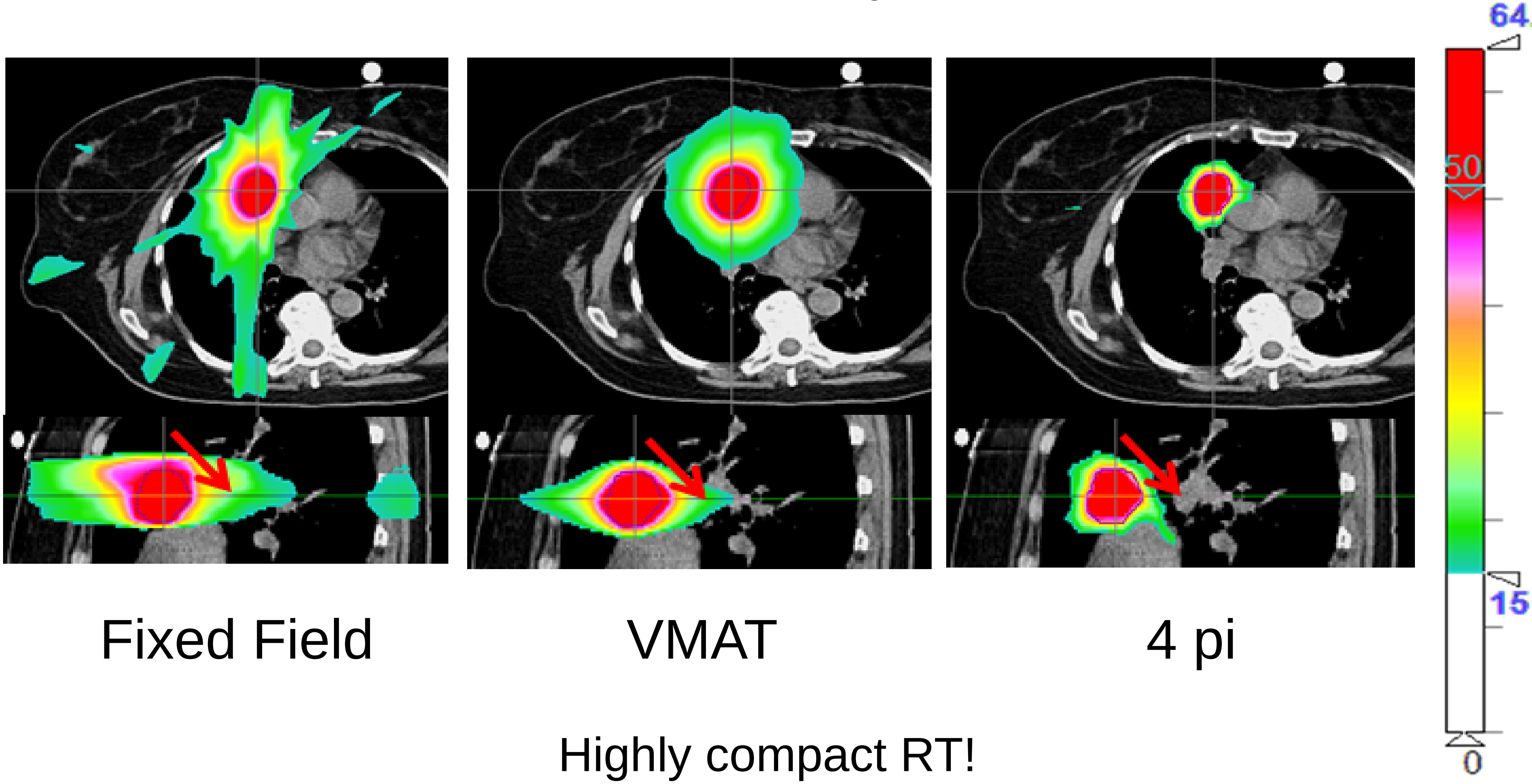
Future SBRT: 4Pi Delivery





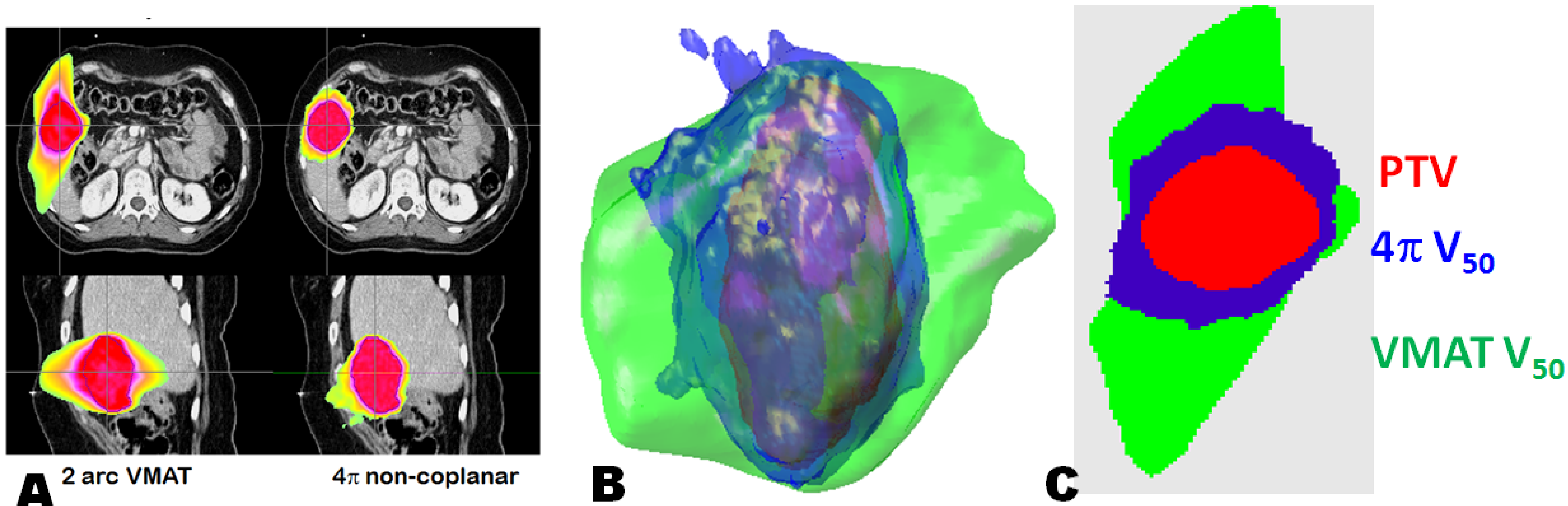
Simulation

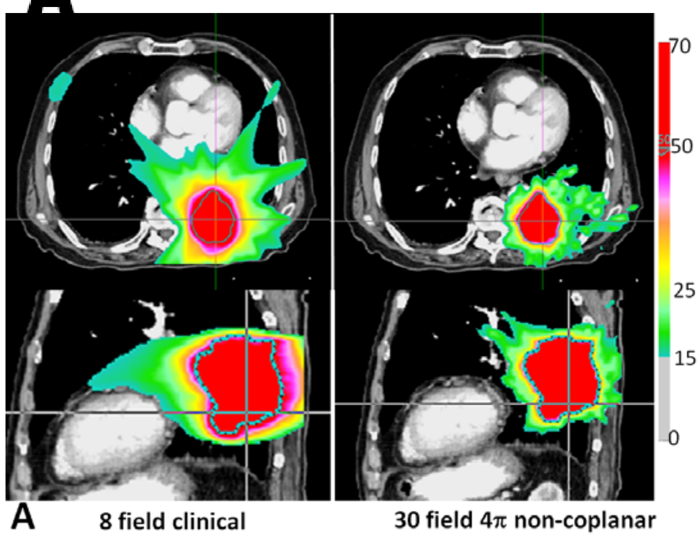
Future SBRT: Dose Conformality / Compactness
4Pi Delivery



Highly compact RT!

