State of the Art for Lung- SBRT

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Standard of Care

- Operable: Surgery
- Borderline Operable: Less surgery
- Medically Inoperable: SBRT (SABR)

Recent Advances in Surgery- VATS

Randomized Trials:

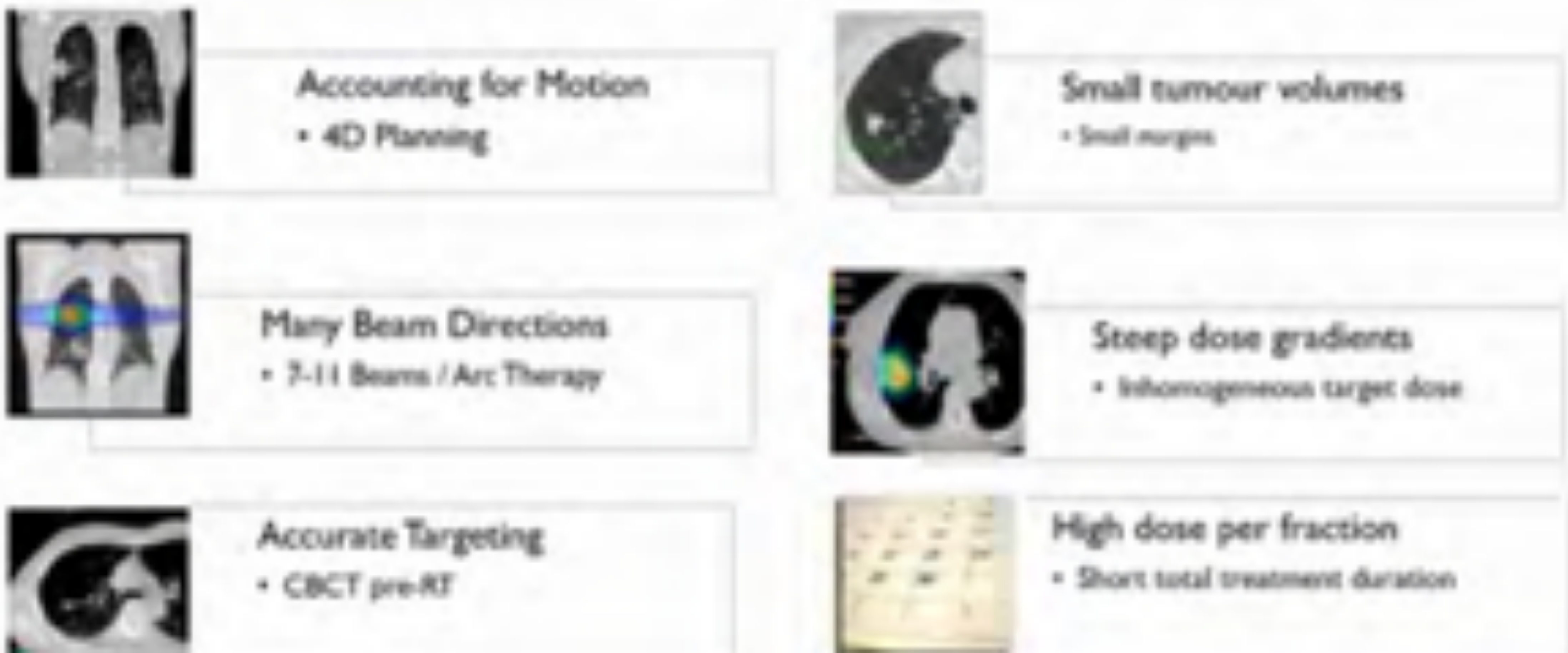
VATS vs. Thoracotomy

- Reduced operative time and blood loss
- Shorter hospital stay
- Less postop pain
- Les to improved quality of life

- NO improvement in long term survival
- 30-day mortality rate 0-30%

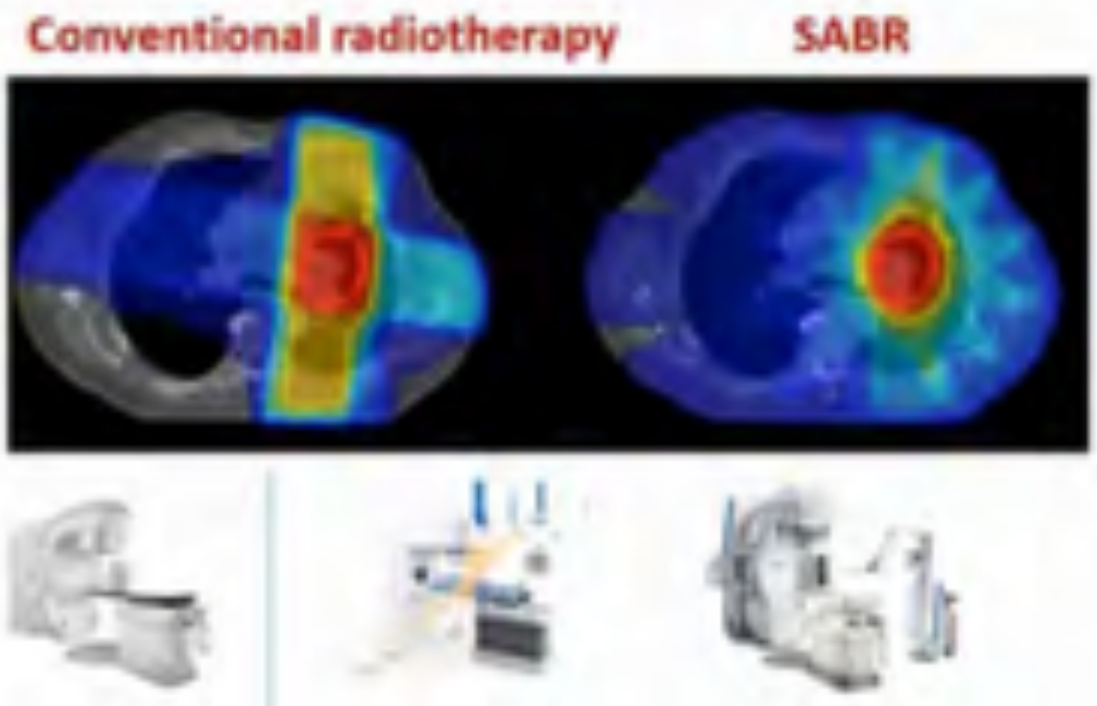
SBRT- Minimally Invasive Radiotherapy

Features of SBRT



SBRT for Frail Patients with Early NSCLC

- Indicated for elderly patients with poor pulmonary or cardiac reserve
  - FEV1 ≤ 50% or < 1 – 1.2 L
  - DLCO ≤ 50%
- Indicated for older patients who refuse surgery
- NCCN guidelines specify SABR is indicated for these patients with node-negative tumors <= 5 cm



Recommendations for PET- SBRT
Overall PET accuracy in the mediastinum 82%

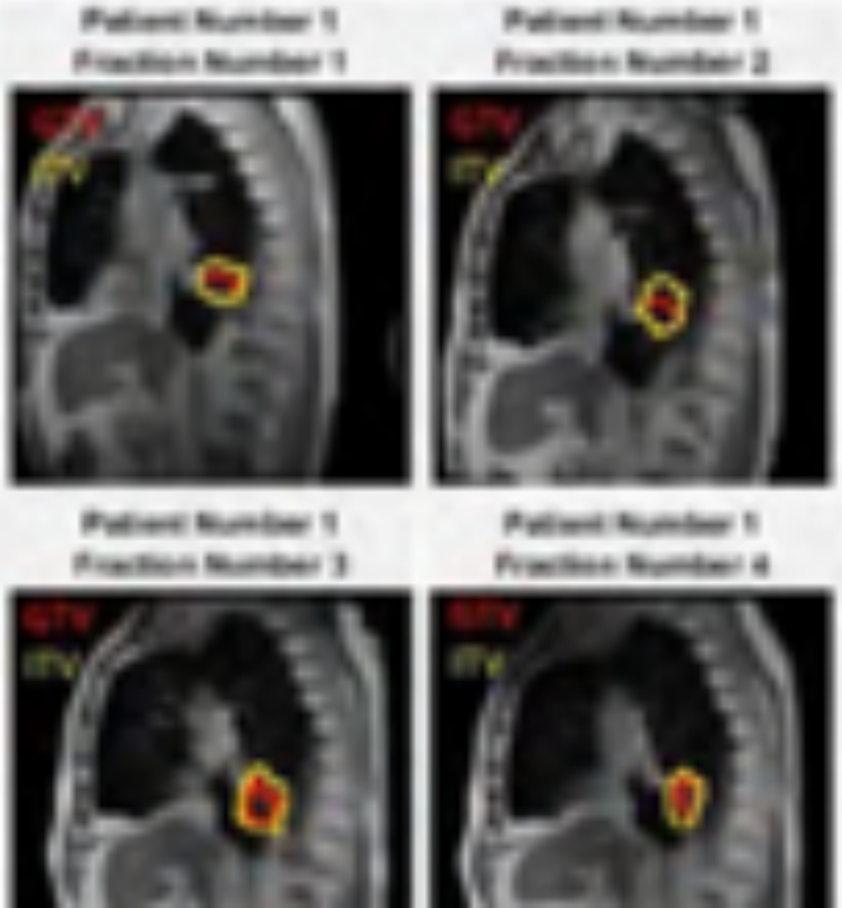
- Patients should be staged ***at a minimum*** with PET-CT which has an accuracy in the mediastinum of ~82%
- ***False positive rates*** of mediastinal involvement can ***approach 25% with PET-CT***
  - should confirm w/ ***invasive mediastinal staging*** prior deciding on therapy
- ***Larger, centrally located, and synchronous tumors*** have higher rates of ***occult mediastinal involvement*** despite PET negativity
  - should consider invasive mediastinal staging prior to definitive SABR
- Patients who are ***borderline resectable*** (high risk) for surgery and who ***undergo SABR should be considered for invasive staging***
  - this may aid decision b/w SABR v. surgery w/ mediastinal resection
- Despite this, ***outcome after SABR*** for early lung cancer w/o invasive mediastinal staging ***appear comparable overall*** c/w those w/ path.

Motion Tracking
CT vs. MR based ITV and max motion

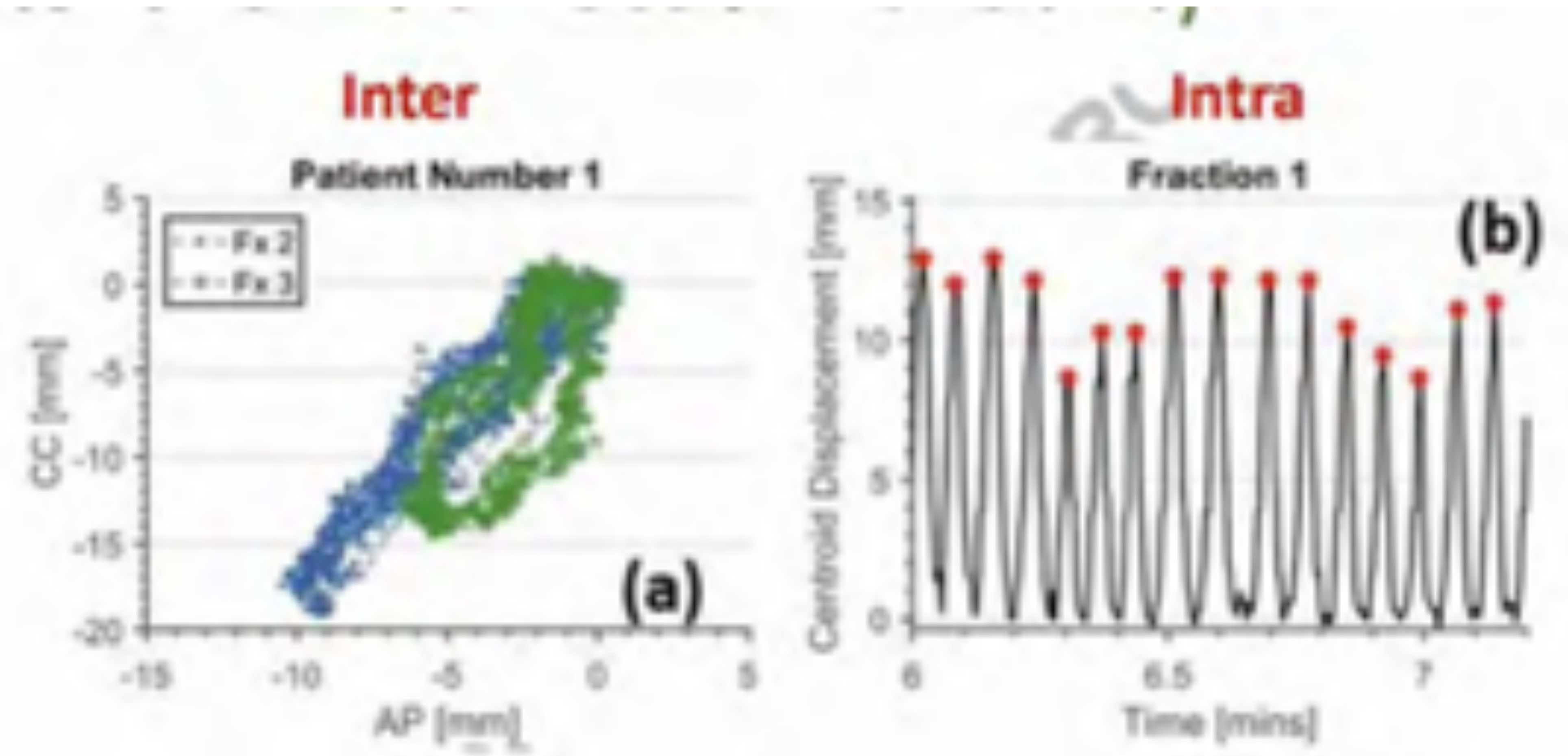
Simulation	Patient 1 Contour size [mm]	Patient 1 Motion [mm]	Patient 2 Contour size [mm]	Patient 2 Motion [mm]	Patient 3 Contour size [mm]	Patient 3 Motion [mm]	Patient 4 Contour size [mm]	Patient 4 Motion [mm]	Patient 5 Contour size [mm]	Patient 5 Motion [mm]
CT GTV	28.7	-	43.2	-	27	-	14.6	-	14.8	-
4D-CT ITV	41.7	13	49.8	6.6	33.6	4.6	21.1	6.5	21.2	6.4
FB MRI ITV	38.9	10.2	59.3	16.1	35.6	8.6	21.9	7.3	23.7	8.9
Location	Right Lower Lung		Right Lower Lung		Right Upper Lung		Right Medial Lung		Right Medial Lung	

* Measured along direction of maximum motion, through the central slice

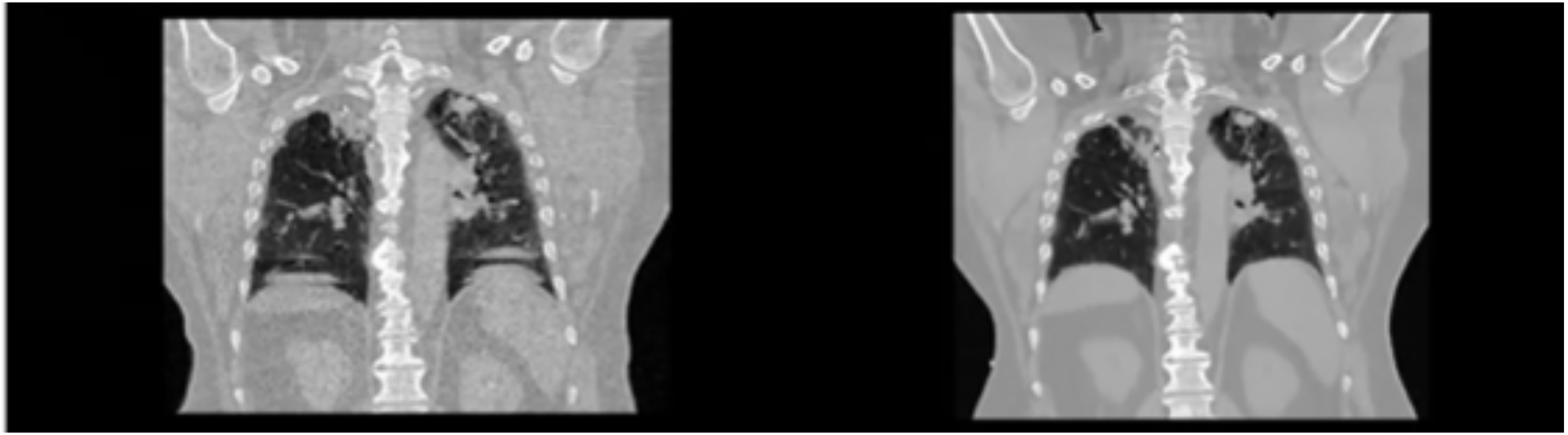
Cine Mode	Patient 1 Mean Motion [mm]	Patient 1 ± [mm]	Patient 2 Mean Motion [mm]	Patient 2 ± [mm]	Patient 3 Mean Motion [mm]	Patient 3 ± [mm]	Patient 4 Mean Motion [mm]	Patient 4 ± [mm]	Patient 5 Mean Motion [mm]	Patient 5 ± [mm]
Fraction 1	11.1	2.0	9.4	2.0	8.4	1.7	1.9	1.2		
Fraction 2	13.7	1.3	11.0	2.2	9.0	1.2	3.5	0.9		
Fraction 3	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]		



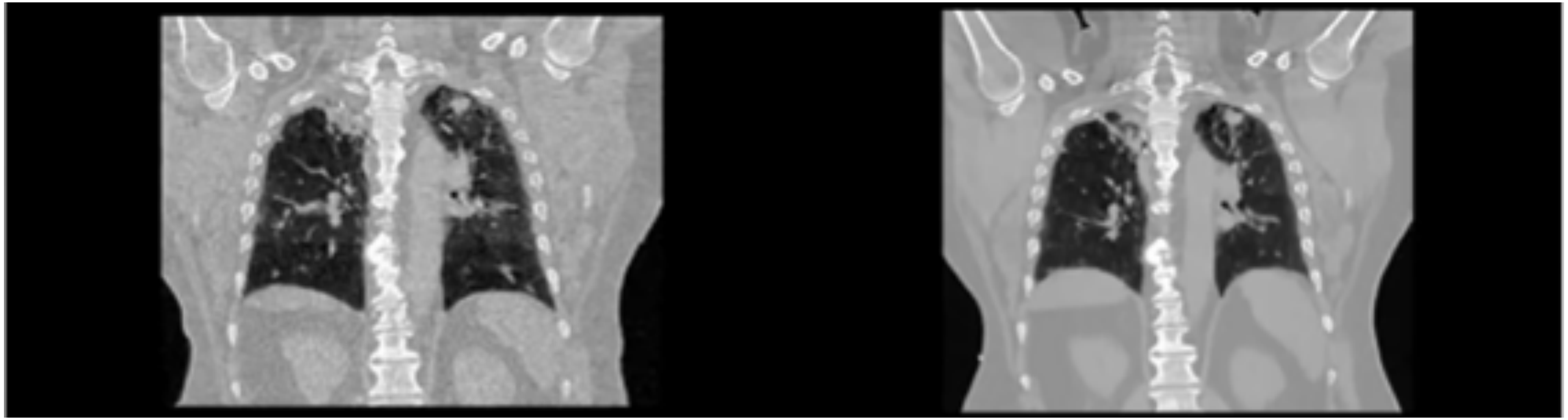
Inter and Intra Fraction Variability



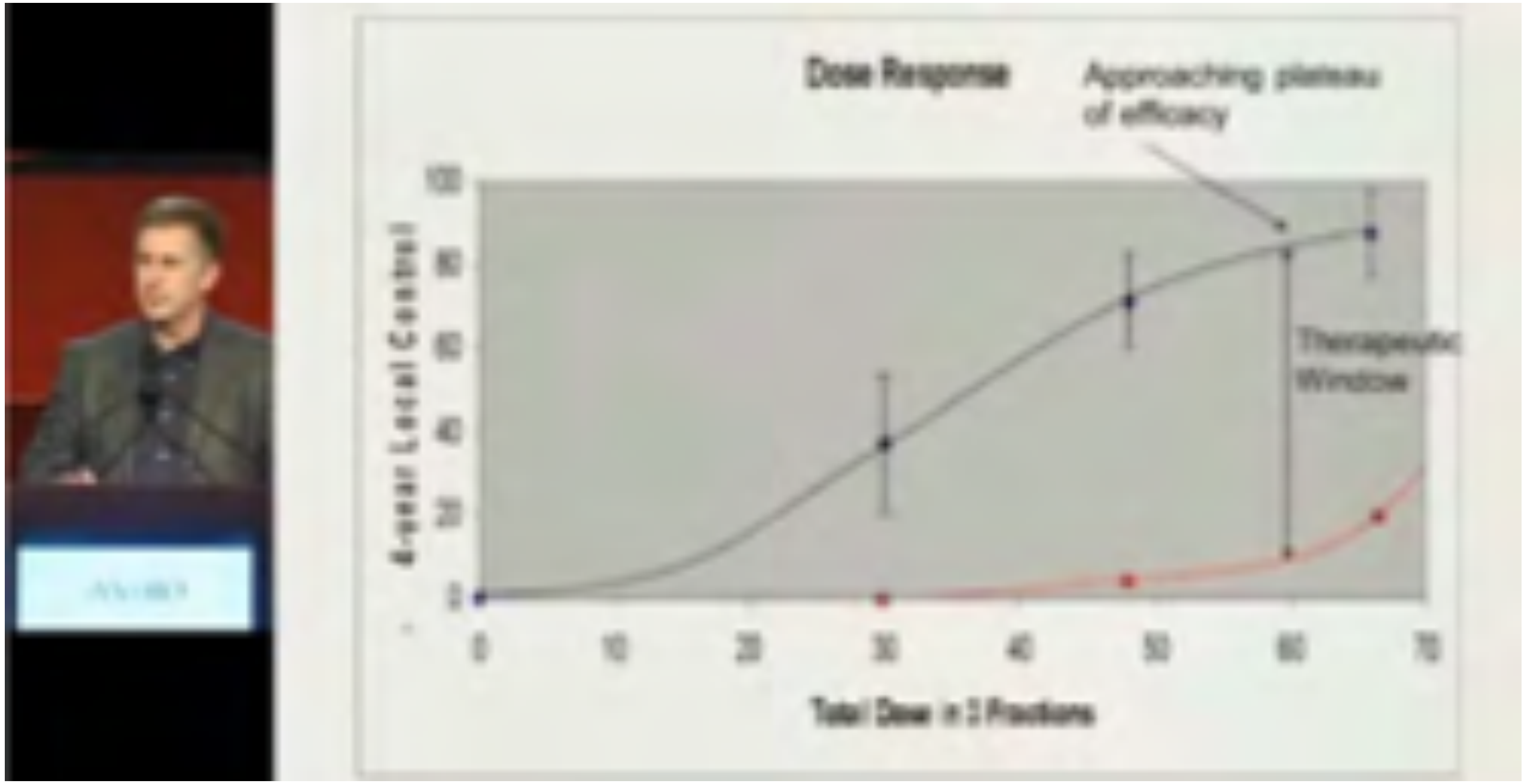
Intra Fraction Variability



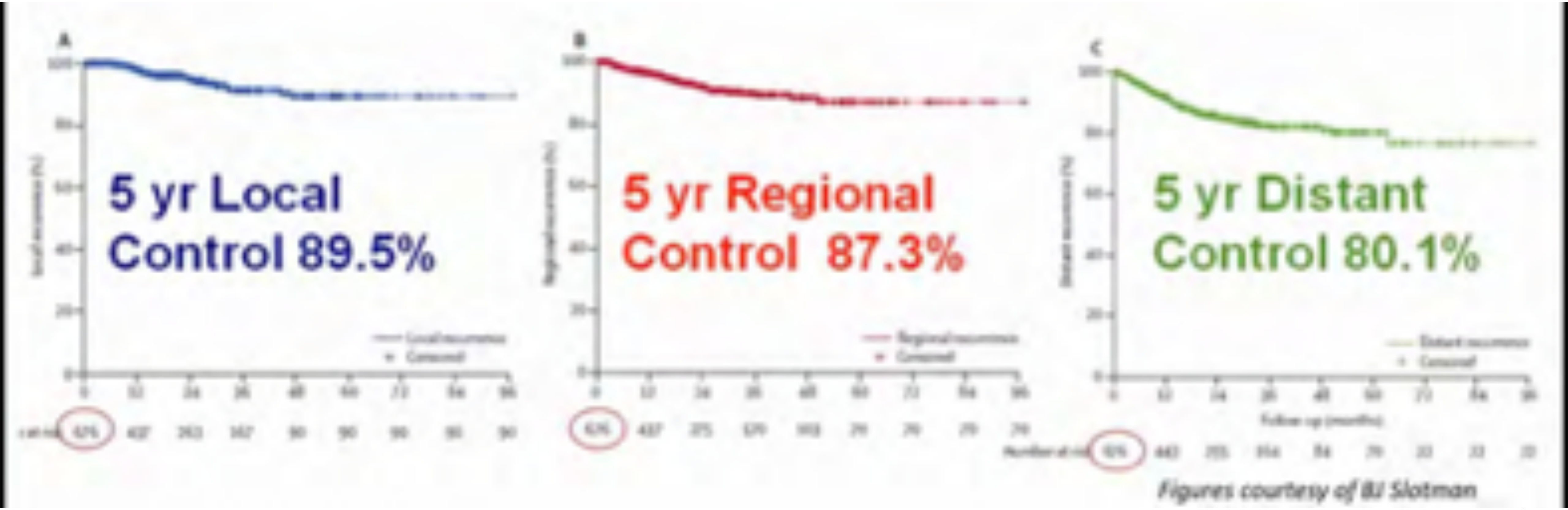
Intra Fraction Variability



SBRT for Stage I NSCLC
Phase I Trial -Indiana University 20 years ago!



Dutch SBRT Series



WGSBRT- TCP Group

Local Control following Stereotactic Body Radiation Therapy for Stage I Non-Small Cell Lung Cancer

Percy Lee, M.D.[1], Billy W. Loo, Jr., M.D., Ph.D.[2], Tithi Biswas, M.D.[3], George X. Ding, Ph.D.[4], Issam M. El Naqa, Ph.D.[5], Andrew Jackson, Ph.D.[6], Feng-Ming Kong, M.D., Ph.D.[7], Tamara LaCouture, M.D.[8], Moyed Miften, Ph.D.[9], Timothy Solberg, Ph.D.[10], Wolfgang A. Tome, Ph.D.[11], An Tai, Ph.D.[12], Ellen Yorke, Ph.D.[6], X. Allen Li, Ph.D.[12]

[1]Department of Radiation Oncology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

- WGSBRT – TCP Group
  - Percy Lee and Allen Li - Co-chairs
  - An Tai
  - Billy W. Loo, Jr.
  - Ellen Yorke
  - Tithi Biswas
  - Issam M. El Naqa
  - Timothy Solberg
  - George X. Ding
  - Andrew Jackson
  - Feng-Ming Kong
  - Moyed Miften
  - Wolfgang A. Tome
  - Tamara LaCouture

WGSBRT- Thoracic TCP

- **Methodology:**
  - 160 clinical studies reviewed on SABR for lung cancer – May 2014
  - Reviews by 12 members of the Thoracic TCP Working Group – primary data
  - Selected re-review by group co-chairs for consistency
  - 47 studies of high quality ultimately included
  - Data modeling by Allen Li and his group (KM/actuarial figure digitized).

- **Objectives:**
  - Better model than LQ, USC for thoracic SABR TCP?
  - More accurate predictions for tumor control by biological and physical dose
  - Discern intrinsic radio sensitivity of lung tumors to SBRT (α/β)

Thoracic TCP Working Group

Isocenter Dose (Gy)		3 fractions	4 fractions	5 fractions
Regrowth	T1	52±1	57±1	60±1
	T2	56±1	62±1	66±1
	T1+T2	54±1	59±1	63±1
LQ	T1+T2	55±1	59±1	63±1
USC	T1+T2	55±1	59±1	63±1

To achieve 3 year Maximal Tumor Control

PTV Dose (Gy)		3 fractions	4 fractions	5 fractions
Regrowth	T1	42±1	46±1	48±1
	T2	45±1	50±1	53±1
	T1+T2	43±1	47±1	50±1
LQ	T1+ T2	44±1	47±1	50±1
USC	T1+T2	44±1	47±1	50±1

Potential Influencers of Tumor Control

Patient Factors:

- Age, histology (in situ vs. invasive), tumor size/volume, tumor location, tumor doubling time, lung function?

Treatment Factors:

- Total dose, dose per fraction, number of fractions?
- Length of treatment? Time effects (BED 100 can be achieved with 3DCRT but takes many weeks). Tumor cell repopulation?
- Treatment techniques. Our study normalized to isocenter

Conventional RT vs. SBRT: SPACE Trial

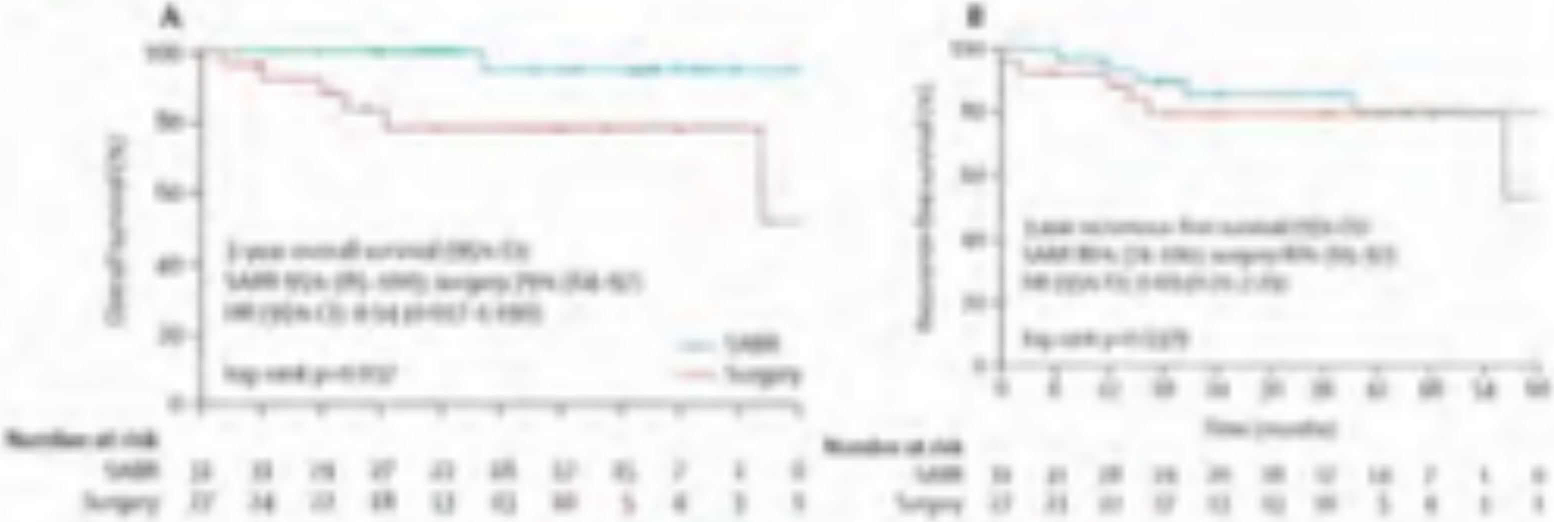
- **SABR** (66 Gy/3fx) vs. **3DCRT** (70 Gy/7wks)

- Stage I peripheral < 5 cm
- 3 year PFS: 62% SABR vs. 58% 3DCRT, OS similar
  - SABR vs. 3DCRT for local control: 72% vs. 59%
- Toxicity profile favored SABR
  - Any grade pneumonitis SABR vs. 3DCRT: 19% vs. 34%
  - Any grade esophagitis SABR vs. 3DCRT: 8% vs. 30%
- SABR
  - Trend to improved control, Higher QoL values, dyspnea, cough, and chest pain

SBRT vs. Standard RT: TROG 09-02. CHISEL. Phase III Local Control 14% vs. 31%

SBRT vs. Surgery: Phase III Studies

- Phase III comparisons have not been feasible thus far
  - High-risk: ACOSOG 4099/RTOG 1021, Stable Mate
- Operable: STARS/ROSEL (Lancet Oncology 2015, n=58)
  - 3-yr OS: 95% (SABR) vs. 79% (surgery)
  - 3-yr RFS: 86% (SABR) vs. 80% (surgery)

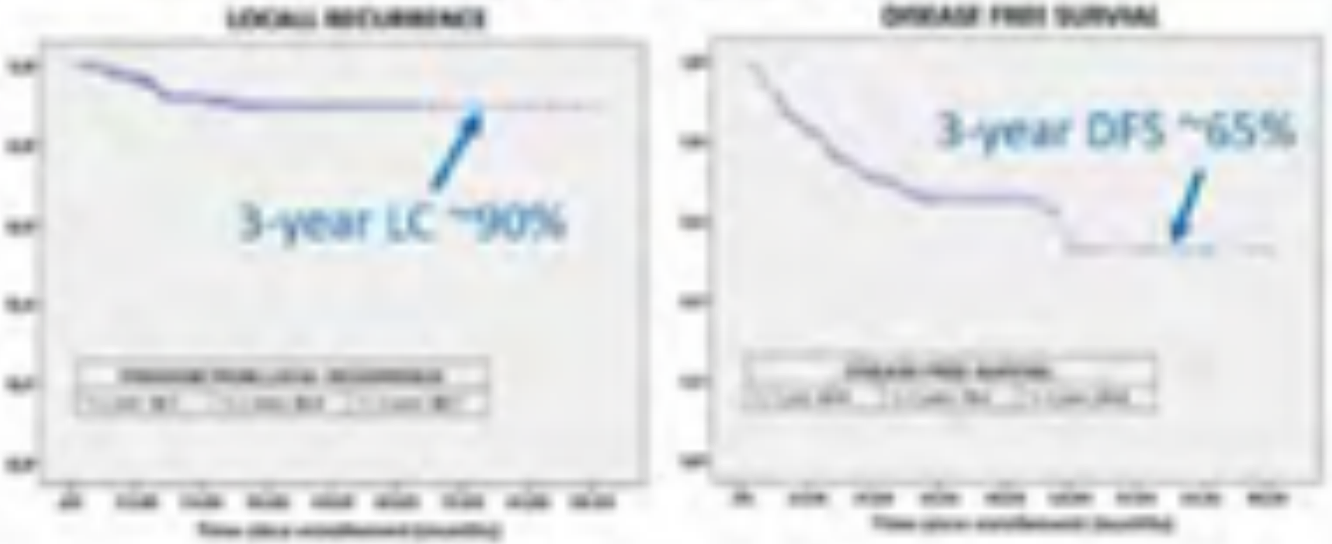


SBRT excellent LC
What about disease recurrence elsewhere?

