

The Future of SBRT



Patrick Kupelian, M.D.
Professor and Vice Chair
University of California Los Angeles
Department of Radiation Oncology
pkupelian@mednet.ucla.edu

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Disclosures

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Accuray

BrainLab

Siemens Medical

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 conformity / 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??	N	o	r
	m	a	l
	t	i	s
	s	p	a
	r	i	n
	g		

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

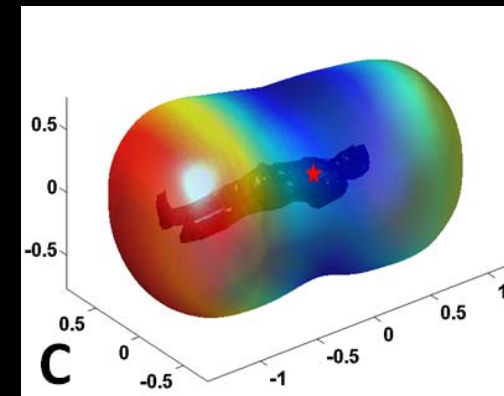
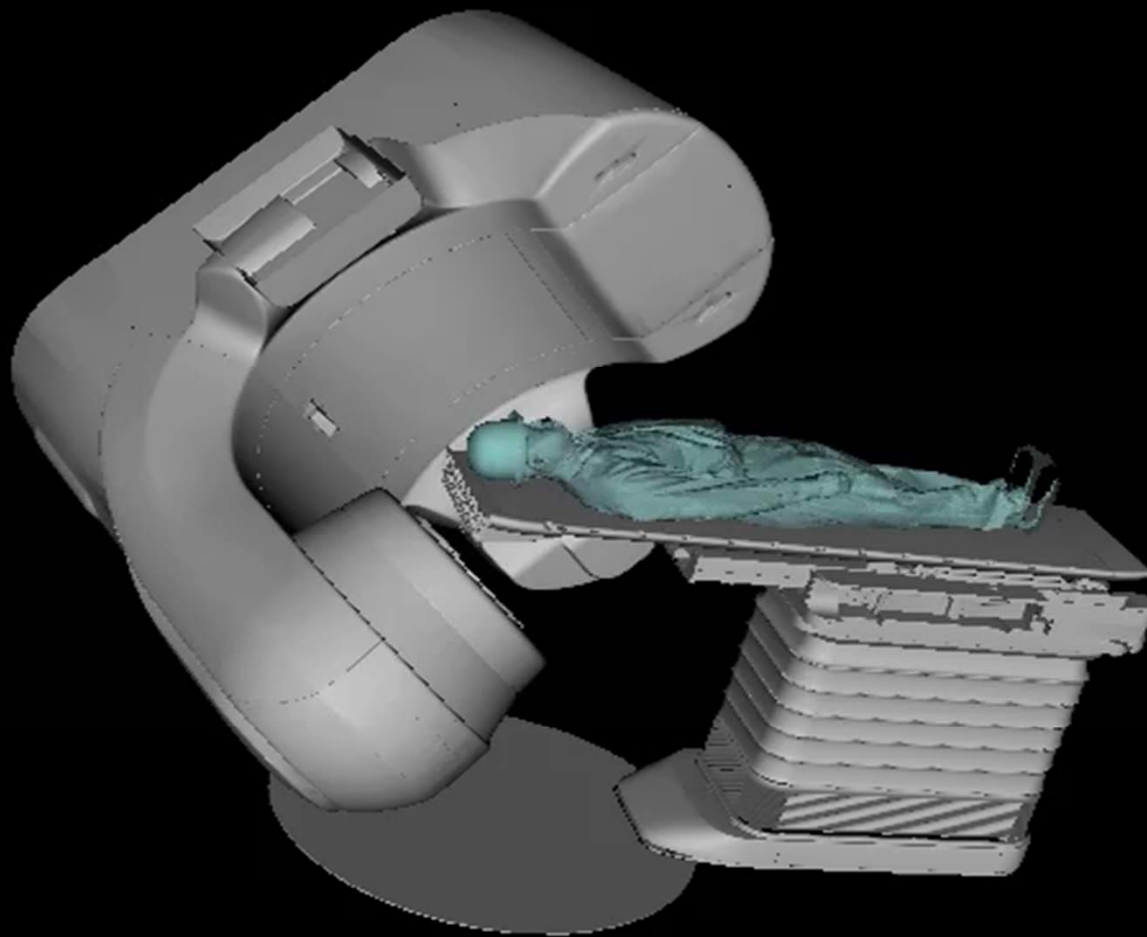
- **Compactness** } *Delivery machine*
- *Localization*
- *Functional information* } *Imaging*
- *Adaptation*

Future SBRT

Evolution of Dose Conformality / Compactness:

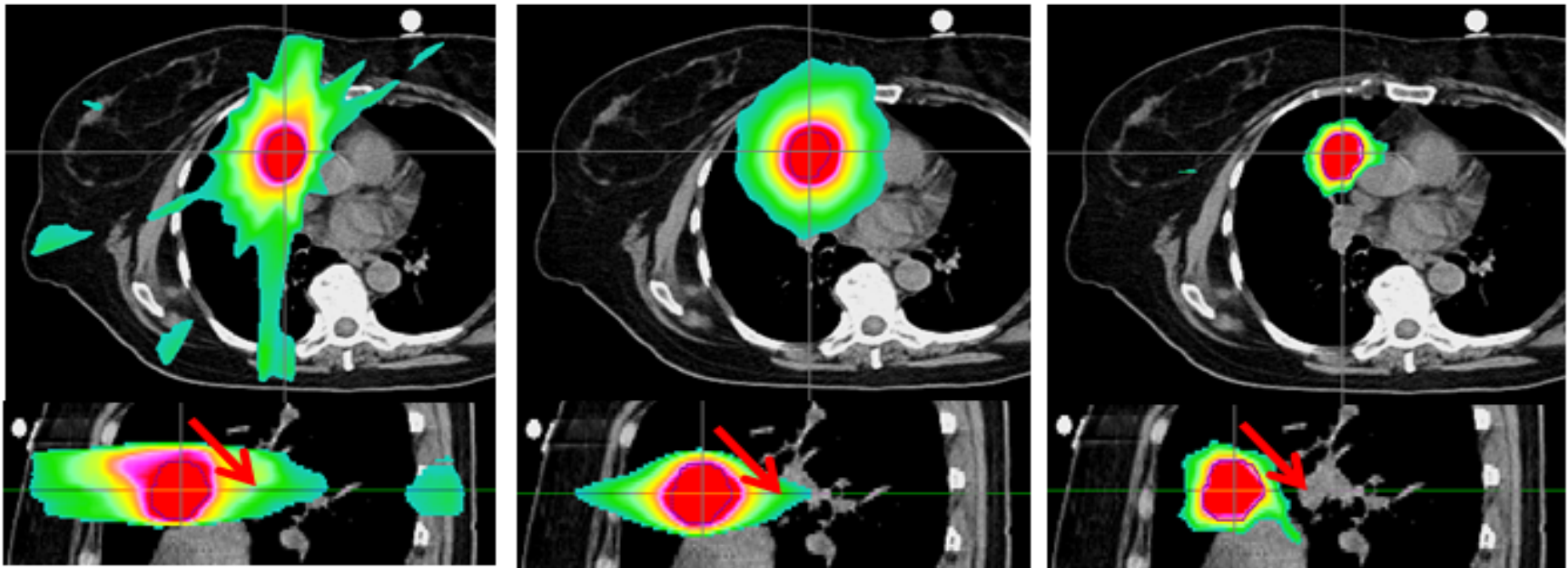
- 3DRT
- IMRT
- Brachytherapy
- Protons / IMPT
- ? 4pi