Future SBRT: Dose Conformality / Compactness
4Pi Delivery





Nguyen. Med Phys. 2014; 41(1):011905.

Dong. IJROBP. 2013;86(3):407-13.

Dong. IJROBP. 2013;85(5):1360-6.

Future SBRT

Technical delivery:
Perfection of the individual fraction delivery

- *Compactness*
- *Localization*
- *Functional information*
- *Adaptation*

} Imaging

Future SBRT

Technical delivery:

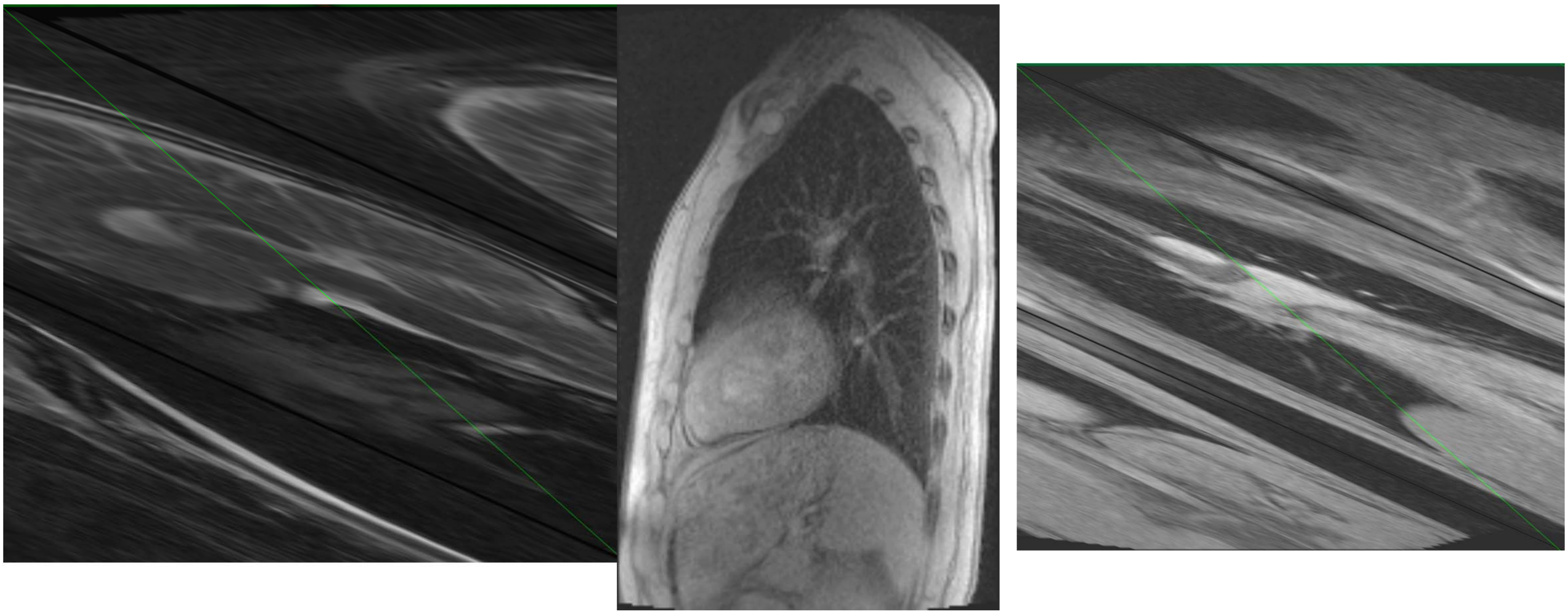
Perfection of the individual fraction delivery

- *Compactness*
- *Localization*
- *Functional information*
- *Adaptation*

} MRI

MRI - 4D Imaging (Planar)