RTOG 0236 5 year update

- Regional recurrences
  - 7 patients with regional failure
    - 2 patients in the original report
    - 5 year local-regional recurrence rate 38%
- Distant recurrences
    - 15 patients with disseminated failure
    - 5 year distant recurrence rate 31%
- 5 year disease free survival only 26%

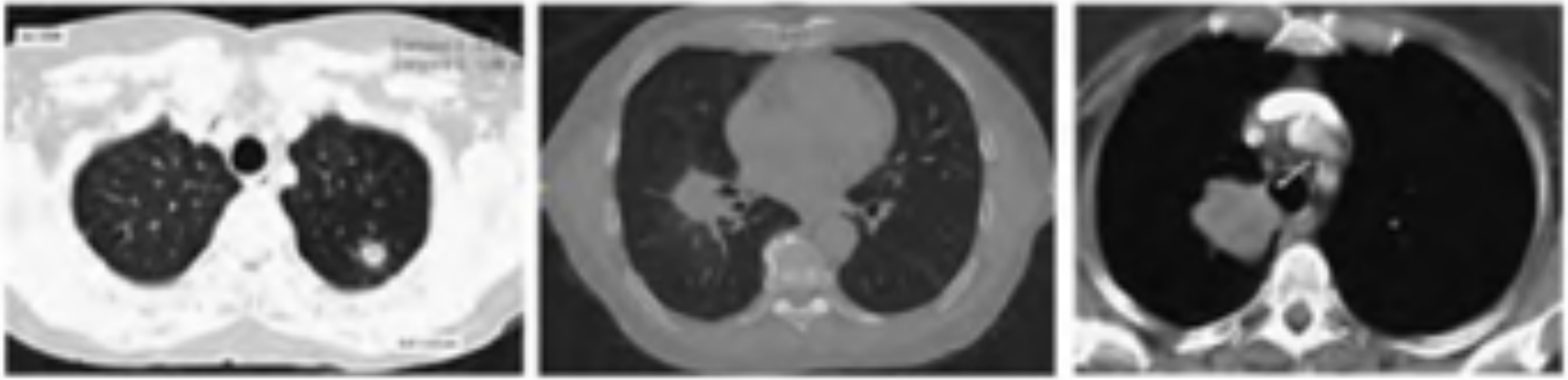
Multicenter Italian Study (n= 196)



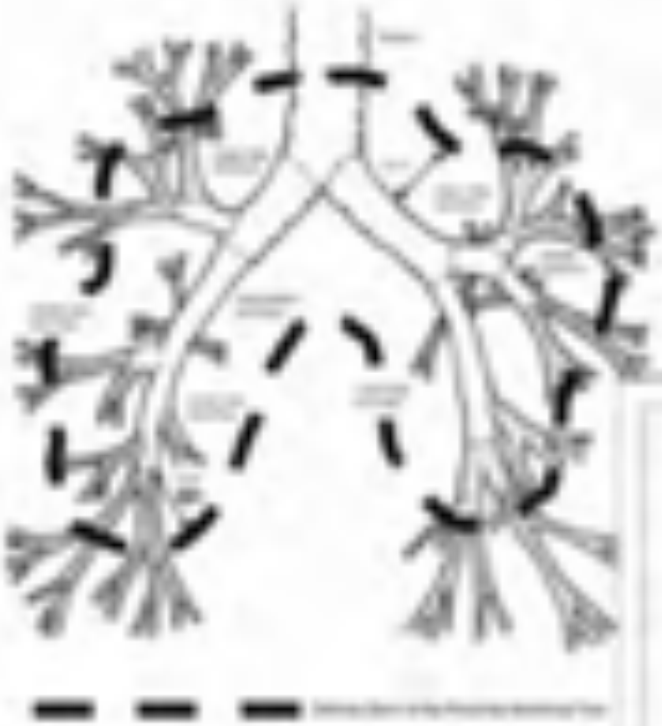
Ricardi U et al., Lung Cancer 2014

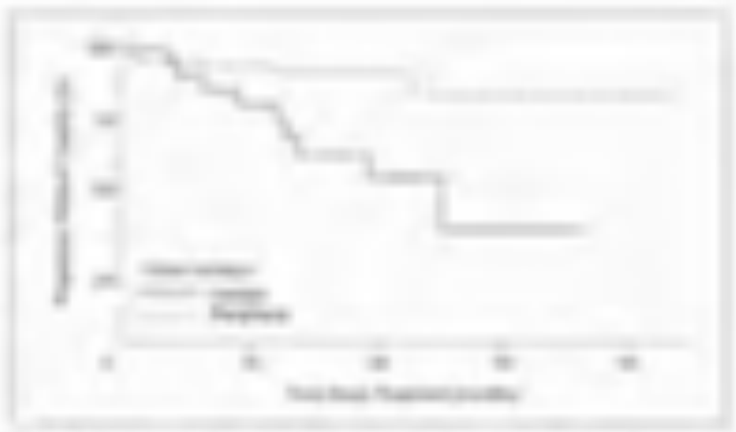
Decision Making Based On Tumor Location

- Peripheral
- Central
- Ultracentral



Central Tumor

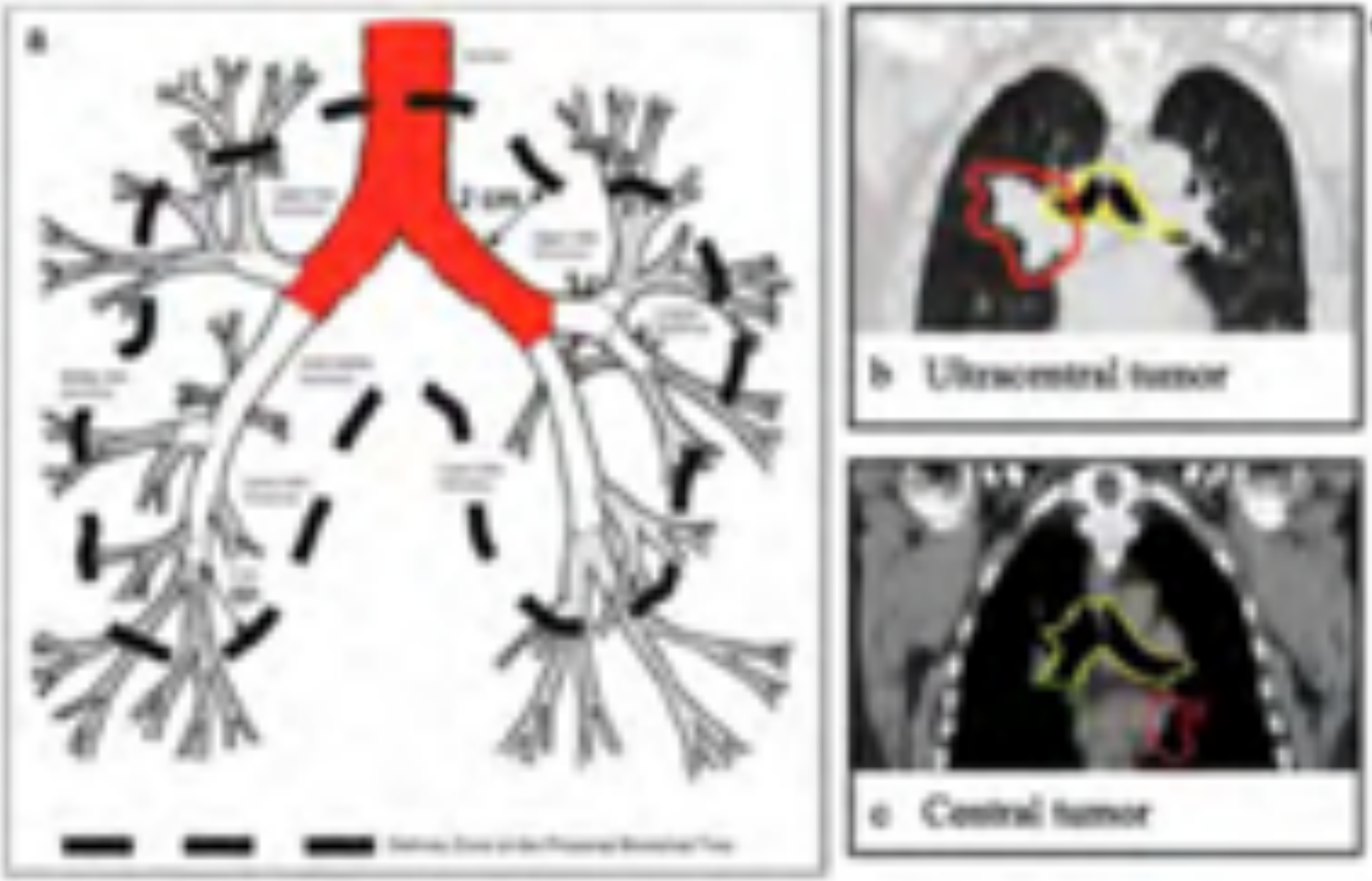




- Central tumor: a tumor with a PTV that overlaps with a 2 cm volume from 2 cm superior to carina extending to the lobar bronchi

Timmerman R et al., JCO 2006

Ultracentral Tumor



- Ultracentral tumor: a tumor with a PTV that overlaps with the trachea and/or main bronchi

Timmerman R et al., JCO 2006
Baker S et al., Radiat Oncol 2016

Peripheral vs. Central Tumor Dosing

- **Peripheral tumors:**
  - 18 gy x 3 planned to PTV (3-6 mm expansion on ITV) with MC calculation engine
  - Or 18 gy x 3 planned to ITV only (large (e.g. > 4 cm) peripheral tumors)
  - Or hypofractionation (60 gy in 8, 65 gy in 10, or 70 gy in 10) for tumors > 5 cm
- **Central tumors:**
  - 12.5 gy x 4, or 10 gy x 5 (3-6 mm expansion on ITV)
  - Or 18 gy x 3 planned to ITV only (abutting aorta, esophagus, heart, great vessels, etc.)
  - Or hypofractionation (60 gy in 8, 65 gy in 10, or 70 gy in 10)
- **Ultracentral tumors:**
  - Hypofractionation (60 gy in 8, 65 gy in 10, or 70 gy in 10)
  - Or Concurrent chemoradiotherapy to 60 Gy +/- durvalumab

Hypothesis for HyCRT and SBRT

- Medically inoperable stage II and III NSCLC
- Local control still ~ 50-60% and survival poor prior to PACIFIC
- Dose escalation beyond 70 Gy with protracted approach is detrimental in randomized cooperative phase III setting (and time consuming)

Hypothesis: Applying technical advances of SABR with hypofractionation, thoughtful margin design, and biological adaptation may reduce toxicity, improve outcomes, shorten treatment course

HyCRT%- SBRT Squeme

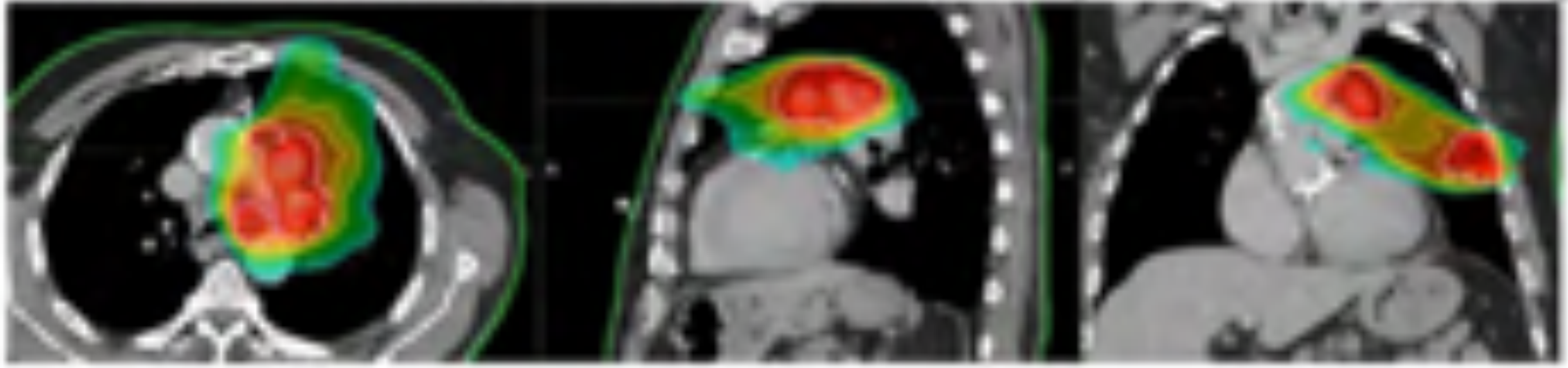
- Eligibility:
  - Stage II/III biopsy proven inoperable NSCLC by AJCC 7th
  - No prior RT in the thorax
- Stopping rules:
  - 7-15 patients per cohort
  - Stopped if rate of treatment-related DLT (non-heme grade ≥ 3) ≤ 90 days was ≥ 33%
  - MTD = immediately prior dose cohort

- 5 Gy Boost: 10 patients (1 DLT)
- 6 Gy Boost: 9 patients (0 DLT)
- 7 Gy Boost: 9 patients (1 DLT)

- Median age: 70 (51 – 88)
- 57% male
- 64% adeno, 36% SCC

Hy CRT- SBRT

76 M with T1bN2M0, cIIIA adeno CA of LUL: 4 Gy x 10 (5 mm PTV margin)



PET response at 40 Gy

SABR boost 6 Gy x 5 (IGTV only)

SBRT for Stage I and Unresectable Stage III

- **Stage I Inoperable**
  - Phase II randomized study of SABR w/ or w/o Nivolumab for early inoperable NSCLC (MD Anderson, recruiting patients)
  - SABR Combining With Avelumab (Anti-PD-L1) for Management of Early Stage Non-Small Cell Lung Cancer (NCT030554, UCSD, recruiting)
  - Pembrolizumab After lung SABR for Medically Inoperable Early Stage Non-Small Cell Lung Cancer (NCT035742220, Case Comprehensive Cancer Center)
  - SABR with Immunotherapy in Early Stage Non-small Cell Lung Cancer: Tolerability and Lung Effects (STILE) (NCT03383302, Royal Marsden NHS Foundation Trust)

- Unresectable Stage III
- RT concurrent with IO followed by IO in LA NSCLC

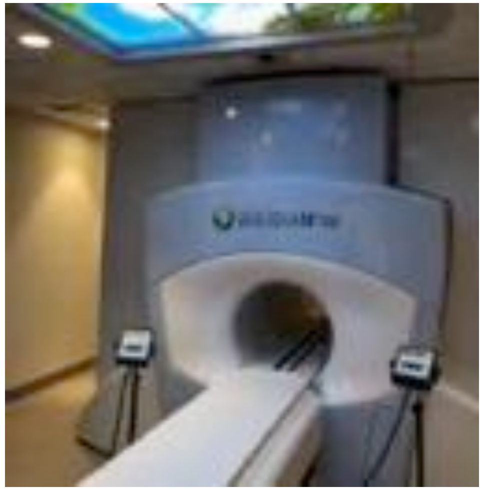
Technology Considerations at Miami Cancer Institute

Linear Accelerators

CyberKnife® M6

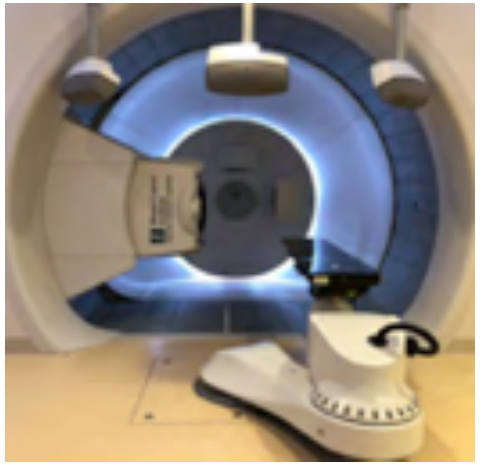
Radixact Tomotherapy

Gamma Knife Icon



MR Linear Accelerator

High Dose Rate Brachytherapy

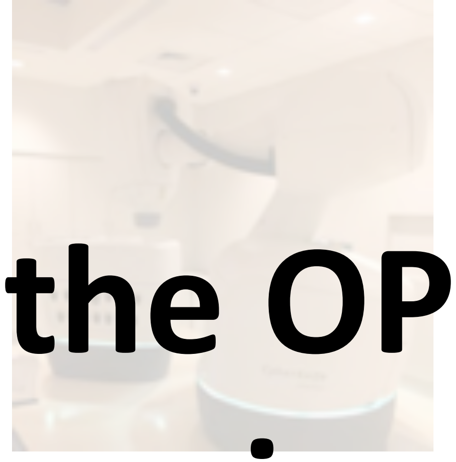


Proton Therapy

Miami Cancer Institute

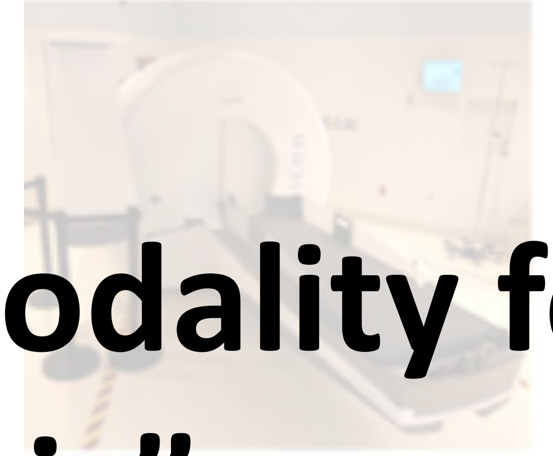
Linear Accelerators

CyberKnife® M6



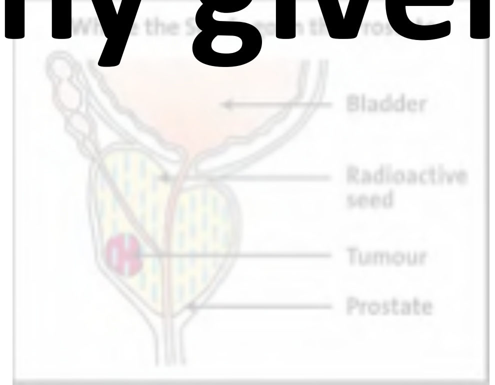
Radixact Tomotherapy

Gamma Knife Icon



“Employ the OPTIMAL modality for any given diagnosis”

MR Linear Accelerator



Low Dose Rate Brachytherapy

High Dose Rate Brachytherapy

Proton Therapy

Radiotherapy Technology

	TrueBeam Linac	Tomo	CyberKnife	Gamma Knife	MR Linac	Proton - PBS
Radiation type	Multiple MVs	6MV-FFF	6MV-FFF	Co-60	6MV-FFF	Multiple p+ MeVs
Isocenter	Isocentric	Non-isocentric	Non-isocentric	Isocentric	Isocentric	Isocentric
IGRT: Inter-fraction	kV-CBCT, kV/kV, MV/MV, SIG, Calypso	MVCT	Stereoscopic kV/kV	kV-CBCT	MR	kV-CBCT, kV/kV, SIG
IGRT: Intra-fraction	kV triggered imaging, Calypso, SIG	Coming soon…	Cine kV	Infrared Marker	Planar Cine MR	Surface Imaging
Ideal clinical indications	Universal	H&N, Comp. Breast, Long Tx Fields, Junction fields	Motion tracking, non-coplanar delivery	Cranial Stereo.	Diaphragmatic motion, adaptive capability	Universal, lower integral dose, pediatrics, re-irradiation

Technology Triage

Early Stage Lung Cancer

CyberKnife
- Trackable?
- Fiducials?
- Arms restriction?
- Large motion

Yes?

TrueBeam
- Breath-hold?
- Compression (ITV)?
- Fast delivery?
- Volumetric imaging?

Yes?

MR Linac
- Breath-hold?
- FB gating?
- Claustrophobic?
- Lateral lesion?
- Volumetric imaging?

Yes?

Protons
- Large motion?
- Insurance?
- Volumetric imaging?
- Breath-hold?

Yes?

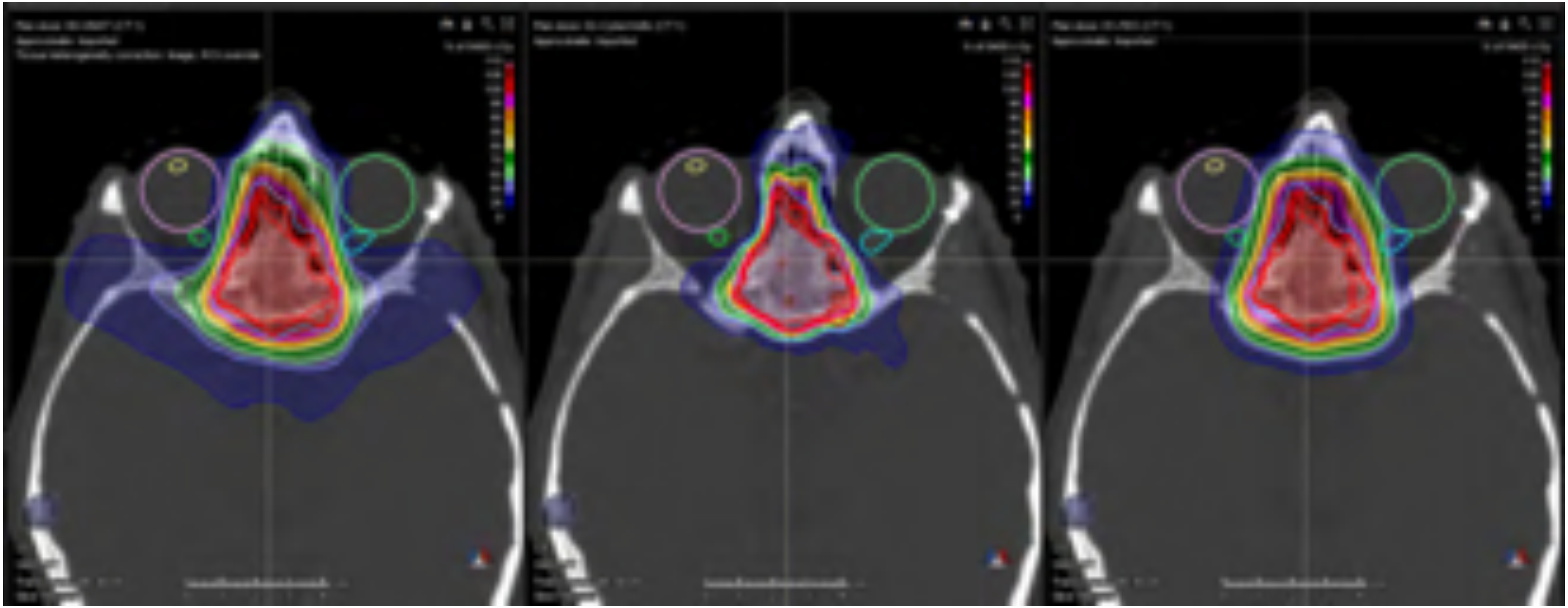
Tomotherapy
- Claustrophobic
- Volumetric imaging?
- Non-coplanar?

Yes?

Comparative Plans

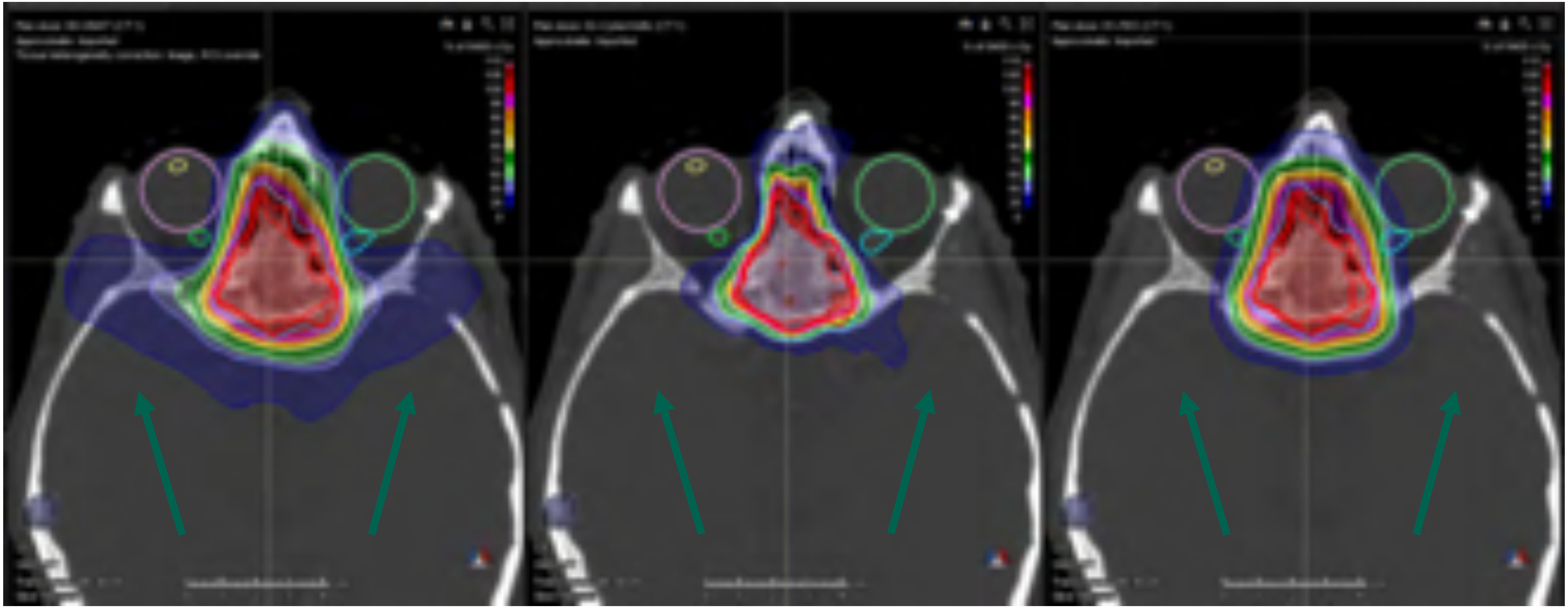
Treat patient with *best* quality plan

Comparative Treatment Planning



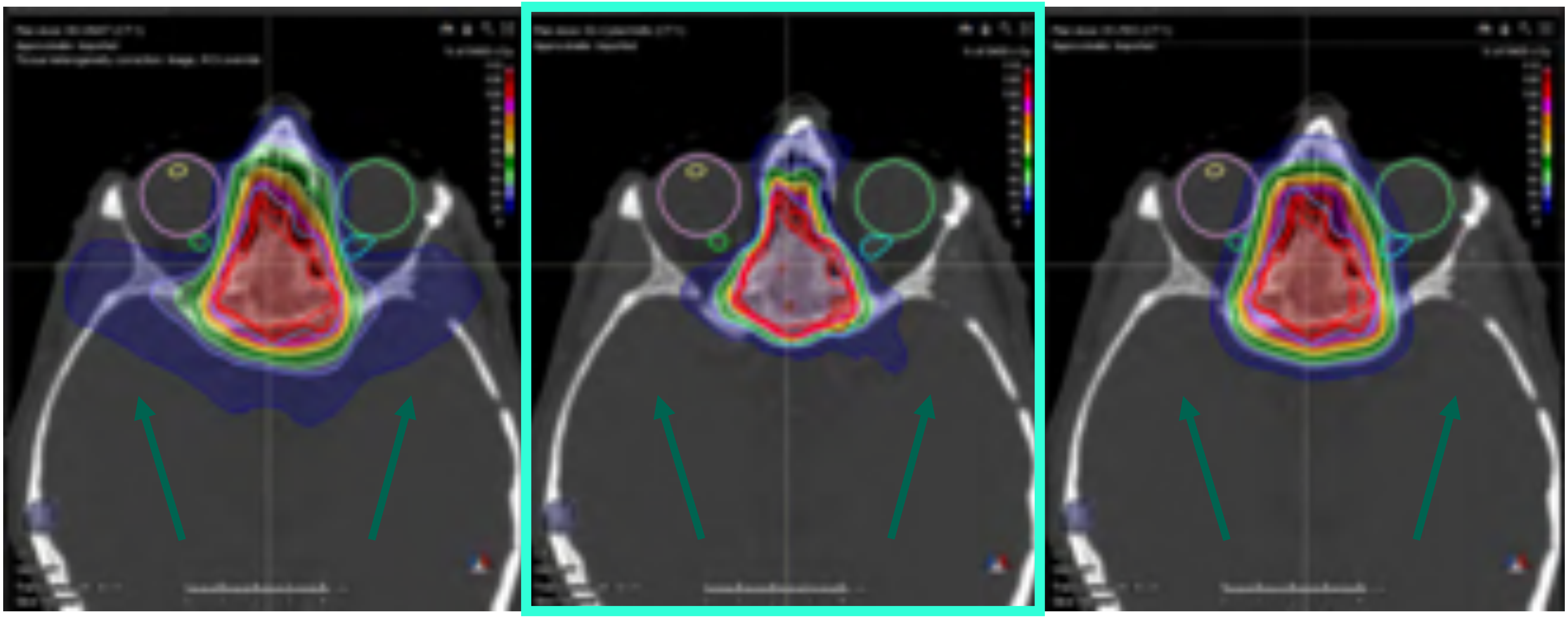
57 yo M with a recurrent meningioma in the frontal skull base