Future SBRT: 4Pi Delivery



Simulation

Future SBRT: Dose Conformality / Compactness 4Pi Delivery

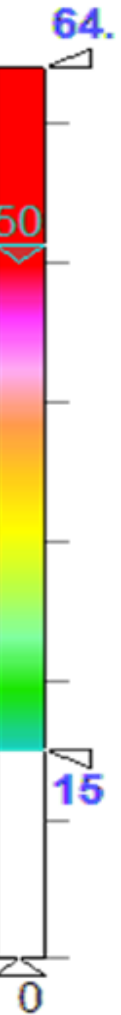


Fixed Field

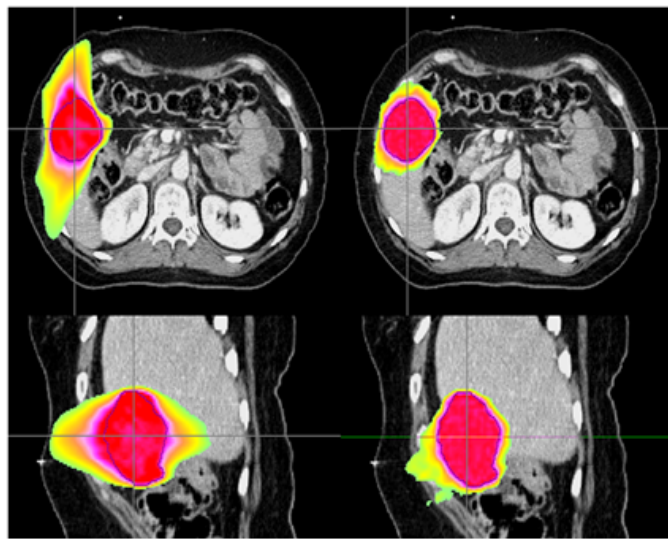
VMAT

4 pi

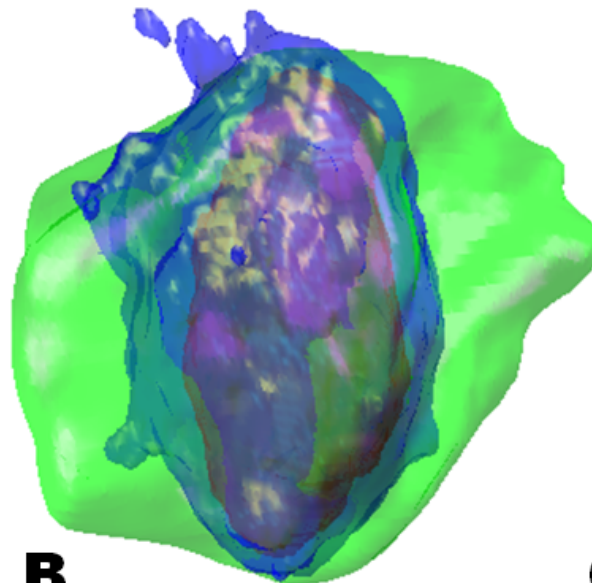
Highly compact RT!



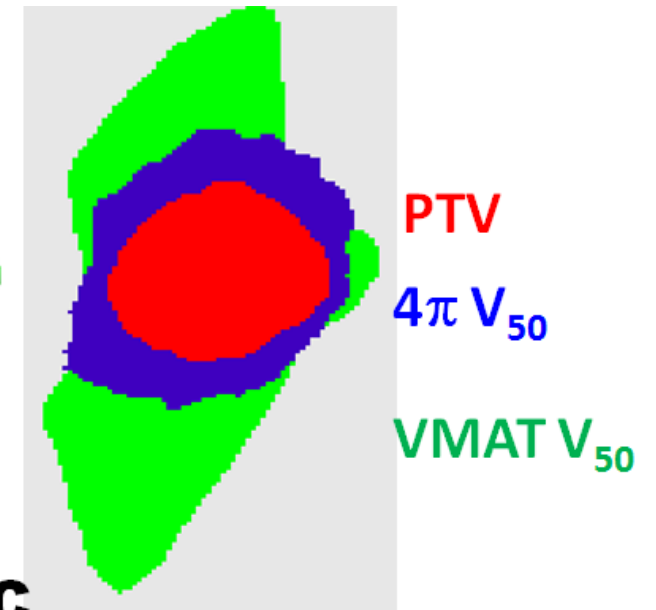
Future SBRT: Dose Conformality / Compactness 4Pi Delivery