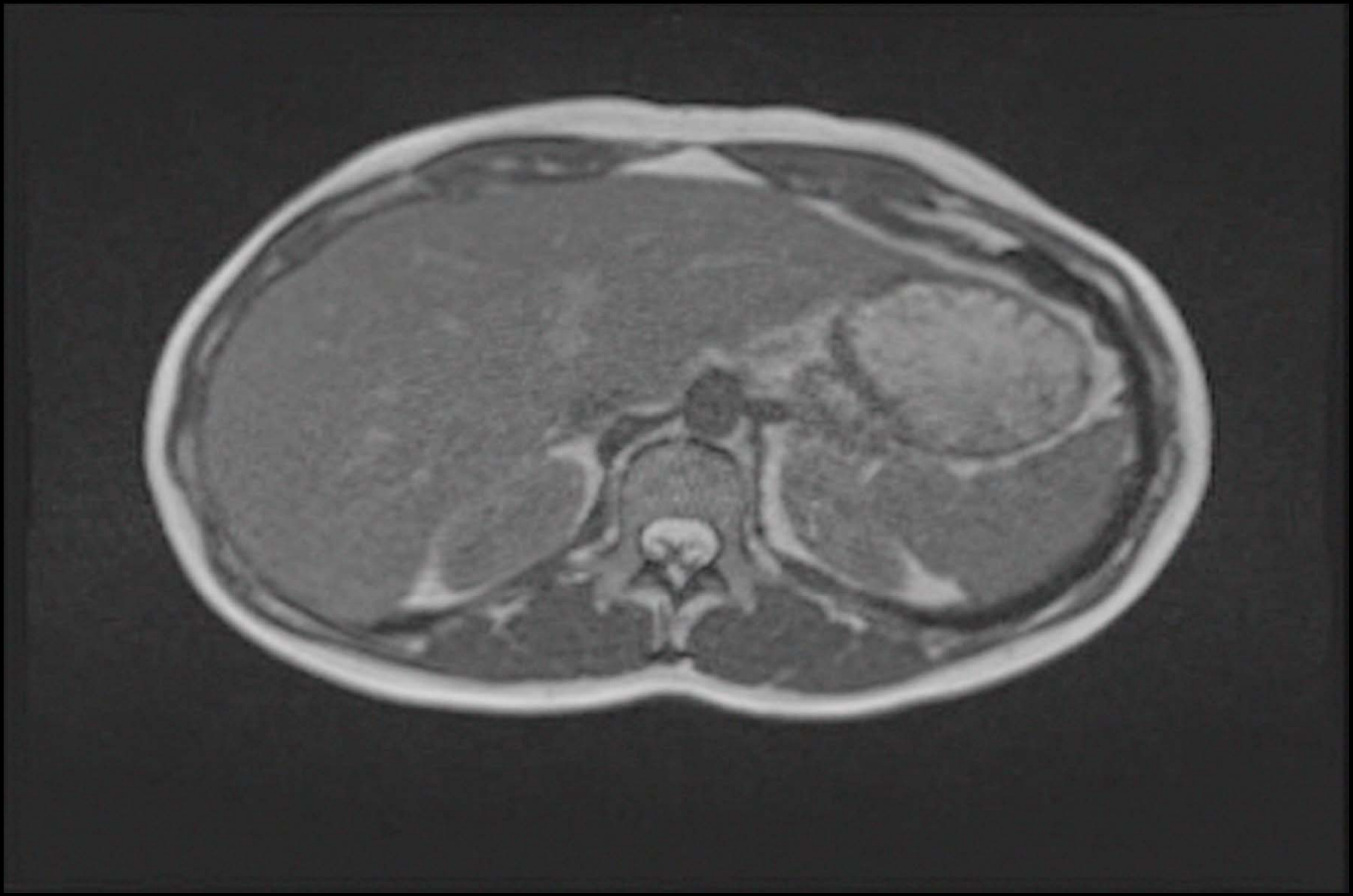
- 2-20 fps, low latency



ViewRay, Courtesy J. Michalski, Wash U. 2014

Pilot (Navigation) Scans

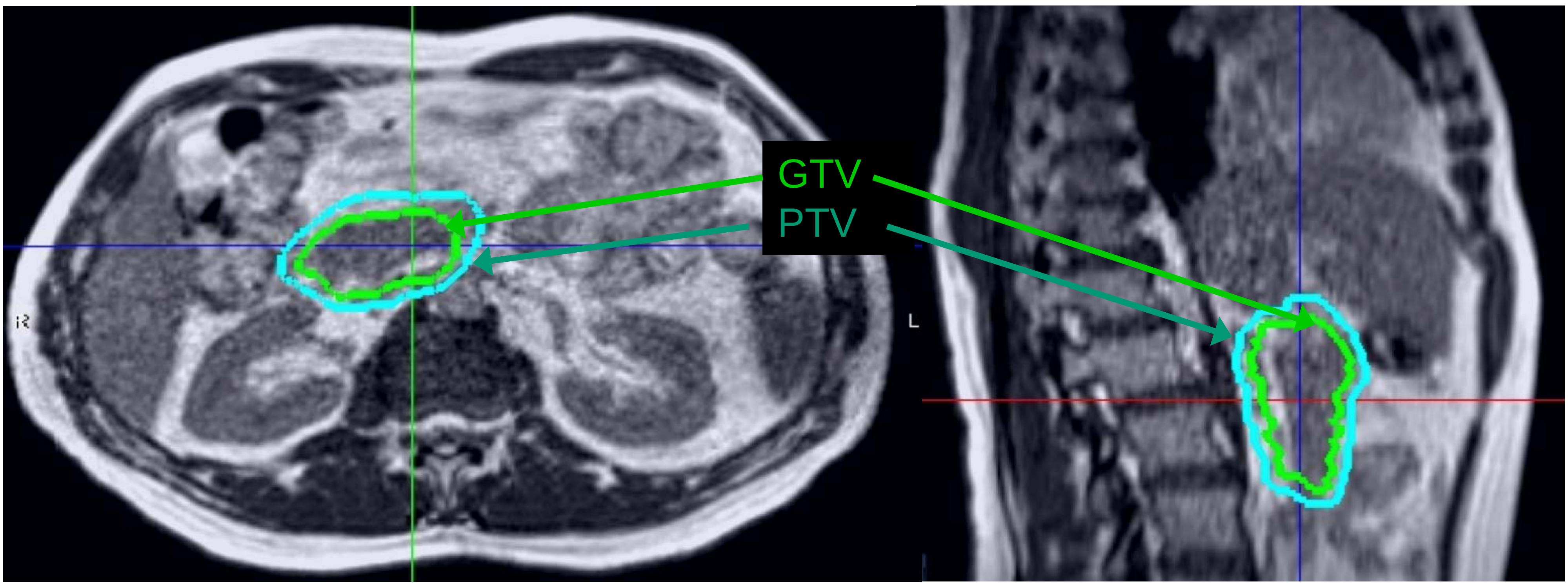
20 sec Pilot Scan



Track Tissues & Control Therapy

MR guided – RT

- 59 yo M with locally advanced pancreatic cancer, s/p FOLFIRINOX x 4 cycles→stable disease
- MR based localization on imaging study



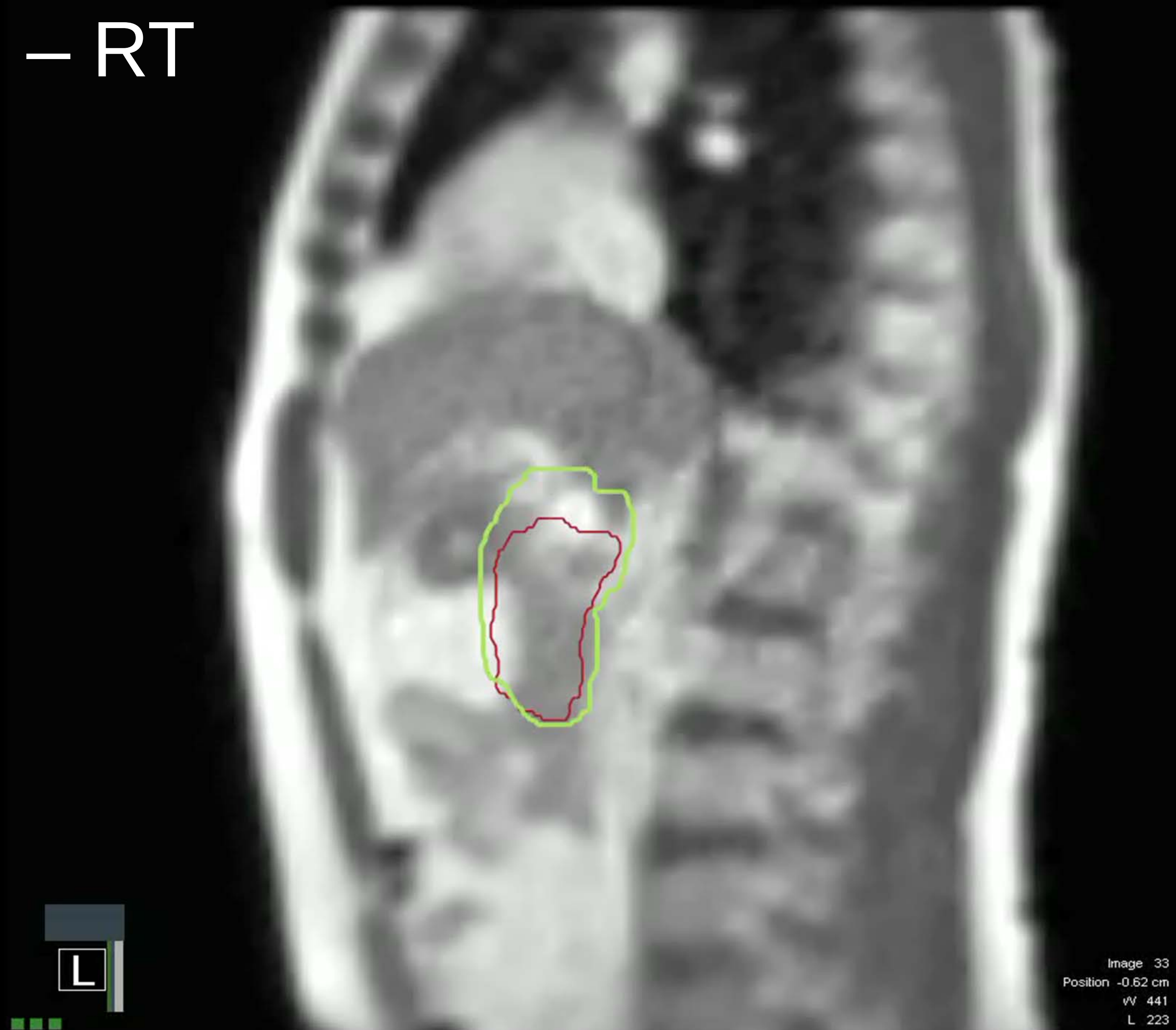
ViewRay, Courtesy J. Michalski, Wash U. 2014