Comparative Treatment Planning



First: evaluate the overall dose distribution to the tumor and surrounding brain

Comparative Treatment Planning



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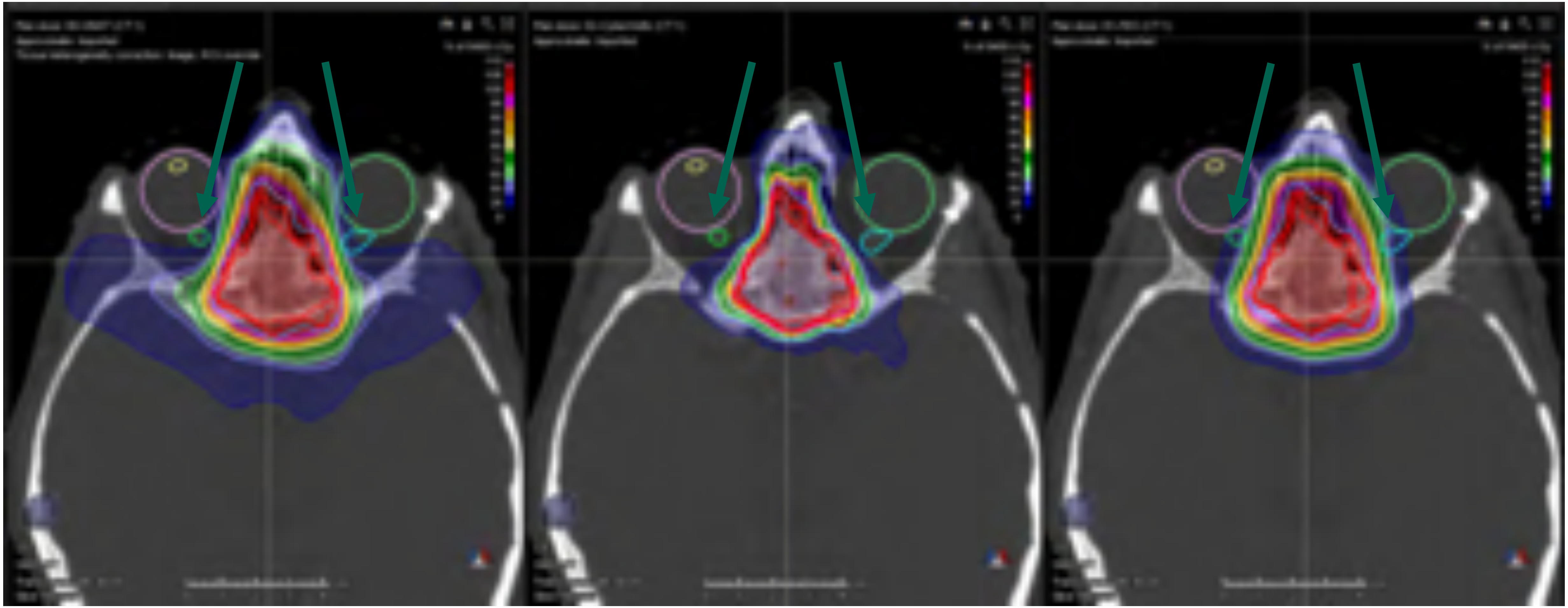
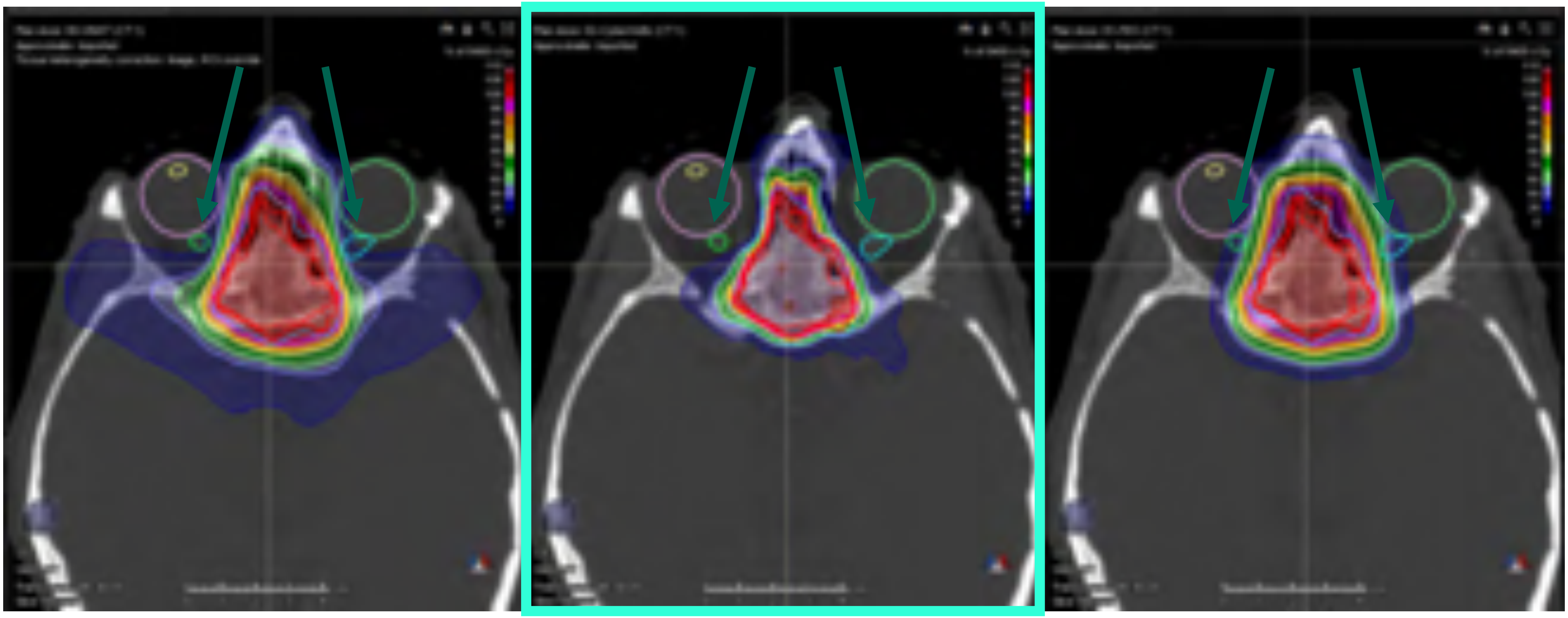


Second: evaluate the dose to the tumor and critical OARs

Comparative Treatment Planning



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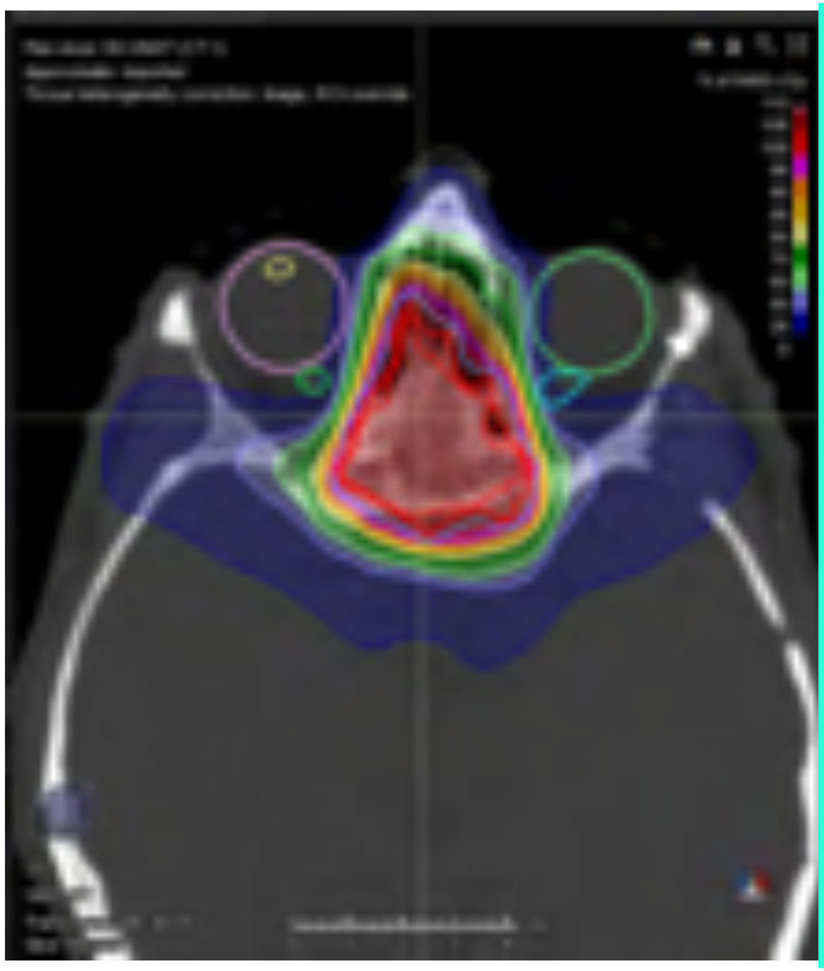
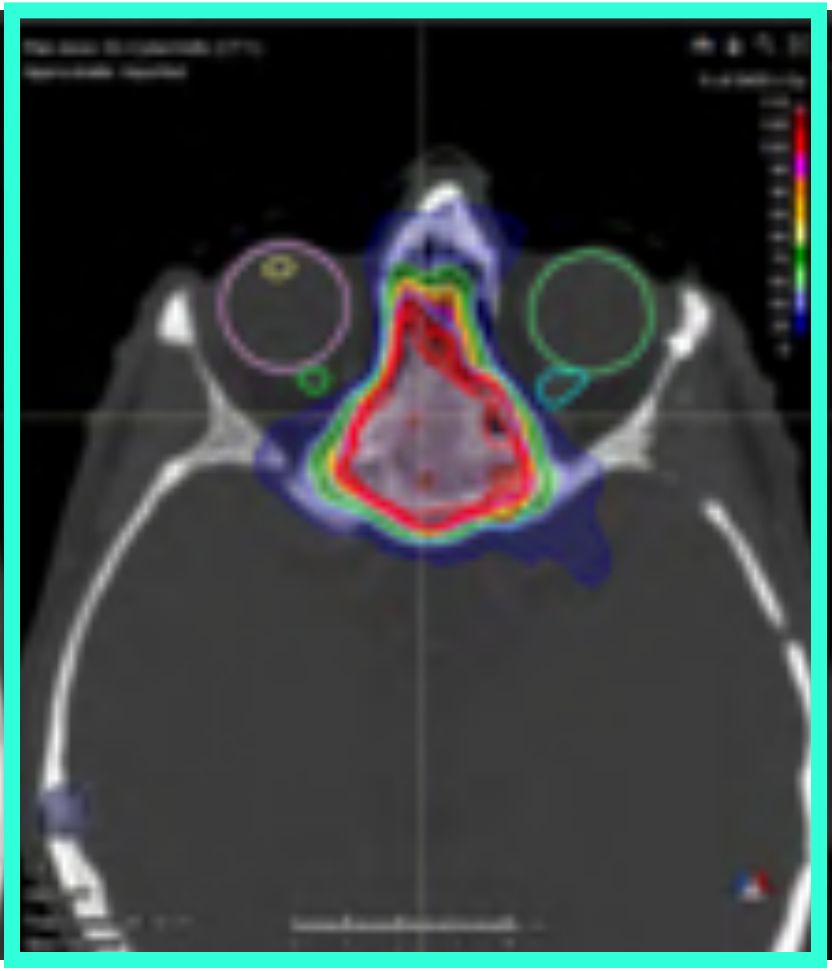
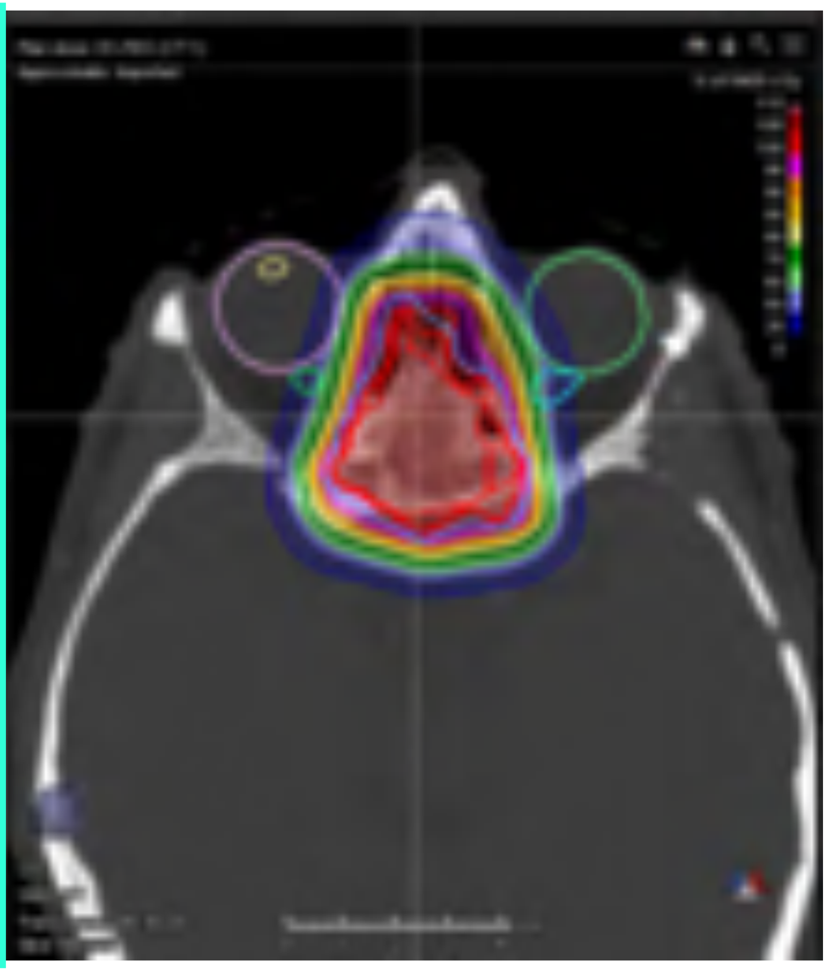
Comparative Treatment Planning



Increased dose to surrounding structures

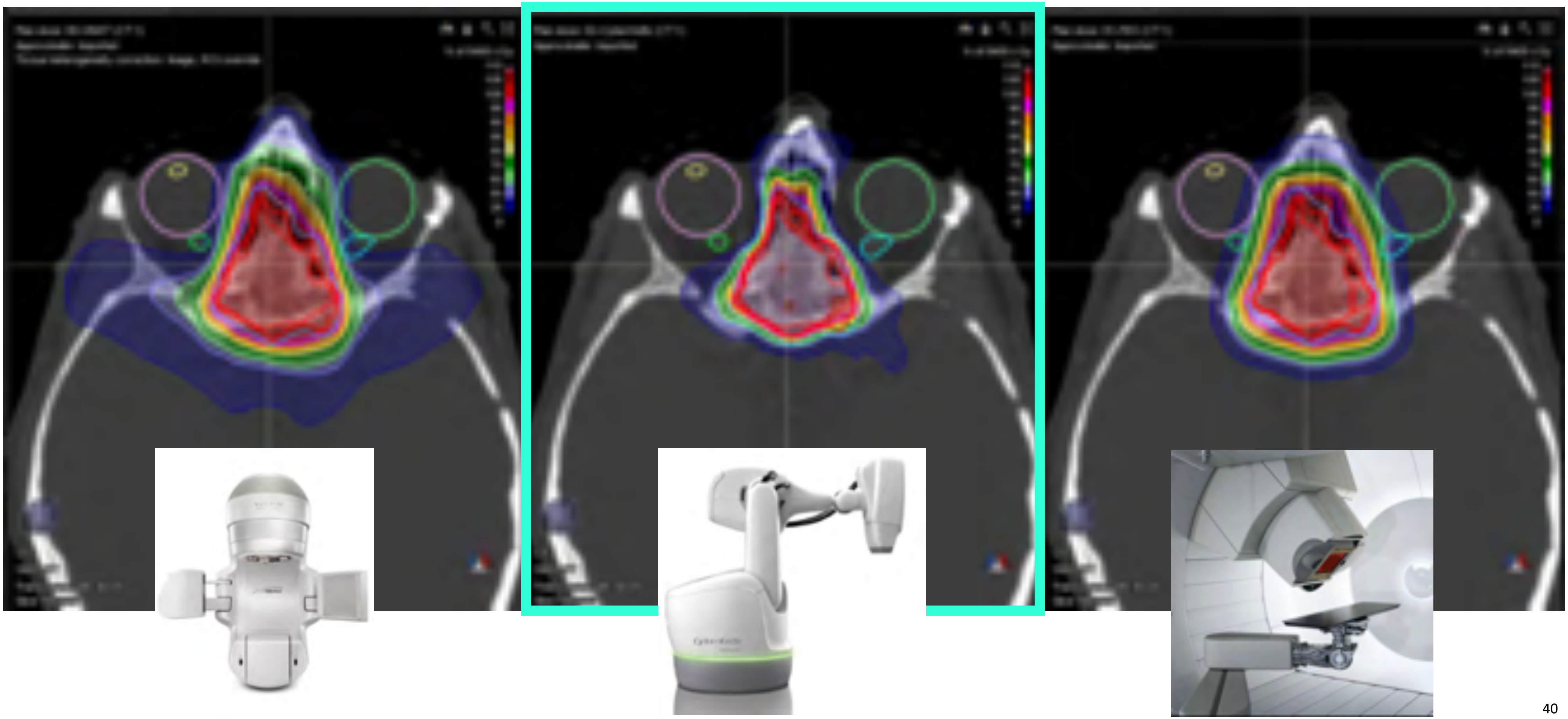


Optimal treatment plan



Increased dose to nearby critical structures

Comparative Treatment Planning



Early Stage NSCLC

- Similar principles across technologies
  - Contouring guidelines
  - Prescription doses
  - Dose constraints
  - Plan evaluation
- Different principles across technologies
  - Simulation
  - Immobilization
  - Tumor localization
  - Treatment delivery

Early Stage NSCLC

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Contouring Guidelines

- Contours performed on planning CT scan*
  - Breath hold
    - CyberKnife
    - TrueBeam / Edge
    - MR linac*
    - Protons
  - Average CT (Abdominal compression device)
    - TrueBeam / Edge
    - Protons

Contouring Guidelines

- Target volume delineation
  - GTV
    - Contoured on the planning CT scan (except the MR linac)
    - Spiculations around the primary tumor are included
  - ITV (if necessary)
    - Union of GTVs in each of 10 phases then registered to the planning dataset
    - Includes the original GTV (if outside any of the phases)
    - Considered for breath hold cases if additional "confirmatory scans" are acquired
  - CTV
    - An isotropic 3 mm expansion to cover microscopic extension of disease
    - Consideration of larger margin based on biology
  - PTV
    - 3 mm margin

Contouring Guidelines

- CTV margin?

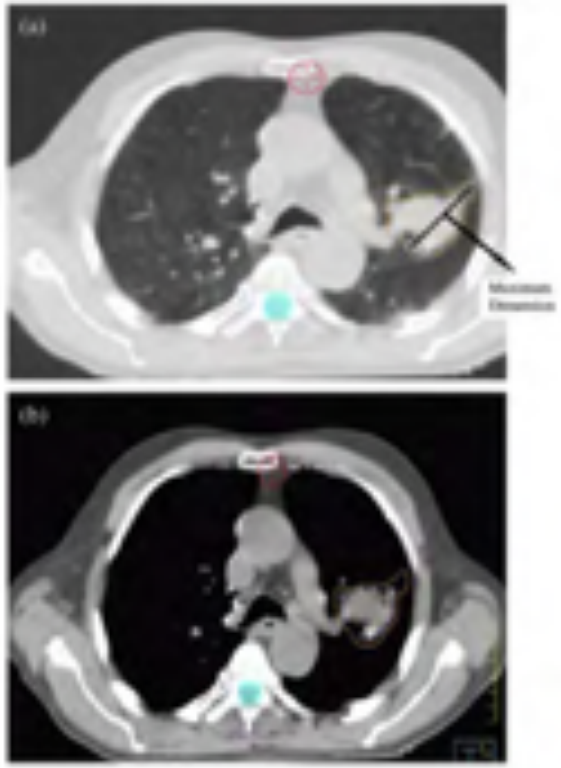


Fig. 1. (a) Maximal tumor size as measured on computed tomography (CT) lung windows. (b) Maximal tumor size by CT lung windows vs. CT mediastinal/soft-tissue windows. Outer contour represents maximal tumor size as measured on CT lung windows; inner contour represents maximal tumor size as measured on CT soft-tissue windows.

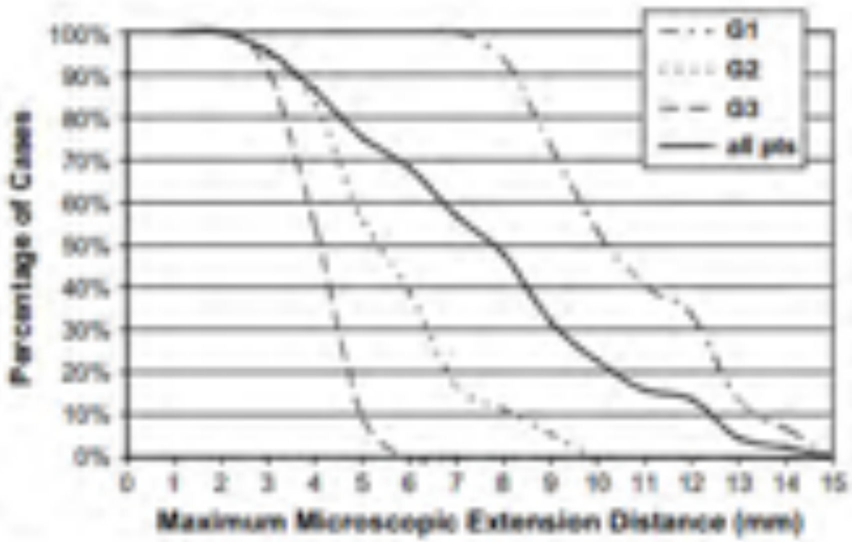


Fig. 2. Relationship between nuclear grade and distance of microscopic extension beyond gross tumor edge.

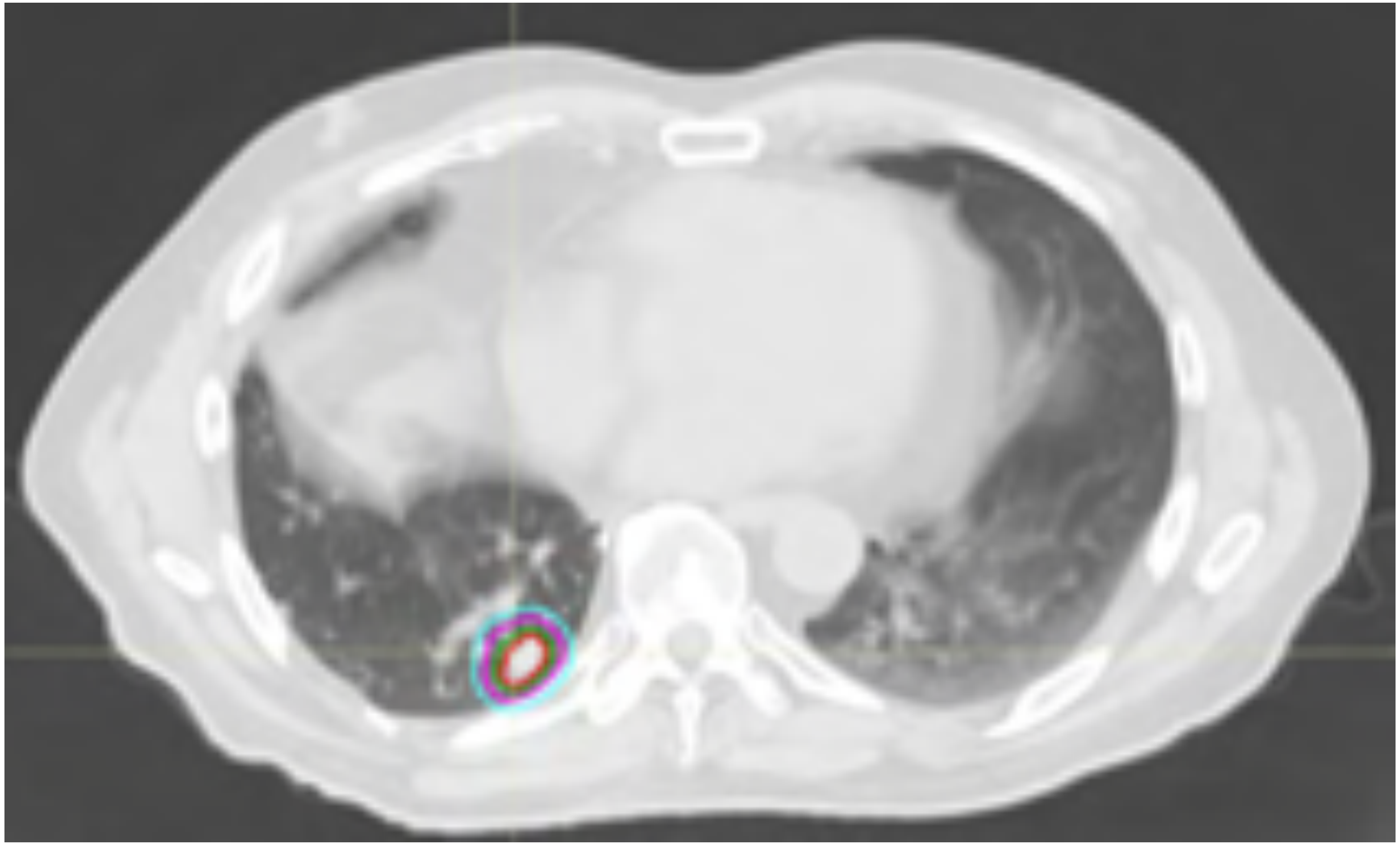
Table 1. Relationship among grade, microscopic extension distance, and adenocarcinoma growth pattern

Adenocarcinoma grade	Patients (n)	Maximal microscopic extension* (mm)	Bronchoalveolar carcinoma involvement (%)
1	11 (31)	10.1 (± 2.1)	34
2	15 (42)	7.0 (± 2.2)	21
3	10 (28)	3.5 (± 0.8)	10
All cases	36 (100)	7.2 (± 3.1)	—
p	—	<0.01	<0.04

* Data presented as mean, with ± SD in parentheses.