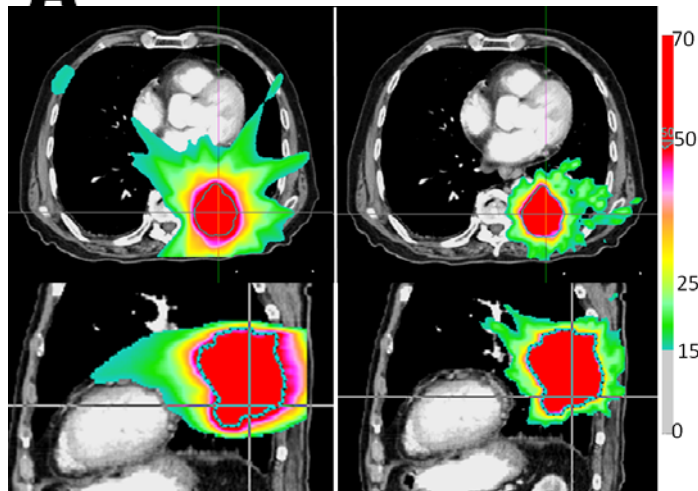
A 2 arc VMAT 4 π non-coplanar



B



C



A 8 field clinical 30 field 4 π non-coplanar

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

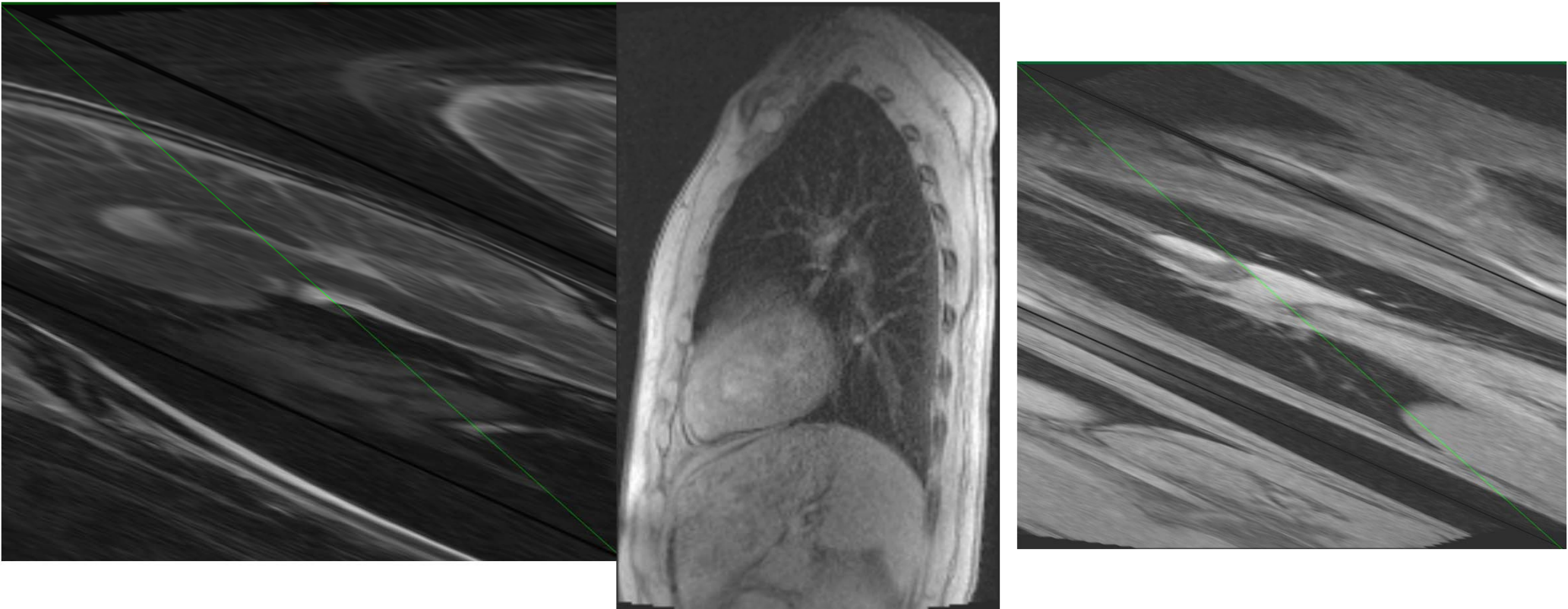
Technical delivery:

Perfection of the individual fraction delivery

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

MRI - 4D Imaging (Planar)