Track Tissues & Control Therapy

MR guided – RT

ViewRay, Courtesy J. Michalski, Wash U. 2014

MR guided – RT



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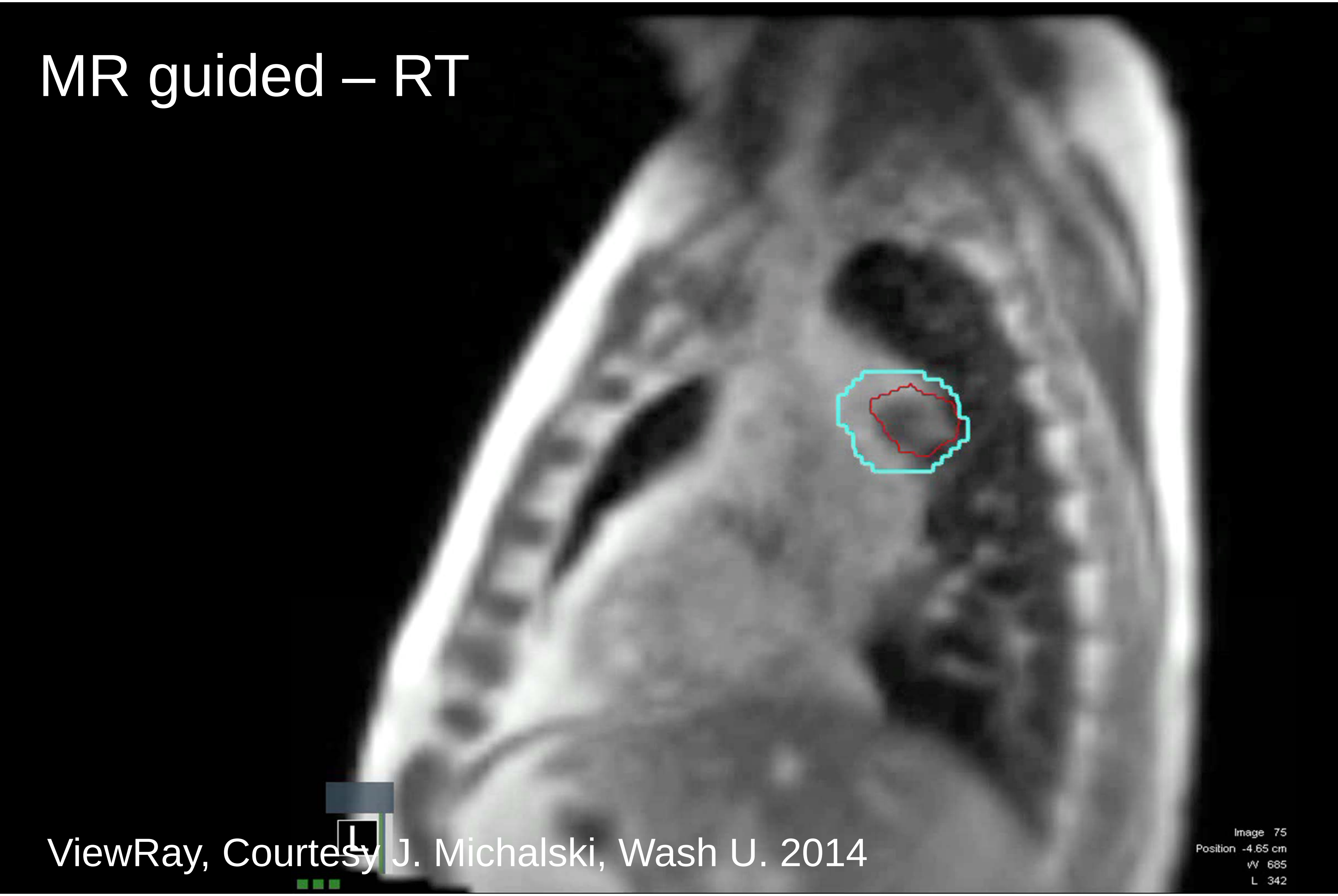
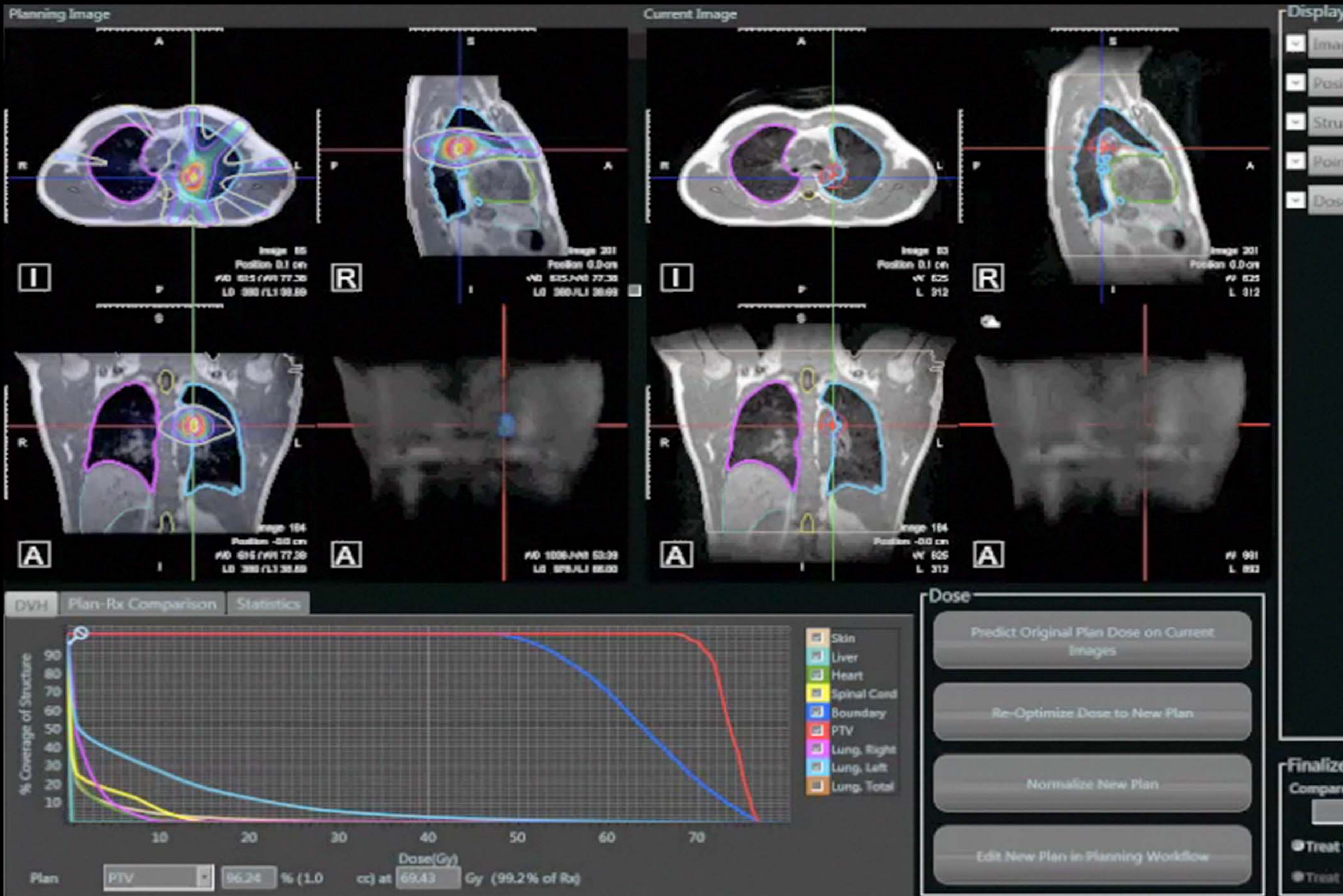
MR guided – RT



