2014 AAPM SUMMER SCHOOL
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SRS/SBRT/SABR: Safely and Accurately Delivering High-Precision, Hypofractionated Treatments

Importance of 4D simulation, Planning, and delivery

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Learning Objectives

- To understand the physiological characteristics of tumor motion in different treatment sites.
- To understand the available technology for 4D planning in SRT.
- To understand startegies for employing ITV and MIPs for dose calculations.

Motivation

Capture the 4th dimension accurately
Deliver the intended plan dose to the tumor
Minimize healthy tissue toxicity -> escalate dose to tumor

Safety Margins

Gold Standard

The 4D radiotherapy process

4D Radiotherapy

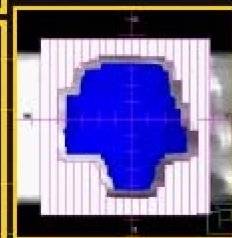
The explicit inclusion of the temporal changes in anatomy during the imaging, planning and delivery of radiotherapy

4D CT Imaging

Acquisition of a sequence of CT image sets over consecutive phases of a breathing cycle

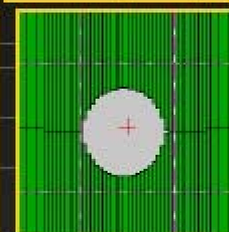
4D Treatment Planning

Designing treatment plans on CT image sets obtained for each phase of the breathing cycle



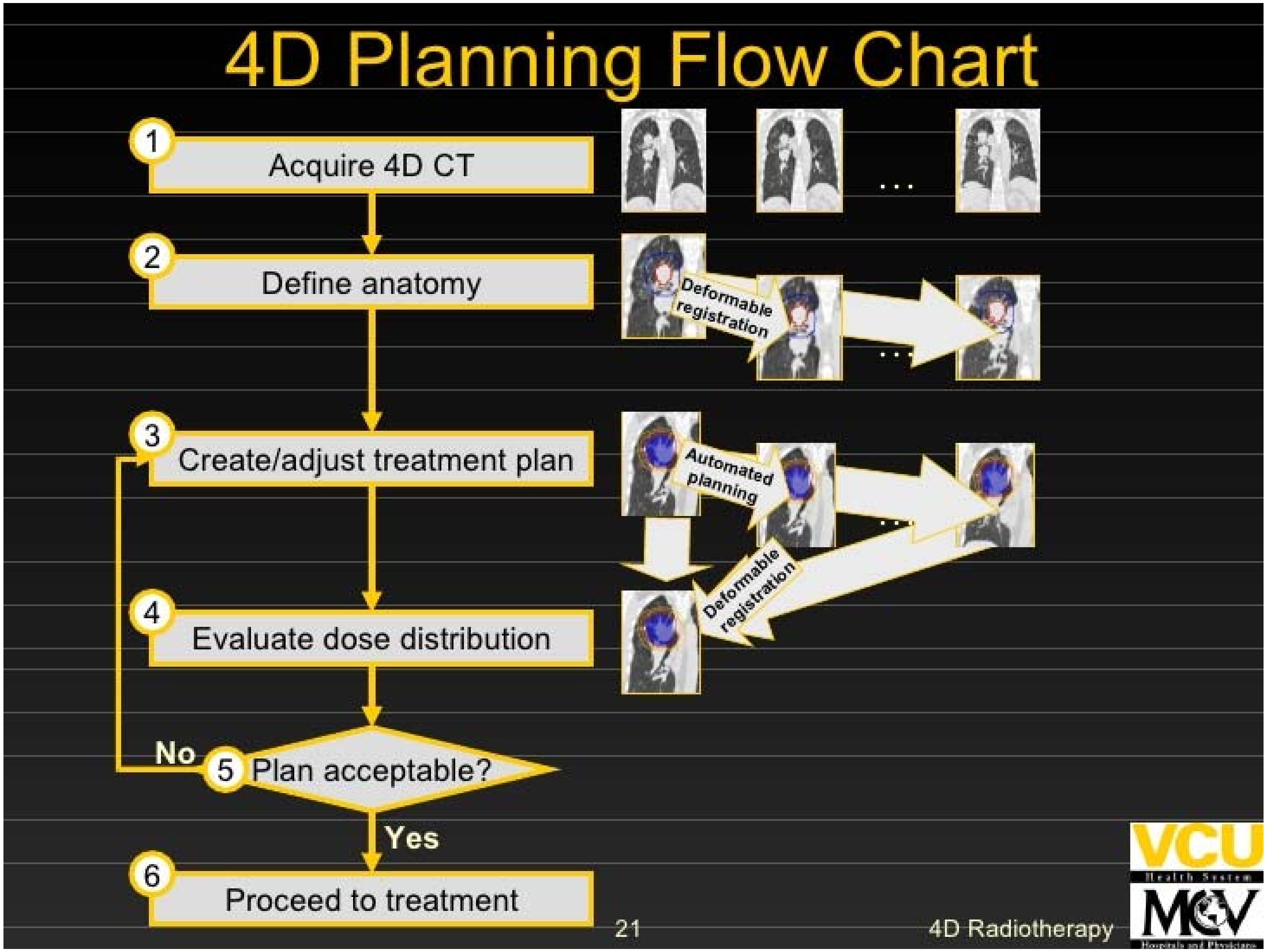
4D Treatment Delivery

Continuous delivery of the 4D treatment plans throughout the breathing cycle



Compliments of Paul Keall

VCU Health System
MCV Hospitals and Physicians



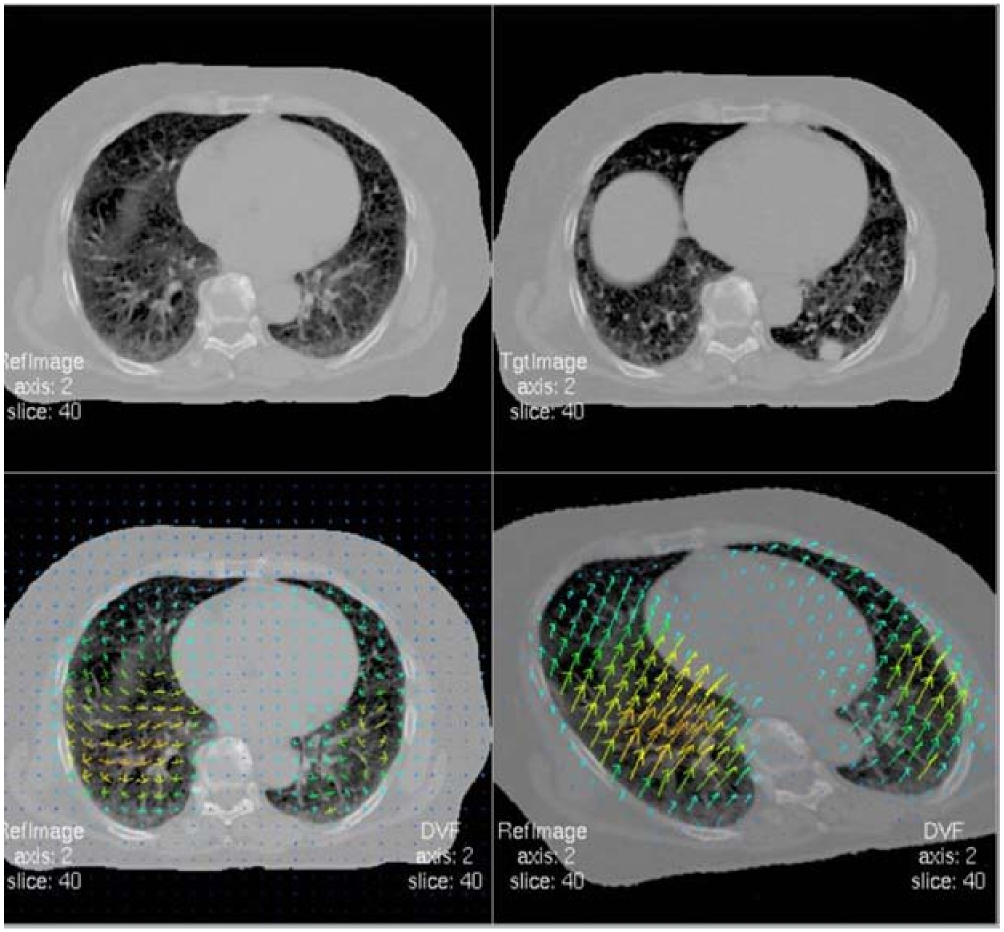
Compliments of Paul Keall

4D treatment planning in the clinic

K. Wijesooriya et al. Med.Phys. 35, 1251 (2008)

manual vs. automated contouring results for a single patient, axial, sagittal and coronal views from Pinnacle 7.7. Red contours are for the inhale phase. Colorwash contours are for the manually drawn exhale phase . Auto contours from inhale to exhale are: black (GTV), yellow (cord, heart), pink (esophagus), white (lungs).