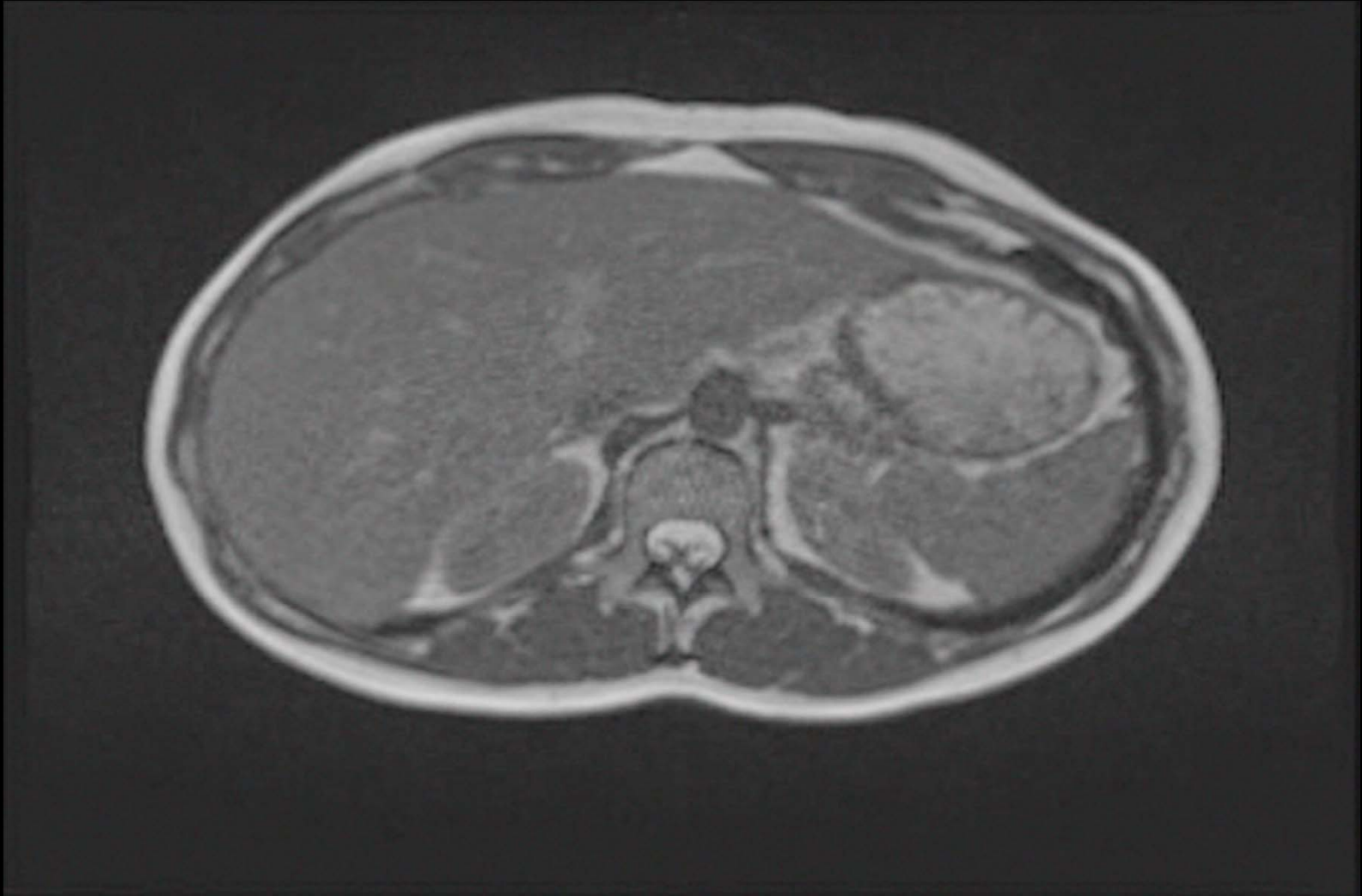
- 2-20 fps, low latency



ViewRay, Courtesy J. Michalski, Wash U. 2014

Pilot (Navigation) Scans

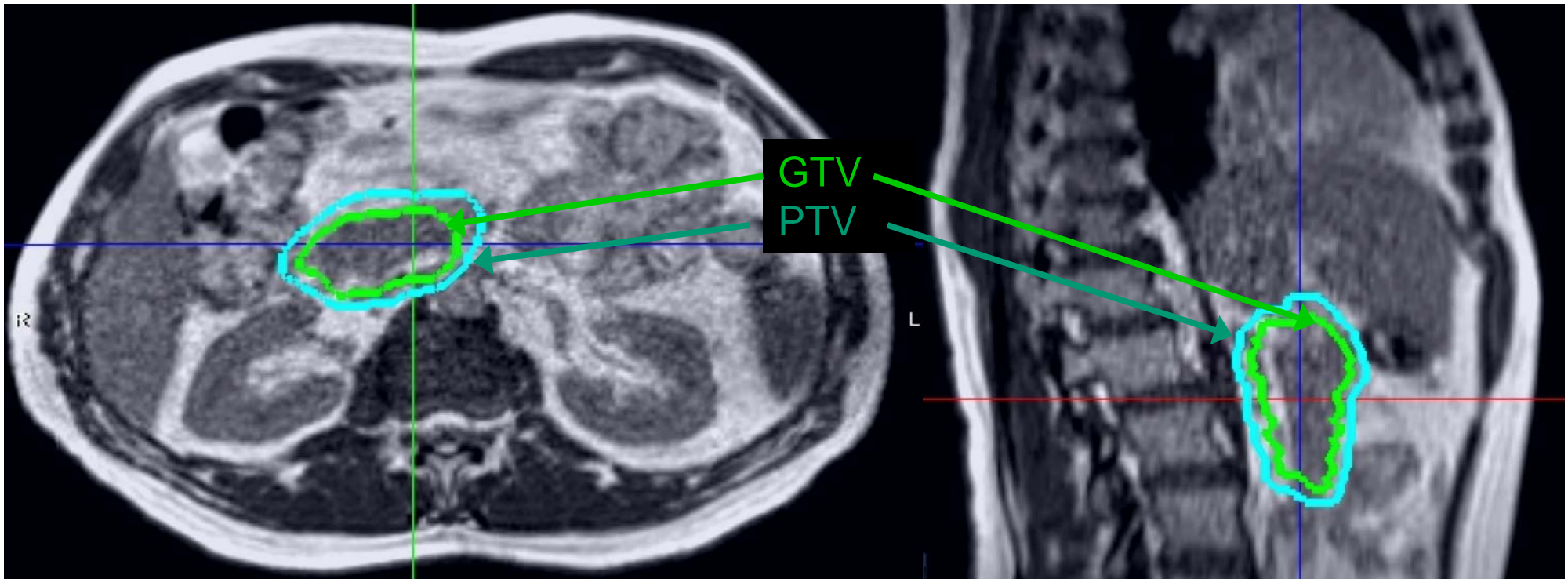
20 sec Pilot Scan



Track Tissues & Control Therapy

MR guided – RT

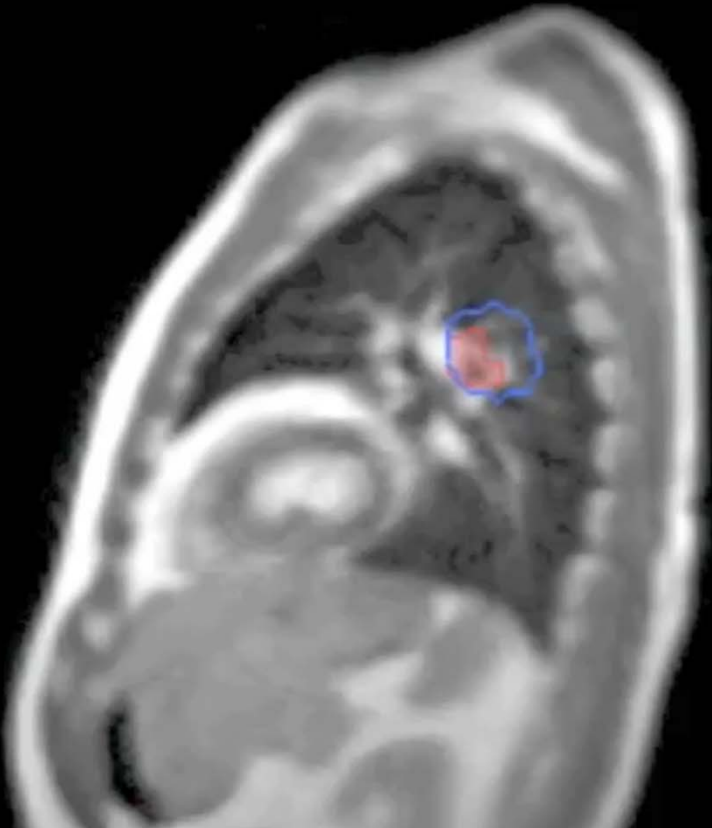
- 59 yo M with locally advanced pancreatic cancer, s/p FOLFIRINOX x 4 cycles → stable disease
- MR based localization on imaging study



ViewRay, Courtesy J. Michalski, Wash U. 2014

Track Tissues & Control Therapy

Enable Treatment
Pause
End Treatment Early



BLAM (D1)


Setup 2: Successive
 Setup 3: Successive
 Setup 4: Successive
 Setup 5: Successive
 Setup 6: Successive
 Setup 7: Successive
 Setup 8: Successive
 Setup 9: Successive
 Setup 10: Successive
 Setup 11: Successive
 Setup 12: Successive
 Setup 13: Successive
 Setup 14: Successive
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 Setup 97: Successive
 Setup 98: Successive
 Setup 99: Successive
 Setup 100: Successive

Target Out of Rounds

Diagrams

● Beam 1 Angle:
 segment of 8

● Beam 2 Angle:
 segment of 8

● Beam 3 Angle:
 segment of 8

Treatment Time

Total Dosed Remaining 0 %

	Head 1		Head 2		Head 3	
	Set	Elapsed	Set	Elapsed	Set	Elapsed
Primary	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>
Secondary	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>	<input type="text" value="0.0"/>

Plan and Machine

Plan type	<input type="text" value="BLAM1"/>	Actual	Target
Fraction Number	<input type="text" value="18"/>	Gantry Angle	<input type="text" value="301.0°"/> <input type="text" value="30.0°"/>
Fraction Primary Dose	<input type="text" value="2.00"/>	Couch Lateral	<input type="text" value="5.4"/> cm <input type="text" value="5.2"/> cm