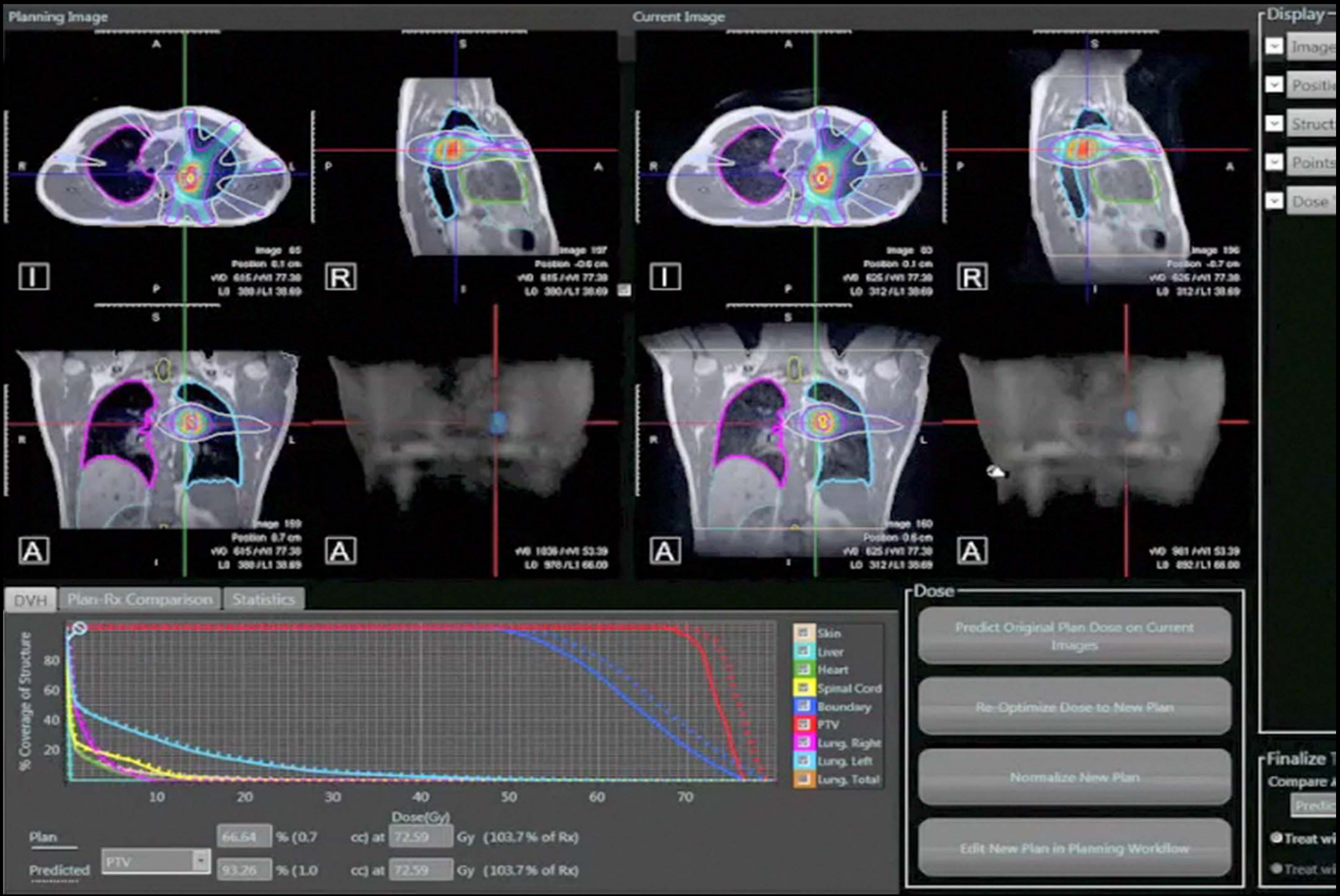
ViewRay, Courtesy J. Michalski, Wash U. 2014