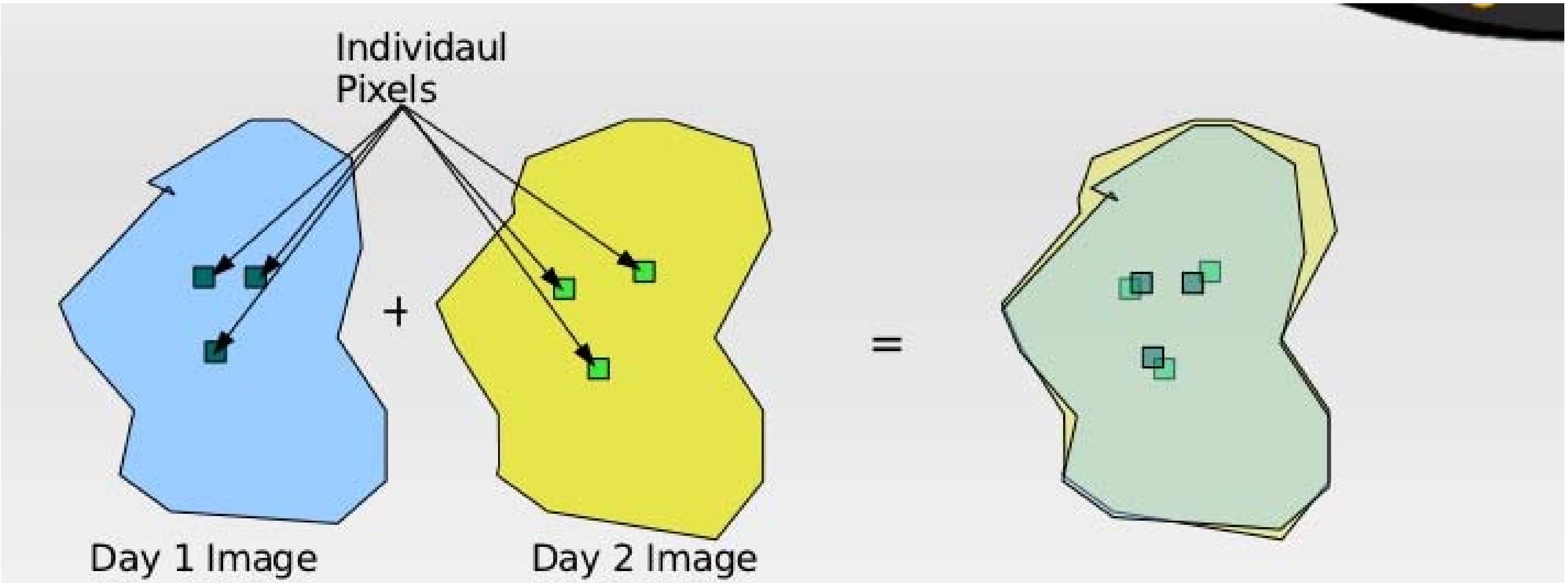
DVF to warp dose distributions to propagate them from end expiratory phase to all other phases



K. Wijesooriya et al. Med.Phys. 35, 1251 (2008).

Deformable Image Registration

- Technique by which a single **moving** voxel is matched on CT slices that are taken in different phases of respiration
- The treatment is planned on a reference CT – usually the end expiration (for Lung)
- Matching the voxels allows the dose to be visualized at each phase of respiration
- **Several** algorithms under evaluation:
  - Finite element method
  - Optical flow technique
  - Large deformation diffeomorphic image registration
  - Splines thin plate and b



Due to the changes in shape of the object the same pixel occupies a different coordinate in the 2nd image

4D Radiotherapy is still clinically prohibitive

- Enormous requirements on:
  - Personnel
  - Computational resources
  - Time resources
- New class of uncertainties
- Calculated dose is good only for a given respiratory pattern –respiratory motion unpredictable
- Clinical benefit is still unknown

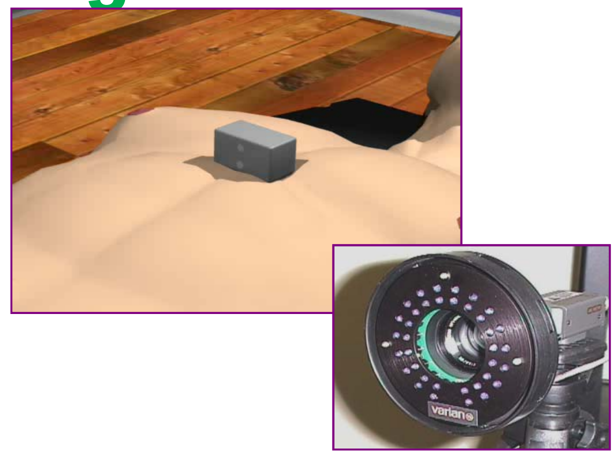
Some examples of limitations…

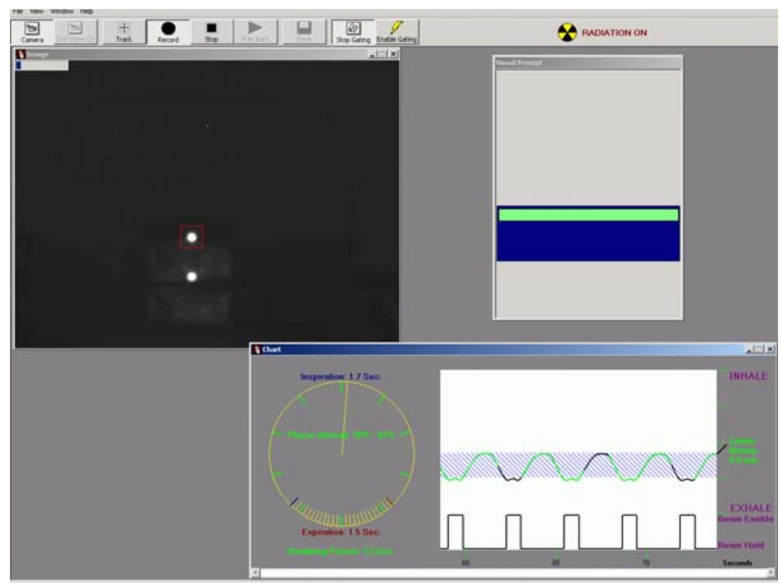
- Incorporating respiratory motion in dynamic IMRT means **MLC motion parameters** become important constraints
- **Tumor tracking** is needed for delivery if true potential is to be realized
- The time delay for dMLC response to a detected motion means that even with tracking **gating** is important

Simplified Approach to 4D Treatment Planning

- 4DCT acquisition
- Accurate tumor volume definition that encompasses all tumor locations – motion envelope
- A 3D plan performed on the ITV + margins
- On an appropriate reference dataset

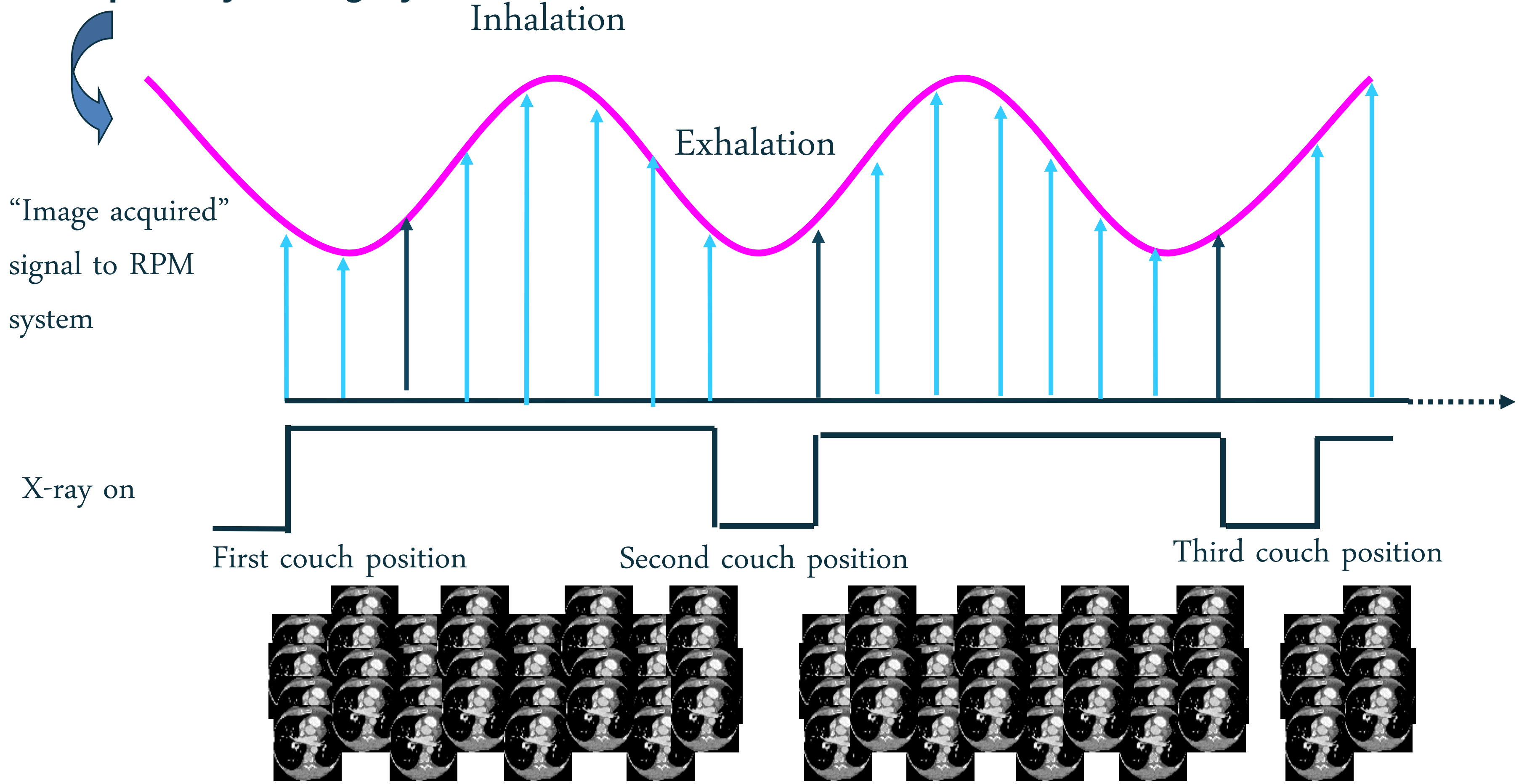
Philips Multi-slice CT Scanners with RPM™ Respiratory Gating





Retrospective 4D CT Image Acquisition - cine mode

Respiration Waveform from RPM Respiratory Gating System



4D CT Image Definitions

Helical CT: Helical CT without 4D CT. Snap shot of the anatomy.