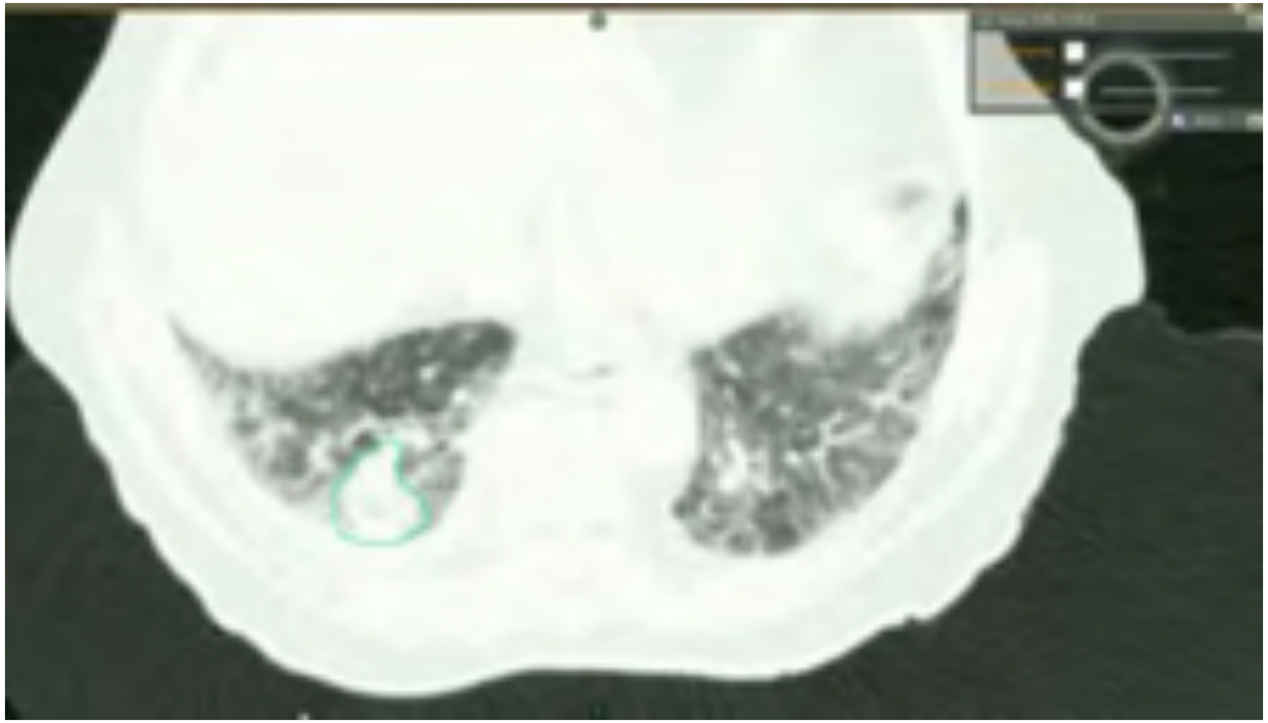
Contouring Guidelines

- Target volume delineation



Contouring Guidelines

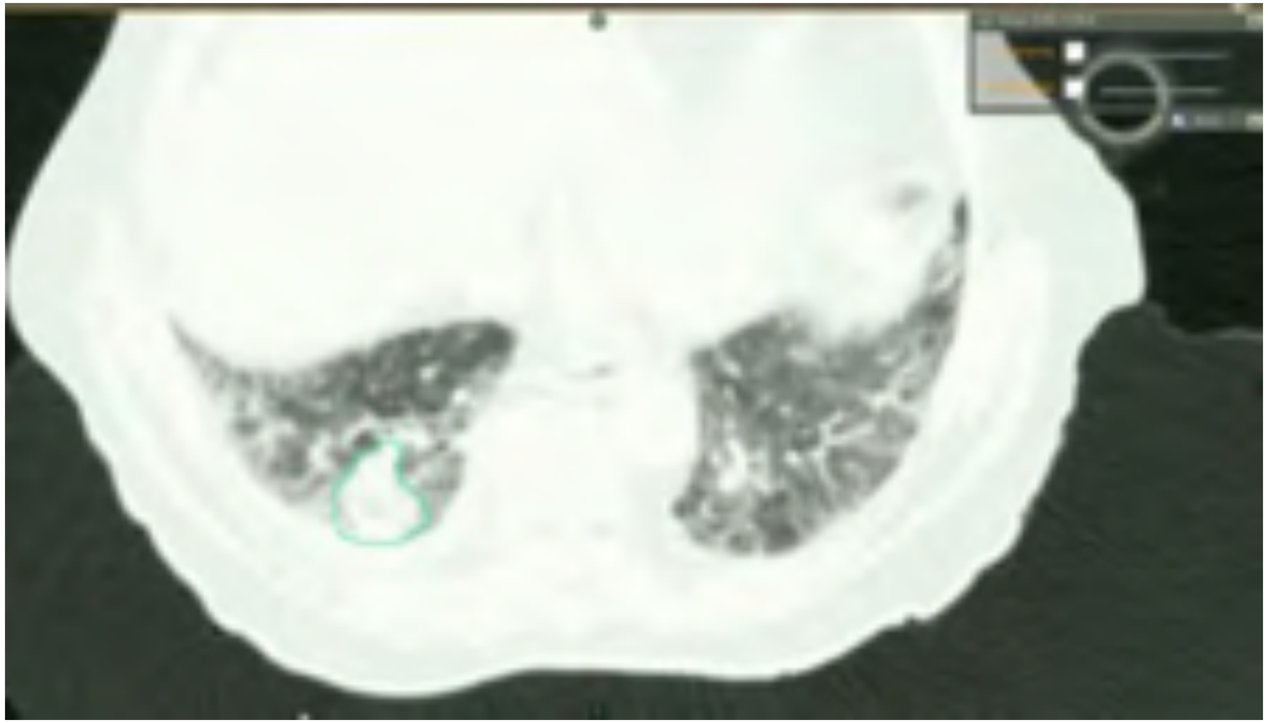
- Target volume delineation



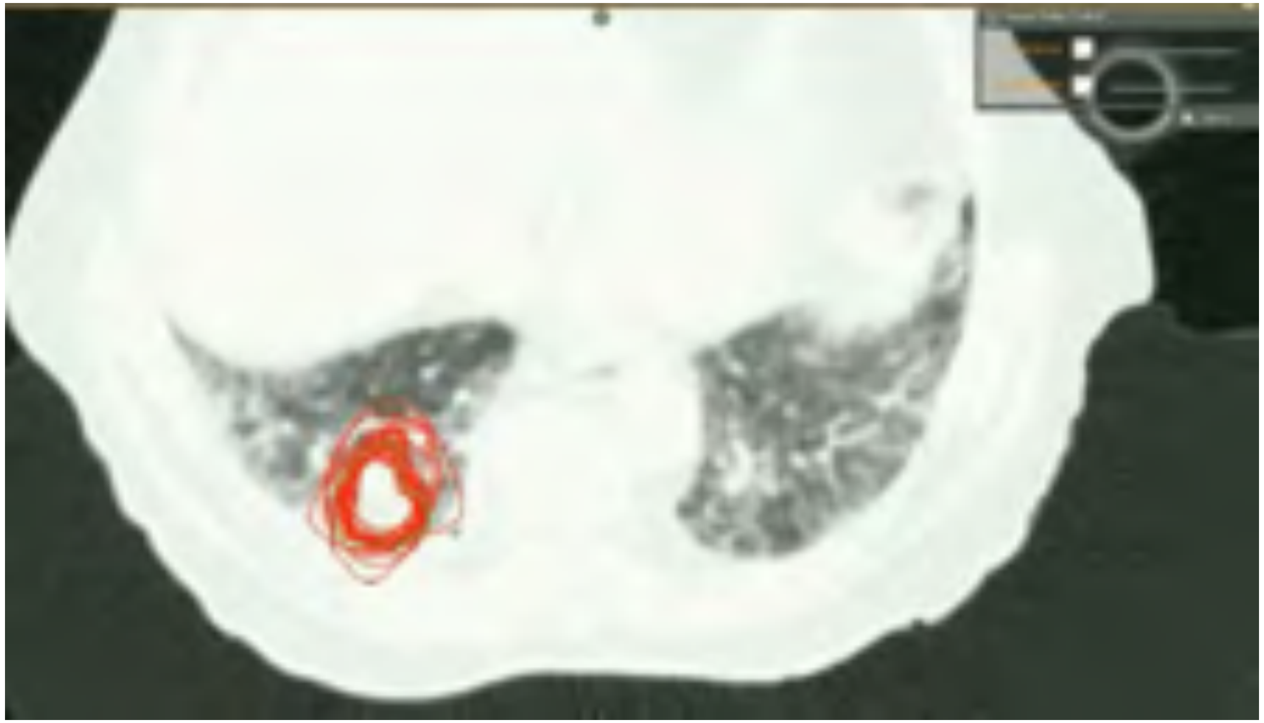
Lung cancer expert

Contouring Guidelines

- Target volume delineation



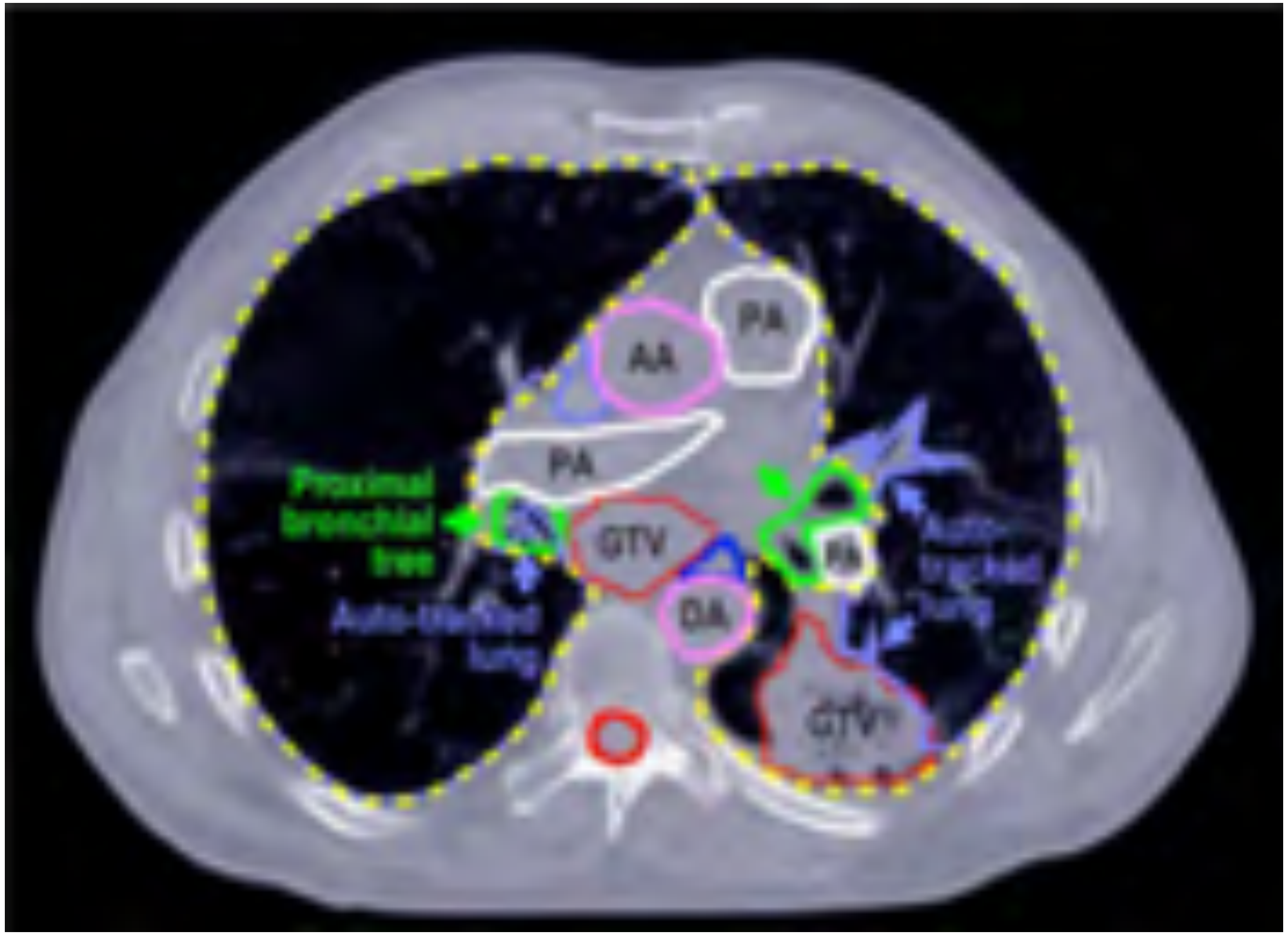
Lung cancer expert



Example contours from class

Contouring Guidelines

- Normal structures
  - Lungs
    - Individual and bilateral lungs
  - Heart
  - Brachial Plexus
  - Trachea
  - Esophagus
  - Proximal bronchial tree
  - Spinal cord
  - Chest wall
    - 2-3 cm rind
  - Skin
    - 3 mm rind



Kong S et al., IJROBP 2011

Prescription Doses

- MCI dose prescription
  - Peripheral Tumors
    - 60 Gy in 5 fractions
  - Central Tumors*
    - 50 Gy in 5 fractions
  - Special indications
    - Medically operable: 54 Gy in 3 fractions
    - Medically frail: 34 Gy in 1 fraction
    - Large tumors (>5 cm): 60 Gy in 8-15 fractions
    - Ultracentral tumors: 60 Gy in 8-15 fractions

Dose Constraints / Plan Evaluation

SBRT PLANNING OBJECTIVES [LUNG]

Patient Name:	DOB:	Date:
MD: Rupesh	Dosimetrist	Physicist

Diagnosis:

Plan:

Target Dose / Volume Objectives

Gy /fx	# fx		Target	Objective Initial	Objective Final (if differs)	Prescribed Dose	Objective Initial	Objective Final (if differs)	Minimum Dose	Objective Initial	Objective Final (if differs)	Maximum Dose	
12	5	✔	GTV	99%		≥ 60 Gy							
12	5	✔	IGTV	99%		≥ 60 Gy							
12	5	✔	CTV	98%		≥ 60 Gy							
12	5	✔	PTV	95%		≥ 60 Gy							
12	5	✔	PTV	mean		65 Gy							

Critical Organs "Hard Constraints" | **Critical Organs: Dose / Volume Objectives**

Vol (%, cc, mean)	Max Dose (Gy)	Point Vol (cc)	Max Point Dose (Gy)		Critical Organ (OAR)	Objective Initial	Objective Final (if differs)	Constraint 1	Objective Initial	Objective Final (if differs)	Constraint 2	Objective Initial	Objective Final (if differs)	Constraint 3	
					Spinal Cord	0.03		≤ 30 Gy							
					Esophagus	0.03		≤ 35 Gy							
					Esophagus	5 cc		≤ 27.5 Gy							
					Chest wall	30 cc		≤ 30 Gy							
					Chest wall	3 cc		≤ 50 Gy							
					Trachea	0.03		≤ 40 Gy							
					Trachea	0.03		≤ 40 Gy							
					Heart	0.03		≤ 40 Gy							
					Skin	10 cc		≤ 30 Gy							
					Skin	0.03		≤ 32 Gy							
					Lungs	1500		≤ 12.5 Gy							
					Lungs	1000		≤ 13.5 Gy							
					Lungs	10%		≤ 20 Gy							
					Heart	15 cc		≤ 32 Gy							
					Brachial Plexus	0.03		≤ 32 Gy							

TG 101; Timmerman tables; RTOG 0813

Comments:

GTV / IGTV / CTV /PTV

GTV = tumor; IGTV; CTV = 3 mm + GTV; PTV = 3 mm + CTV

Initials / Date

ROI/Objectives Done:

Plan Approved:

Individualized Treatment Planning Directive

MCI SBRT Planning Evaluation Sheet

Patient Name | MCI #:

Physician | Site

Total Dose [Gy] | Fraction #

PTV Parameters

PTV Volume [cc]		PITV	#DIV/0!
Vol of PTV receiving Pres Dose [		$R_{50\%}$	#DIV/0!
100% Pres. Isodose Vol. [cc]		Homogeneity Ind.	#DIV/0!
50% Pres. Isodose Vol. [cc]		Target Coverage	#DIV/0!
Max Dose at 2.0cm ring [Gy]		Max. D_{2cm} [%]	#DIV/0!

$D_{98\%}$ [Gy]

$D_{2\%}$ [Gy]

Normal Tissue Parameters

Critical OAR	Critical Vol. [cc]	Plan Critical Dose [Gy] Act.	Plan Critical Dose [Gy] Tol.	Plan Max Dose Pt. Act.	Plan Max Dose Pt. Tol.	Met Criteria? [Yes / No]

Planning Evaluation Sheet

Early Stage NSCLC

- Similar principles across technologies
  - Contouring guidelines
  - Prescription doses
  - Dose constraints
  - Plan evaluation
- Different principles across technologies
  - Simulation
  - Immobilization
  - Tumor localization
  - Treatment delivery

Technology Triage

Early Stage Lung Cancer

CyberKnife
- Trackable?
- Fiducials?
- Arms restriction?
- Large motion

Yes?

TrueBeam
- Breath-hold?
- Compression (ITV)?
- Fast delivery?
- Volumetric imaging?

Yes?

MR Linac
- Breath-hold?
- FB gating?
- Claustrophobic?
- Lateral lesion?
- Volumetric imaging?

Yes?

Protons
- Large motion?
- Insurance?
- Volumetric imaging?
- Breath-hold?

Yes?

Tomotherapy
- Claustrophobic
- Volumetric imaging?
- Non-coplanar?

Yes?

Comparative Plans

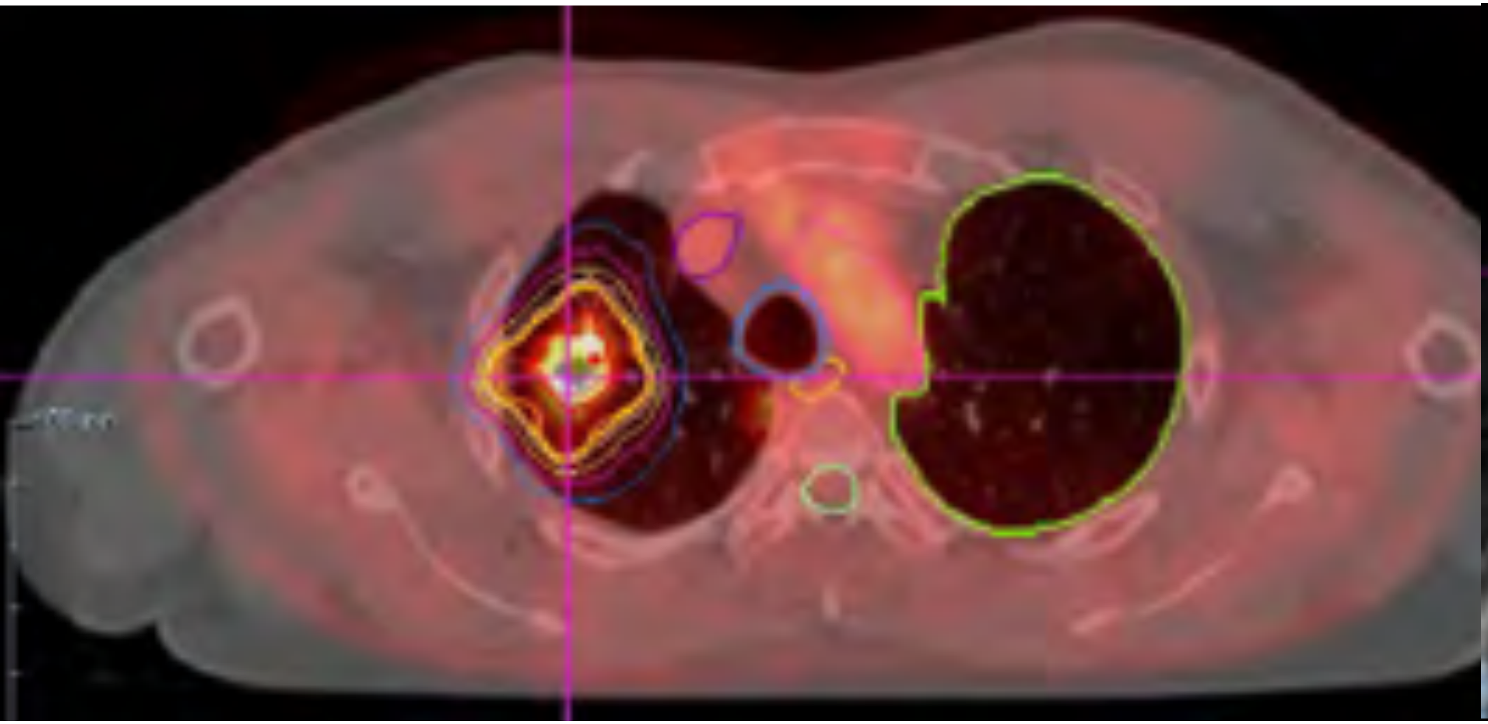
Treat patient with *best* quality plan

CyberKnife

- Triage considerations
  - Patient
    - Able to maintain treatment position for extended period of time (25-50 mins)
    - Unable to tolerate breath-hold delivery
    - Reproducible breathing pattern—needed for good correlation model
    - Significant tumor motion despite abdominal compression or does not tolerate compression
  - Tumor
    - Peripherally (island) located tumors
    - Fiducials placed
    - Abutting chest wall

Case Examples

60 Gy in 5 fractions prescribed to the 75% IDL

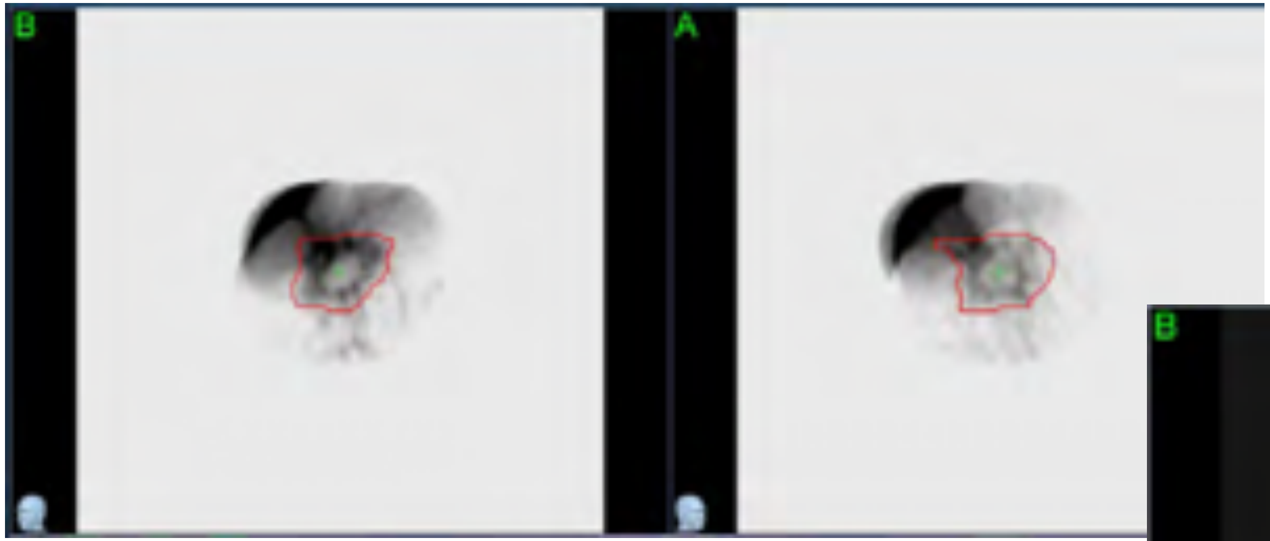


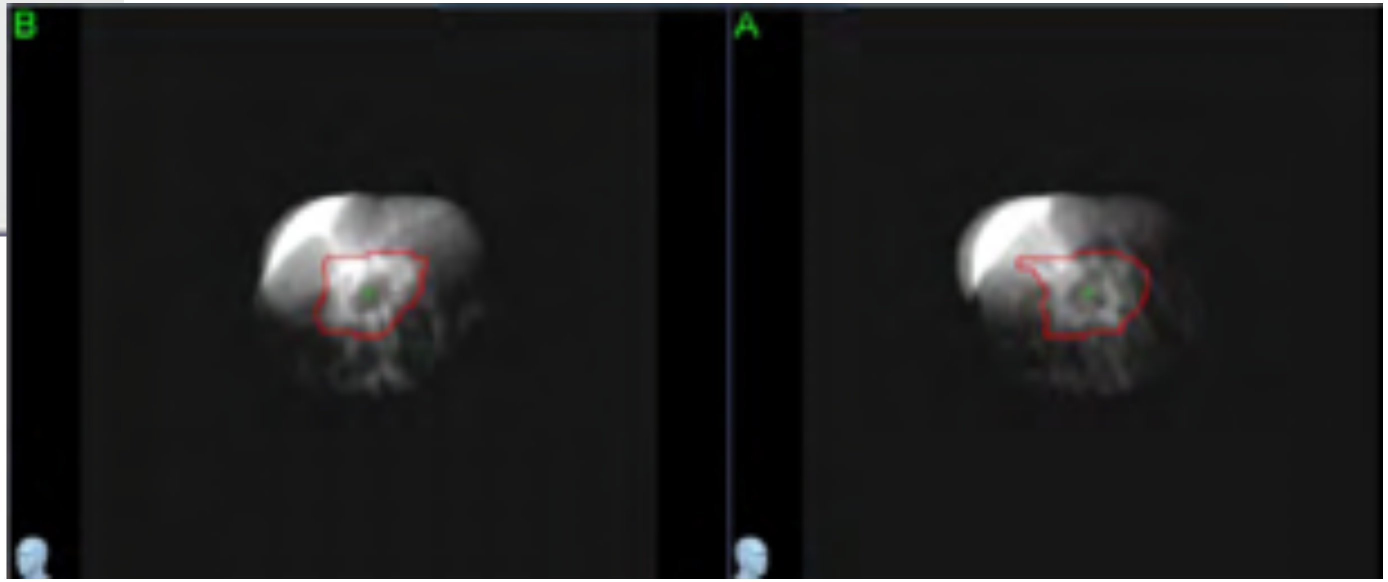
Stage IB, T2aN0M0, adenocarcinoma [EGFR negative, lepidic predominant] s/p cryoablation with progressive disease

Case Examples

- Case triage features
  - Adenocarcinoma with lepidic predominant features
    - Extra CTV margin needed, eliminate ITV to reduce lung exposure
  - Need to stay off chest wall
    - Non-isocentric delivery
  - Cavitary mass with spiculations not ideal for other tracking modalities
    - Potential for low correlation or tracking ability with MR linac
  - Unable to tolerate breath hold

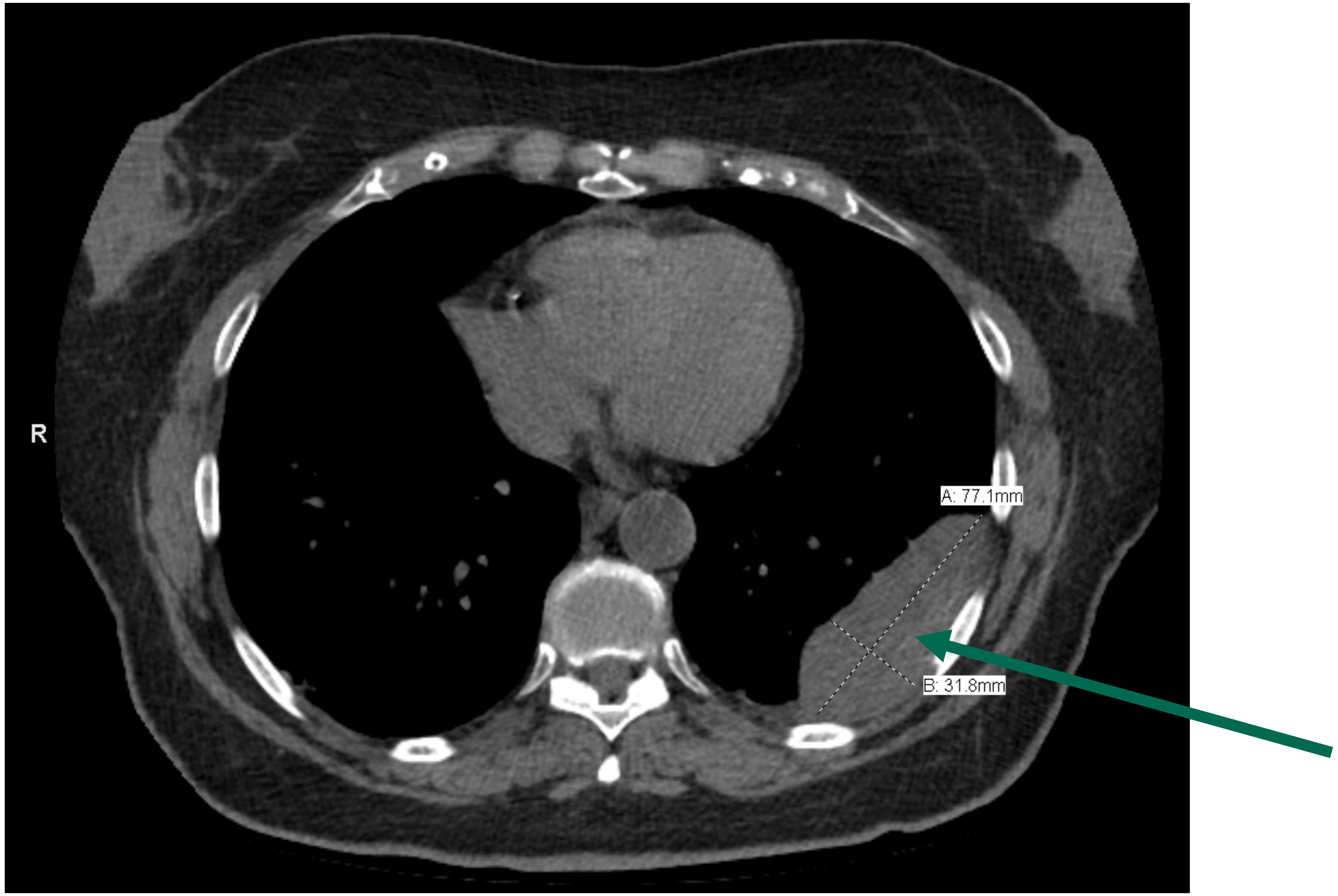
Case Examples





Stage IB, T2aN0M0, adenocarcinoma [EGFR negative, lepidic predominant] s/p cryoablation with progressive disease

Case Examples



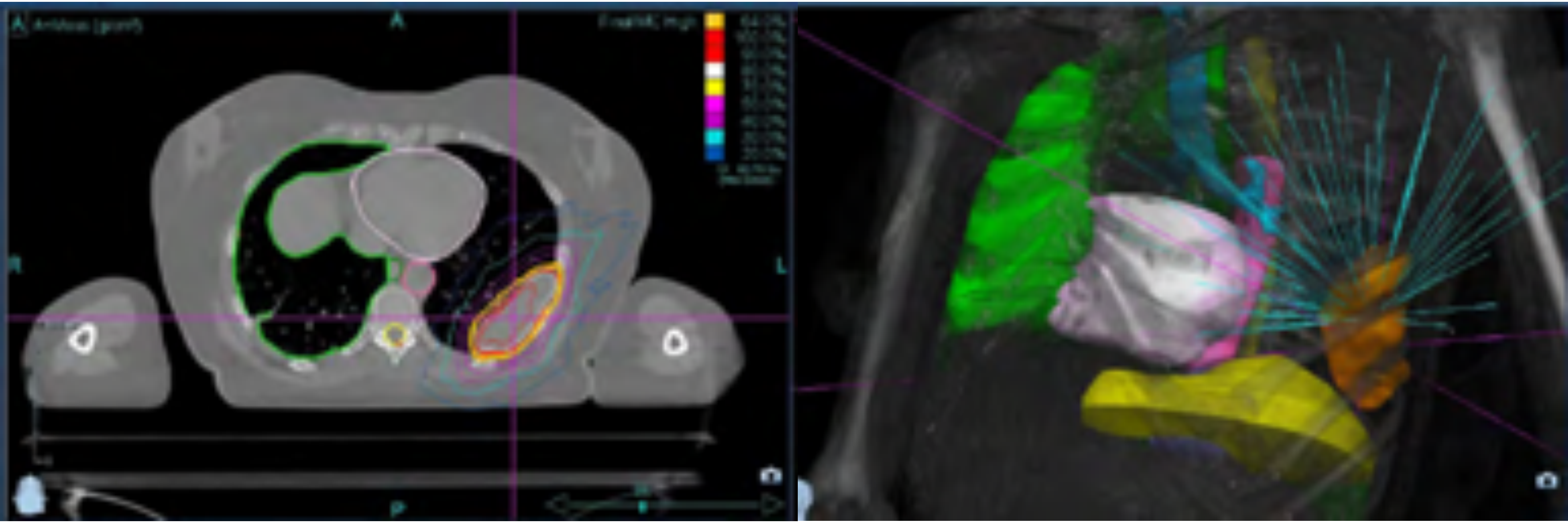
85 yo lady with Stage IV NSCLC (EGFR-m) with oligoprogression of a left lower lobe mass on targeted therapy

Case Examples

- Case triage features
  - Need to stay off chest wall
    - Non-isocentric delivery
  - Unable to tolerate breath hold
    - Patient compliance
  - Excellent baseline lung function
    - Significant motion (>1 cm) with maximal abdominal compression

Case Examples

60 Gy in 15 fractions



85 yo lady with Stage IV NSCLC (EGFR-m) with oligoprogression of a left lower lobe mass on targeted therapy

Case Examples

60 Gy in 15 fractions

Dose Statistics Table	Dx Vx Values	Plan Information	Dose Points	
Name	**Dose (Gy)**	**Dose (%)**	**Volume (cm³)**	**Volume (%)**
Chestwall	17.03	18.2	250.00	85.2
Chestwall	34.76	37.1	120.00	40.9
Chestwall	44.35	47.3	60.00	20.5
Chestwall	58.12	62.0	15.00	5.1
Total Lung	20.00	21.3	400.30	12.1
Total Lung	10.00	10.7	1013.38	30.6

Rapid fall-off at the chest wall interface without overdosing lung

85 yo lady with Stage IV NSCLC (EGFR-m) with oligoprogression of a left lower lobe mass on targeted therapy

Technology Triage

Early Stage Lung Cancer

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- Fiducials?
- Arms restriction?
- Large motion

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Yes?

Tomotherapy
- Claustrophobic
- Volumetric imaging?
- Non-coplanar?

Yes?