Automatically Identify & Locate Tissues

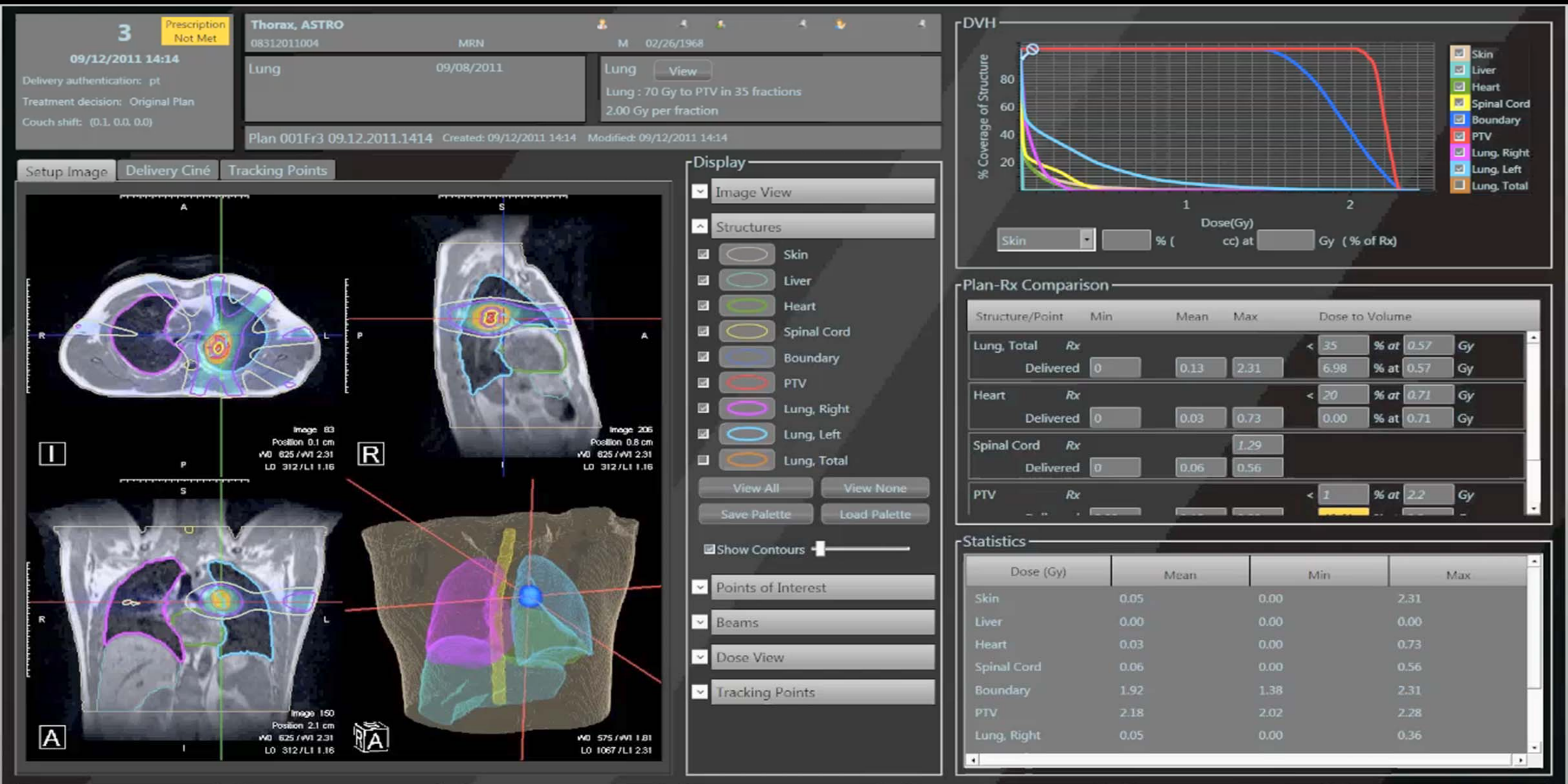
Predict Dose On Demand



Optimize On Demand



Physician’s Workstation: Overall review and supervision

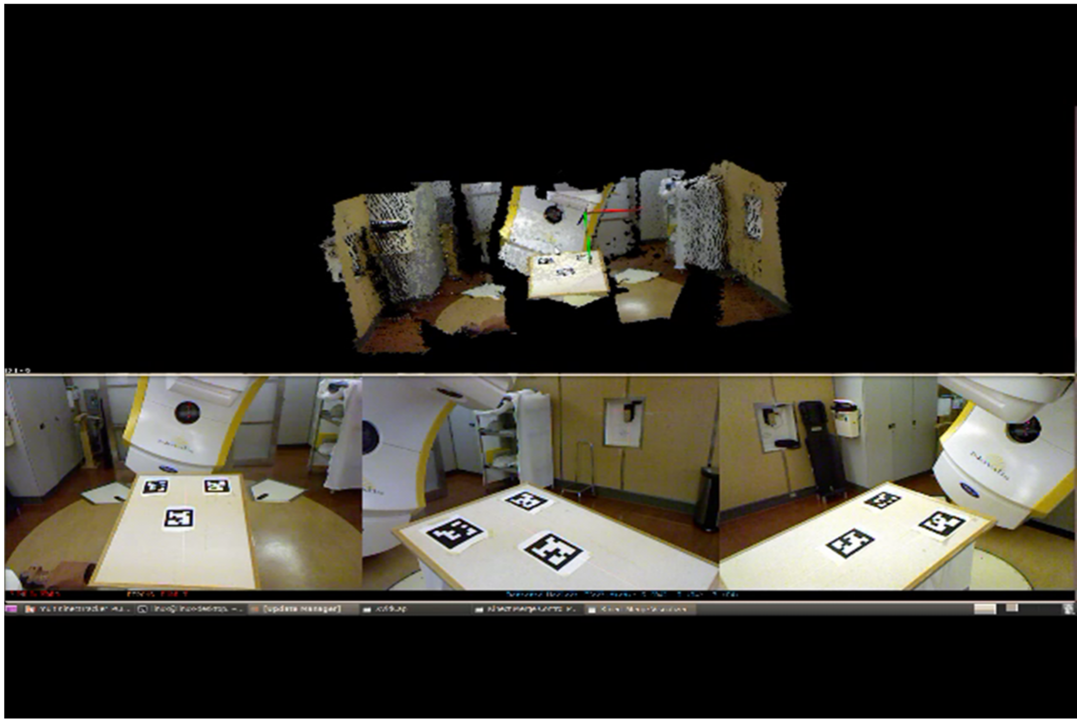


RT Delivery: Safety / Monitoring

- Treatment room workflows mirror operating rooms
  1. Slower rhythm; checklists, timeouts, etc…
  2. Increase automation
  3. Patient identification
  4. Treatment site recognition
  5. Treatment site monitoring
  6. Display of patient CT (internal anatomy)
  7. Collision monitoring
  8. Recording of treatment sessions

3D Virtualization of Treatment Room

- New generation of 3D cameras
  - Provide color images + 3D surface
  - Multiple cameras linked together (positioned at different locations in room) camera generate real-time digital model of treatment room



Positioning / Monitoring Example

Future SBRT: New Knowledge

- **Biology of (very) large fractions:** **New science**

  Understanding of underlying mechanisms

  Vasculature, Immune response, DNA damage, etc…

- **Technical delivery** **New approach**

  Perfection of the individual fraction compact delivery:

  Imaging, Planning, On-line and off-line assessments, Adaptation

  Safety considerations

  Standardization / Automation / (Real Time) Monitoring

- **Clinical impact of large fractions:** **New perspectives**

  Clinical Trials

  Registries

  Case Reviews

Hypofractionated RT:

Current Clinical Use

Current Use of Hypofractionation

Hypofractionation = Small targets

- CNS sites (SRS, FSRT, SBRT)
- Lung cancers (Early stages)
- Partial breast RT
- Abdominal sites (Liver, Pancreas, Kidney)
- Localized prostate cancers
- Spine SBRT / Oligometastatic cites
- HDR: GYN

Where is hypofractionation not used?

Conventional fractionation = Large targets

- Large CNS targets: Gliomas, meningiomas, whole brain
- Head and Neck cancers
- Most breast cancers
- Most advanced lung cancers
- Large Pelvic targets (GI or GYN)

Future Use of Hypofractionation

Breaking down large targets?
Smaller targets within larger targets?

- Large CNS targets: e.g. GBM stem cell niches
- Head and Neck cancers:
  - Dose pain gross disease
  - Targeted nodal RT only
- Breast cancers: Partial breast / targeted nodal RT
- Advanced lung cancers:
  - SBRT to residual disease
  - Hypofractionation for gross dz

Novel Indications

- Oligometastatic disease / Drug resistant areas
- SBRT as immune response modulator / combination with other immune modulators: abscopal effects
- CNS benign conditions
- Bladder Ca / Rectal Ca

CNS

Hypofractionation / SRS

CNS - SRS

Current indications:

- Trigeminal Nerve RT
- Metastatic Disease: $\leq$6 lesions
- Spine SBRT

New indications (?):

- Recurrent GBMs
- Dose painting in primary GBM RT (mpMRI)
- Back pain: Dorsal nerve root zones
- Parkinson's / Tremors
- OCD
- Excessive flushing
- Excessive sweating

Lung SBRT

Best example of SBRT success:
Early Stage Lung Cancer

Elements:

1. Small target: No elective nodal irradiation
2. Ablative Doses
3. Image Guidance: Motion Management

Extensive experience in Japan
US experience (Timmerman et al)
Multiple institutional experiences
Current RTOG trials

Will probably become the standard of care in the era of Lung cancer CT screening.

Advanced Lung Cancer Hypofractionation/SBRT

RADIATION THERAPY ONCOLOGY GROUP
American College of Radiology Imaging Network

RTOG 1106/ACRIN 6697

RANDOMIZED PHASE II TRIAL OF INDIVIDUALIZED ADAPTIVE RADIOTHERAPY USING DURING-TREATMENT FDG-PET/CT AND MODERN TECHNOLOGY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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STRATIFY		RANDOMIZE[3]	
	MLD 1. >14 Gy 2. ≤ 14 Gy **PreGTV** 1. ≥ 200 cc 2. < 200 cc **Histology** 1. Squamous 2. Non-Squamous		**Arm 1: Concurrent Chemoradiotherapy** RT to 50 Gy in 25 fractions in 5 weeks [4]Carboplatin and paclitaxel weekly **Arm 2: Concurrent Chemoradiotherapy** RT to 47.5-49.5 Gy in 17-22 fractions in 3-4 weeks [4]Carboplatin and paclitaxel weekly

ALL PATIENTS: During-RT FDG-PET/CT Scan

Arm 1: At fraction 20-23 (weeks 4-4.5)

Arm 2: At fraction ~14-21 (weeks 3-4)

Arm 1: Continuation of radiotherapy, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

10 Gy in 5 fractions; overall total of 60 Gy in 30 daily fractions in 6 weeks

Arm 2: Adaptive radiotherapy, based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

34-37.8 Gy in 8-13 fractions; overall total of up to 85.5 Gy in 30 daily fractions in 6 weeks
Individualized to MLD 20 Gy

ALL PATIENTS: Consolidative Chemotherapy

Arms 1 and 2: Carboplatin and paclitaxel q21 days X 3

IGRT is mandatory for this study (see Section 5.1).