MIP (Maximum Intensity Projection image) : Reflect the highest data (**hyper-dense**) value encountered along the viewing ray for each pixel of volumetric data, giving rise to a full intensity display of the brightest object along each ray on the projection image

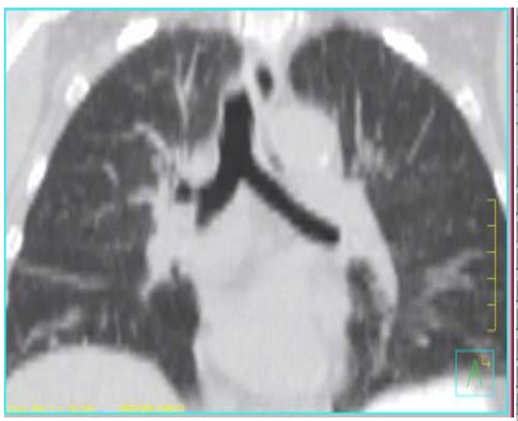
So if you are interested in identifying high contrast objects (lung tumor, stents etc..) better to have a MIP

4D CT Image Definitions

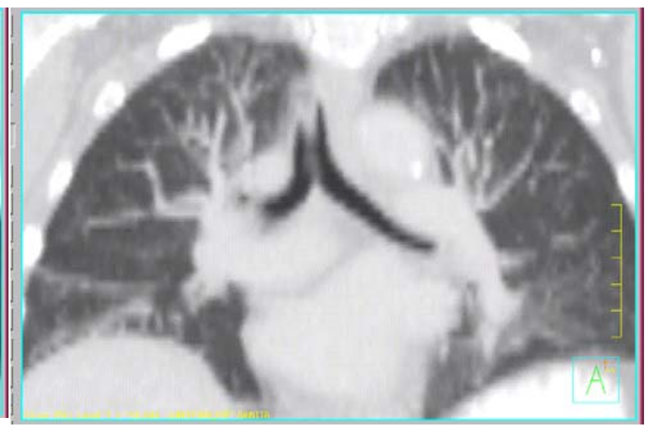
MinIP (Minimum Intensity Projection image): projections reflect the lowest data (**hypo-dense**) value encountered along the viewing ray for each pixel of volumetric data.

So if you are interested in identifying low contrast objects (liver, pancreas etc..) better to have a MinIP

4D CT Image Definitions



Helical



MIP

MinIP

4DCT imaging studies: References

Nakamura M, Narita Y, Sawada A, et al. Impact of motion velocity on four-dimensional target volumes: A phantom study. Med Phys 2009;36:1610–1617.

Abdelnour AF, Nehmeh SA, Pan T, et al. Phase and amplitude binning for 4D-CT imaging. Phys Med Biol 2007;52:3515–3529.

Biederer J, Dinkel J, Remmert G, et al. 4D-imaging of the lung: Reproducibility of lesion size and displacement on helical CT, MRI, and cone beam CT in a ventilated ex vivo system. Int J Radiat Oncol Biol Phys 2009;73:919–926.

Sources of Error in 4DCT

Irregular patient breathing – regular and reproducible breathing by coaching
CT image reconstruction algorithm
Resorting of reconstructed CT images with respiratory signal (phase/amplitude or combination of two)

Mismatch of respiratory phase between adjacent couch positions

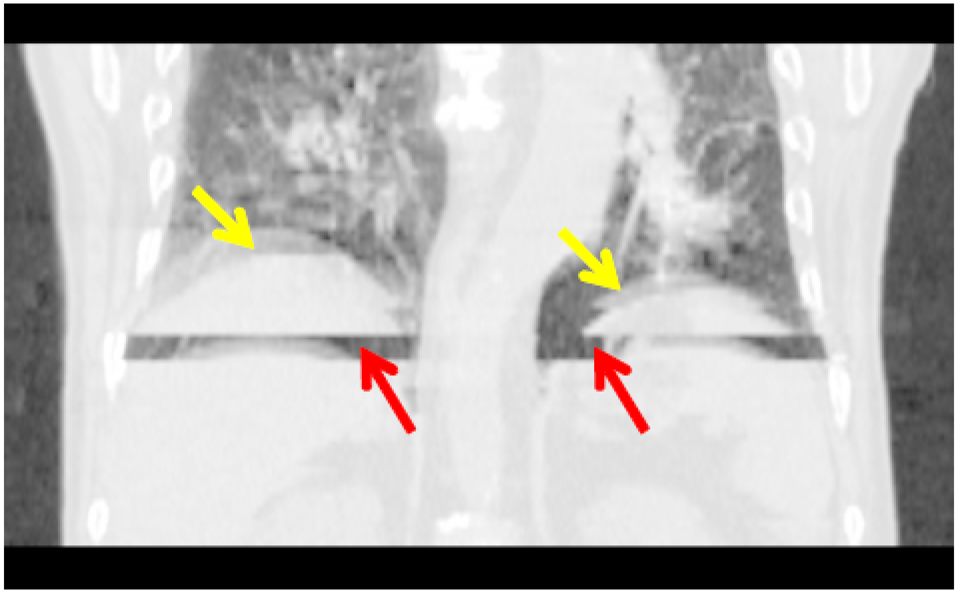


FIG. 1. Examples of misalignment artifacts and motion-blurring artifacts. Upper arrows show misalignment artifacts resulting from mismatches in respiratory phase between adjacent couch positions. The diaphragm is imaged as two disconnected parts. Lower arrows show motion-blurring artifacts. The edges of the diaphragm become blurred due to poor temporal resolution of the CT scanner to the velocity of the diaphragm.

Nakamura M, Narita Y, Sawada A, et al. "Impact of motion velocity on four-dimensional target volumes: A phantom study", Med Phys;36:1610–1617; 2009

Amplitude binning is better than phase binning

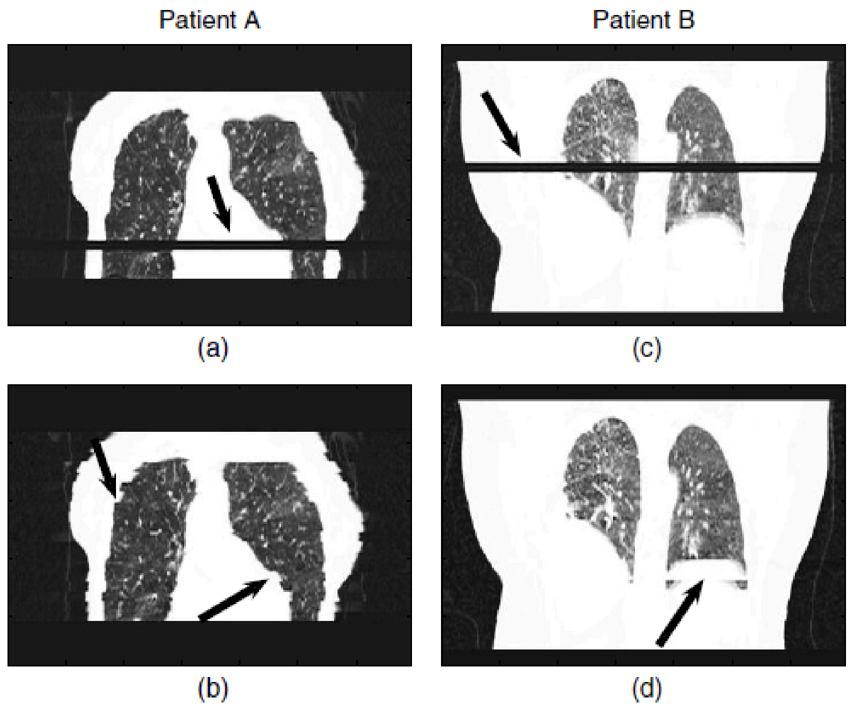
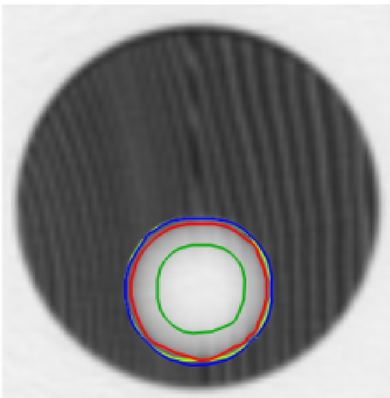


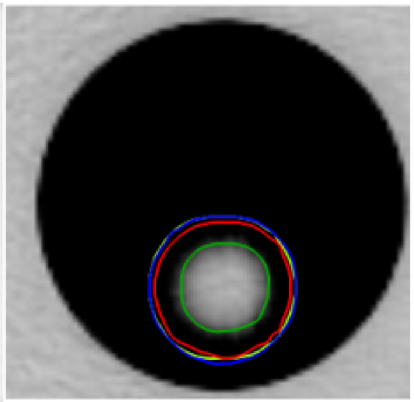
Figure 12. Coronal lung images for patient A (figures 12(a) and (b)) at bin 35% ± 5%, and patient B (figures 12(c) and (d)) at bin 65% ± 5%. Top images show a case of amplitude binning, while the bottom images show phase binning at the same respective bins. Note the missing slices near the bottom of figure 12(a) and the middle of figure 12(c). While the top images are smooth and have no visible artifacts (except for missing slices), the phase binned image 12(b) exhibits artifacts on the chest wall and along the torso. The diaphragm of figure 12(d) suffers anomalies where the arrow is pointing.

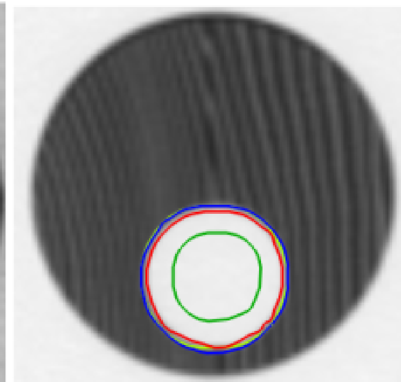
Abdelnour AF, Nehmeh SA, Pan T, et al. Phase and amplitude binning for 4D-CT imaging. Phys Med Biol 2007;52:3515– 3529.