MR guided – RT



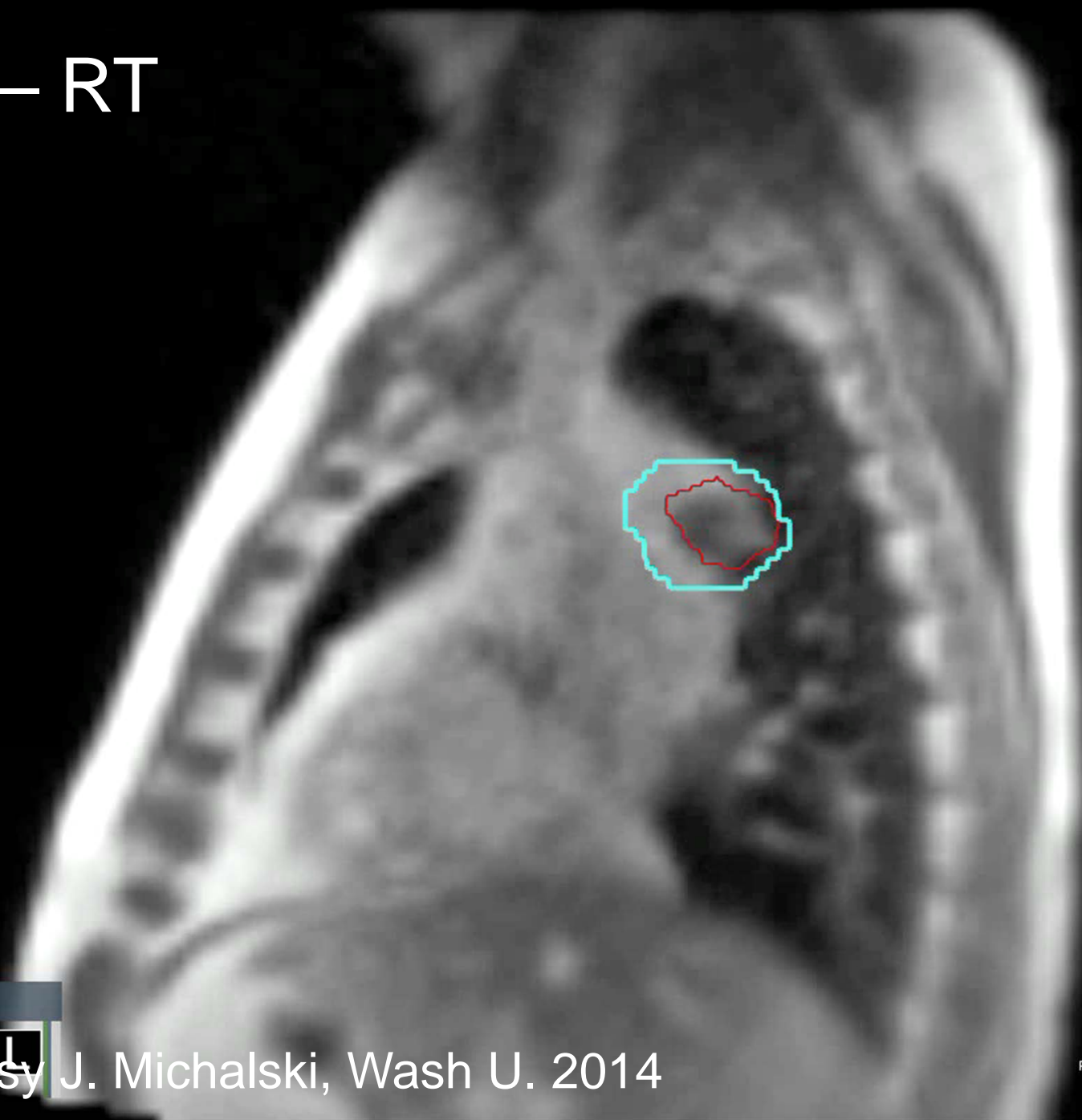
ViewRay, Courtesy J. Michalski, Wash U. 2014

MR guided – RT



ViewRay, Courtesy J. Michalski, Wash U. 2014

MR guided – RT



ViewRay, Courtesy J. Michalski, Wash U. 2014

Image 75
Position -4.65 cm
w 685
L 342

Automatically Identify & Locate Tissues

Image Volumes

Pilot Imaging

Pilot Time: 15

Acquire Pilot

Set-Up Imaging

Use Navigator

Lateral: 0

Axial: 0

Vertical: 0

FOV: 40 x 35 x 35

Resolution: 1.5 mm x 3.0 mm

Volume Time: 180

Acquire Volume

Plan Image

Current Image

Process and Plan

Get Deformation and Auto-Contour

Auto-Contour Skin: Threshold 149, Margin 5

Get Couch Shift

Manual Automatic

Rigid Deformable

Set Isocenter Manually

Find Shift From Fusion

Couch Location

	Plan Position	Actual Position	Displayed Shift
Lateral	-5.4 cm	-5.1 cm	0 cm
Vertical	-9.0 cm	-8.6 cm	0 cm
Axial	220.8 cm	220.9 cm	0 cm

Display

Level: 313

Presets

Show MPR Lines

Colormap Overlay

Current Plan

Predict Dose On Demand

Planning Image

Image 05
Position 0.1 cm
#0 025 / #1 77.26
L0 380 / L1 98.69

Image 301
Position 0.0 cm
#0 025 / #1 77.26
L0 380 / L1 98.69

Image 104
Position -0.0 cm
#0 095 / #1 77.26
L0 380 / L1 98.69

Current Image

Image 03
Position 0.1 cm
025
L 312

Image 301
Position 0.0 cm
025
L 312

Image 104
Position -0.0 cm
025
L 312

Display

- Imag
- Posit
- Struc
- Point
- Dose

Dose

Predict Original Plan Dose on Current Images

Re-Optimize Dose to New Plan

Normalize New Plan

Edit New Plan in Planning Workflow

Finalize

Compare

Treat w

Treat w

DVH | Plan-Rx Comparison | Statistics

Plan: PTV 96.24 % (1.0 cc) at 69.43 Gy (99.2% of Rx)