N=138

Personalized RT prescriptions

Table 6.1.2a: Individualized Doses and Fraction Sizes for Arm 2 (Based on 74 Gy Screening Plan)

	(1) Mean Lung Dose for the screening plan (74 Gy PTV dose)	(2) Initial Dose per fx (Gy)	(3) # Fractions for ~50 Gy EQD2 Tumor Dose	(4) Physical Dose at this time point (Gy)	(5) Minimum # Fractions Before 2nd PET scan	(6) Adaptive Phase Largest allowed Boost Dose per fx (Gy)	(7) Adaptive Phase # of Fractions	(8) Adaptive Phase Largest allowed Physical Boost Dose (Gy)	(9) Largest allowed Total Physical Prescription Dose (Gy)
a)	<13.5	2.85	17	48.45	14	2.85	13	37.05	85.5
b)	13.5	2.85	17	48.45	14	2.85	13	37.05	85.5
c)	13.9	2.80	17	47.6	14	2.9	13	37.7	85.3
d)	14.3	2.75	18	49.5	15	3	12	36	85.5
e)	14.7	2.70	18	48.6	15	3.05	12	36.6	85.2
f)	15.1	2.65	18	47.7	15	3.15	12	37.8	85.5
g)	15.5	2.60	19	49.4	16	3.25	11	35.75	85.2
h)	16.0	2.55	19	48.45	16	3.3	11	36.3	84.8
i)	16.5	2.50	19	47.5	16	3.4	11	37.4	84.9
j)	17.0	2.45	20	49	17	3.55	10	35.5	84.5
k)	17.6	2.40	20	48	17	3.65	10	36.5	84.5
l)	18.1	2.35	21	49.35	18	3.85	9	34.65	84.0

Keep total 30 fractions:

Fraction size range: 2.35 to 3.85 Gy

SBRT for residual disease after conventional RT

International Journal of
Radiation Oncology
biology • physics

www.redjournal.org

Clinical Investigation: Thoracic Cancer

Stereotactic Body Radiation Therapy Can Be Used Safely to Boost Residual Disease in Locally Advanced Non-Small Cell Lung Cancer: A Prospective Study

Jonathan Feddock, MD,* Susanne M. Arnold, MD,*,† Brent J. Shelton, PhD,‡ Partha Sinha, MD,§ Gary Conrad, MD,§ Li Chen, PhD,‡ John Rinehart, MD,† and Ronald C. McGarry, MD, PhD*

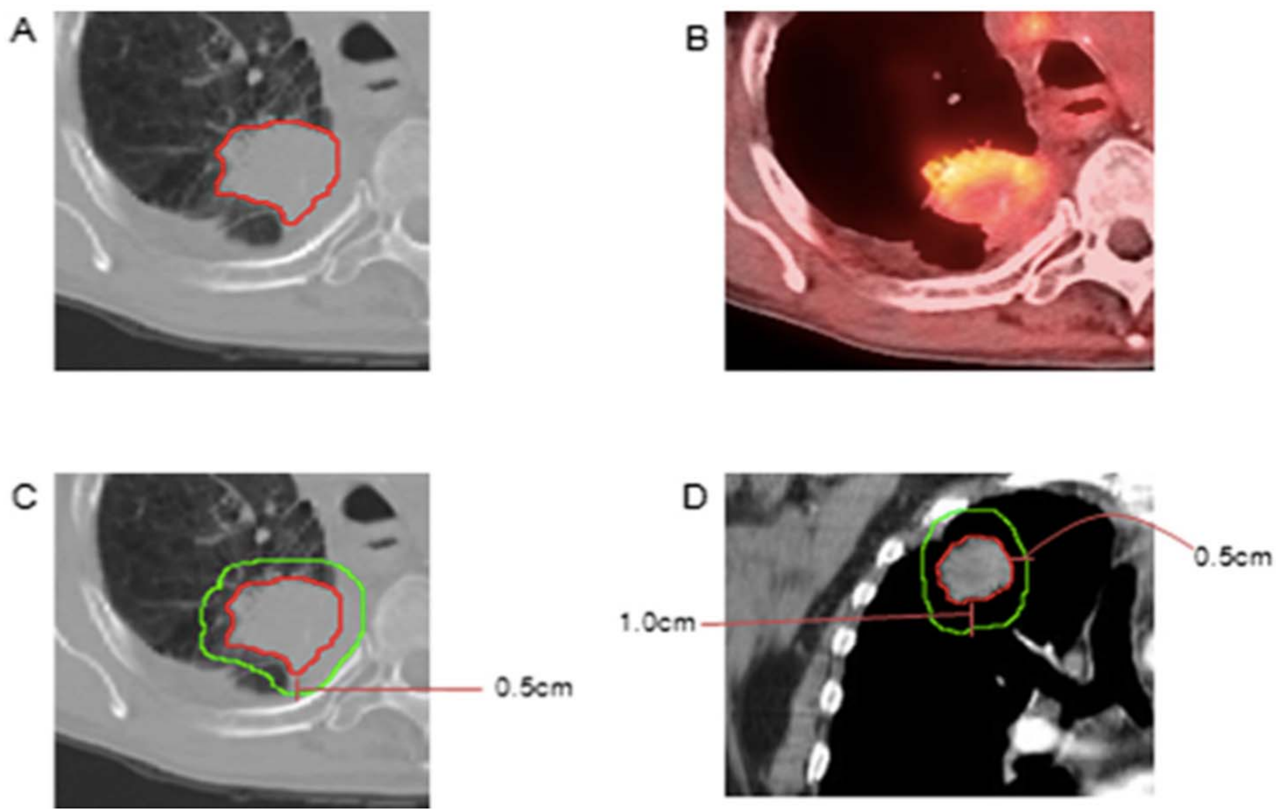
*Departments of *Radiation Medicine, †Medical Oncology, ‡Biostatistics, and §Radiology, University of Kentucky, Lexington, Kentucky*

Received Sep 20, 2012, and in revised form Nov 6, 2012. Accepted for publication Nov 7, 2012

SBRT Boost to Residual Disease

Feddock J et al. IJROBP, 85, 1325-1331, 2013

PET-CT one month following conventional CRT (60 Gy)
An additional 20 Gy in 2 SBRT fractions in 1 week.
Central lesions: 6.5 Gy x 3 = 19.5 Gy



SBRT Boost to Residual Disease

Feddock J et al. IJROBP, 85, 1325-1331, 2013

62 patients screened. 35 eligible to boost.