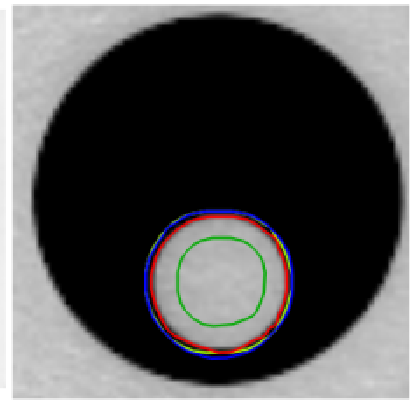
W/L Matters

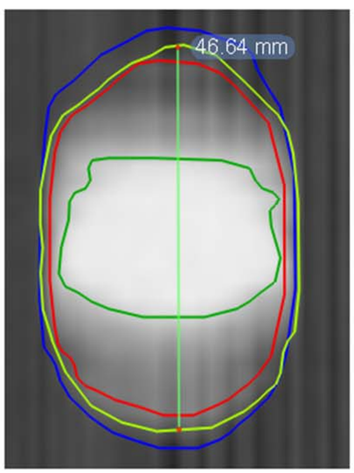
4 contours: yellow is untagged_LW, green is untagged_MW, blue is fullmip_LW, red is fullmip_MW


Untagged_LW

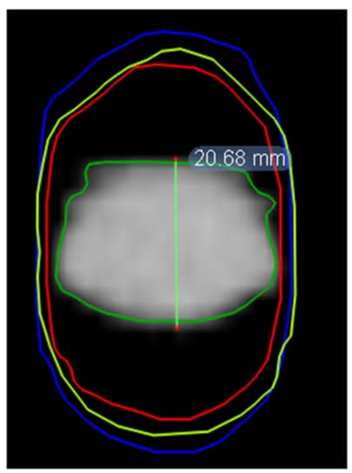

Untagged_MW


FullMIP_LW

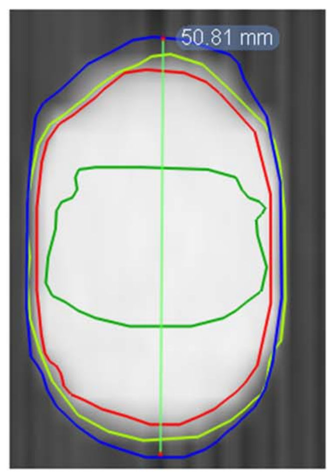

FullMIP_MW



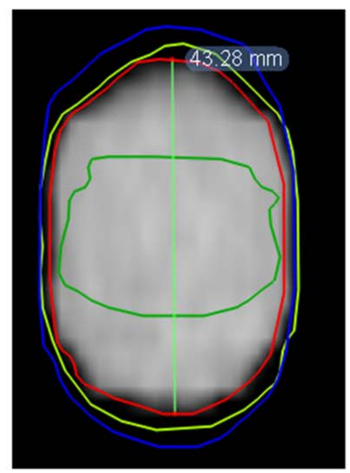
Untagged_LW



Untagged_MW

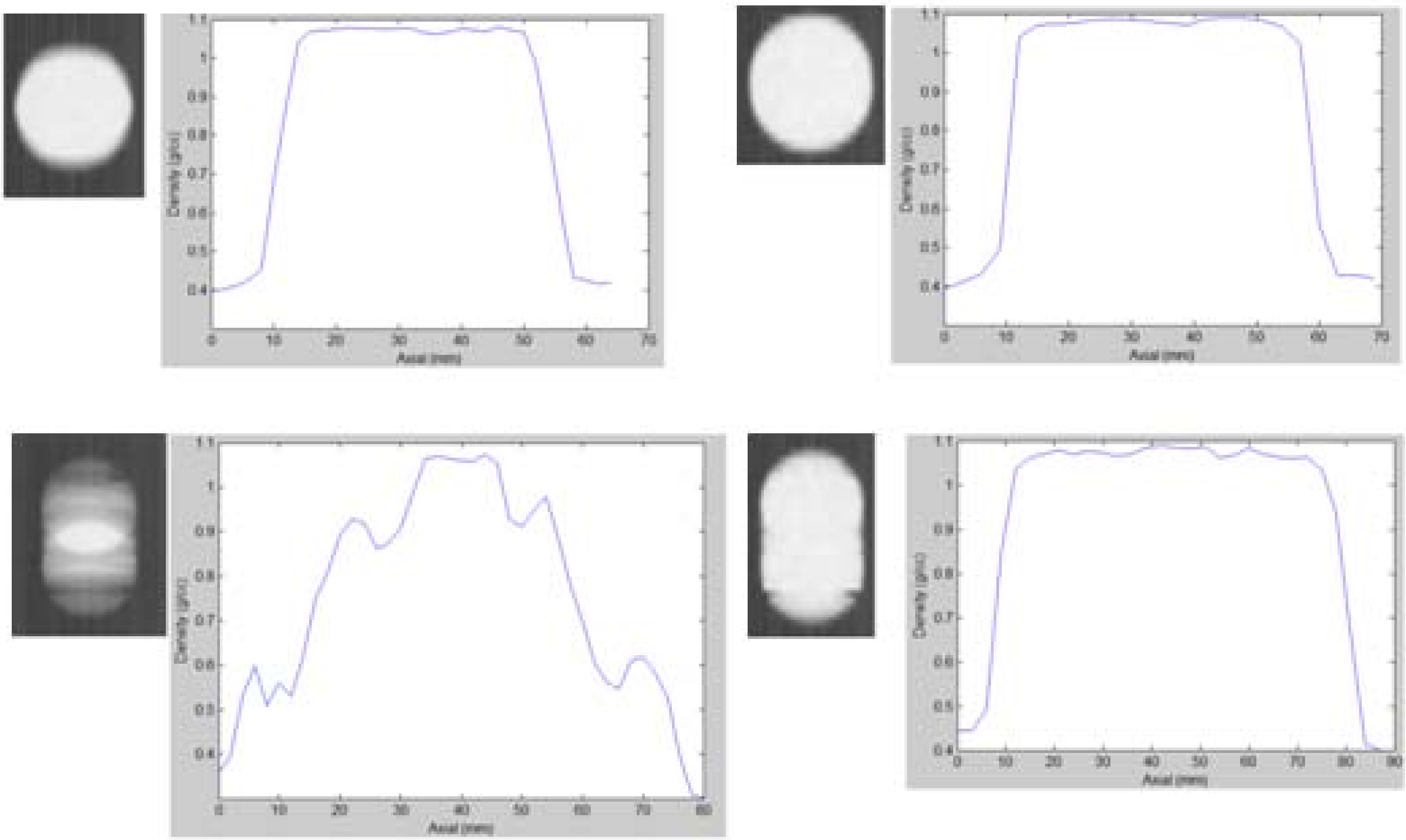


FullMIP_LW

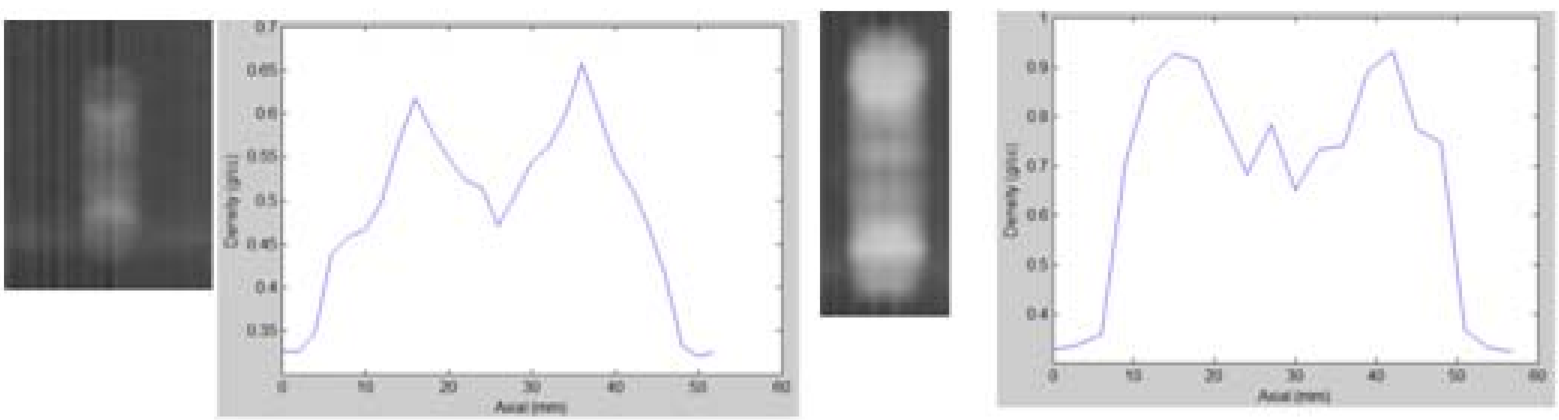


FullMIP_MW

Effects of motion amplitude and tumor diameter

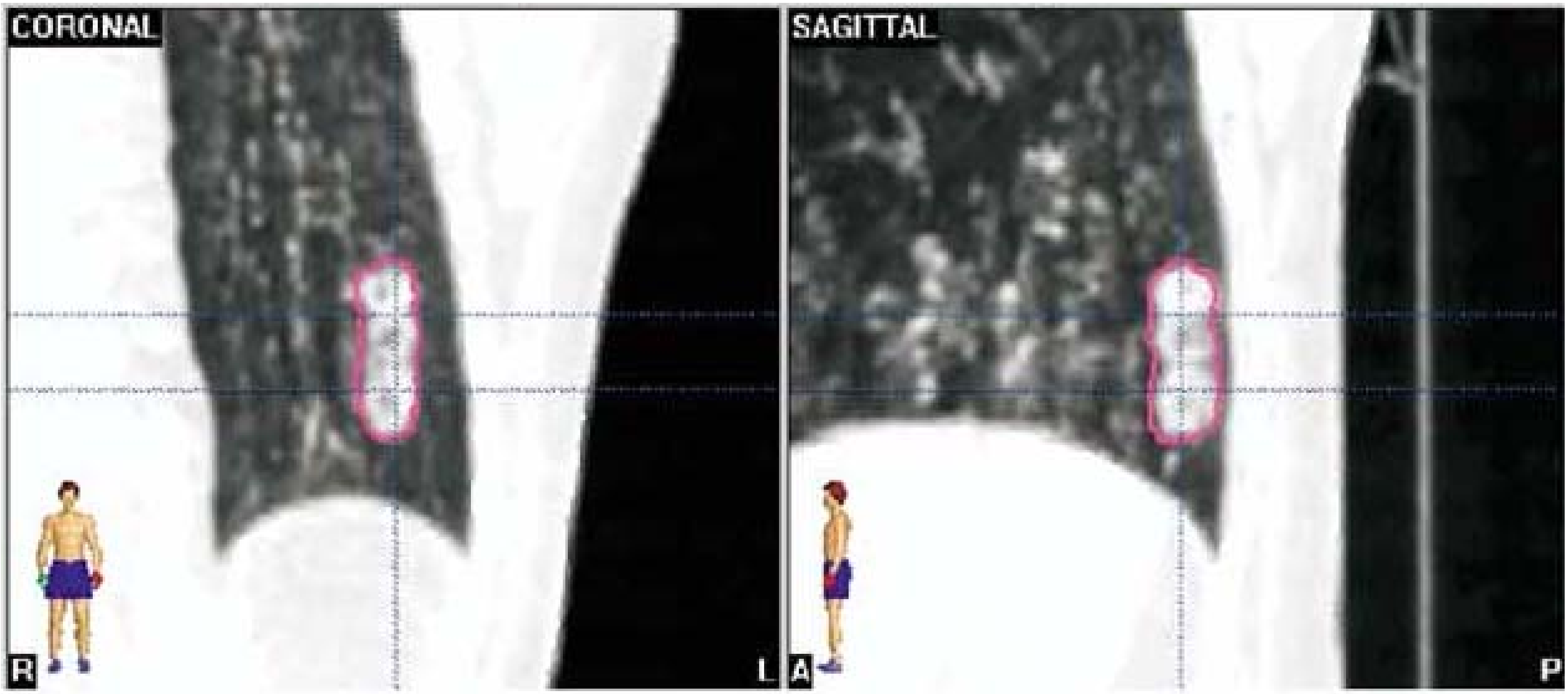


Effects of motion amplitude and tumor diameter