Optimize On Demand

Planning Image

Image 85
Position 0.1 cm
v# 815 /w# 77.38
L0 300 /L1 38.69

Image 157
Position -0.6 cm
v# 815 /w# 77.38
L0 300 /L1 38.69

Image 159
Position 0.7 cm
v# 815 /w# 77.38
L0 300 /L1 38.69

Current Image

Image 83
Position 0.1 cm
v# 825 /w# 77.38
L0 312 /L1 38.69

Image 156
Position -0.7 cm
v# 825 /w# 77.38
L0 312 /L1 38.69

Image 160
Position 0.6 cm
v# 825 /w# 77.38
L0 312 /L1 38.69

Display

- Image
- Position
- Structure
- Points
- Dose

DVH | Plan-Rx Comparison | Statistics

Plan	66.64	% (0.7)	cc	at 72.59	Gy (103.7% of Rx)
Predicted PTV	93.26	% (1.0)	cc	at 72.59	Gy (103.7% of Rx)

Dose

Predict Original Plan Dose on Current Images

Re-Optimize Dose to New Plan

Normalize New Plan

Edit New Plan in Planning Workflow

Finalize T

Compare A

Predict

Treat w

Treat w

Physician's Workstation: Overall review and supervision

3 Prescription Not Met

09/12/2011 14:14

Delivery authentication: pt
Treatment decision: Original Plan
Couch shift: (0.1, 0.0, 0.0)

Thorax, ASTRO
08312011004 MRN M 02/26/1968

Lung 09/08/2011

Lung View
Lung : 70 Gy to PTV in 35 fractions
2.00 Gy per fraction

Plan 001Fr3 09.12.2011.1414 Created: 09/12/2011 14:14 Modified: 09/12/2011 14:14

Setup Image Delivery Ciné Tracking Points

DVH

Plan-Rx Comparison

Structure/Point	Min	Mean	Max	Dose to Volume
Lung, Total Rx	< 35	% at 0.57	Gy	
Delivered	0	0.13	2.31	6.98 % at 0.57 Gy
Heart Rx	< 20	% at 0.71	Gy	
Delivered	0	0.03	0.73	0.00 % at 0.71 Gy
Spinal Cord Rx			1.29	
Delivered	0	0.06	0.56	
PTV Rx	< 1	% at 2.2	Gy	

Statistics

Dose (Gy)	Mean	Min	Max
Skin	0.05	0.00	2.31
Liver	0.00	0.00	0.00
Heart	0.03	0.00	0.73
Spinal Cord	0.06	0.00	0.56
Boundary	1.92	1.38	2.31
PTV	2.18	2.02	2.28
Lung, Right	0.05	0.00	0.36

Display

Image View

Structures

- Skin
- Liver
- Heart
- Spinal Cord
- Boundary
- PTV
- Lung, Right
- Lung, Left
- Lung, Total

View All View None

Save Palette Load Palette

Show Contours

Points of Interest

- Beams
- Dose View
- Tracking Points

RT Delivery: Safety / Monitoring

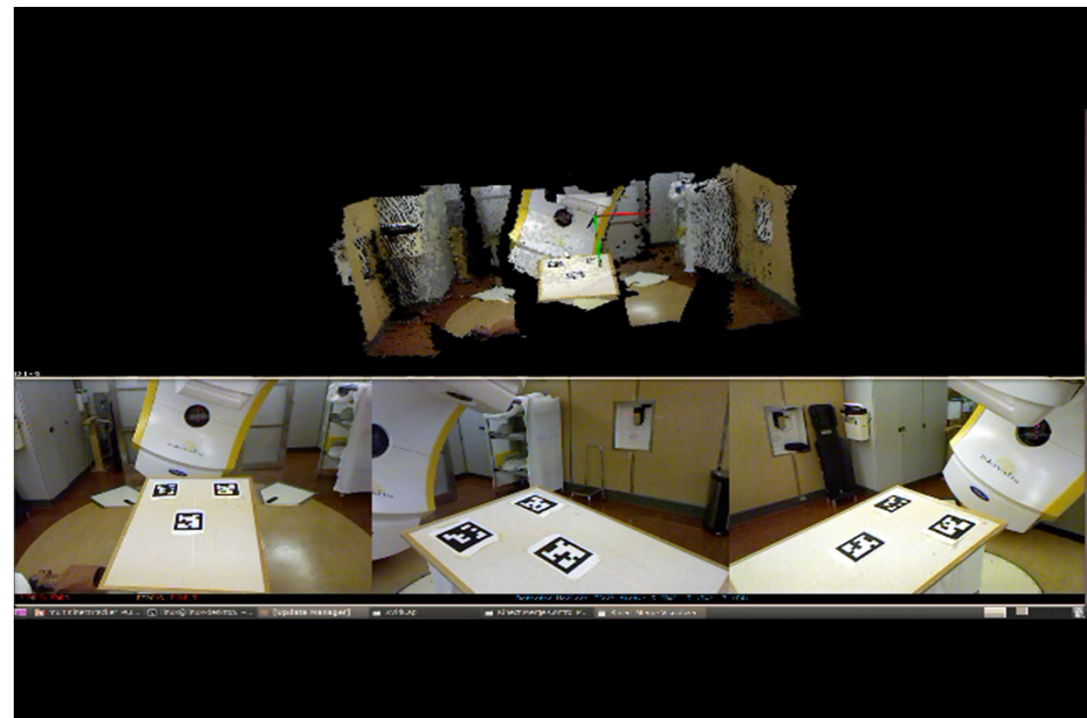
- Treatment room workflows mirror operating rooms
 1. Slower rhythm; checklists, timeouts, etc...
 2. Increase automation
 3. Patient identification
 4. Treatment site recognition
 5. Treatment site monitoring
 6. Display of patient CT (internal anatomy)
 7. Collision monitoring
 8. Recording of treatment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

3D Virtualization of Treatment Room

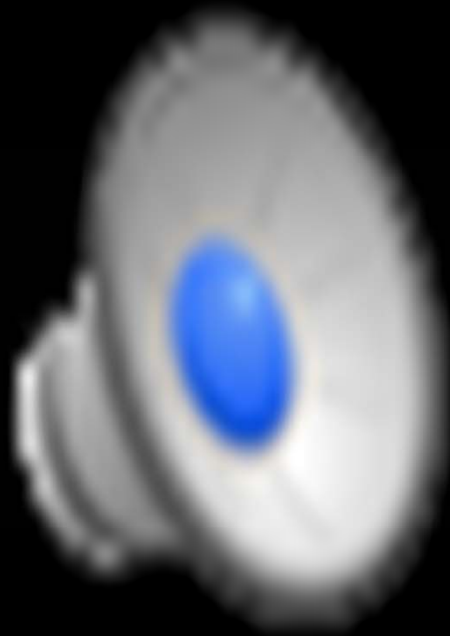
- New generation of 3D cameras
 - Provide color images + 3D surface
 - Multiple cameras linked together (positioned at different locations in room) camera generate real-time digital model of treatment room




KINECT
for XBOX 360.