Exclusion reasons: 31% persistent nodal disease
31% systemic progression
15% no residual local disease

Median follow-up: 13 mos

- Local control: 83%
- No Gr 4-5 Rad Pneumonitis.
- Acute grade 3 RP: 4 patients (12%)
- Late and persistent grade 3 RP: 1 patient (3%)

“No dosimetric parameters evaluated for SBRT protocol treatment, including MLD, V2.5, V5, V10, and V20, correlated with RP development”

Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer

Phase I/II Protocol (UCLA) - PI: Percy Lee

PET-CT, 4D CT Simulation

↓

4 Gy x 10 fractions Involved Field RT

↓

PET-CT, 4D CT Re-Simulation / **Adaptation**

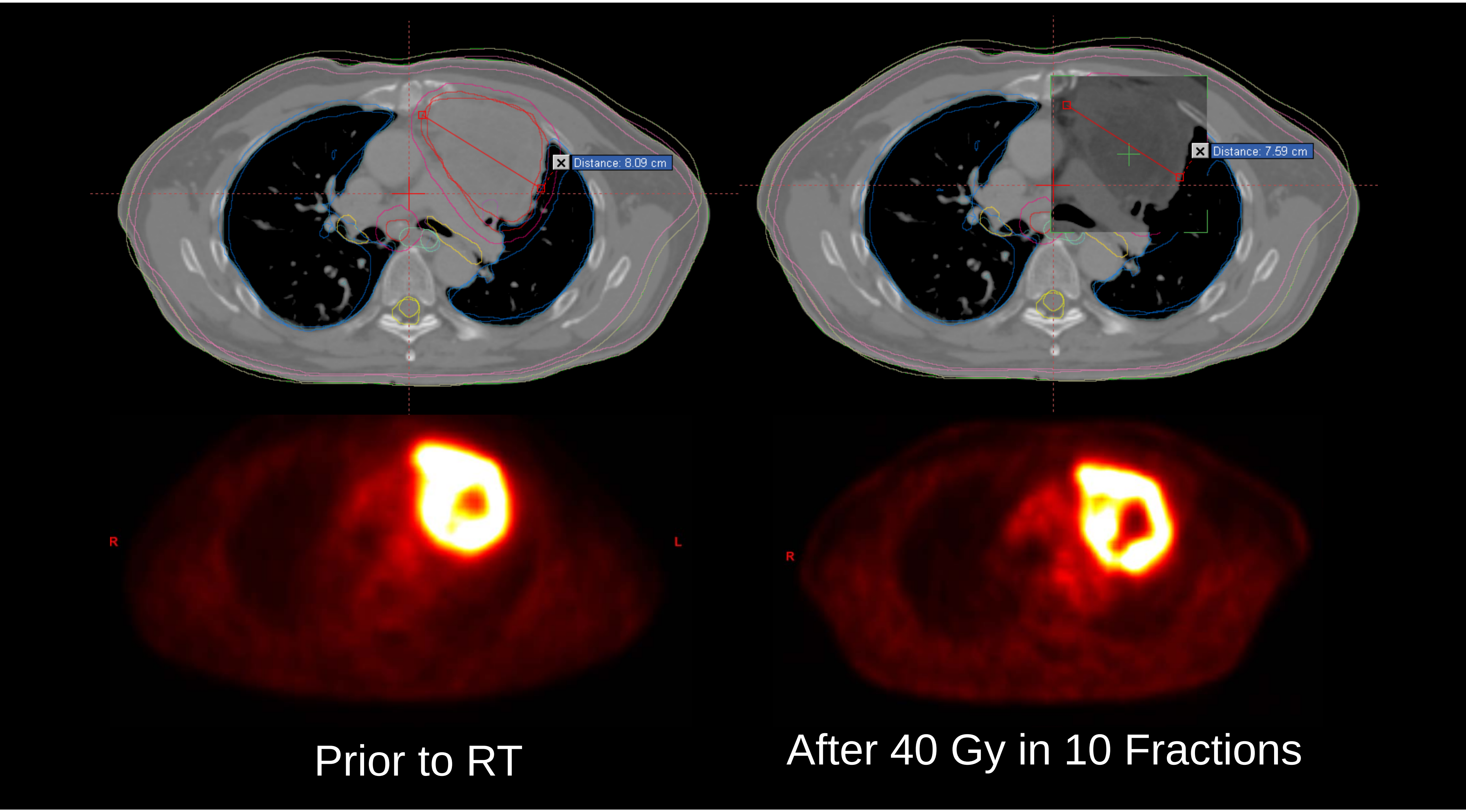
(at the 8^{th} or 9^{th} fraction)

Dose-escalation cohorts: SBRT Boosts

5 Gy x 5	or	6 Gy x 5	or	7 Gy x 5
N=15		N=15		N=15

3 WEEK COURSE

Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer



Prostate SBRT

Prostate SBRT Doses

Dose ranges:	BED	
6.70 x 5 = 33.5 Gy	146	Madsen IJROBP 2007
7.25 x 5 = 36.25 Gy	168	King IJROBP 2009; King IJROBP 2011; Friedland TCRT 2009; Katz BMC Urol 2010; Wiegner IJROBP 2010; Bolzicco TCRT 2010; Aluwini J Endourol 2010; Freeman RO 2010; Townsend AJCO 2011; Kang Tumori 2011; Jabbari IJROBP 2011; Mantz IJROBP 2011
7.5 x 5 = 37.5 Gy	178	
9.0 x 4 = 36.0 Gy	198	Fuller IJROBP 2008
8.0 x 5 = 40.0 Gy	200	King RO 2013
9.0 x 5 = 45.0 Gy	248	Boike JCO 2011 / Kim ASTRO 2013
9.5 x 5 = 47.5 Gy	273	
10.0 x 5 = 50.0 Gy	300	
24 x 1 = 24 Gy	312	Greco, Lisbon

UCLA High-Risk Prostate Ca SBRT Trial

SBRT: Not delivery platform specific.

CT/MRI planning

8 Gy x 5 (40 Gy*) to prostate PTV

5 Gy x 5 (25 Gy) to pelvic LN (optional)

SV: Full dose or 5 Gy x 5 (respecting ROI constraints)

*Minimum dose, 30-50% heterogeneous ‘Hot Shell’

Head and Neck?

UCLA Head & Neck Postop “SBRT” Trial

Postoperative Head and Neck cancers

No change in volumes

3 Dose levels:

7 Gy x 5 (35 Gy)

6 Gy x 5 (30 Gy)

5 Gy x 5 (25 Gy)

Conclusions

Fewer and larger size fractions, seem associated with better (or at least) equivalent outcomes in most cancers.

SBRT treatments are associated with increased workloads, scrutiny and safety.

The higher therapeutic ratio of currently used hypofractionated regimens is expanding indications.

Dose / fractionation schemes are still unclear and need proper outcomes documentation with appropriate clinical trials or case registries.

The Future of SBRT

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areas if desired. Volume adjustments would be routine as would be individualization of dose, which makes sense given the large variation of tumor size and burden in patients with head and neck cancers, and the biologic differences of individual tumors, as obvious currently in HPVþ vs HPV cases.[51] Adjustments would allow better normal tissue sparing, particularly salivary gland sparing. DW MRI could also allow for assessment of changes within the salivary glands predicting for late effects.[52] However, further improvement will come from identifying nodal areas that are microscopically involved. Although unimaginable today, as with lung cancer currently, elective nodal irradiation could be abandoned for head and neck cancers, replaced with more targeted nodal irradiation, thus decreasing treatment volumes and making head and neck RT a much more tolerable treatment than what it is today.

Ablation of Pancreatic Cancers or Liver Cancers

Upper abdominal targets have presented a challenge owing to

relatively aggressive biology, sensitive OARs such as the small bowel, and significant motion and deformation issues.[53] Pancreatic cancer is a particularly difficult disease to approach with RT. In localized pancreatic cancers, the efficacy of radiation therapy could be improved with larger than conven- tional fraction sizes.[54] Definition of peripancreatic (eg, vascu- lature involvement) and intrapancreatic (cancer tissue) targets would allow dose painting, with in-room MRI being used to track those targets