Very small tumors 5cc or less, with large motion amplitudes >1.5cm, due to sampling resolution will show discrete volumes even in FULL_MIP in mediastinum window.

Maximum intensity projection of a highly mobile tumor

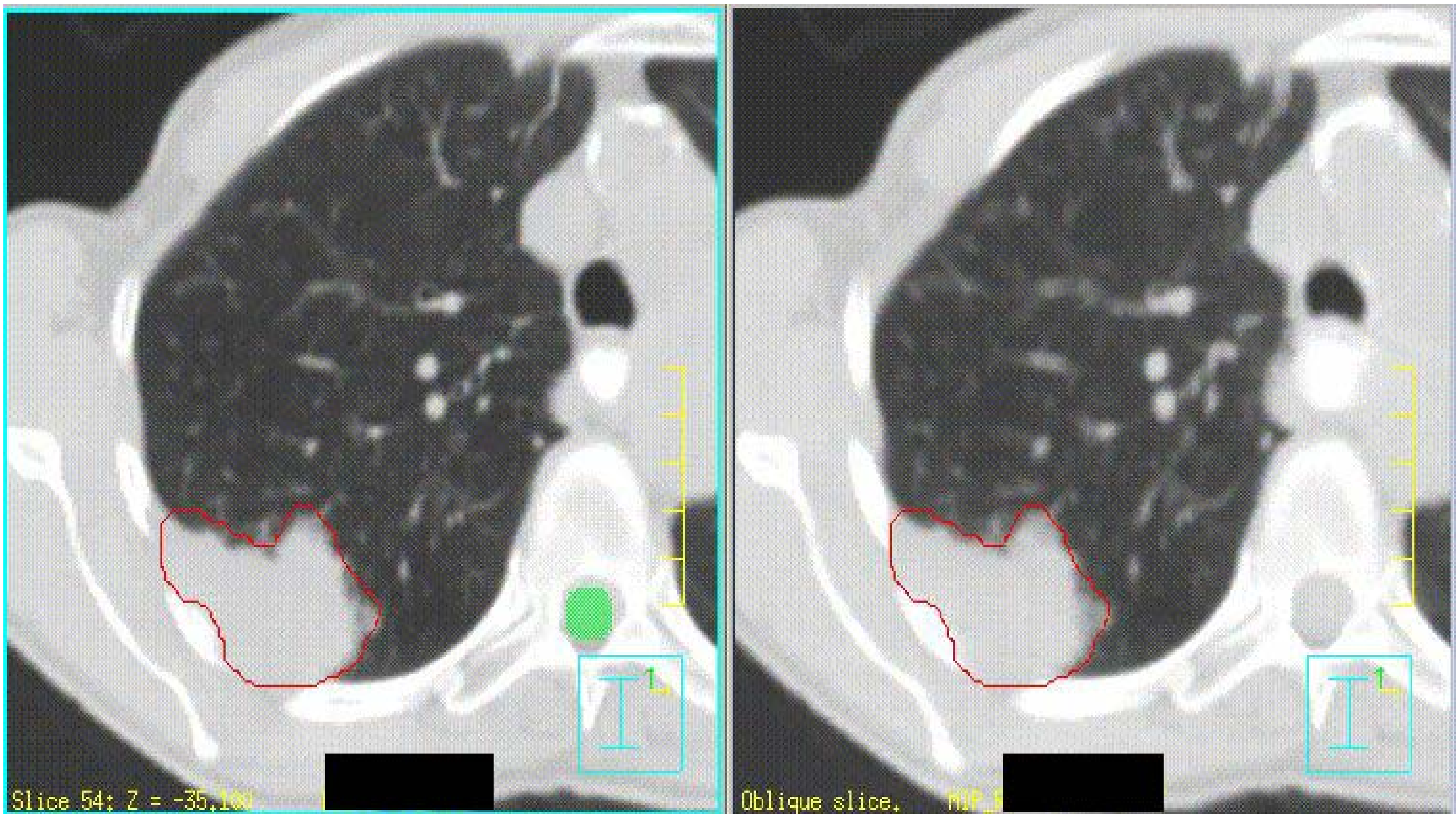


Underberg RWM et al IJROBP 2005; 63:253-260

MIPs can be problematic

- Drawback for target delineation: where background and tumor have similar HU, tumor is not as clearly defined
- Example: Caudal extent of ITV may not be correct due to overlap with diaphragm
- Review individual phases
- For this case, send additional scans, e.g. max inhale and max exhale scans to help MD assess tumor motion

Tumors adjacent to CW – Helpful to review phases



Tumor adjacent to diaphragm

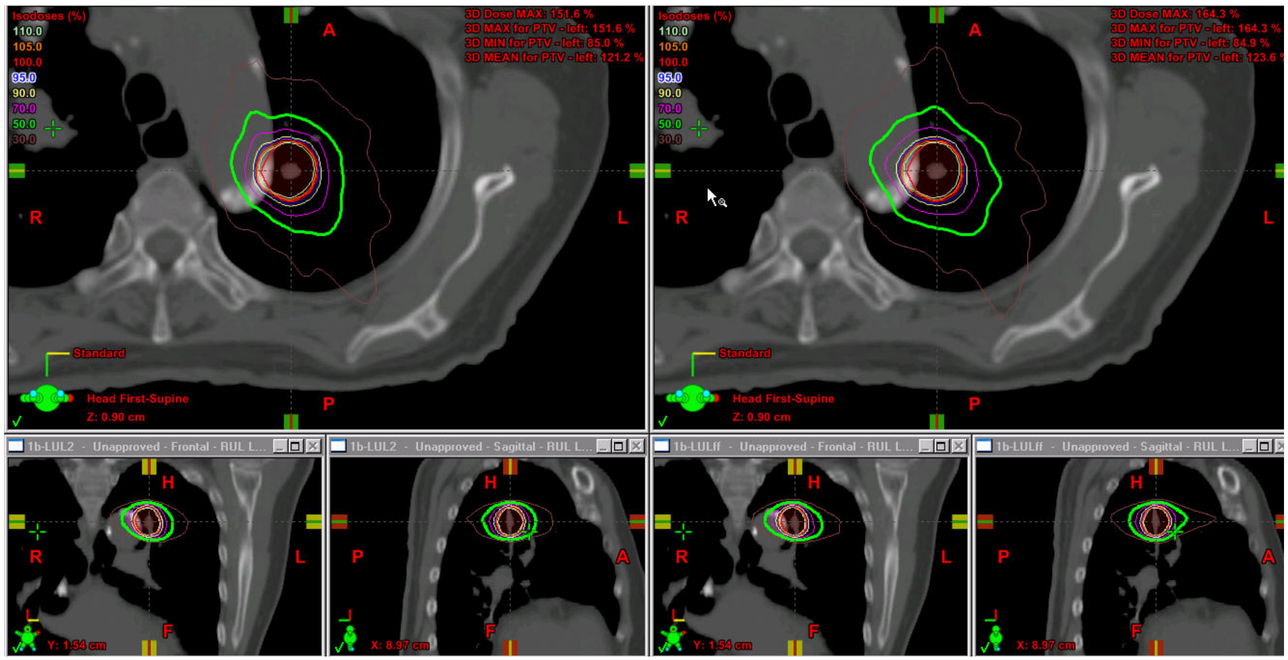
(a) (b) (c)