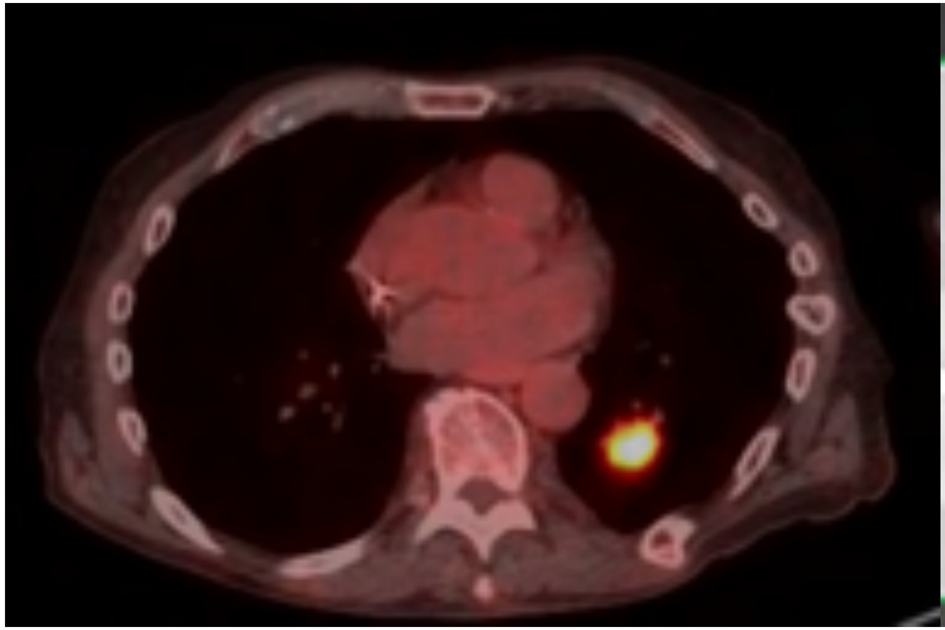
Comparative Plans

Treat patient with *best* quality plan

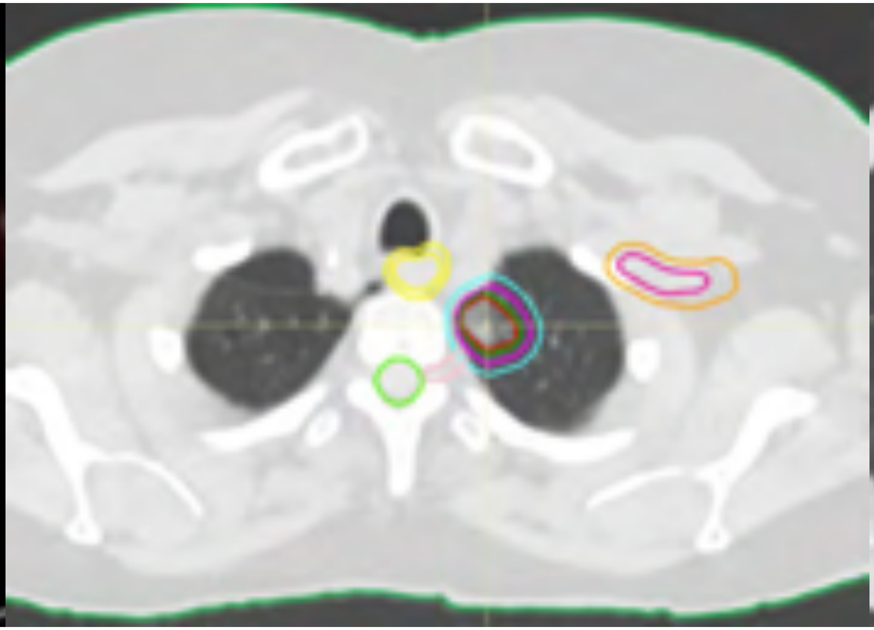
TrueBeam / Edge

- Triage considerations
  - Patient
    - For patients that need to be treated expeditiously
    - Limited or minimal tumor motion with abdominal compression
  - Tumor
    - Central tumors where CT anatomy may be beneficial for patient alignment and/or OAR evaluation
    - Small tumors unable to be tracked (without fiducials)
    - Tumors with significant ground-glass components not well visualized with other IGRT methods

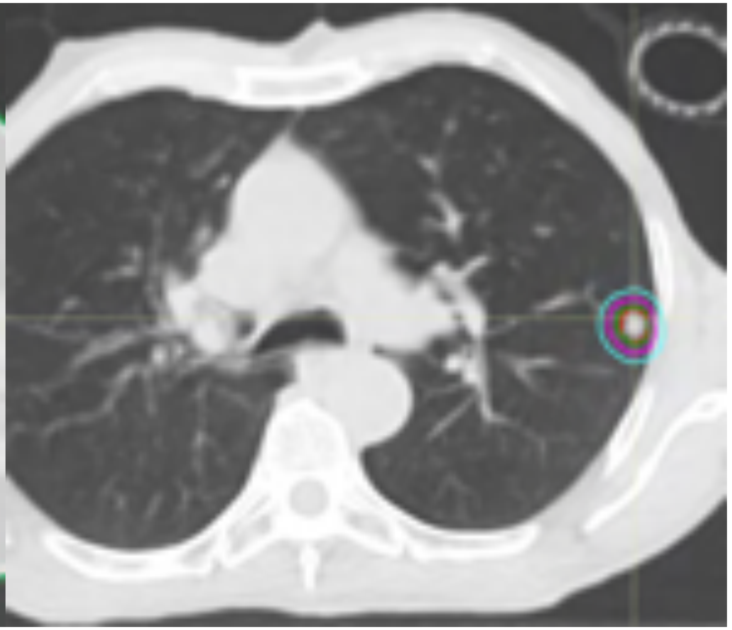
Case Examples



Planned for CK, patient unable to tolerate time on table for tracking test to assess respiratory model

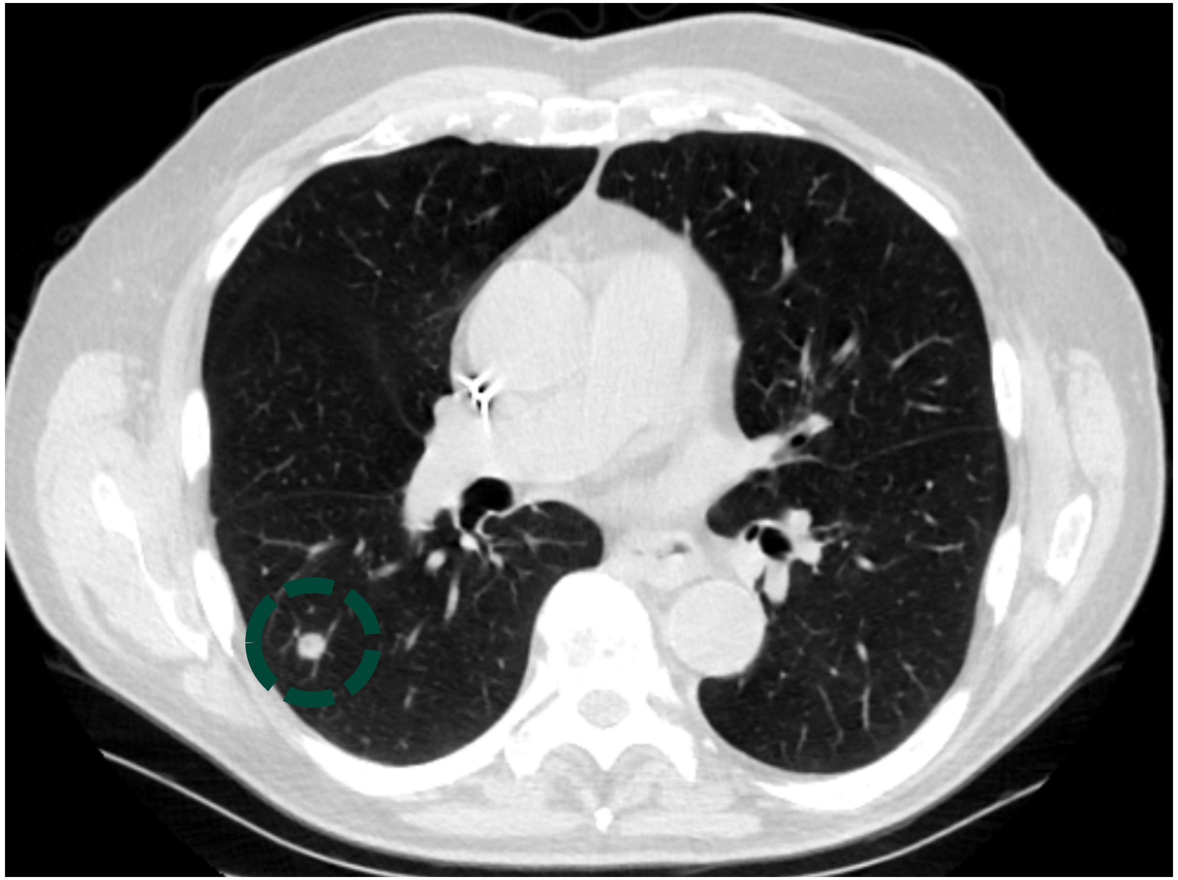


Apical centrally located tumor close to esophagus, brachial plexus, etc.

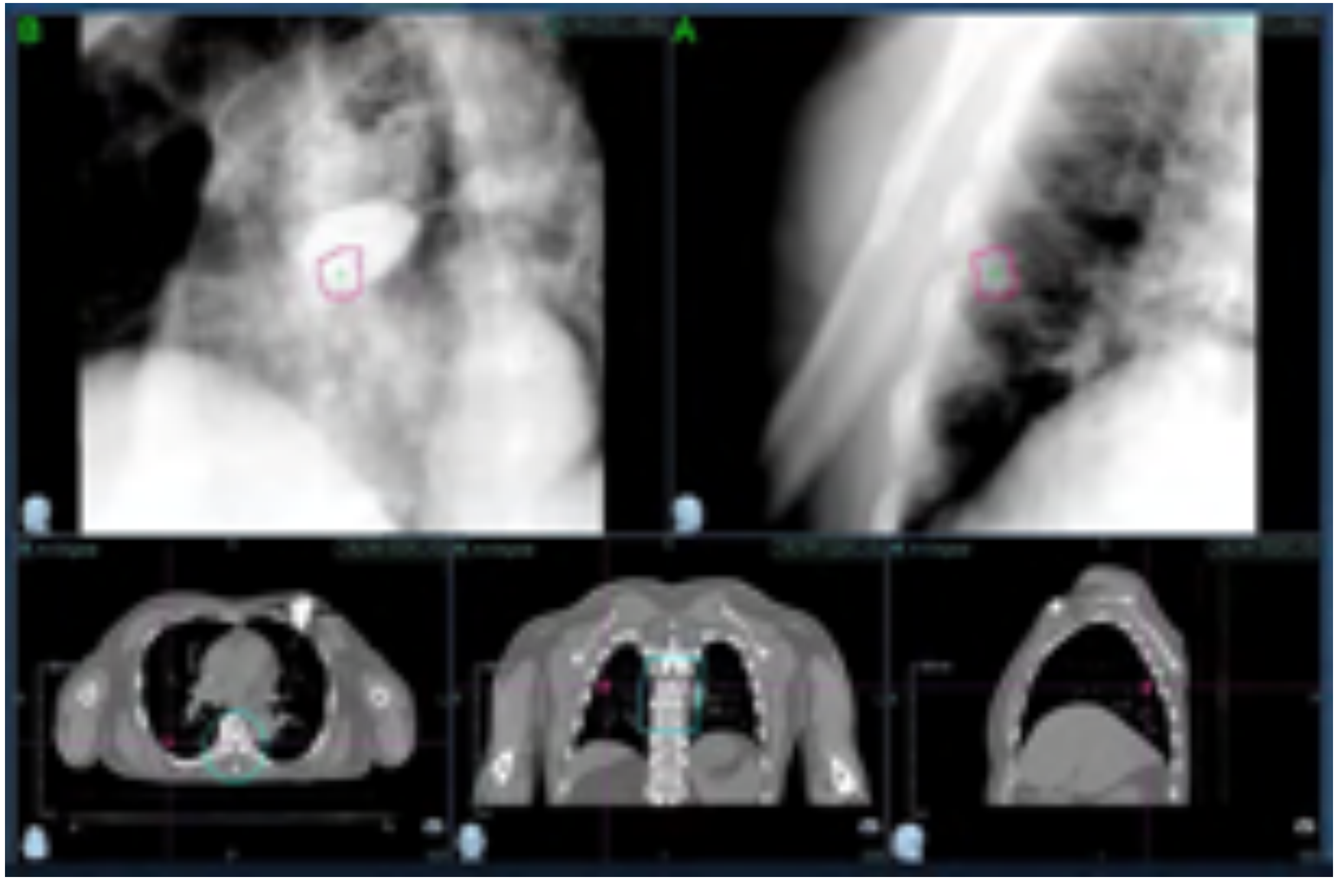


Potentially too small for real-time tracking

Case Examples

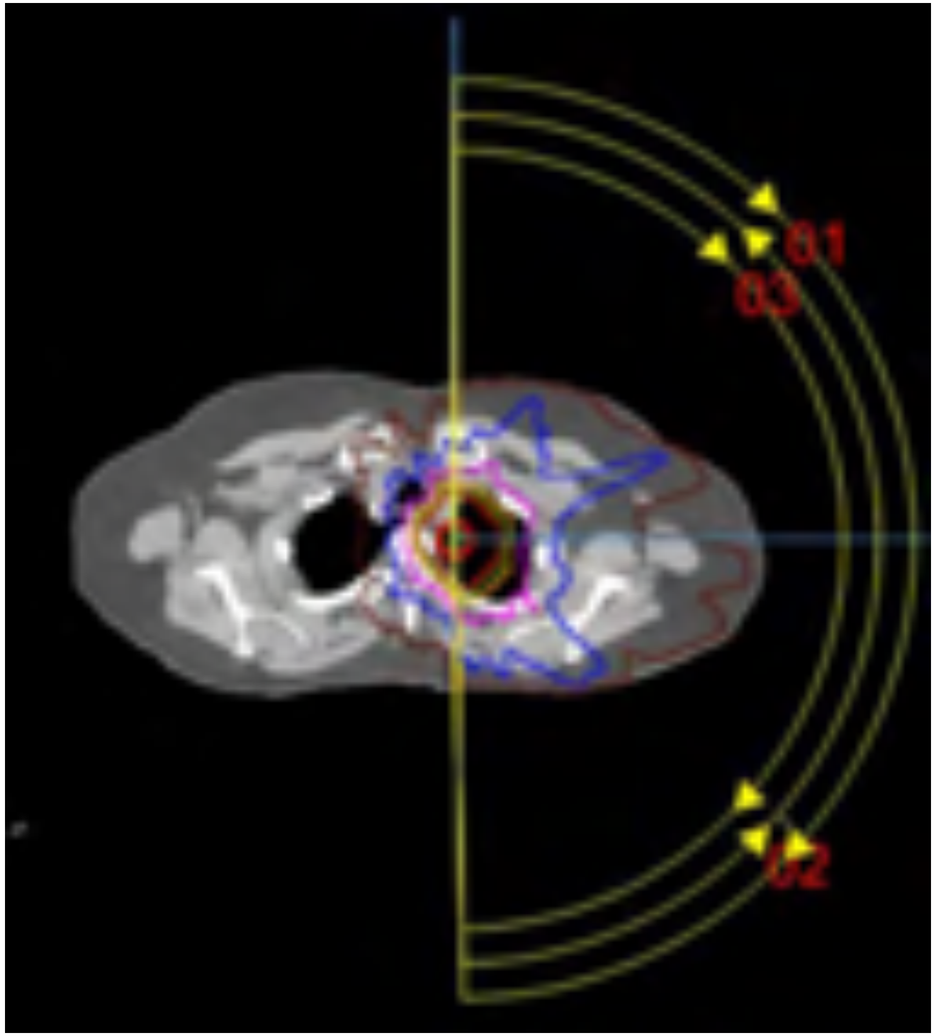


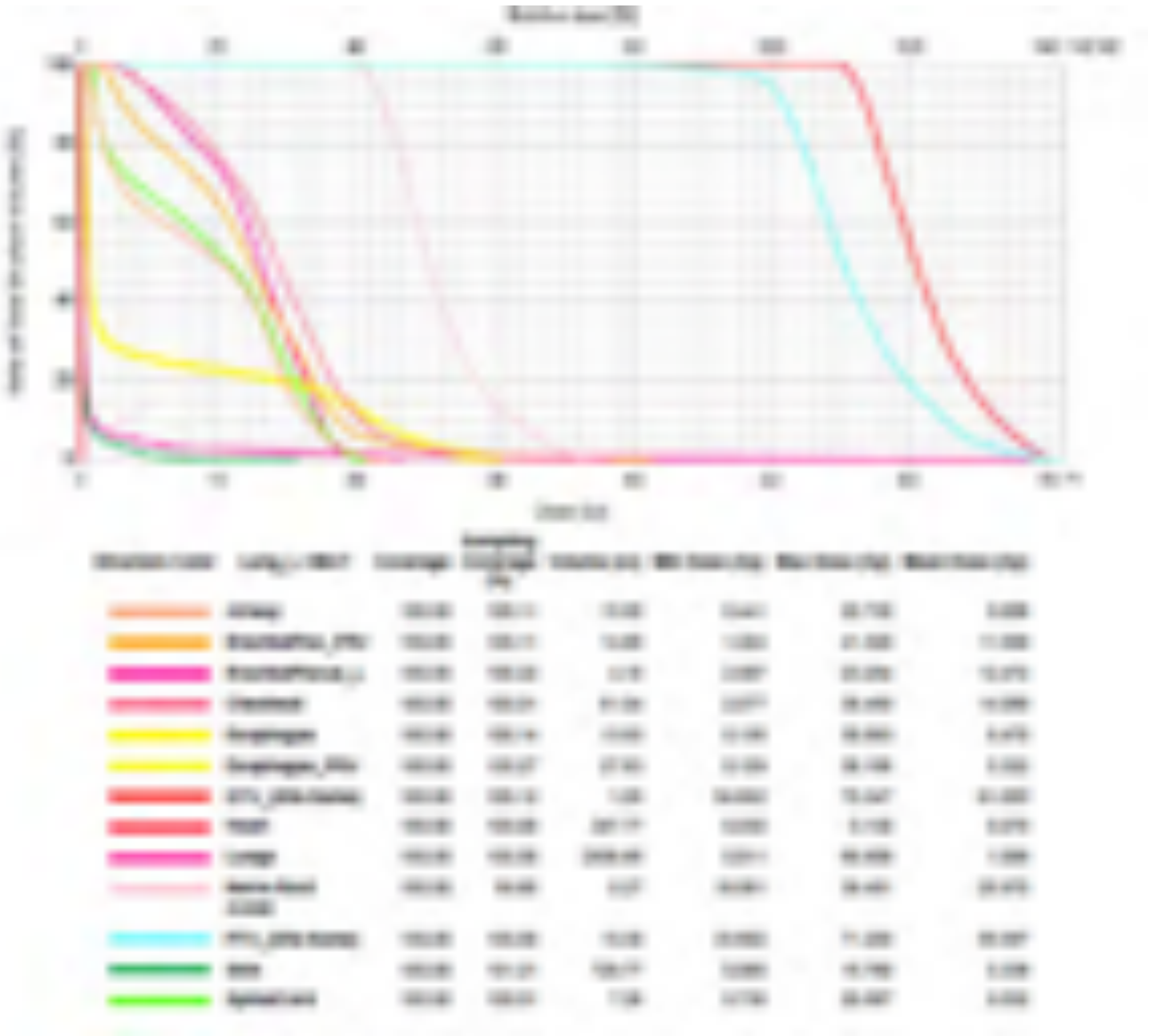
81 yo medically inoperable gentleman with a T1N0M0 NSCLC of the right lower lung



1. Unable to develop a respiratory model due to pacemaker position with camera B projection
2. Estimated X kVs per fraction through the pacemaker during treatment

Case Examples





Technology Triage

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- Breath-hold?

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- Volumetric imaging?
- Non-coplanar?

Yes?

Comparative Plans

Treat patient with *best* quality plan

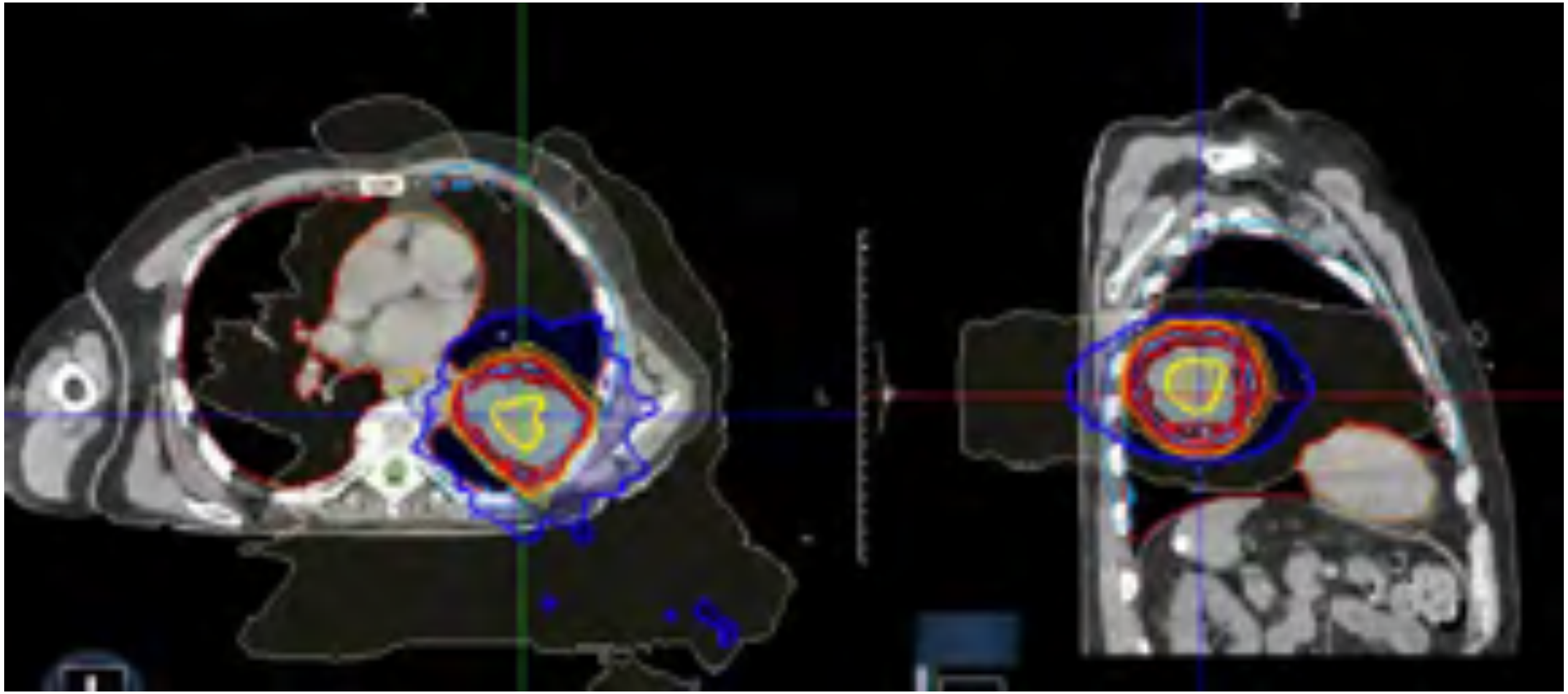
MR Linac

- Triage considerations
  - Patient
    - Tolerate breath hold
    - MR compatible (pacemaker, metal hardware, etc.)
    - Tolerate extended set-up treatment time
    - Tolerate tight space in bore (not claustrophobic)
    - Interstitial lung disease
    - Single fraction treatment
  - Tumor
    - Beware of peripheral tumors (patient offset in bore and reduced geometrical accuracy due to static field inhomogeneity)
    - Beware of small tumors unable to be tracked (<10mm)
    - Beware of non-solid tumors (poor correlation and tracking)

MR Linac Workflow

- Identify a target for anatomical tracking
  - Region of interest to be treated
  - Critical structure to avoid treating
- Create a boundary to identify tracking region
- Visualize the tracking algorithm as it deforms the anatomical target and each subsequent cine frame
- Treatment if target within boundary, radiation paused if target moves outside boundary

Case Examples



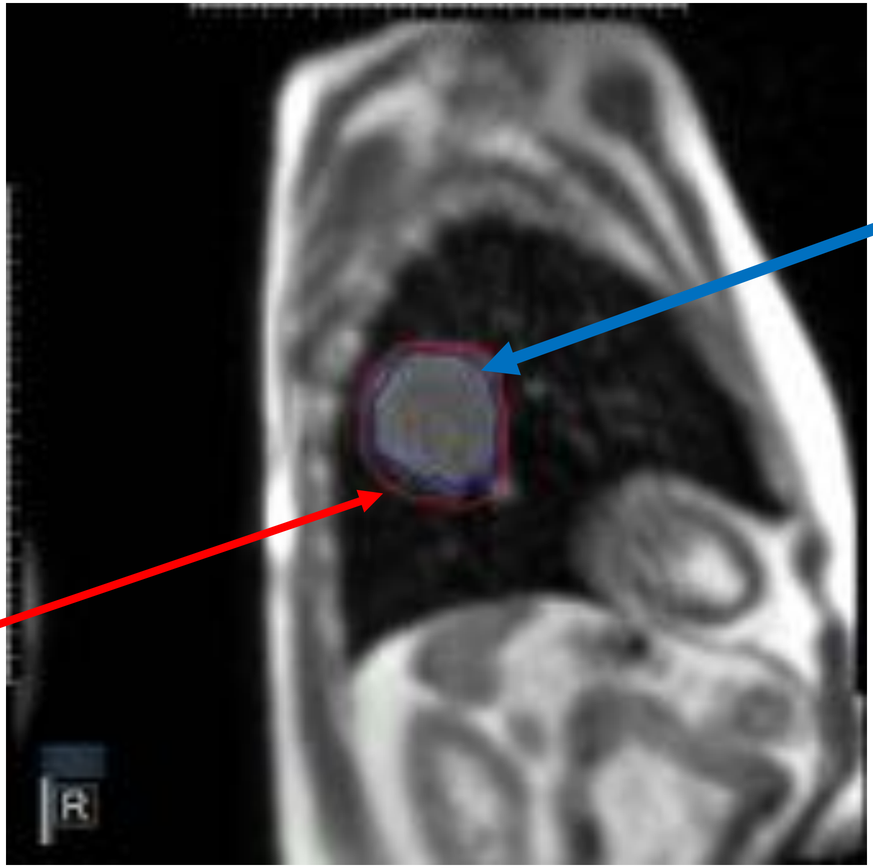
Isodose Lines

Rx Dose = 60.00 Gy

Dose (Gy)	Rx (%)
76.00	126.7
66.00	110.0
60.00	100.0
57.00	95.0
54.00	90.0
48.00	80.0
30.00	50.0
5.00	8.3

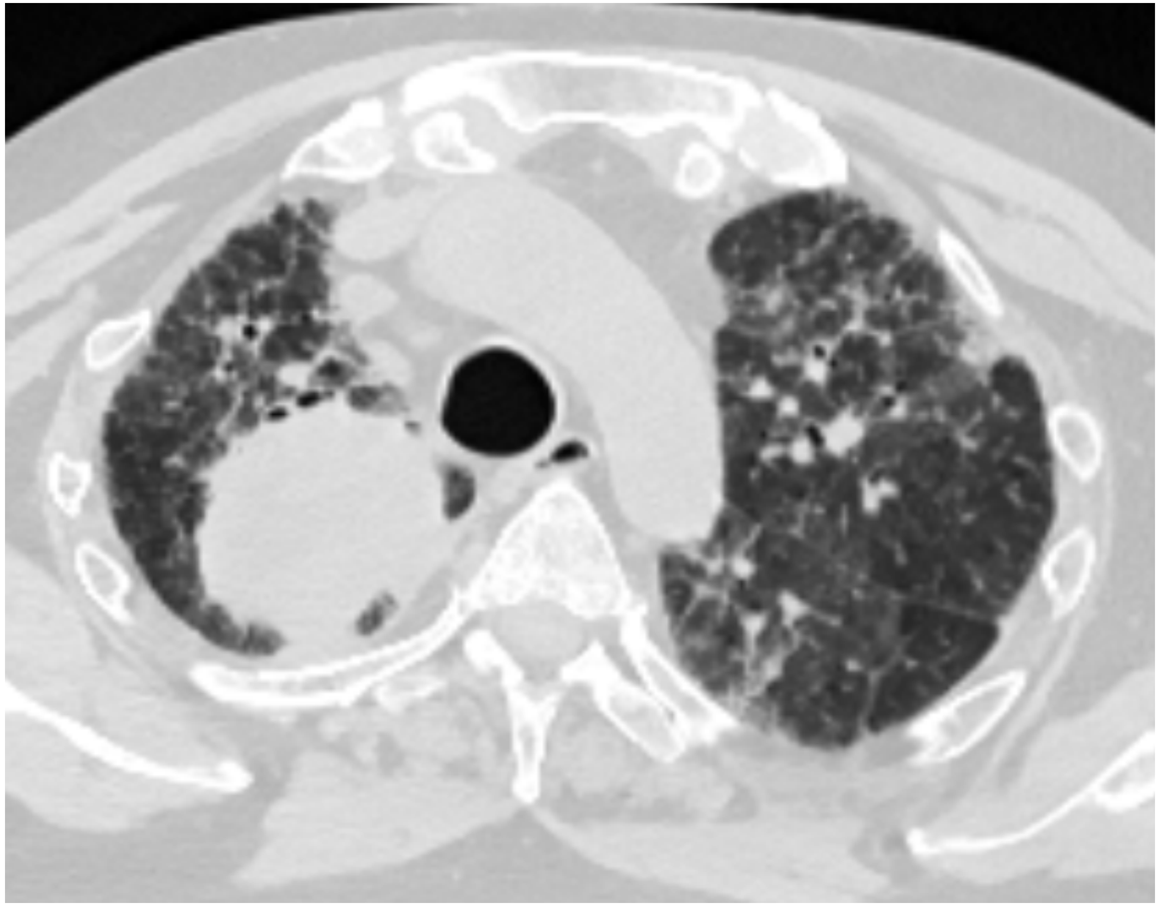
Locally advanced colorectal cancer with metachronous oligometastatic disease to the lung

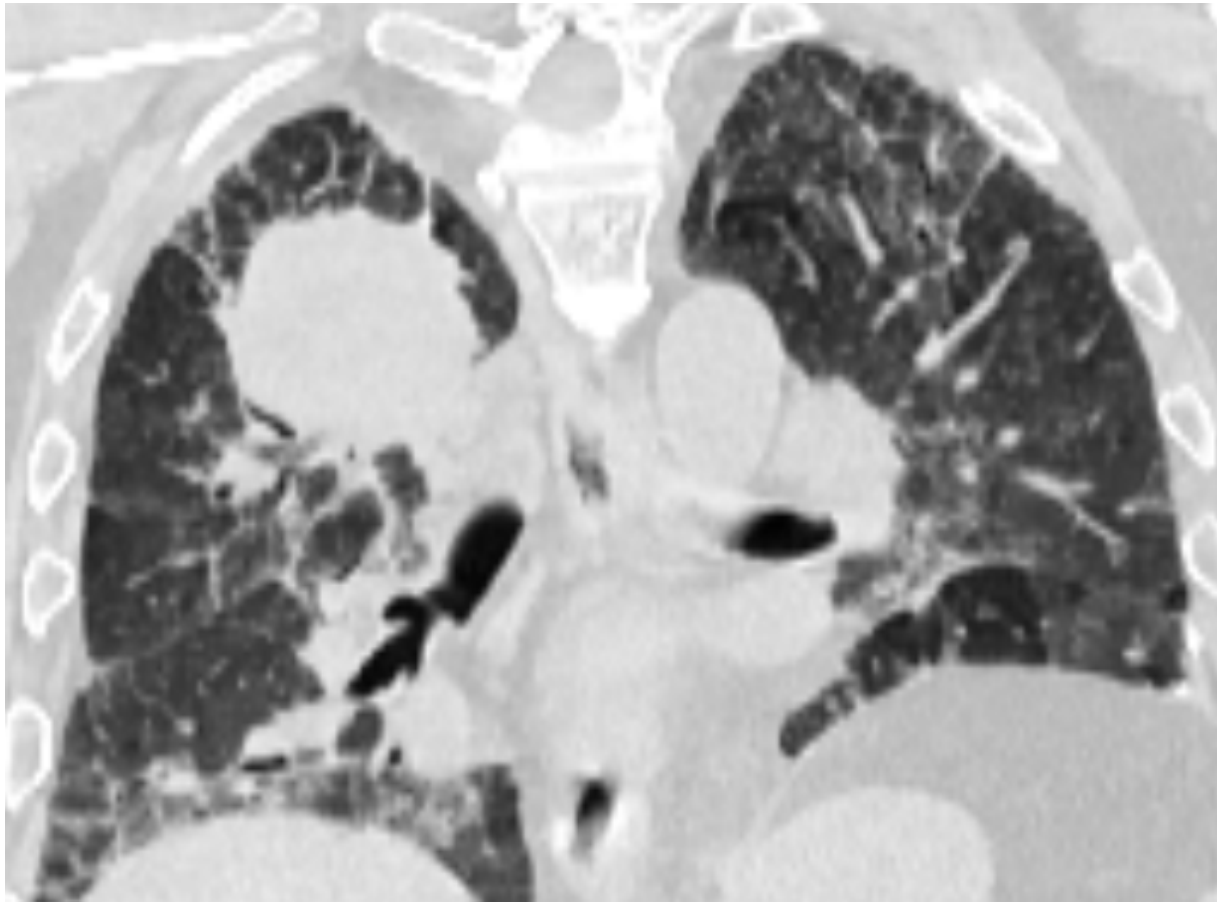
Case Examples



Tracking structure defined at time of planning with boundary
Adjusted each day by physician with evaluation of tracking ability