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 sites

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: ≤ 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)**

Principal Investigator

Radiation Oncology/Translational Research

Feng-Ming (Spring) Kong, MD, PhD

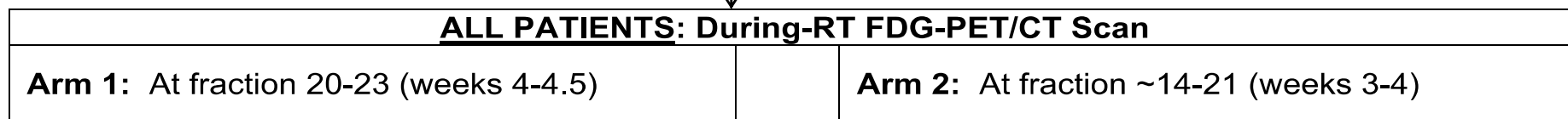
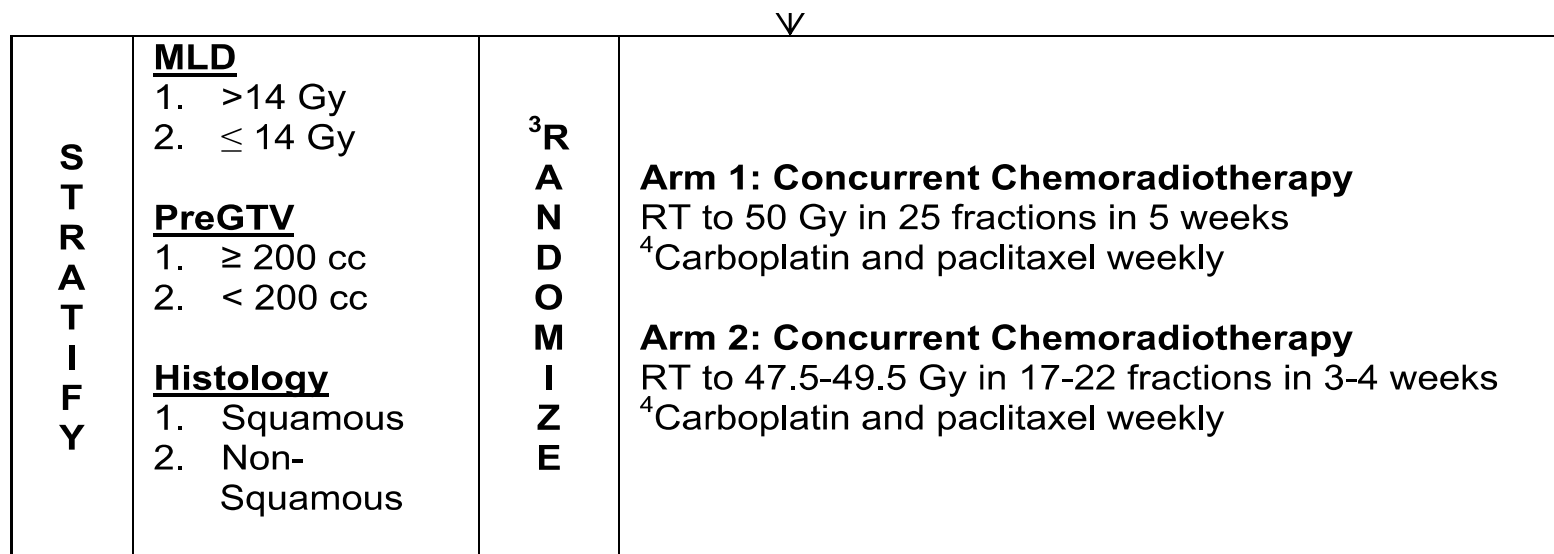
University of Michigan

1500 E. Medical Center Dr./UH B2 C490, SPC 5010

Ann Arbor, MI 48109

734-936-7810/FAX 734-763-7370

fengkong@umich.edu

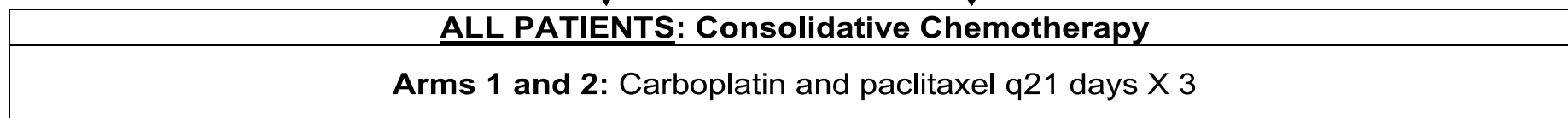


Arm 1: Continuation of radiotherapy, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

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



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)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
	Mean Lung Dose for the screening plan (74 Gy PTV dose)	Initial Dose per fx (Gy)	# Fractions for ~50 Gy EQD2 Tumor Dose	Physical Dose at this time point (Gy)	Minimum # Fractions Before 2 nd PET scan	Adaptive Phase Largest allowed Boost Dose per fx (Gy)	Adaptive Phase # of Fractions	Adaptive Phase Largest allowed Physical Boost Dose (Gy)	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