Underberg RWM et al IJROBP 2005; 63:253-260

UVA planning for lung

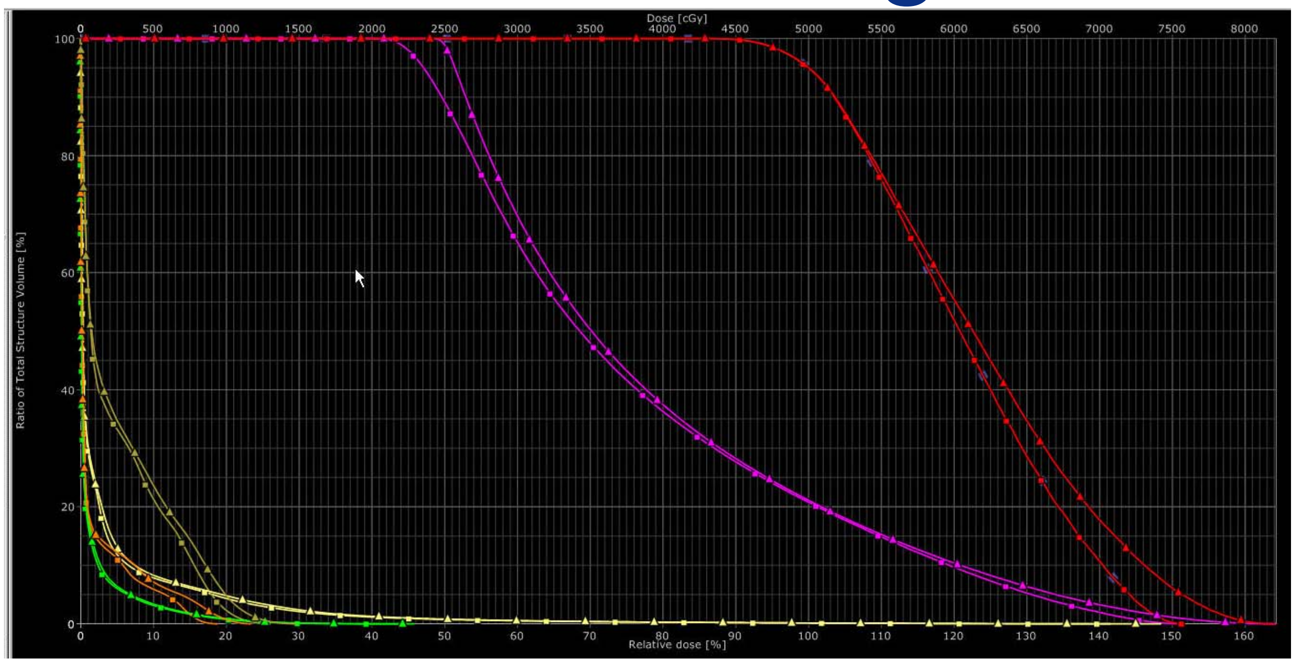
- Scan the full thorax/abdomen
- Obtain the 10 phased 4D CT image sets
- Reconstruct a MIP image Using the 10 4D CT image sets – if treat with no gating
- Reconstruct a MIP image Using the gated window (eg:30% -70%)4D CT image sets – if treat with gating
- Plan on average intensity image with ITV defined from MIP/PET images

FFF VMAT for lung SBRT



Left – FFF; Right –FF. Notice the better conformity of the 50% isodose (green) line in FFF beams in all three dimensions.

FFF VMAT for lung SBRT



FFF beams(in squares) and FF beams (in triangles). PTV – red, 50% prescription isodose – pink, dose distribution beyond 2cm from PTV – green, cord – orange, esophagus – khaki, and total lung –GTV – yellow. Notice that in all cases, FFF beams give a lower out of field dose to different extent when both plans are normalized to cover 95% of PTV to receive the prescription dose

FFF VMAT for lung SBRT

Parameter	Mean	STD	Mean	STD	*p*-value
	Percentage difference		Absolute difference		
Prescription Isodose Surface Coverage:					
% PTV covered by 100% Rx dose:	-0.01%	0.04%	-0.01	0.03	0.330
% PTV covered by 90% Rx dose:	0.00%	0.05%	0.00	0.05	0.834
Target Dose Heterogeneity:					
MAX point dose (Gy):	-0.31%	2.09%	-0.27	1.83	0.520
High Dose Spillage:					
Location: 105% volume/PTV volume	-0.09%	0.17%	-0.01	0.03	0.028
Volume: Rx isodoe volume/PTV volume	-0.98%	1.67%	-0.01	0.02	0.017
Low Dose Spillage:					
Max dose > 2.0 cm from PTV:	-0.81%	2.97%	-0.47	1.71	0.237
Volume: 50% Rx isodose volume/PTV volume	-3.01%	3.33%	-0.13	0.14	0.001
Lung Constraints (Parallel Tissue)					
V20.0 Gy (cc)	-2.38%	3.08%	-3.48	6.74	0.032
V12.4 Gy (cc)	-2.27%	1.73%	-7.05	9.42	0.003
V11.6 Gy (cc)	-2.26%	1.44%	-6.85	7.59	0.001
Integral Dose (Gy.L)					
Normal tissue	-2.21%	2.00%	-0.76	0.84	0.001
Ipsilateral lung	-2.43%	1.46%	-0.26	0.21	0.000

Table 3. Mean and standard deviation for conformality criteria, lung doses, and integral doses as a percentage difference and as absolute difference for patients of RTOG 0915 (peripheral tumors).

0915 Reductions with FFF

- Reductions (mean, STD, *p*-value, maximum) are:
- High dose spillage location (-0.09%, 0.17%, 0.028, -0.57%)
- High dose spillage volume (-0.98%, 1.67%, 0.017, **-6.1%)**
- Low dose spillage volume (-3.01%, 3.33%, 0.001, **-11.59%)**
- V20 (2.38%, 3.08%, 0.032, **-8.77%)**
- V12.4 (2.27%, 1.73%, 0.003, **-4.99%)**
- V11.6 (2.26%, 1.44, 0.001, **5.00%**)

FFF VMAT for lung SBRT

Parameter	Mean	STD	Mean	STD	*p*-value
	Percentage difference		Absolute difference		
Prescription Isodose Surface Coverage:					
% PTV covered by 100% Rx dose:	0.00%	0.00%	0.00	0.00	na
% PTV covered by 90% Rx dose:	-0.10%	0.33%	-0.10	0.34	0.352
Target Dose Heterogeneity:					
Point dose @ iso center (Gy):	-0.04%	0.02%	0.01	1.32	0.980
High Dose Spillage:					
Location: 105% volume/PTV volume	-0.11%	0.22%	-0.02	0.03	0.150
Volume: Rx isodoe volume/PTV volume	-0.74%	1.40%	-0.01	0.02	0.131
Low Dose Spillage:					
Max dose > 2.0 cm from PTV:	-0.16%	4.89%	0.23	1.81	0.684
Volume: 50% Rx isodose volume/PTV volume	-3.27%	3.87%	-0.15	0.19	0.026
Lung Constraints (Parallel Tissue)					
V20.0 Gy	-3.63%	2.97%	-4.20	3.51	0.004
V13.5 Gy	-4.47%	4.48%	-10.01	13.96	0.041
V12.5 Gy	-4.29%	4.51%	-11.34	16.29	0.046
Integral Dose (Gy.L)					
Normal tissue	-2.08%	1.87%	-0.57	0.49	0.005
Ipsilateral lung	-2.57%	1.74%	-0.25	0.20	0.004

Table 5. Mean and standard deviation for conformality criteria, lung doses, and integral doses as a percentage difference and as absolute difference for patients of RTOG 0813 (central tumors).

0813 Reductions with FFF

- Reductions (mean, STD, *p*-value, maximum) are:
- Low dose spillage volume (-3.27%, 3.87%, 0.026, **-11.23%)**
- V20 (3.63%, 2.97%, 0.004, **9.88%**)
- V13.5 (4.47%, 4.48%, 0.04, **12.77%**)
- V12.5 (4.29, 4.51, 0.04, **11.75%**).

1. What type of image/images should be used for tumor volume delineation when the lung tumor is attached to the diaphragm?

- 9% 1. Maximum intensity projection image (MIP)
- 80% 2. MIP image and the phase images of inhalation phases
- 6% 3. Time average (untagged) image
- 0% 4. 3DCT image with no time information
- 5% 5. Minimum intensity projection image

- Answer: 2
- References: Underberg RWM et al IJROBP 2005; 63:253-260

What dataset should be chosen for planning?

- Dose computation should be close to cumulative 4D dose computed using all datasets
  - Rosu M, Balter JM, Chetty IJ, Kessler ML, McShan DL, Balter P, et al. How extensive of a 4D dataset is needed to estimate cumulative dose distribution plan evaluation metrics in conformal lung therapy? Med Phys 2007;34:233–45.
- Anatomy of this image set should correlate well with the tumor image of pre-treatment image (CBCT/MVCT)
- Average intensity image should be used for planning

2. What is the optimum dataset for dose calculation of a lung Tx?

0%	1.	3DCT image which carries a snap shot of the tumor position
10%	2.	Maximum intensity projection image (MIP)
2%	3.	Minimum intensity projection image (Minip)
88%	4.	Time average (untagged) image
0%	5.	CBCT image

- Answer: 4
- References:

- • MA Admiraal, D.Schuring, CW Hurkmans "Dose calculations accounting for breathing motion in stereotactic lung radiotherapy based on 4D-CT and the internal target volume", Radiotherapy and oncology 86 (2008) 55-60
- • Yuan Tian, Zhiheng Wang, Hong Ge, Tian Zhang, Jing Cai, Christopher Kelsey, David Yoo, Fang-Fang Yin. "Dosimetric Comparison of Treatment Plans Based on Free Breathing, Maximum and Average Intensity Projection CTs for Lung Cancer SBRT." Med Phys 39:2754-2760 (2012)