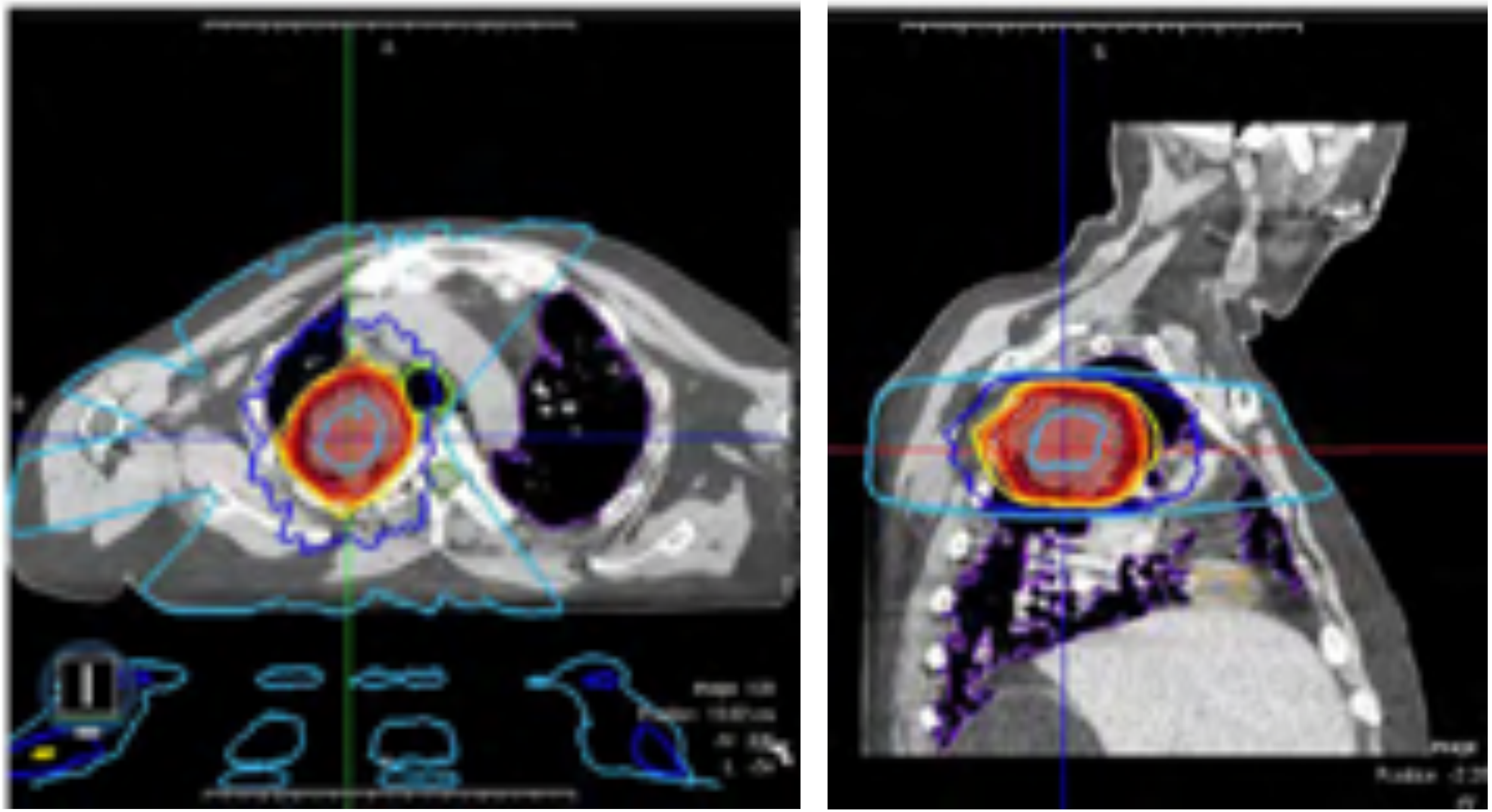
Case Examples





65-year-old w/ T2bN0M0 NSCLC, severe COPD

Case Examples



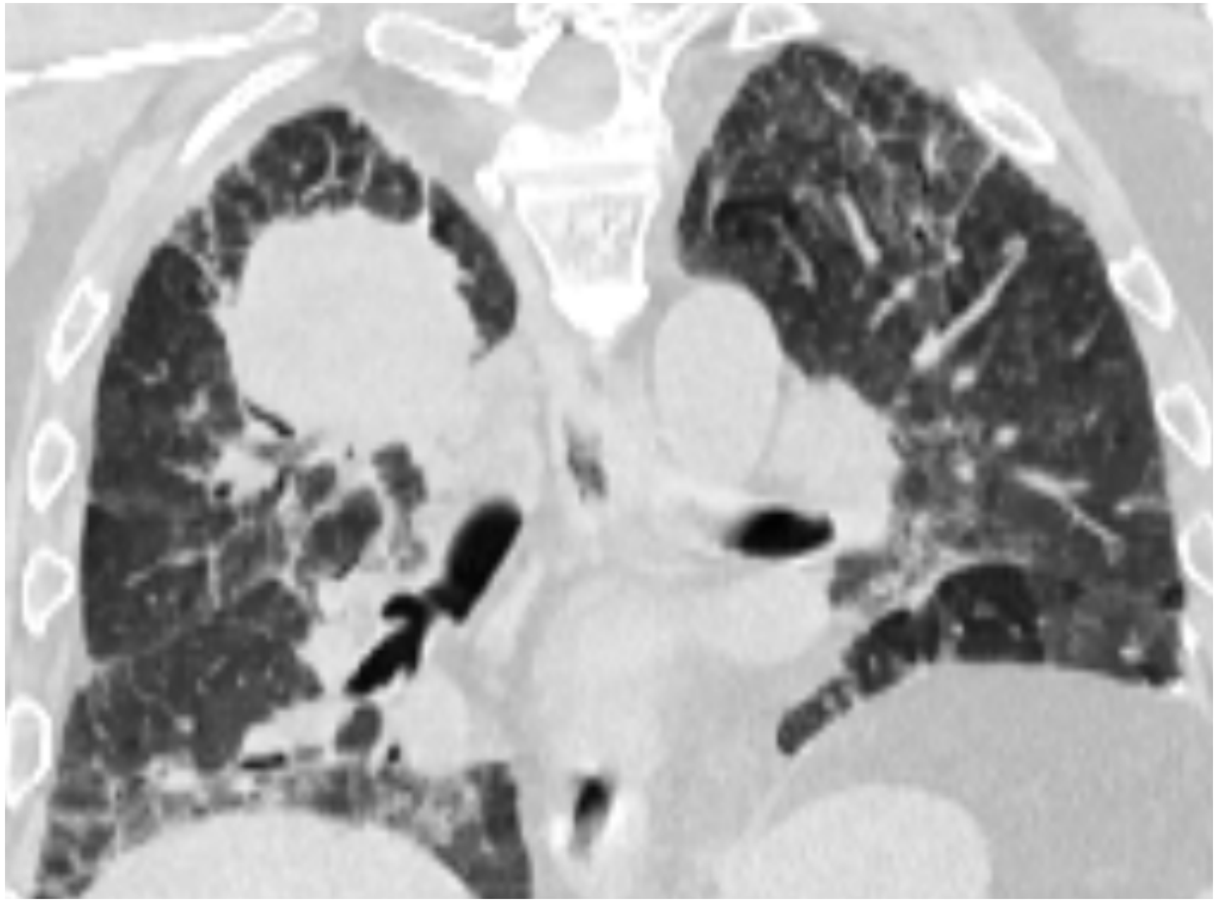
Isodose Lines

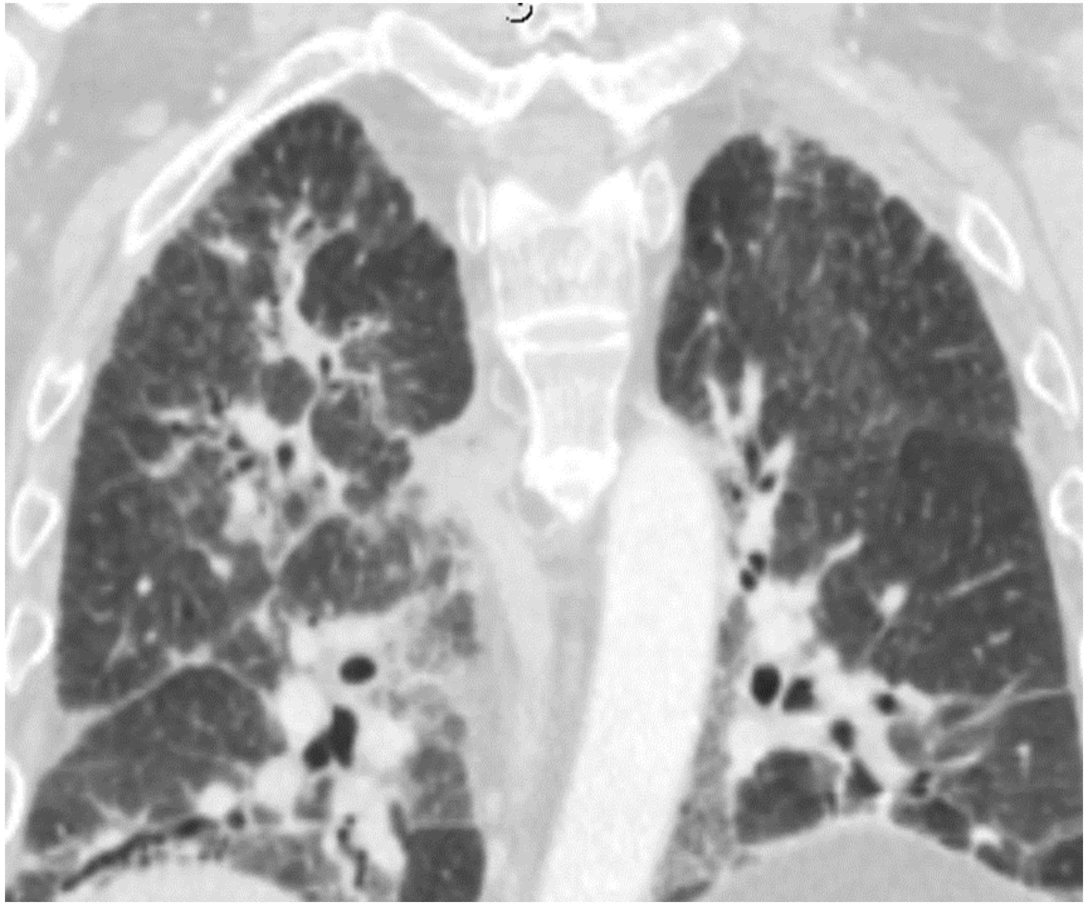
Rx Dose = 40.00 Gy

Dose (Gy)	Rx (%)
50.00	125.0
40.00	100.0
38.00	95.0
36.00	90.0
32.00	80.0
20.00	50.0
10.00	25.0

65-year-old w/ T2bN0M0 NSCLC, severe COPD

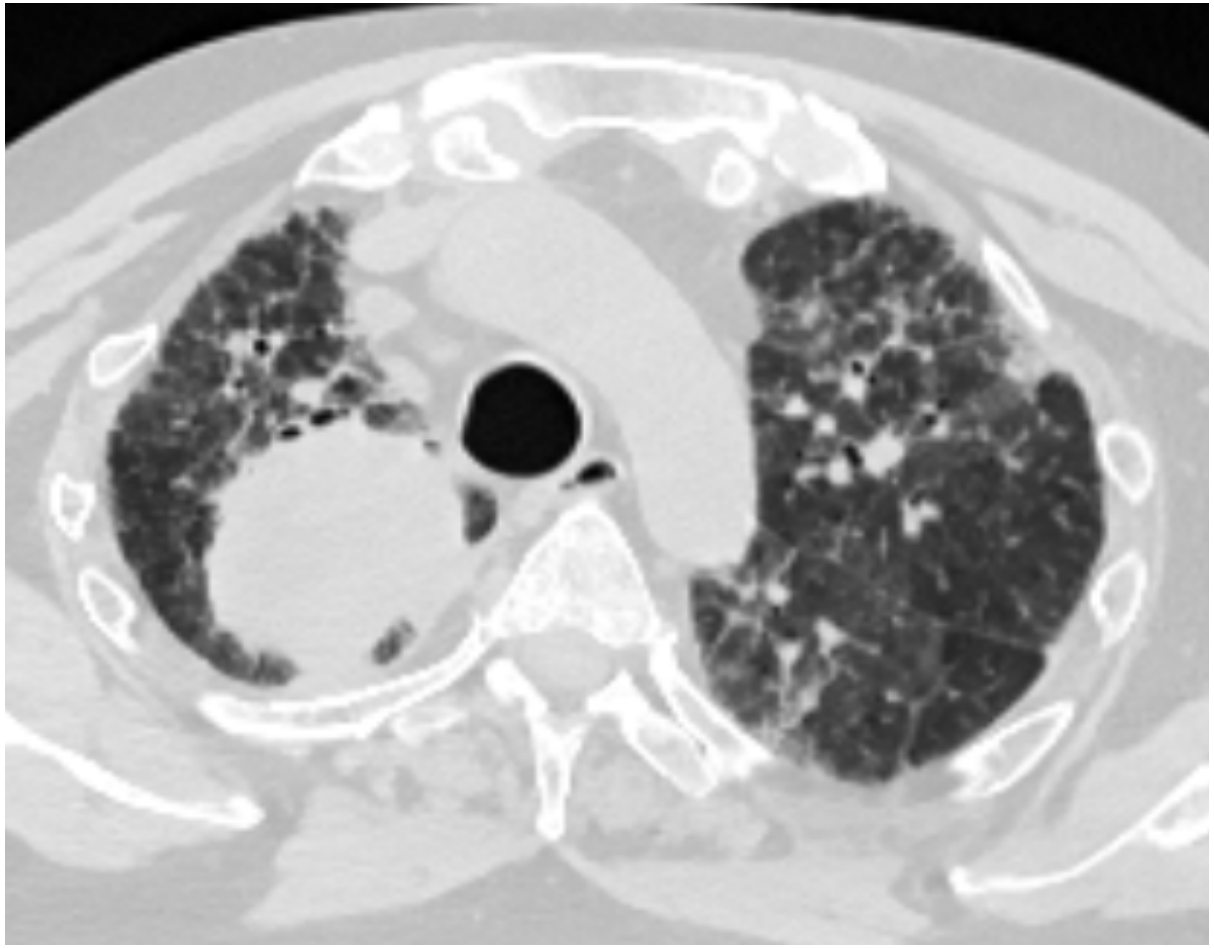
Case Examples

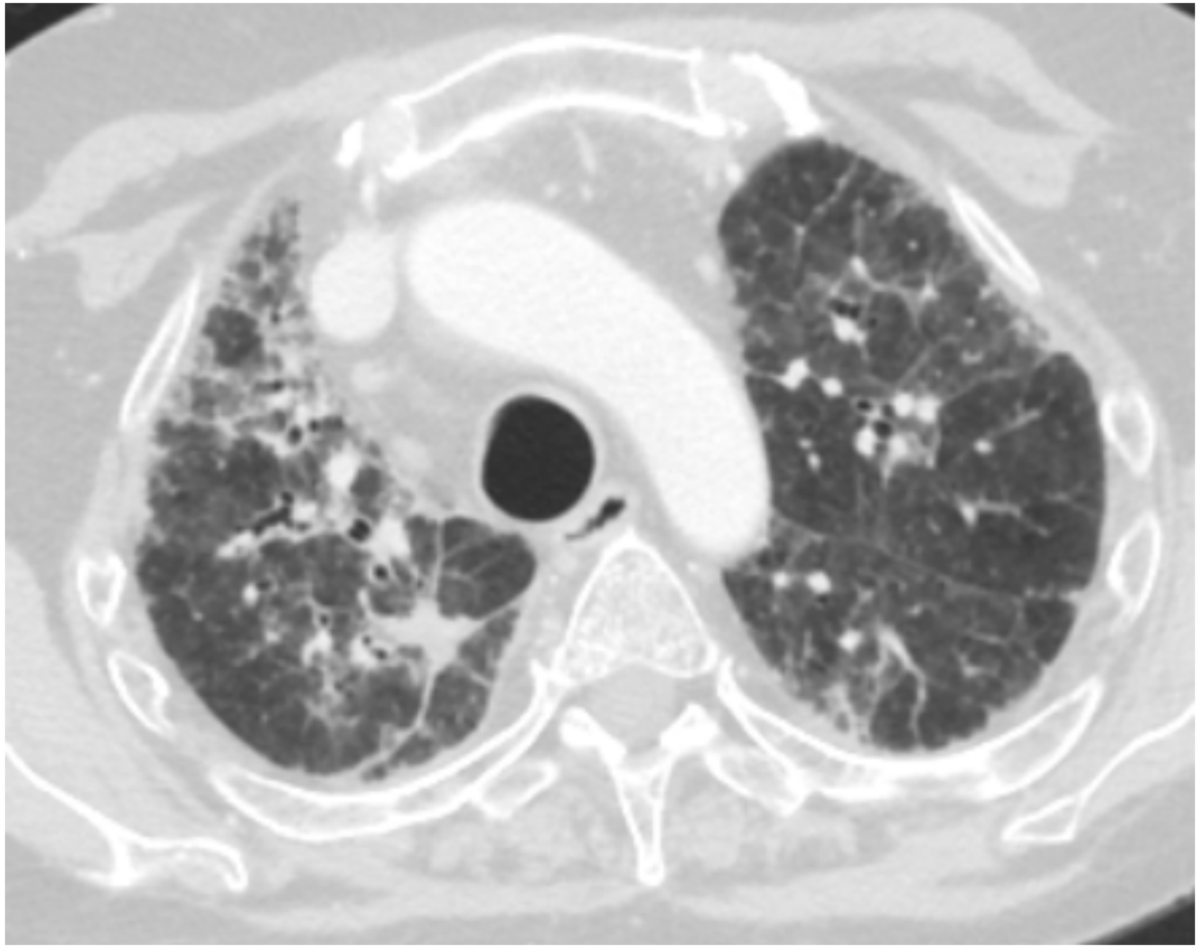




65-year-old w/ T2bN0M0 NSCLC, severe COPD

Case Examples

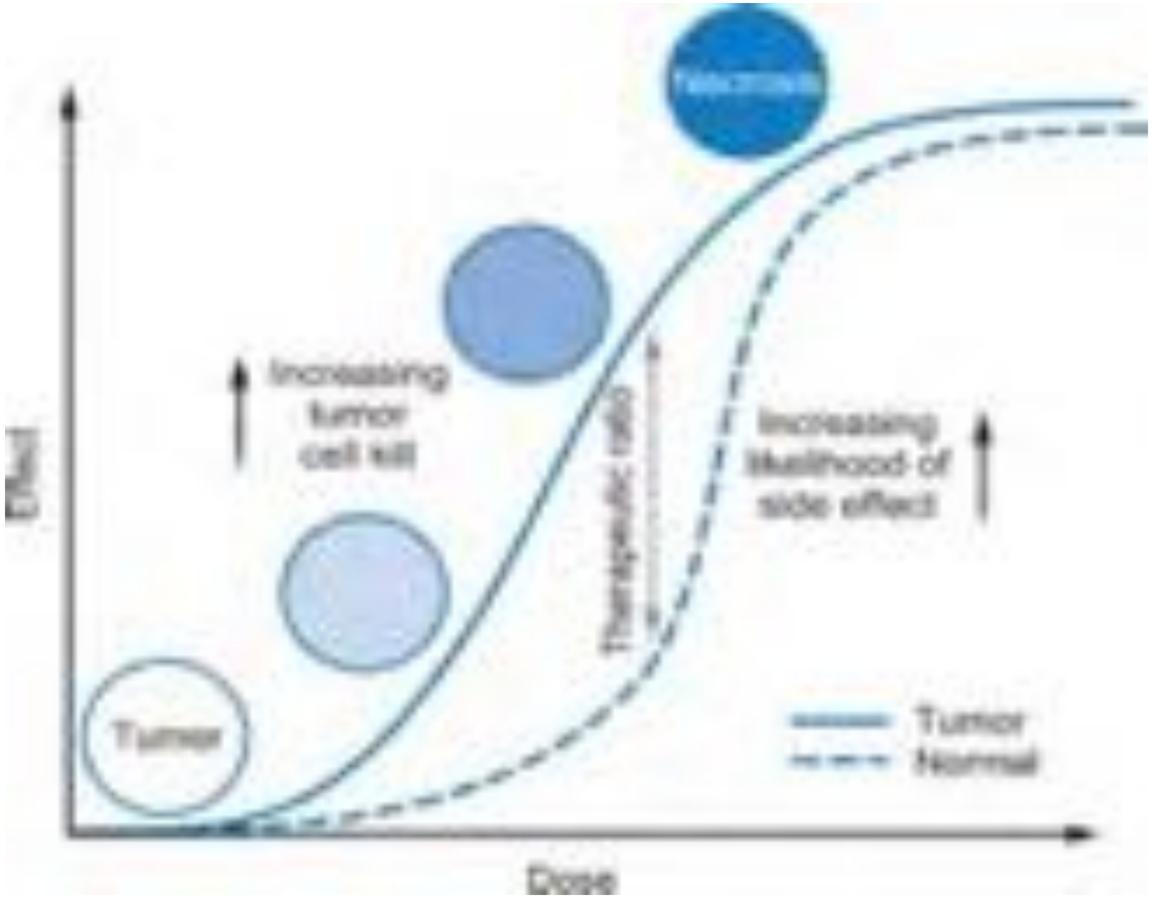




65-year-old w/ T2bN0M0 NSCLC, severe COPD

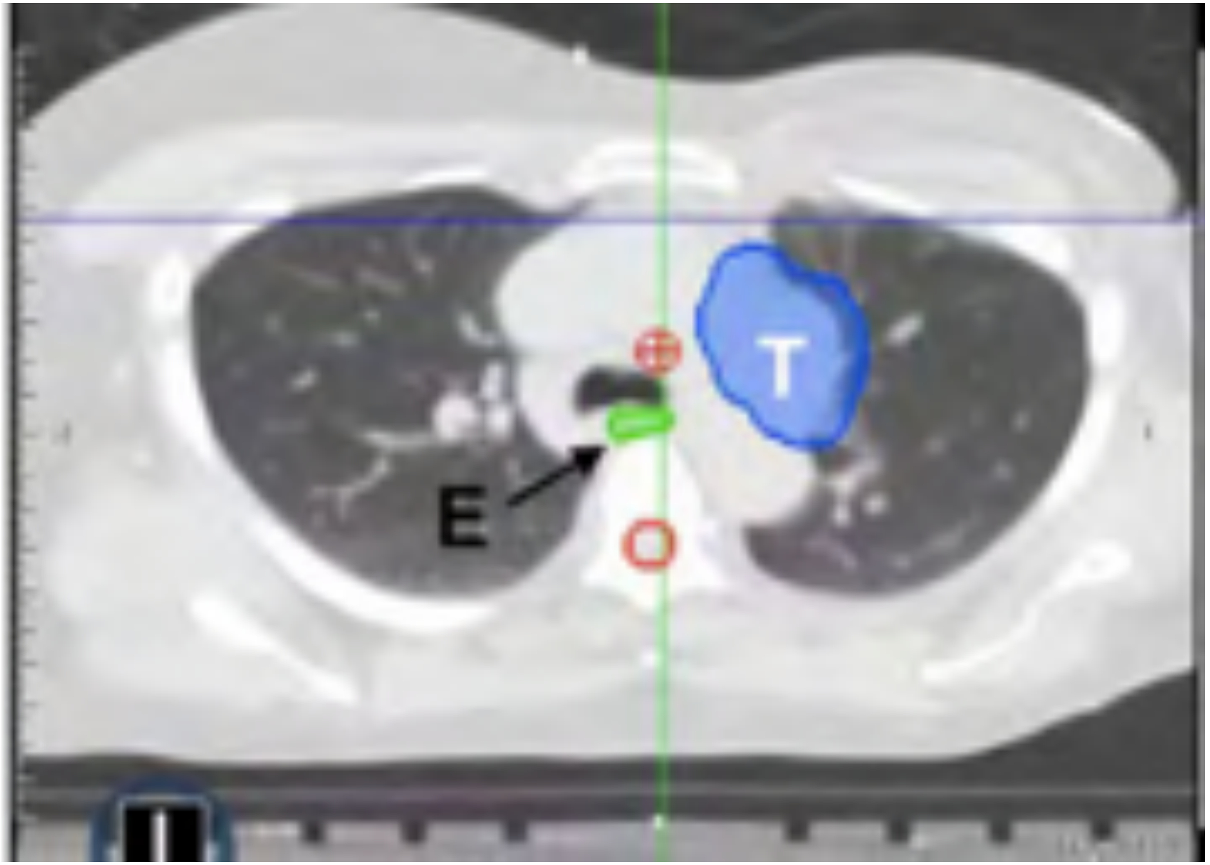
Plan Adaptation

The promise of plan adaptation



MR Linac Workflow

The promise of plan adaptation

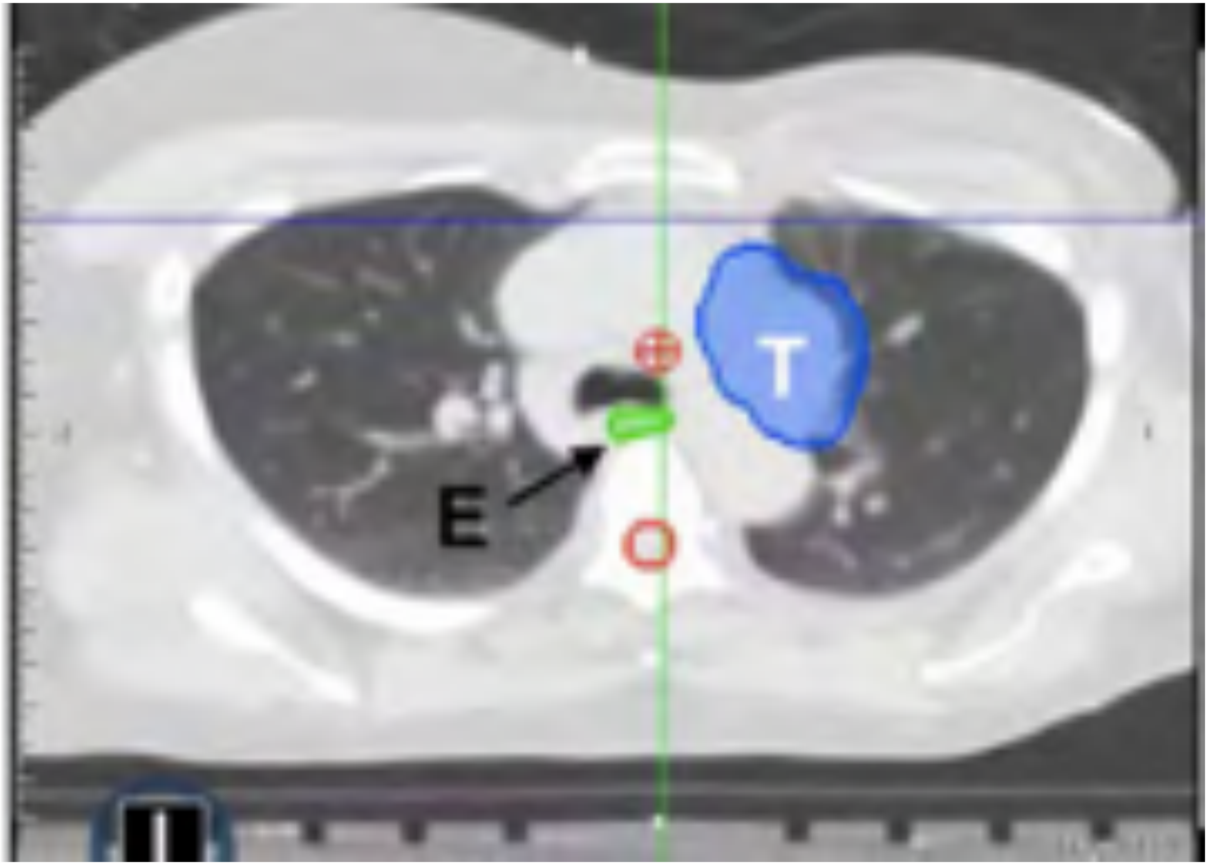


Simulation CT scan

Henke L et al., IJROBP 2017

MR Linac Workflow

The promise of plan adaptation



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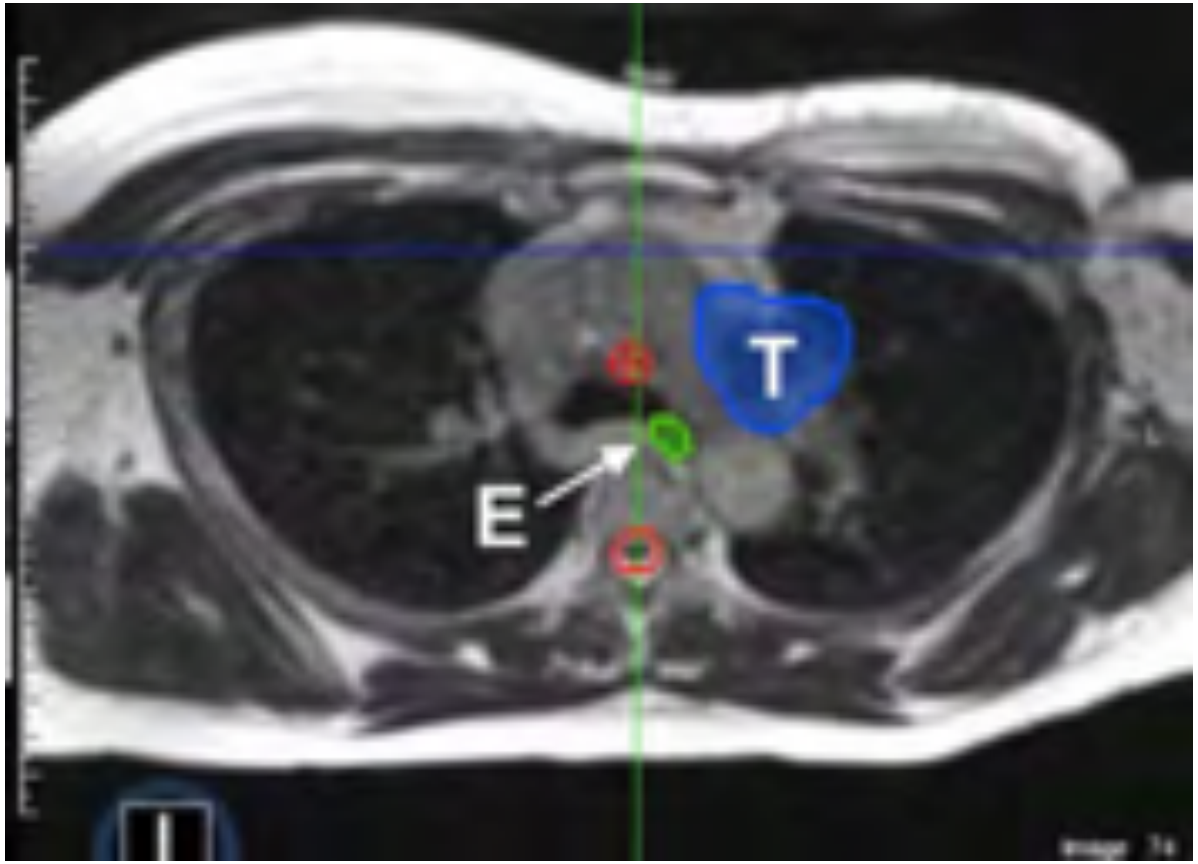
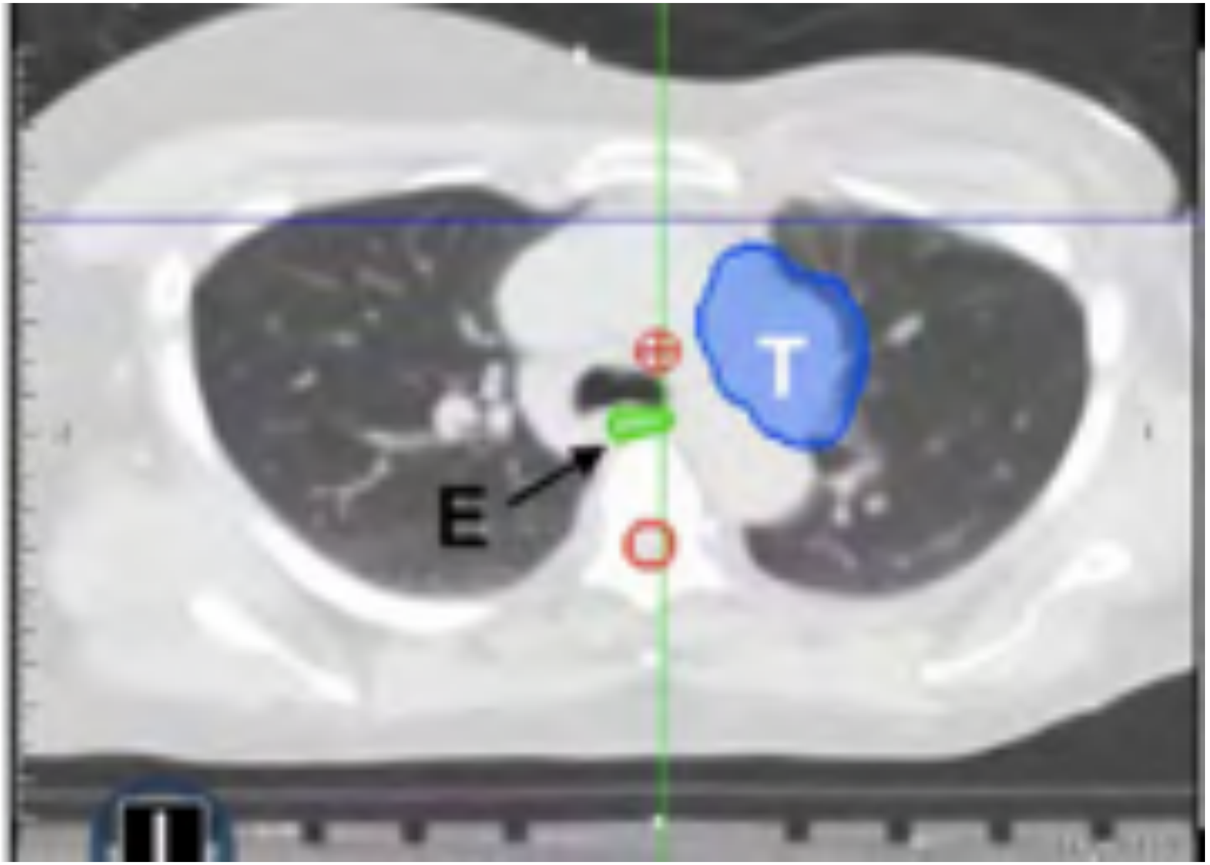