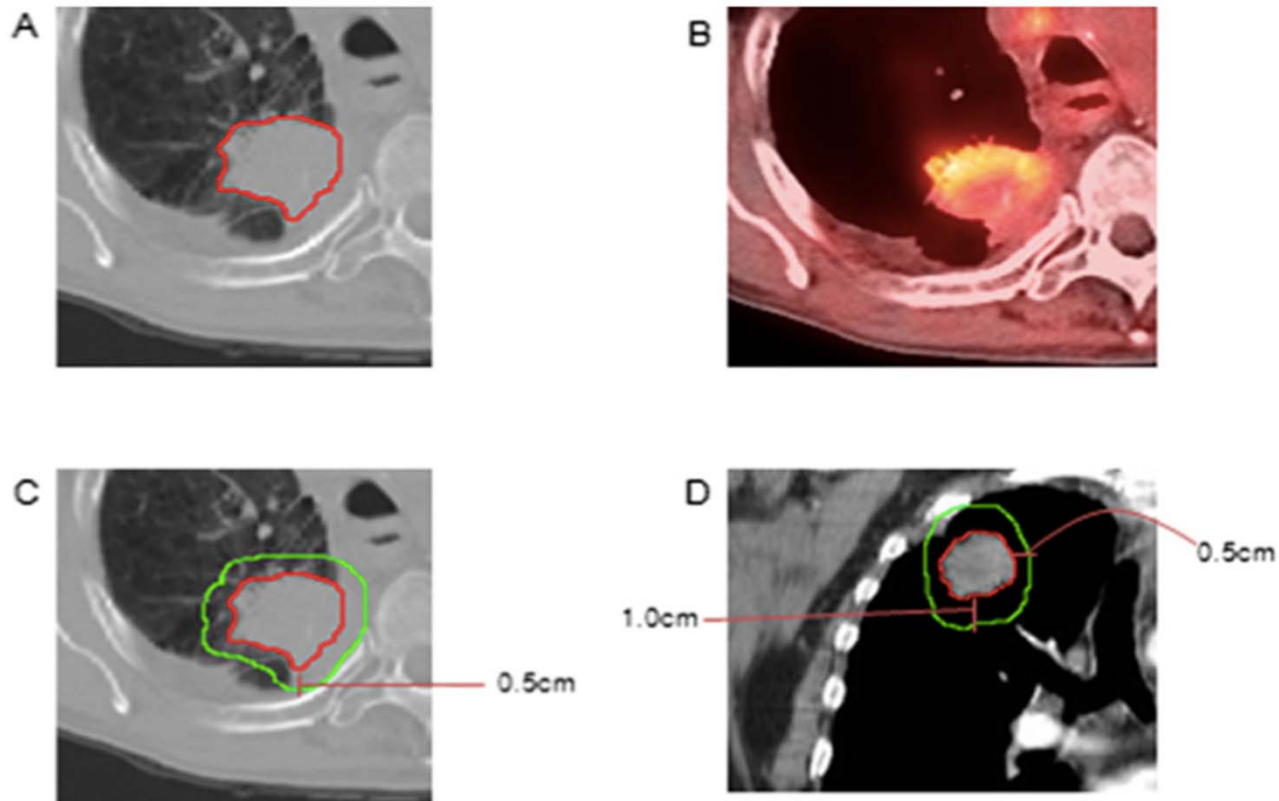
SBRT Boost to Residual Disease

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 8th or 9th fraction)

Dose-escalation cohorts: SBRT Boosts



5 Gy x 5

N=15

or

6 Gy x 5

N=15

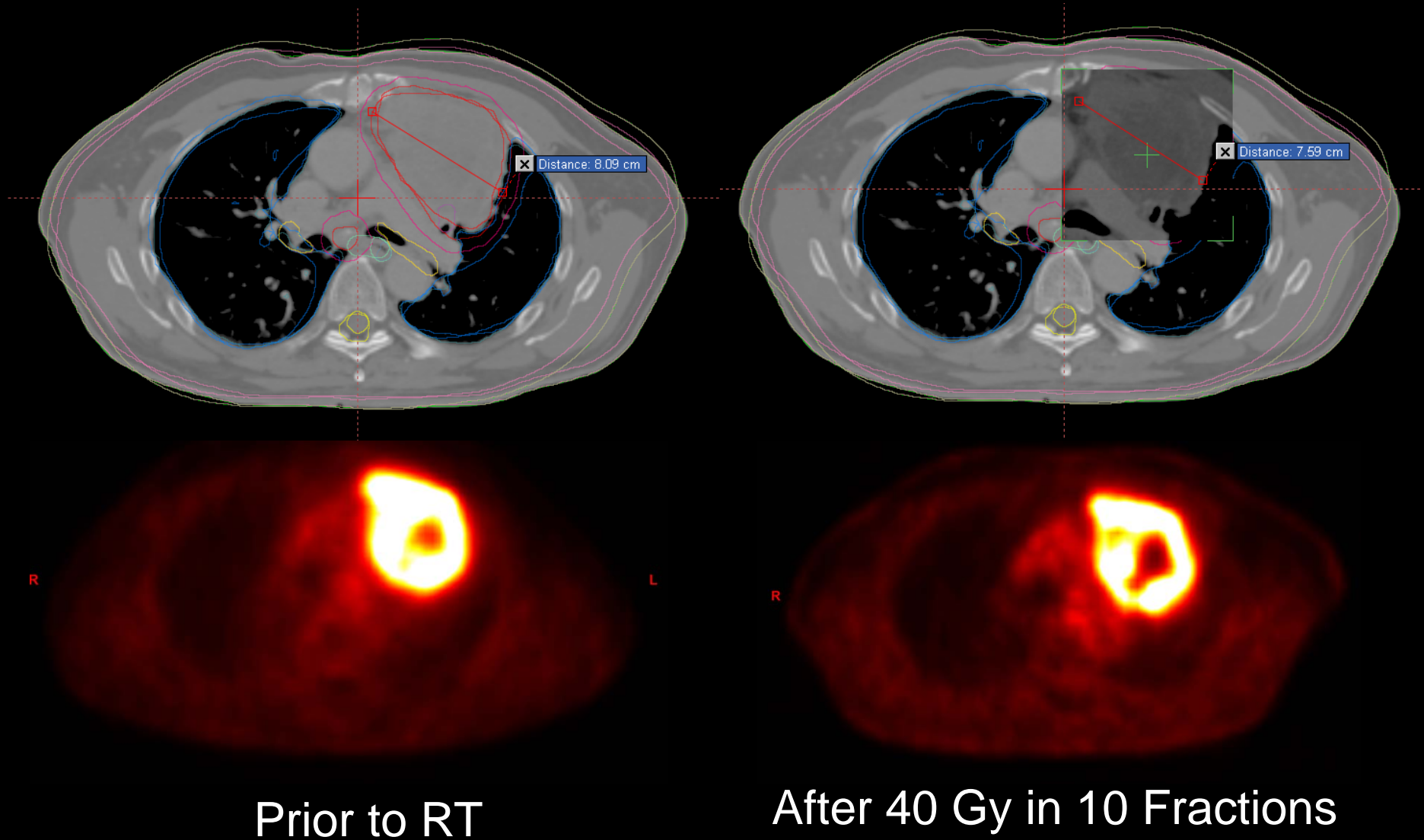
or

7 Gy x 5

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:

$$6.70 \times 5 = 33.5 \text{ Gy}$$

$$7.25 \times 5 = 36.25 \text{ Gy}$$

$$7.5 \times 5 = 37.5 \text{ Gy}$$

$$9.0 \times 4 = 36.0 \text{ Gy}$$

$$8.0 \times 5 = 40.0 \text{ Gy}$$

$$9.0 \times 5 = 45.0 \text{ Gy}$$

$$9.5 \times 5 = 47.5 \text{ Gy}$$

$$10.0 \times 5 = 50.0 \text{ Gy}$$

$$24 \times 1 = 24 \text{ Gy}$$

BED

146 Madsen IJROBP 2007

168

178

198 Fuller IJROBP 2008

200 King RO 2013

248

273

300

312 Greco, Lisbon

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

Boike JCO 2011 / Kim ASTRO 2013

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



Patrick Kupelian, M.D.
Professor and Vice Chair
University of California Los Angeles
Department of Radiation Oncology
pkupelian@mednet.ucla.edu

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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 HPV⁺ 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 conventional fraction sizes.⁵⁴ Definition of peripancreatic (eg, vasculature involvement) and intrapancreatic (cancer tissue) targets would allow dose painting, with in-room MRI being used to track those targets