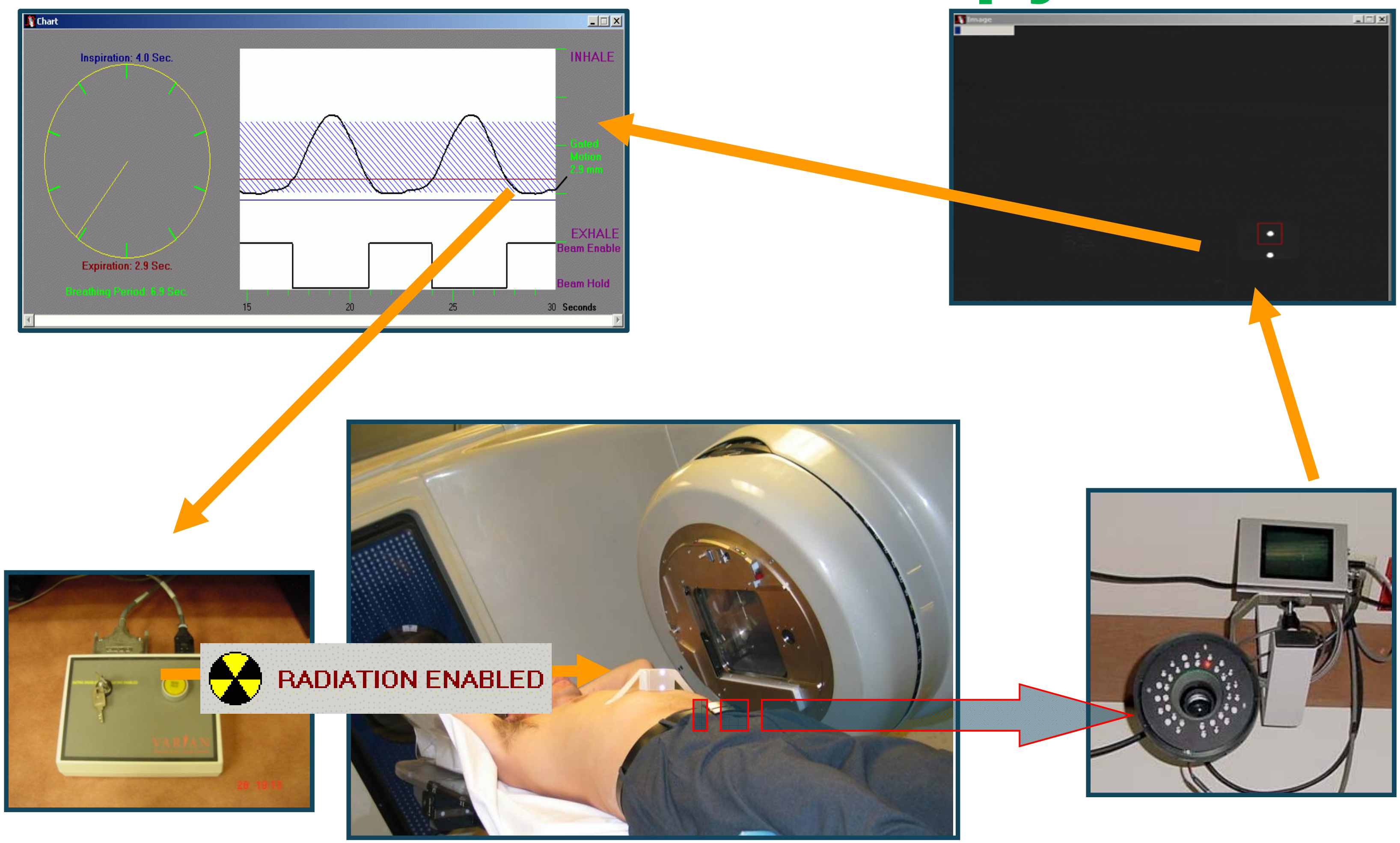
3. Which of the following is accepted as a lung SBRT planning technique?

2%	1. CBCT image is used for ITV definition and dose calculation
0%	2. 3D CT image used for ITV definition
1%	3. 3DCT image used for dose calculation
92%	4. ITV is defined by the MIP image and the time averaged image used for dose calculation
5%	5. ITV is defined by the MINiP image and the time averaged image used for dose calculation

- Answer: 4
- References:

- • Guckenberger M, Wilbert J, Krieger T, et al. Four-dimensional treatment planning for stereotactic body radiotherapy. Int J Radiat Oncol Biol Phys 2007;69:276–85.
- • MA Admiraal, D.Schuring, CW Hurkmans "Dose calculations accounting for breathing motion in stereotactic lung radiotherapy based on 4D-CT and the internal target volume", Radiotherapy and oncology 86 (2008) 55-60
- • Kaus MR, Brock KK, Pekar V, et al. Assessment of a model based deformable image registration approach for radiation therapy planning. Int J Radiat Oncol Biol Phys 2007;68:572–80.

Gated Radiotherapy

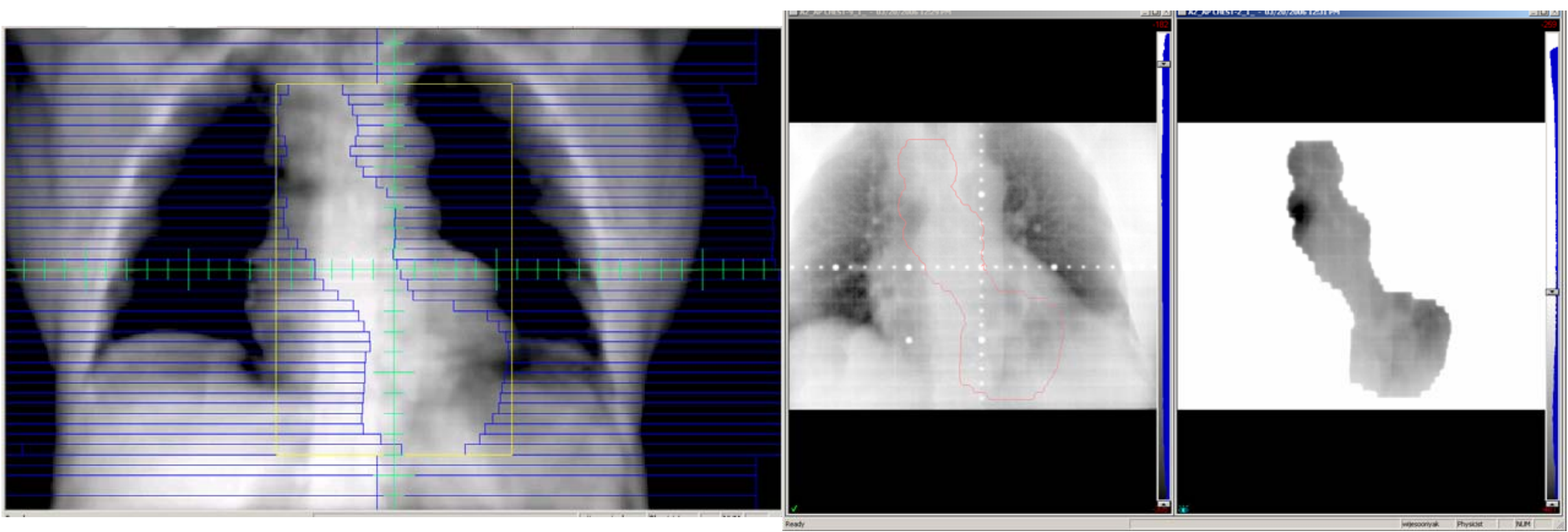


To Ensure an Accurate Externally Gated Treatment, five QA Steps

1. During Simulation, the reference home position should be accurately measured (4DCT)
2. During Tx planning, patient and tumor geometry corresponding to the gating window should be used

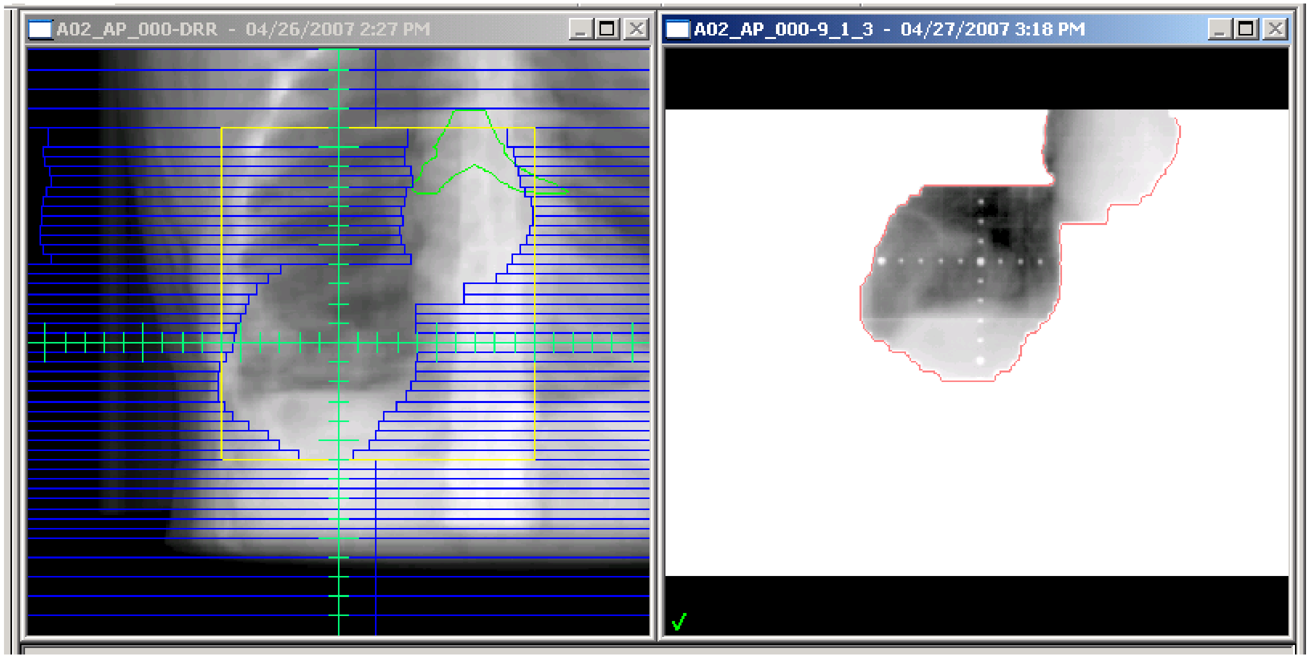
To ensure an Accurate Externally Gated Treatment, five QA steps

3. During patient setup tumor home position at this fractionation should be matched to the reference home position – image guidance (x-ray, Ultrasound, implanted E.M transponders), lung: tumor or diaphragm, liver: implanted fiducial markers



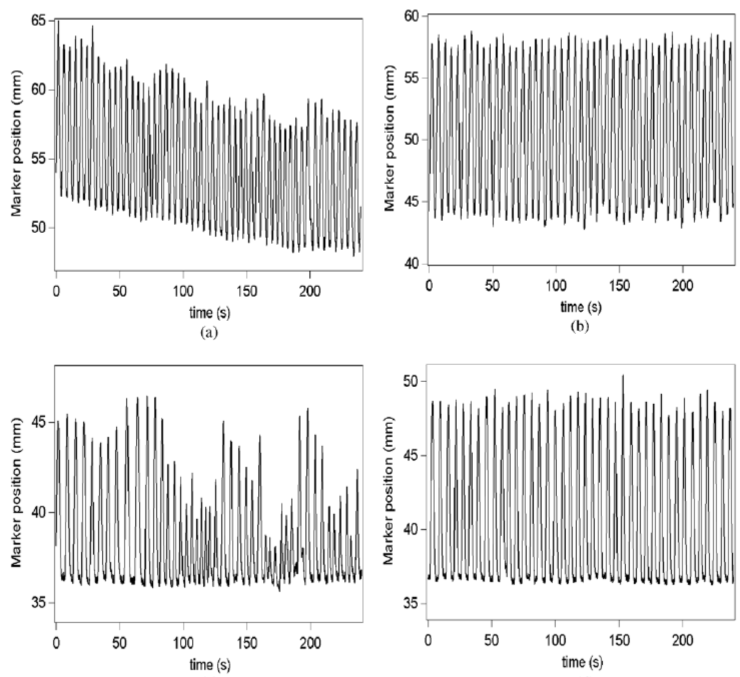
To ensure an Accurate Externally Gated Treatment, five QA steps