Treatment Fraction

Henke L et al., IJROBP 2017

MR Linac Workflow

The promise of plan adaptation



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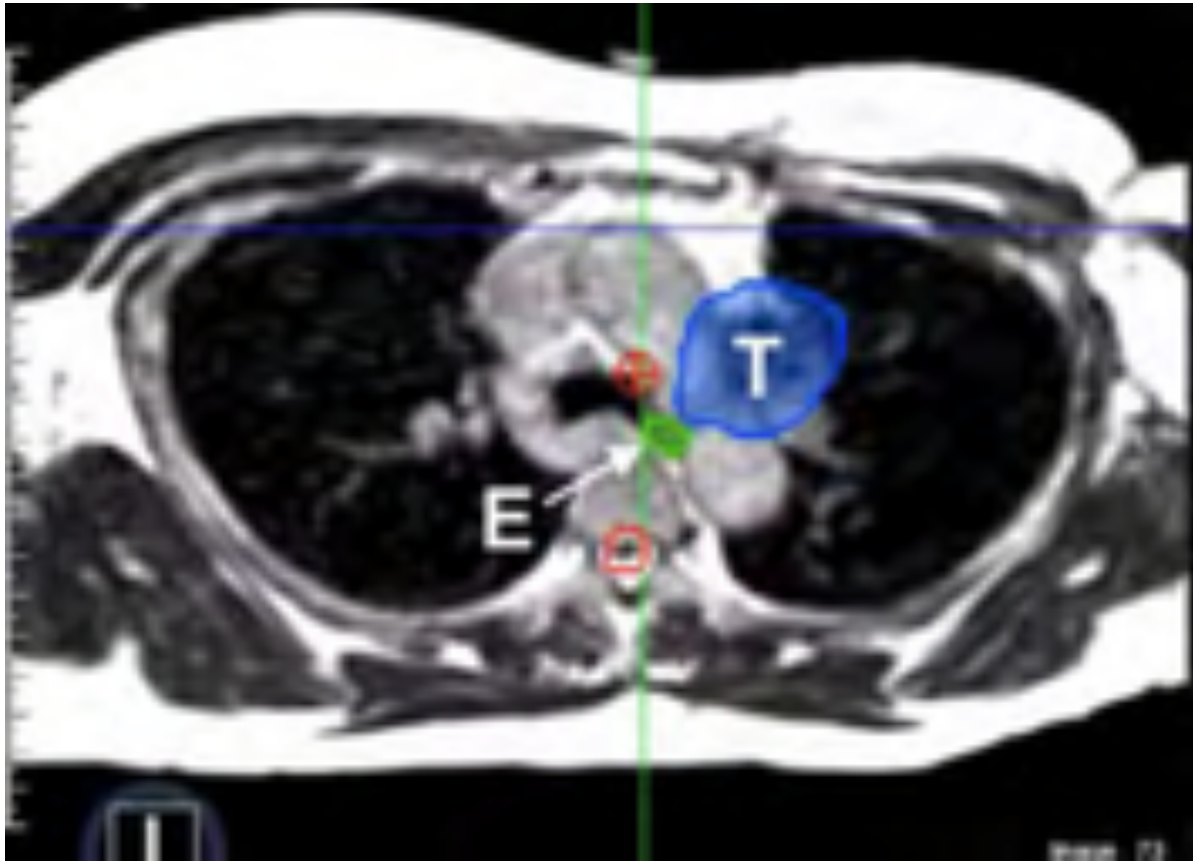
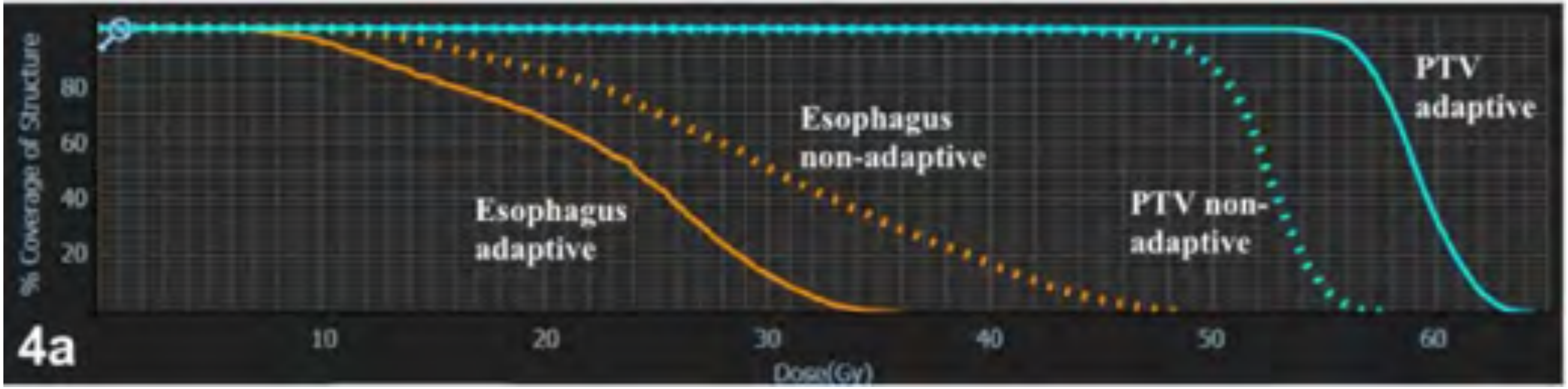


Treatment Fraction

Henke L et al., IJROBP 2017

MR Linac Workflow

The promise of plan adaptation



Comparison of simulation plan to current anatomy using prior plan

Adaptive plan reduces dose to the esophagus
Adaptive plan improves tumor coverage
Adaptive plan allows for potential for dose-escalation

Henke L et al., IJROBP 2017

Technology Triage

Early Stage Lung Cancer

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- Volumetric imaging?
- Non-coplanar?

Yes?

Comparative Plans

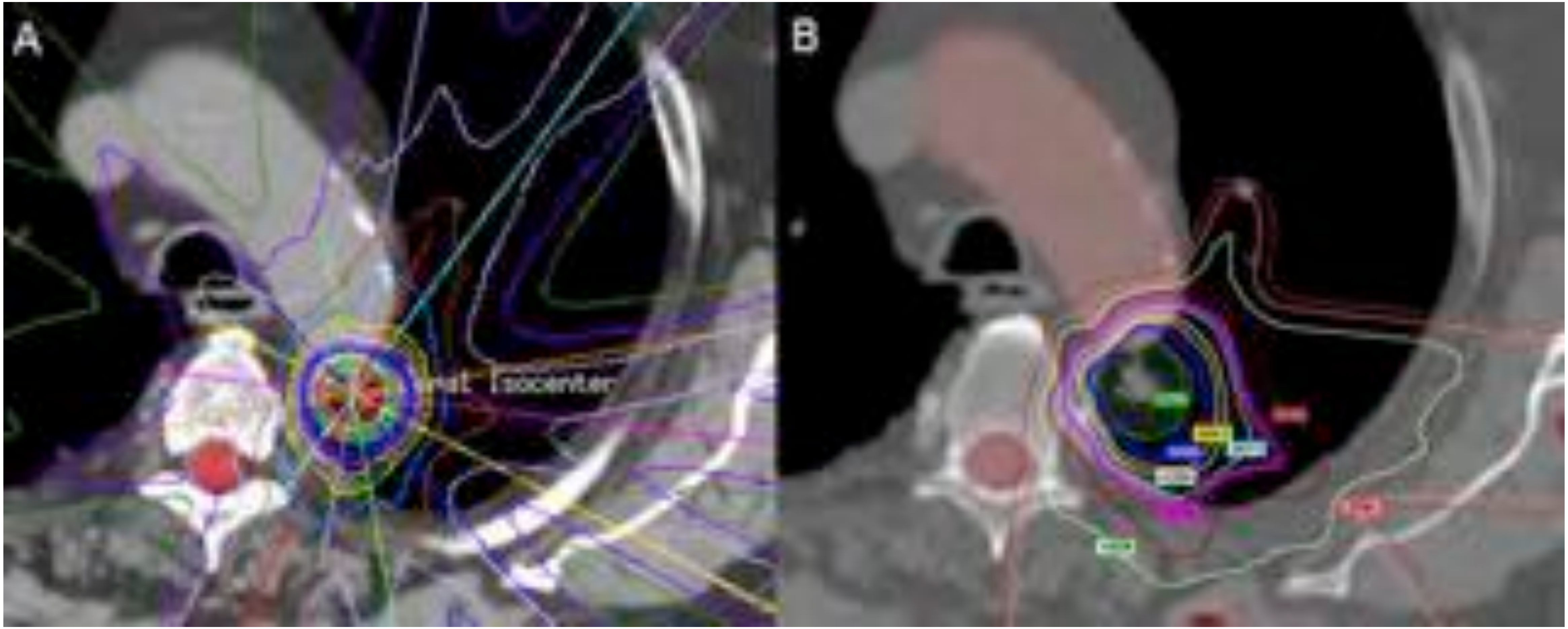
Treat patient with *best* quality plan

Proton Therapy

- Rationale
  - Reduce dose to normal tissues
  - More safely allows treatment of tumors close to critical organs potentially not treatable with photon therapy
  - More safely allows for dose escalation
  - More safely allows for retreatment of locally recurrent tumors potentially not treatable with photon therapy
- Potential benefits
  - Reduce treatment toxicities
  - Chance of cure not otherwise achievable with photon therapy
  - Improvement in local control
  - Improvement in local tumor control and progression-free survival compared with definitive photon radiotherapy
  - Chance of cure not otherwise achievable with photon therapy

Simone C et al., Cancer J. 2014

Proton Therapy

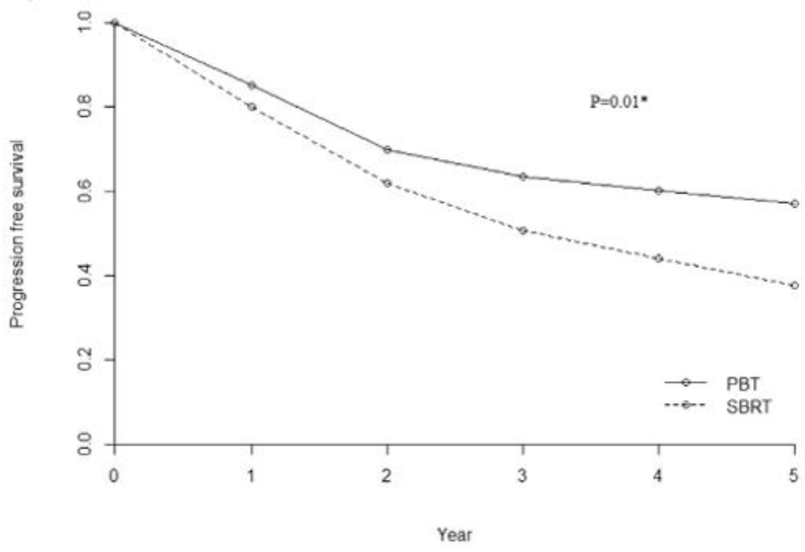


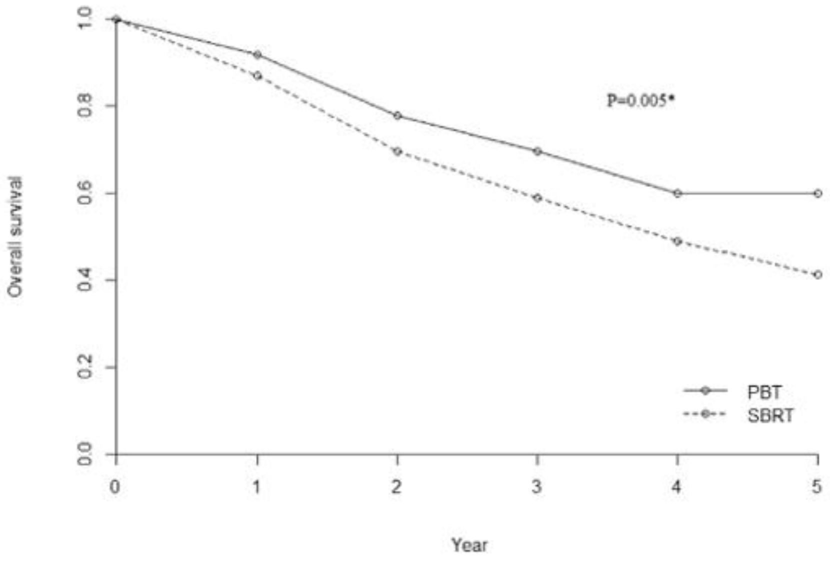
Photon SBRT **Proton SBRT**

Nantavithya C et al., IJROBP 2018

Proton Therapy

- Meta-analysis of 72 photon SBRT studies and 9 hypo-fractionated PBT studies
  - Patients treated with PBT had larger tumors
    - Larger median tumor size (2.9 vs. 2.4 cm, p=0.02)
    - Less likely to have T1 disease (57% vs. 71%, p=0.05)

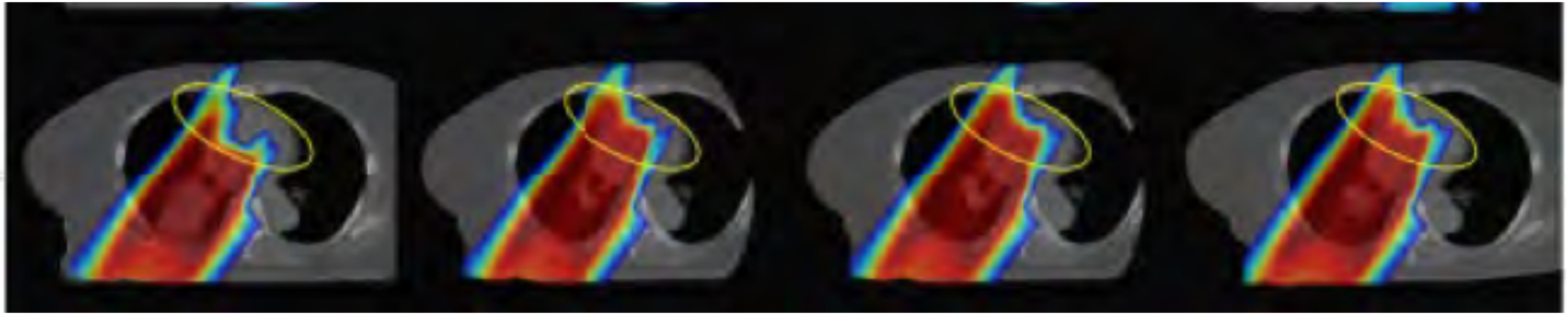




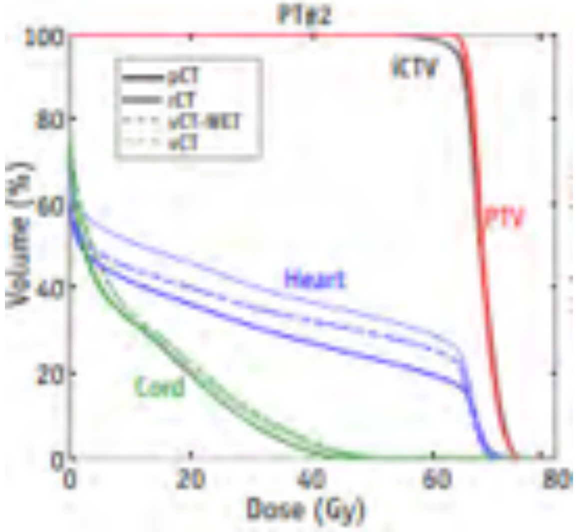
- Grade 3 pneumonitis (0.9% vs. 3.4%, *p*=0.001)

Chi AC et al., Radiother Oncol 2017

Proton Therapy



Tumor shrinkage during treatment



Over-ranging:

1. Increase in dose delivered to the spinal cord
2. Increase in dose delivered to the heart

Veiga et al., IJROBP 2016

Technology Triage – Putting it All Together

Early Stage Lung Cancer

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Tomotherapy
- Claustrophobic
- Volumetric imaging?
- Non-coplanar?

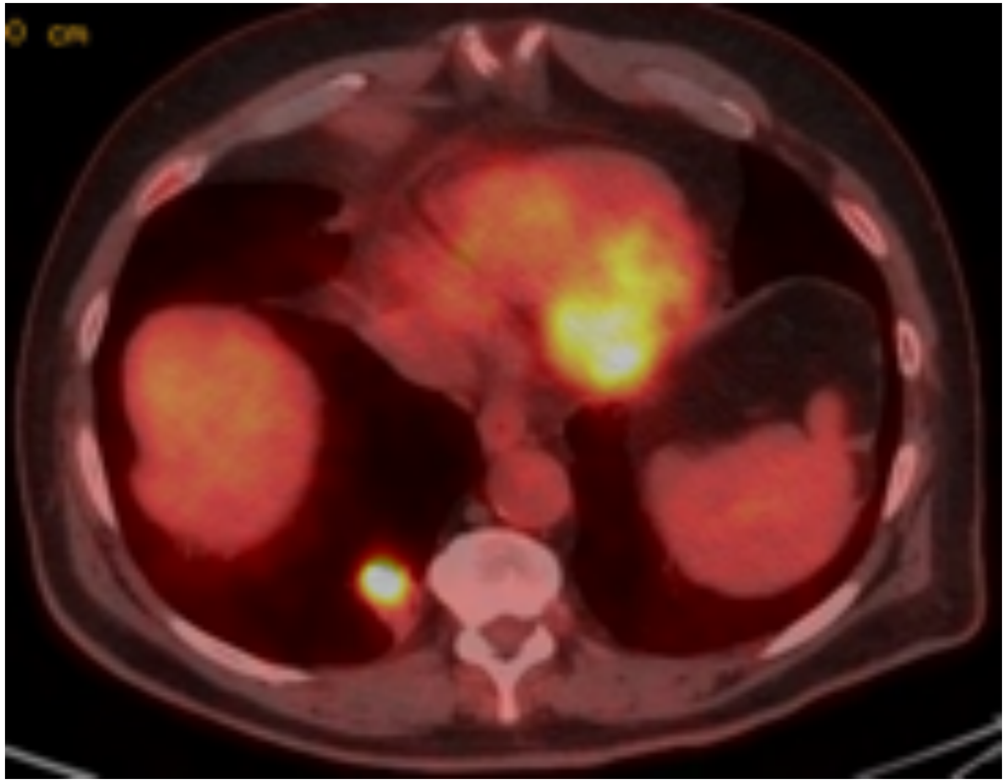
Yes?

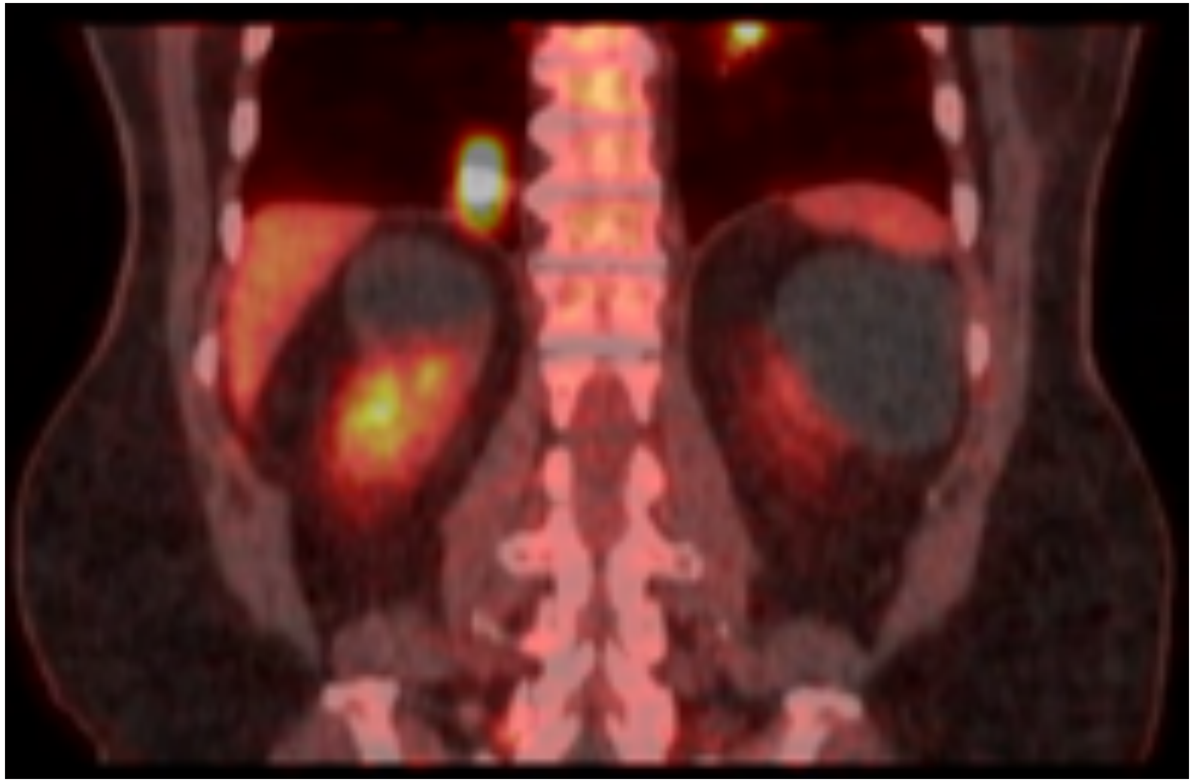
Comparative Plans

Treat patient with *best* quality plan

Case Example

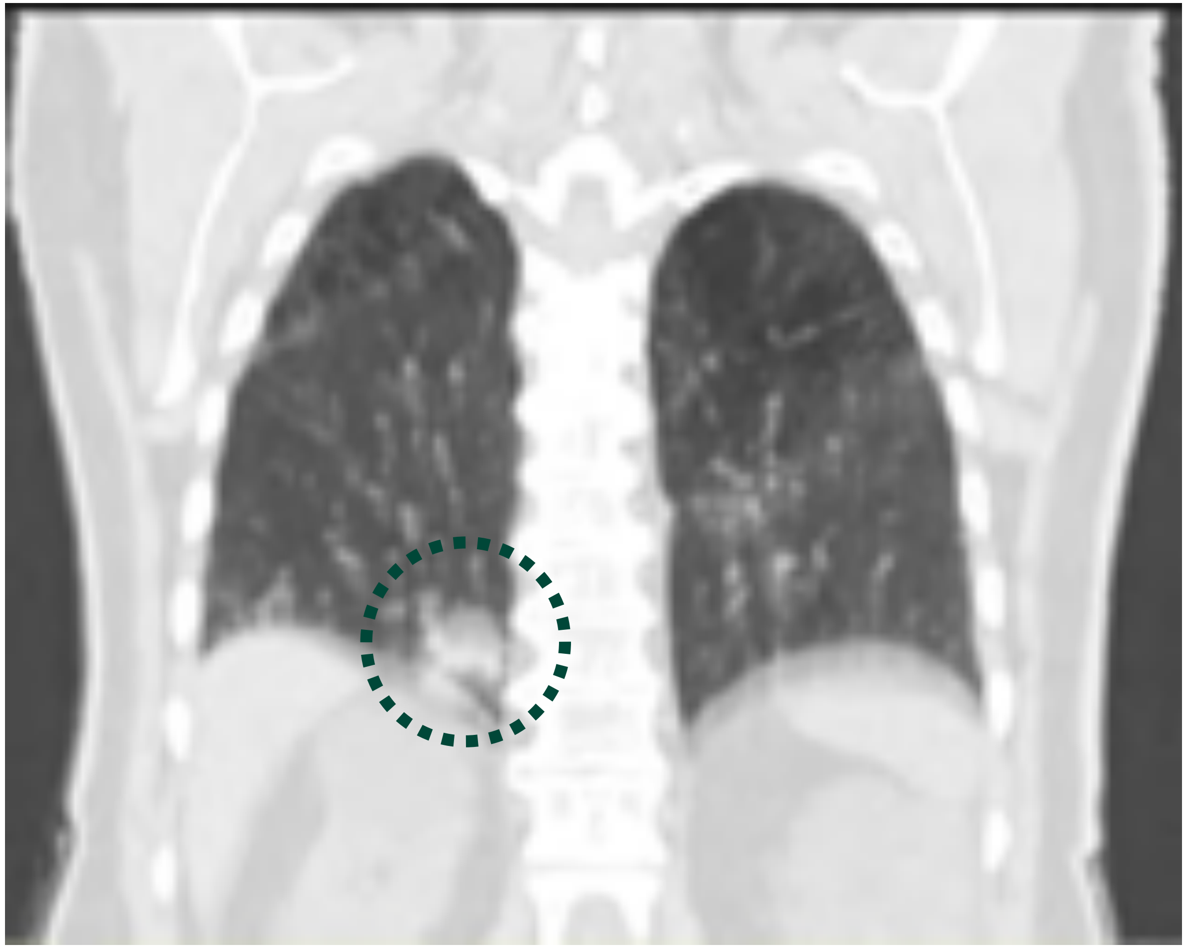
- 73 yo M with RLL and LLL squamous cell carcinomas, synchronous primaries vs. metastatic disease, s/p 4 cycles of carboplatin/taxol/pembrolizumab and 6 cycles of maintenance pembrolizumab with interval oligo-progression of the right lower lung mass





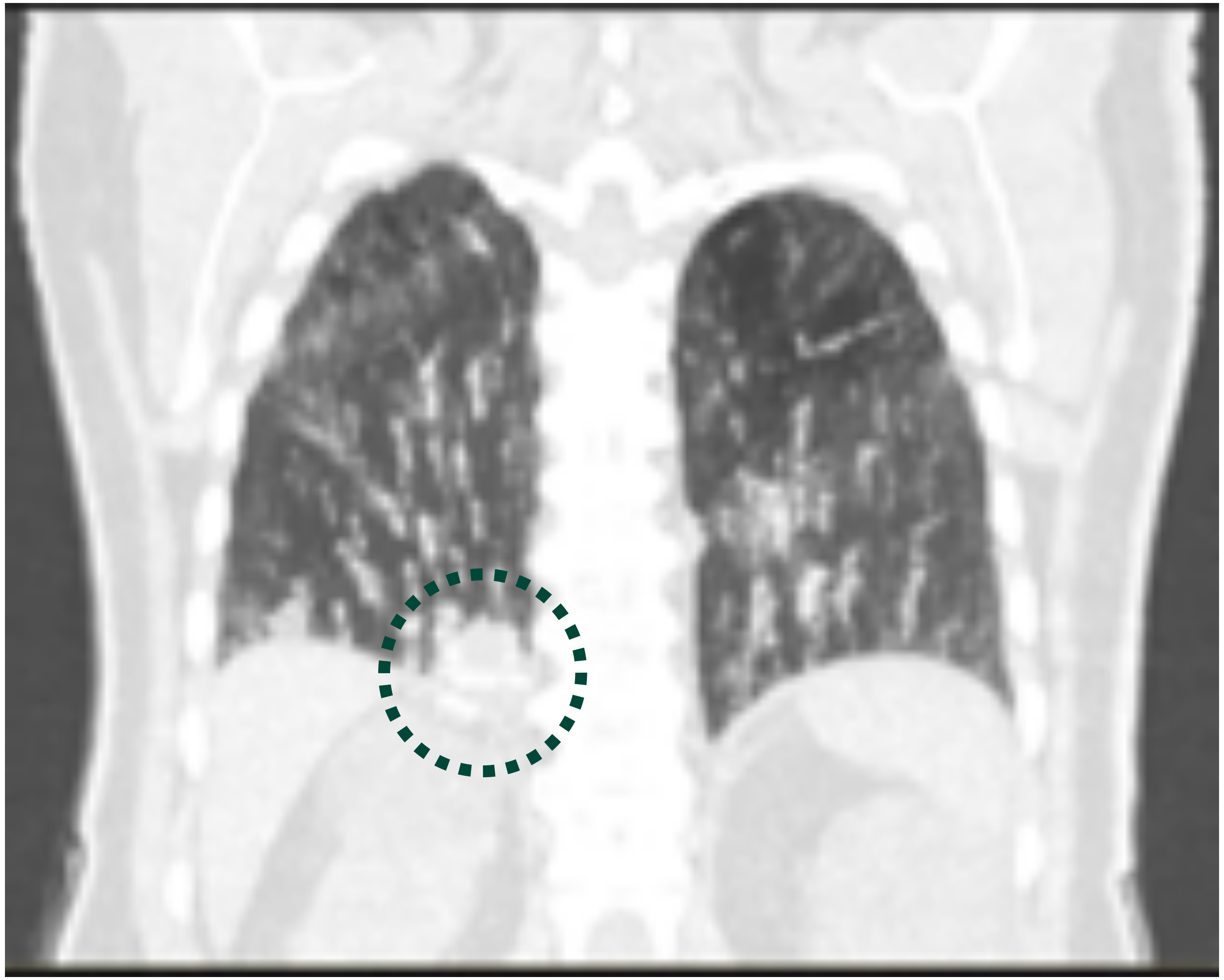
Simulation (for 3 modalities)

- Planned CT simulation
  - Supine
  - Arms above head
  - Vac-Lok device
  - Abdominal compression belt
  - 4D CT to assess respiratory motion
  - No contrast



Average CT for planning

CT Simulation



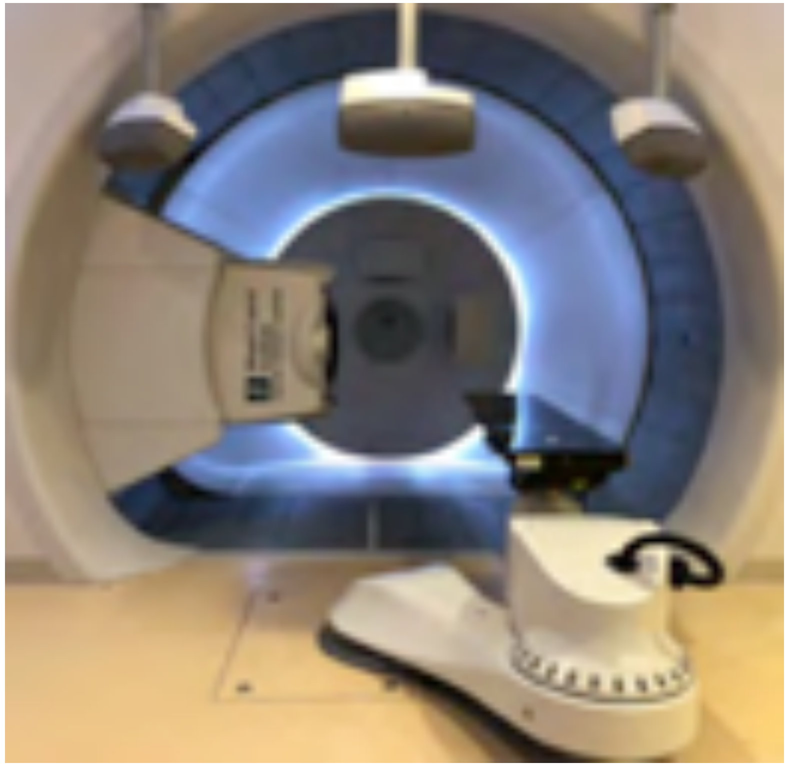
Significant (>1.5cm) respiratory excursion **despite** maximal abdominal compression:

1. **> 2x size** in treatment volume due to respiratory excursion
2. Inability to delineate the edges of the tumor given surrounding vascularity
3. Potential for **undercoverage** or **overtreatment** at inferior extent of disease due to challenges delineating the tumor edge from diaphragm and surrounding organs-at-risk

Alternative Treatment Platforms

- Significant increase in the treated volume with ITV approach
- Difficulty accurately registering CBCT at delivery due to CBCT motion artifacts
- Gating option would require fiducials

- Significant increase in the treated volume with ITV approach
- Potential difficulty accurately registering with MVCT at time of treatment delivery
- No gating or tracking solution yet



- Significant increase in the treated volume with ITV approach
- Difficulty accurately registering CBCT at delivery due to CBCT motion artifacts
- Non-synchronization of spot delivery and respiratory motion (interplay)