3. During patient setup tumor home position at this fractionation should be matched to the reference home position – image guidance (x-ray, Ultrasound, implanted E.M transponders), lung: tumor or diaphragm, liver: implanted fiducial markers – to avoid inter-fraction variation

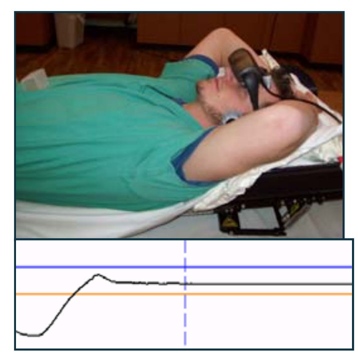


To Ensure an Accurate Externally Gated Treatment, Five QA Steps Continued…

4. During Tx delivery, measures should be taken to ensure constant tumor home position (tumor should be at the same position when the beam is on) breath coaching, visual aids- stable EOE position by two straight lines for amplitude gating



(A), and (c) - free breathing – baseline shift & irregular breathing
(b), and (d) - audio-visual coaching



Neicu T, Berbeco R, Wolfgang J et al. “synchronized moving aperture radiation therapy (SMART): improvement of breathing pattern reproducibility using respiratory coaching”, Phys Med Biol 51: 617-636, 2006.

To Ensure an Accurate Externally Gated Treatment, Five QA Steps Continued…

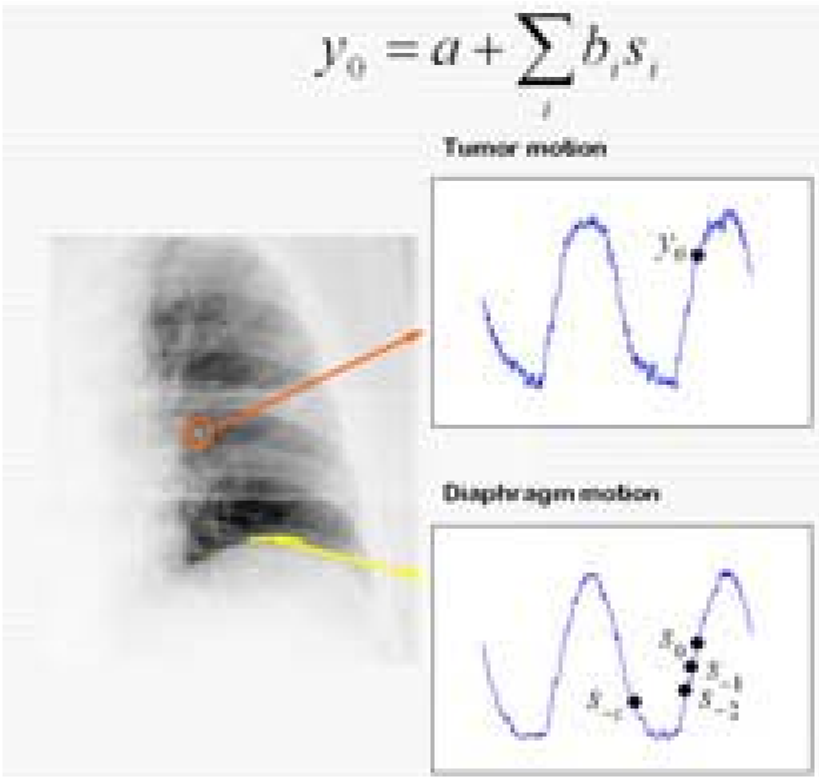
5. During Tx delivery, tumor positions corresponding to the gating window should be measured and compared with the reference home position, either on or offline. EPID in cine mode for small patients and non-IMRTs (Ref: berbeco RI, Neicu T, Rietzel E et al. “A technique for respiratory-gated radiotherapy treatment verification with an EPID in cine mode”, Phys Med Biol 50:3669-3679 2005), OBI KV images for others

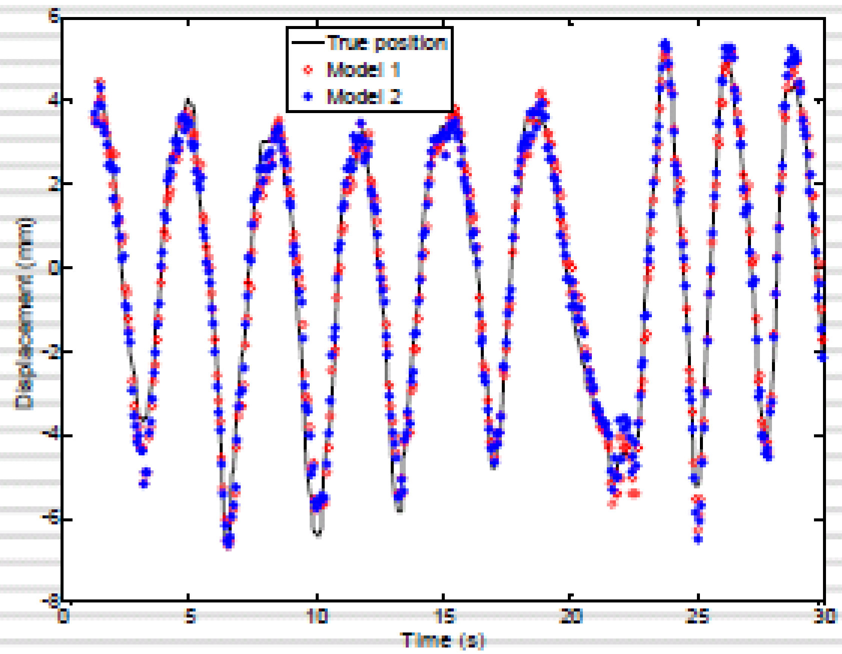
How to ensure treatment accuracy when internal target position is predicted using external surrogates

Surrogates used to generate gating signals

1. External surrogates: markers placed on the patients outside surface
   1. Varian RPM system
   2. Active breathing control using spirometery
   3. Siemens Anzai pressure belt: bellows system
   4. Medspira respiratory monitoring bellows system

Diaphragm as an internal surrogate





Mean error ~ 1 mm

Maximum error (e95) ~ 2 mm

Cervino et al. Phys Med Biol 54(11):3529-3541, 2009

Three Phases of 4D QA

- Typical QA measures
- Initial testing of equipment and clinical procedures: CT scanner, fluoroscope, linac, gating…..
- Frequent QA examination during early stage on implementation

Keall PJ, Mageras GS, Balter JM, etal. The management of respiratory motion in radiation oncology report of AAPM TG 76, Med Phys; 33:3874-3900 2006

Jiang S., Wolfgang J, Mageras GS " Quality assurance challenges for motion-adaptive radiation therapy: gating, breath holding, and four-dimensional computed tomography", IJROBP 71(1):S103-S107 2008

4DCT scan QA

Hurkmans, CW, vanLieshout,M. et al. "Quality assurance of 4DC scan techniques in multicenter phase III trial of surgery versus stereotactic radiotherapy non-small-cell lung cancer [ROSEL] study, IJROBP 80(3), 918-927, (2011)

- 9 centers, 8 Philips, siemens,GE CT scanners, 1 Siemens PET-CT scaner
- Widely varying imaging protocols
- No strong correlation found between specific scan protocol parameters and observed results
- Average MIP volume deviations 1.9% (φ15, R =15mm), and 12.3% (φ15,R =25mm) , -0.9% (φ30, R =15)
- End expiration volume deviations – 13.4%, φ15; 2.5%, φ30
- End inspiration volume deviations – 20.7%, φ15; 4.5%, φ30
- Mid ventilation volume deviations – 32.6%, φ15; 8.0%, φ30
- Variation in mid-ventilation origin position – mean, -0.2mm; range -3.6-4.2
- Variation in MIP origin position – mean, -0.1mm; range, -2.5 -2.5
- Range motion is underestimated – mean, -1.5mm; range, -5.5-1

Future of 4D QA

- Extend the QA to measure/evaluate 4D dose delivery:
  - Estimate from 4D planning
  - Perform phantom measurements
  - Evaluate actual 4D dose delivery

Some publications on interplay

Yu Cx, Jaffray DA, Wong JW, “Effects of intra-fraction motion on the delivery of dynamic intensity modulation”, Phys Med Biol. 1998, 43(1):91-104.

Bortfeld T., “Effects of intra-fraction motion on IMRT dose delivery: statistical analysis and simulation”, Phys Med Biol 47: 2203-2220, 2002.

Engelsman M, Damen EM, De Jaeger K, van Ingen KM, Mijnheer, BJ, “ The effects of breathing and set-up errors on the cumulative dose to a lung tumor”, Radiotherapy Oncol., 60(1):95-105, 2001.

Chui CS, Yorke, E, Hong L, “The effects of intra-fraction organ motion on the delivery of intensity-modulated field with a multileaf collimator”, Med Phys 30(7): 1736-46 2003.

Duan J, Shen S., Fiveash JB, Popple RA, Brezovich IA, “Dosimetric and radiobiological impact of dose fractionation on respiratory motion induced IMRT delivery errors: a volumetric dose measurement study”, Med Phys 34(3):923-34, 2007

Seco J, Sharp GC, Turcotte J, Gierga D, Bortfeld T, paganetti H. “ Effects of organ motion on IMRT traetments with segments of few monitor units”, Med Phys. 37 5850 2010.

Summary | Conclusion

1. Motion envelope should be measured prior to ITV definition
2. Particular care should be given to tumors attached to chest wall/diaphragm
3. Planning CT should be a time averaged CT image
4. Gated image reference position should be verified prior to Tx
5. End to end QA program should be established prior to going clinical

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