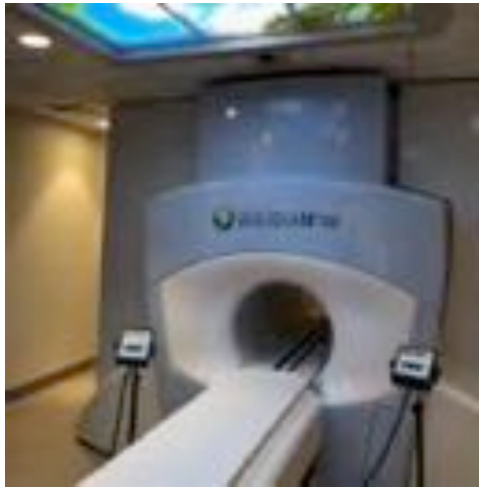
Lung SBRT Program Options

Linear Accelerators

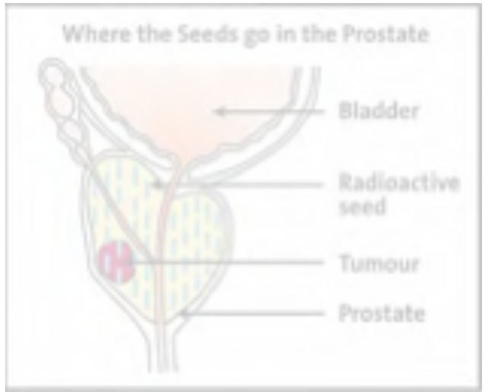
CyberKnife® M6

Radixact Tomotherapy

Gamma Knife Icon

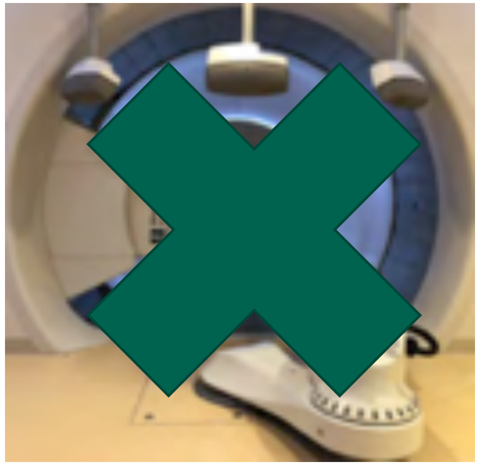


MR Linear Accelerator



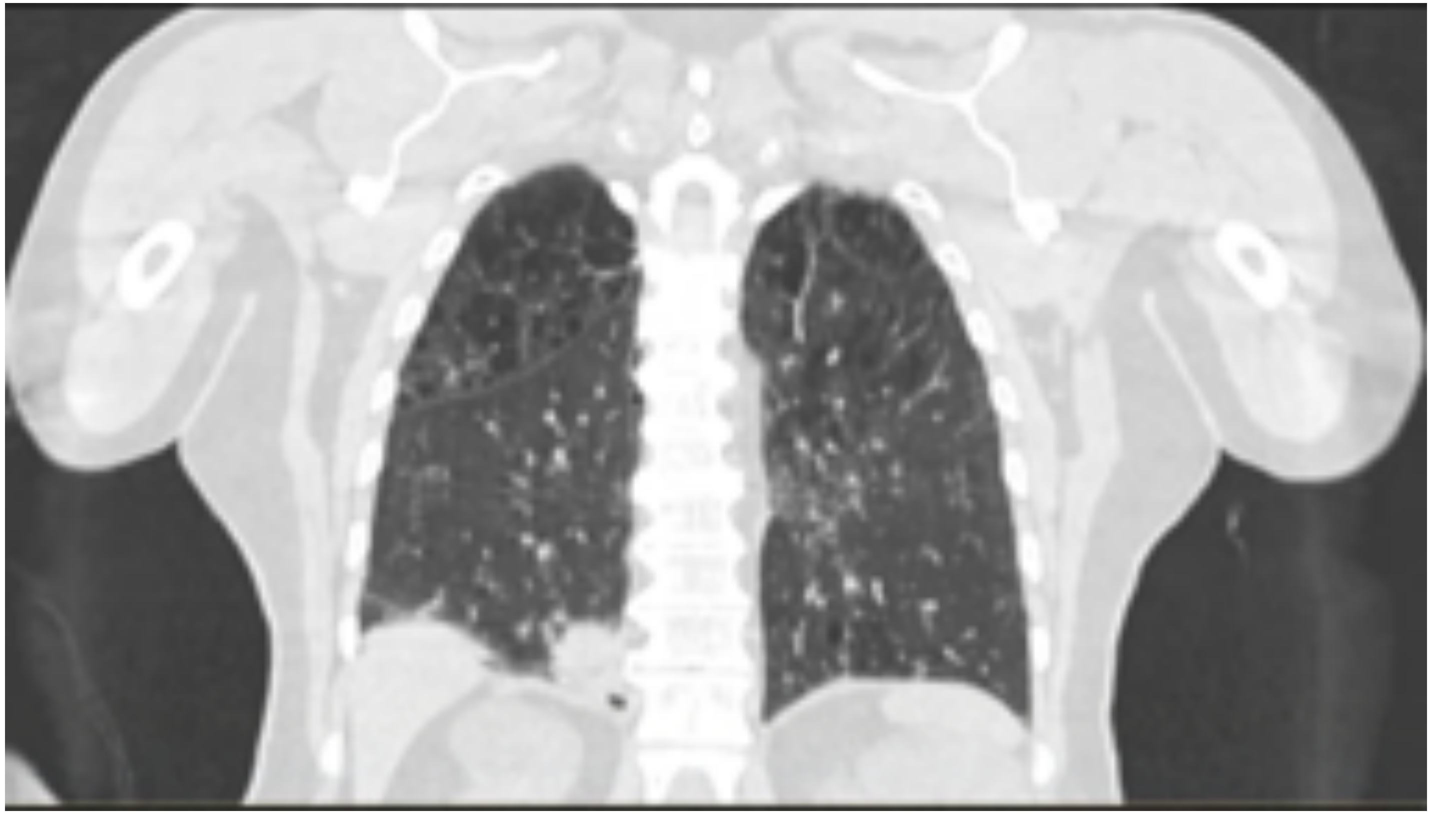
Low Dose Rate Brachytherapy

High Dose Rate Brachytherapy



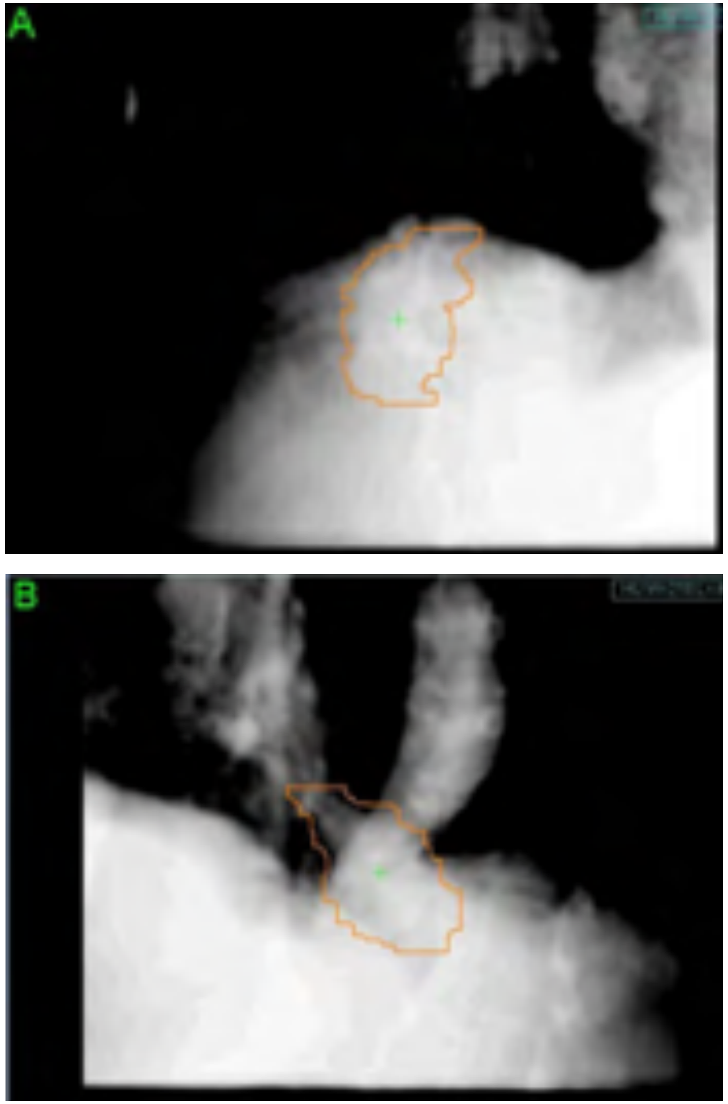
Proton Therapy

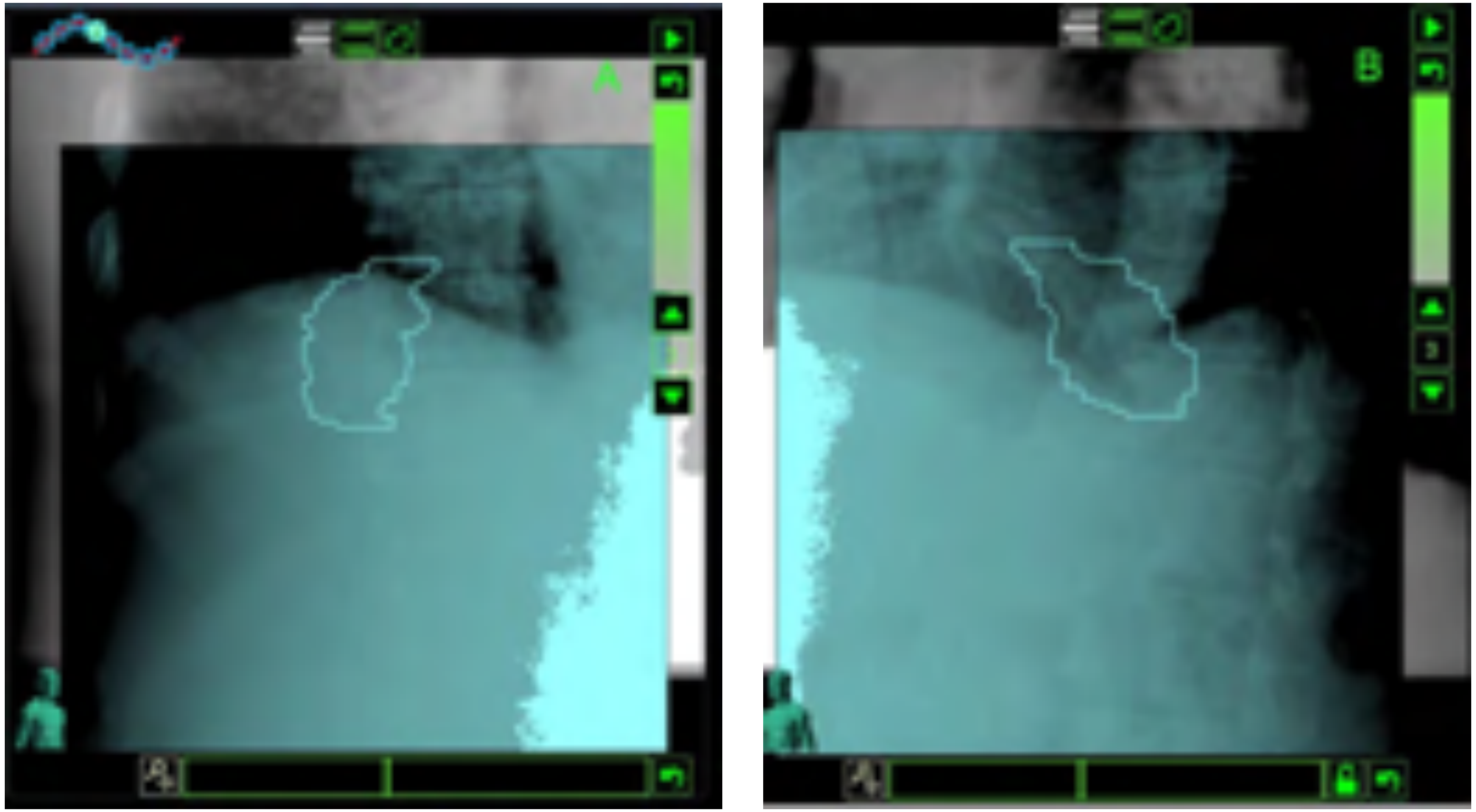
Alternative Treatment Platforms



Exploration of treatment alternative with automatic and continuous tracking and synchronized treatment delivery

Alternative Treatment Platforms





Tracking plan with the DRR generated from the exhale CT along with a randomly picked set of kV images taken during the tracking test shows system **difficulty** in differentiating tumor from surrounding structures.

No respiratory correlation model could be generated.

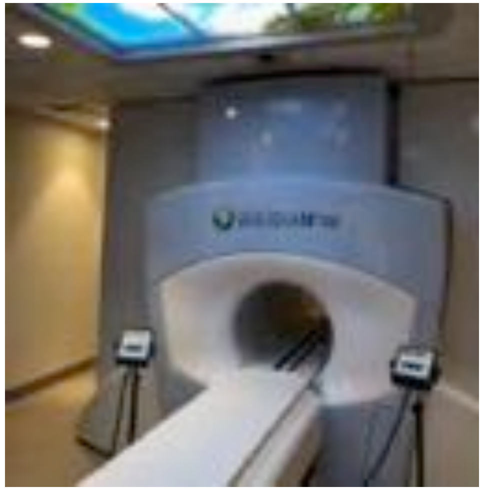
Lung SBRT Program Options

Linear Accelerators

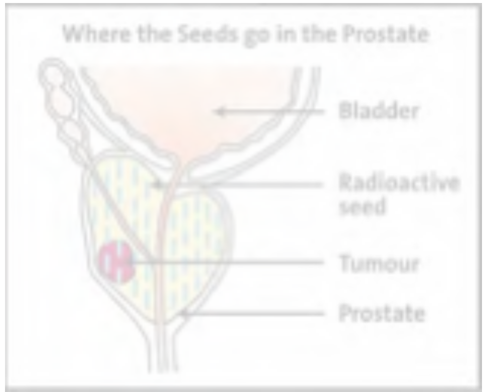
CyberKnife® M6

Radixact Tomotherapy

Gamma Knife Icon

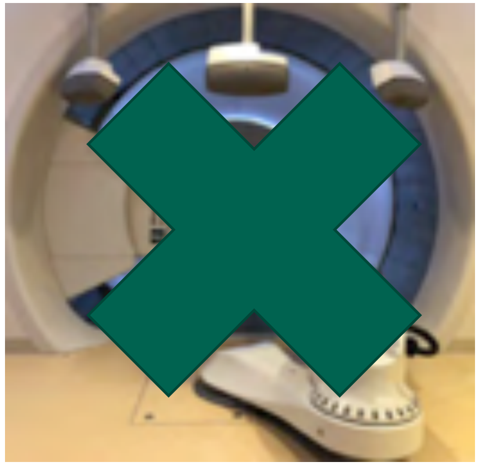


MR Linear Accelerator



Low Dose Rate Brachytherapy

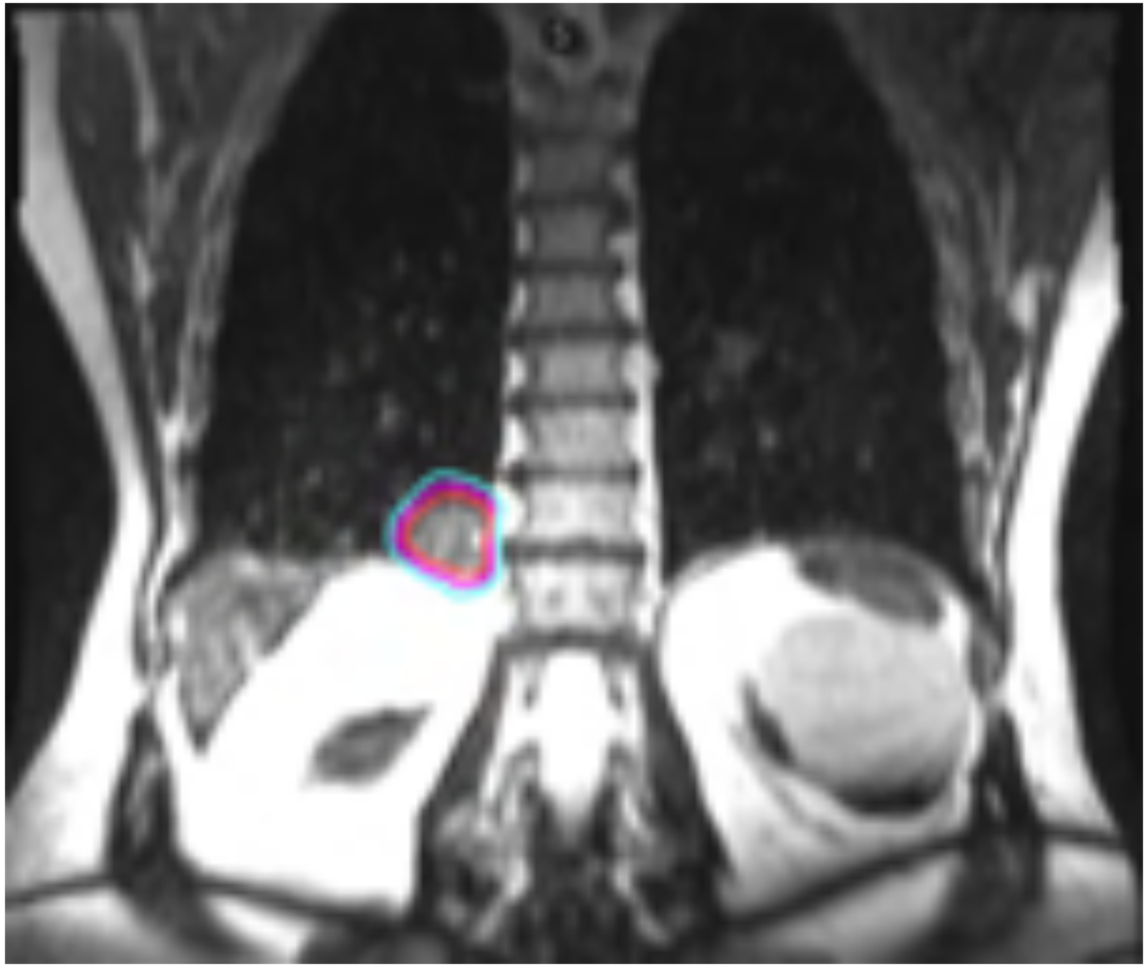
High Dose Rate Brachytherapy



Proton Therapy

MR Linac Simulation and Treatment

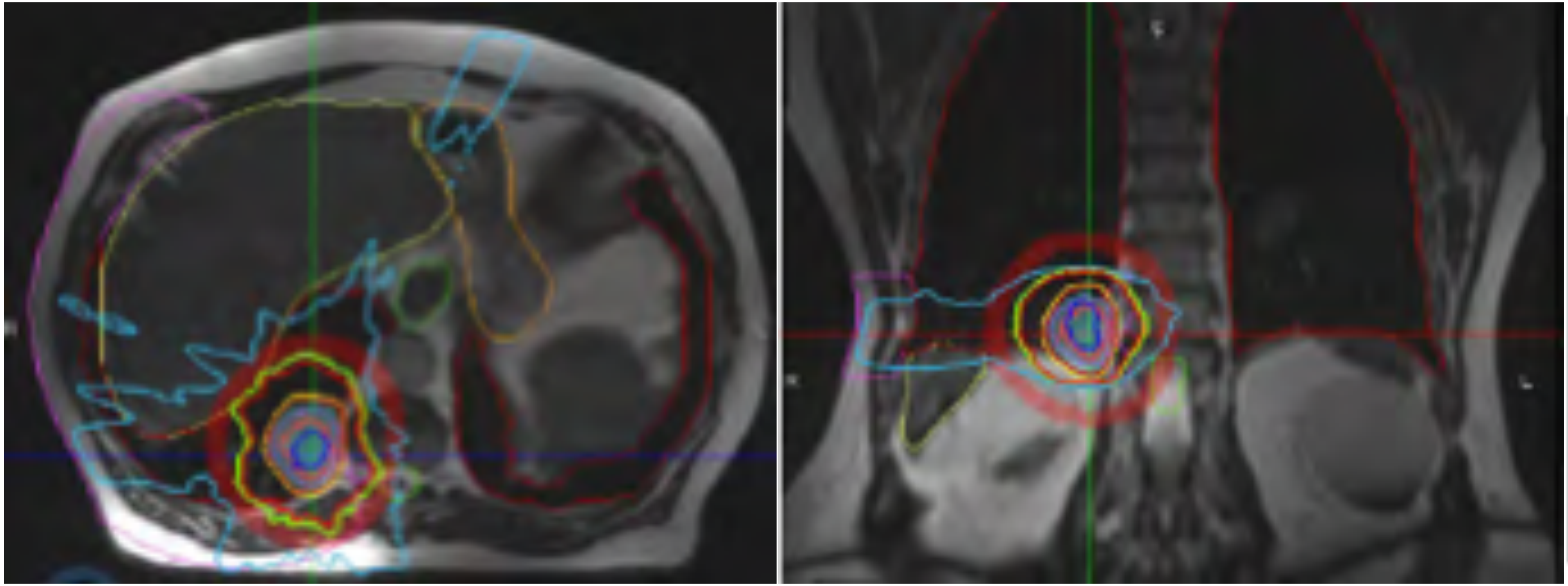
- Planned MRI Simulation
  - Supine
  - Arms above head
  - No contrast
  - No compression belt
  - Mid inhalation breath hold scan
  - 4 frames per sec
  - 3 mm margin with 5% ROI



GTV = 16.12 cc   CTV = 26.99 cc   PTV = 43.94 cc

MR Linac Simulation and Treatment

50 Gy in 5 fractions

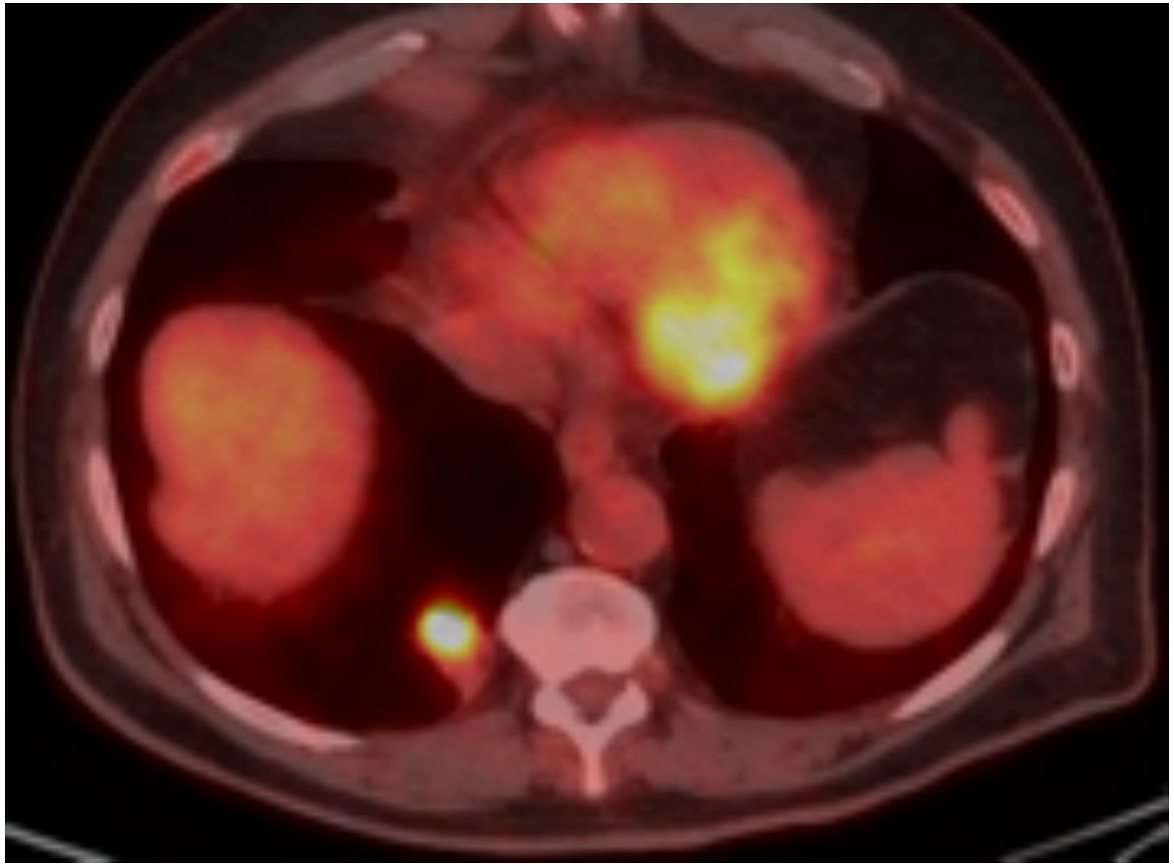


Isodose Lines

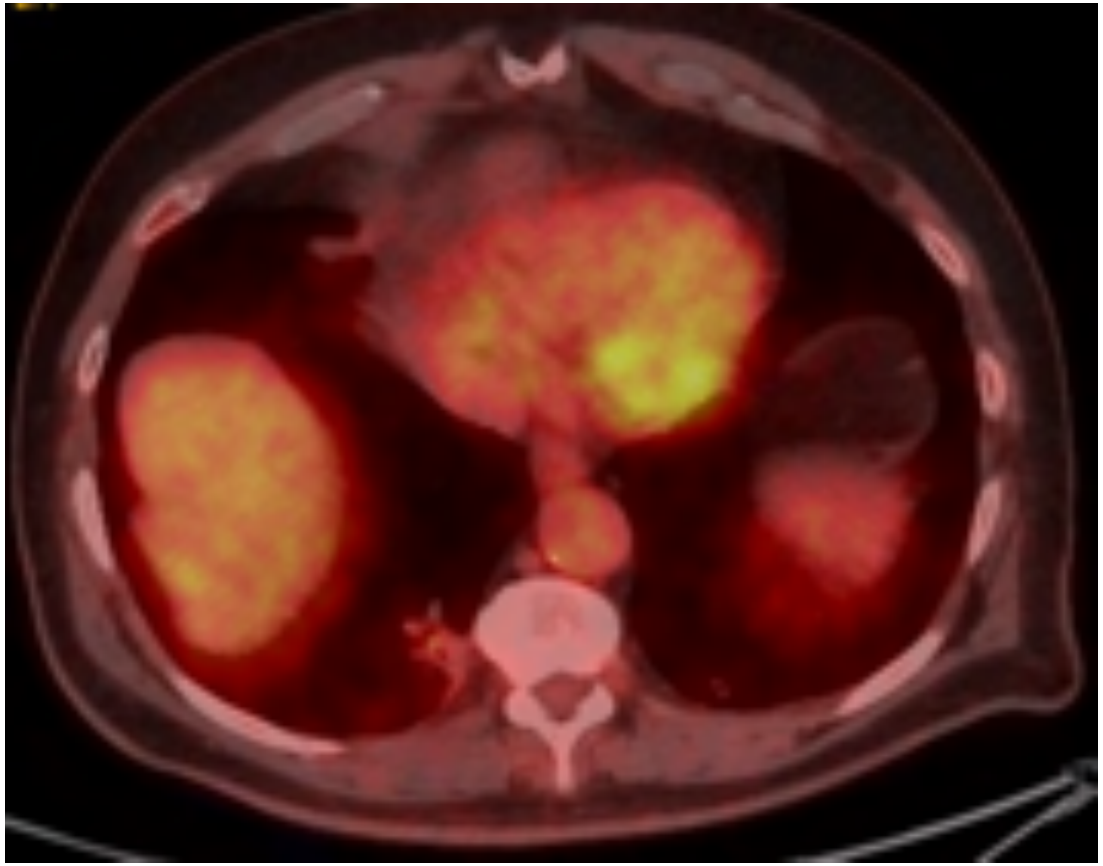
Rx Dose = 50.00 Gy

Dose (Gy)	Rx (%)
65.00	130.0
60.00	120.0
50.00	100.0
47.50	95.0
27.50	55.0
25.00	50.0
16.50	33.0

MR Linac Simulation and Treatment



Pre-treatment PET/CT



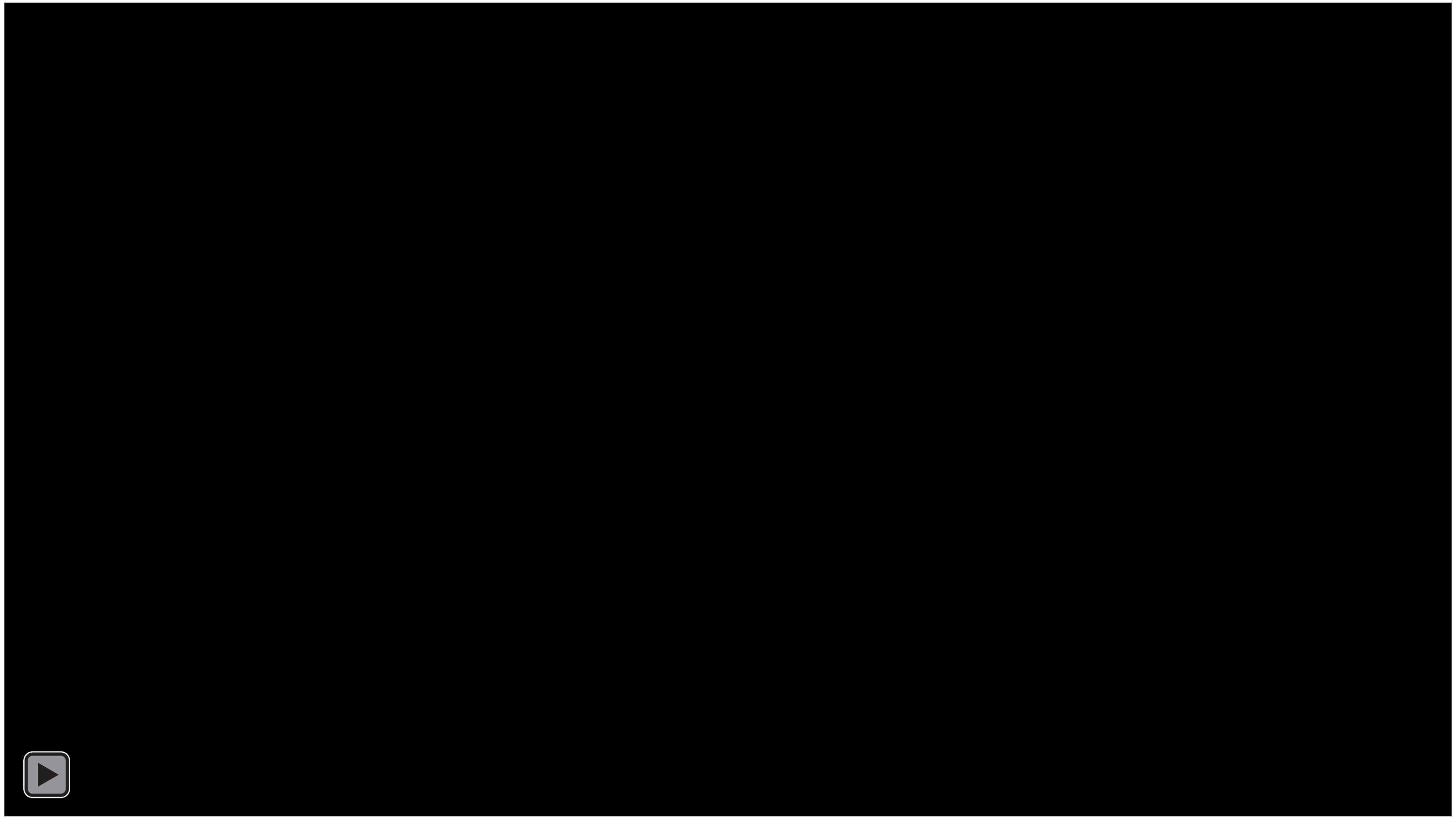
8 week post-treatment PET/CT

Post-treatment PET/CT revealed significant **metabolic** and **radiographic** response in the treated disease in the RLL

Summary

- ***Lung cancer screening*** is an important initiative, and should be ***implemented thoughtfully***
- Tremendous advances made in ***precision-oriented, accurately delivered*** radiotherapy for all stages of lung cancer in the last decade
- SABR is ***standard for frail patients*** with early stage lung cancer patients who cannot have or refuses surgery
  - Addition of ***immunotherapy*** may further improve outcomes of SABR
- Addition of ***immunotherapy after chemotherapy and radiation*** for locally advanced lung cancer helps patients live longer
- ***Radiation to metastatic sites*** with ***SABR*** along with systemic treatments in ***selected patients*** with ***minimal disease burden*** with stage IV lung cancer may help patients live longer and improve quality of life

Conclusions



When working with competing technology platforms ... Teamwork is key!