Lung SBRT
4D simulation, Planning, and QA

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Learning Objectives

- To understand the physiological characteristics of tumor motion in different treatment sites.
- To understand what data set to employ for ITV definition and dose calculation
- To understand the available technology for planning in SBRT
- To understand the importance in performing and End to end QA for any new motion management system introduced into a clinical program

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Motivation

- SBRT, if misdirected or used too liberally, could lead to debilitating toxicity
- Lung SBRT due to motion complicates the situation
- Capture the 4th dimension accurately
- Deliver the intended plan dose to the tumor
- Minimize healthy tissue toxicity -> escalate dose to tumor

Safety Margins

Measurements of tumor motion

- Lung tumors: ***Liu HH et al IJROBP 2007; 68: 531-540 – 152 patients***
  - Up to 3cm inferior motion
  - 95% of lung tumors move <1.3cm I/S, <0.4cm L/R, and <0.6cm A/P
  - Tumor motion is highly correlated with diaphragm motion and tumor location in S/I
- Abdominal tumors: ***Bradner GS et al IJROBP 2006; 65: 554-560 – 13 patients***
  - Up to 2.5cm inferiorly for all tumors, motion up to 1.2 cm A/P observed for liver and kidneys
  - Mean S/I displacements: Liver 1.3cm; Spleen 1.3 cm; Kidneys 1.2cm

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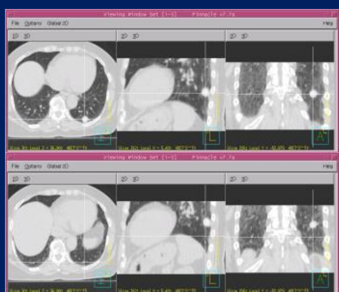
GTV motion inhale vs. exhale



Inhalation

Exhalation

2.5 cm displacement in cranio-caudal direction

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GTV motion with time

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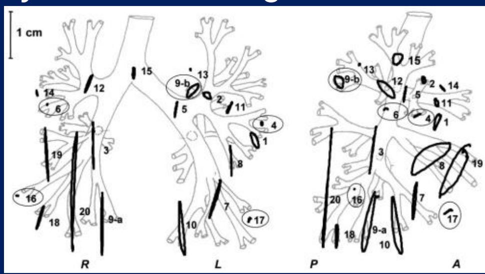
Hysteresis of lung tumor motion



1- 5mm hysteresis of breathing trajectories measured

Seppenwoolde Y. et al. "Precise and real-time measurement of 3D tumor motion in lung due to breathing and heartbeat measured during radiotherapy" IJROBP 2002; 53:822-834

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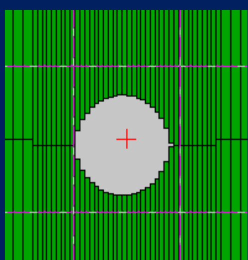
Ideally what we want to do (IGRT)



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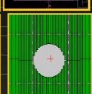
Gold Standard
4D Radiotherapy

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	

Courtesy of Paul Keall

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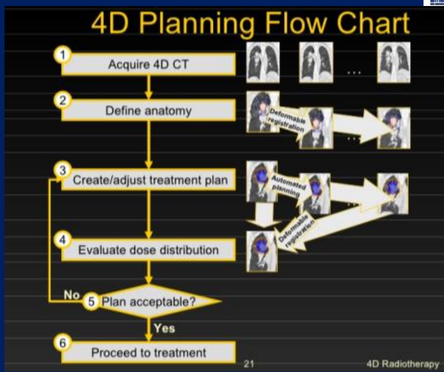
4D Planning Flow Chart



Courtesy of Paul Keall

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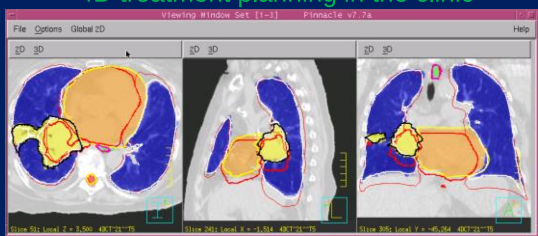
4D treatment planning in the clinic



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).

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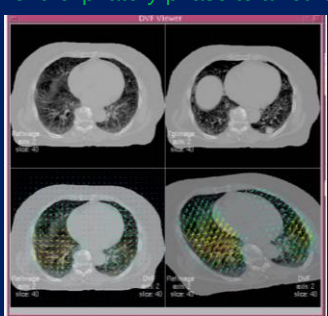
DVF to warp dose distributions to propagate them from end expiratory phase to all other phases



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

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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

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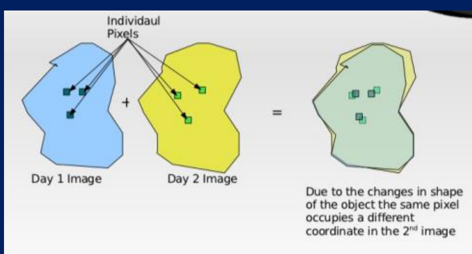

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4D Radiotherapy is still clinically prohibitive

- 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…

- Computing resource intensive – Parallel calculations require **computer clusters** at present
- No **commercial** TPS allows 4 D dose calculation
- Respiratory motion is **unpredictable** – calculated dose good for a certain pattern only
- 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

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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

Accounting for respiratory motion at simulation

- Respiratory correlated CT/4DCT
  - Cine CT – couch stationary while repeat CT for images acquired corresponding to different phases of respiratory cycle, couch incremented
  - *Low D. et al. Med Phys. 2003; 30:1254-1263*
  - *Pan T. et al. Med Phys. 2004; 31: 333-340*
  - Helical CT – reducing the pitch 0.5-0.1, and adjusting CT parameters such that CT beam on for at least on respiratory cycle at each couch position.
  - *Keall P J. et al. Phys. Med. Biol. 2004; 49:2053-2067*
  - *Pan T. et al. Med Phys. 2005; 32: 627-634*

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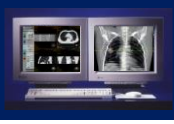
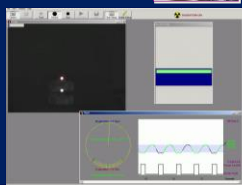
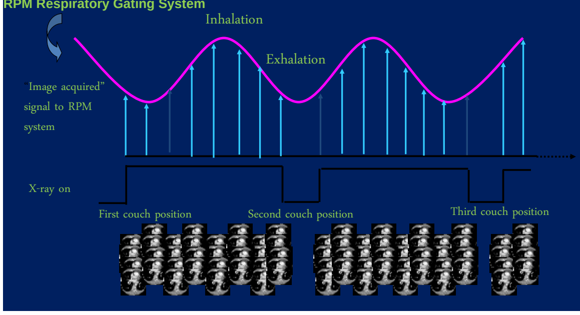
Philips Multi-slice CT Scanners with RPM^{TM} Respiratory Gating





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

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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

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4D CT Image Definitions

Helical MIP MinIP

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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)

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Mismatch of respiratory phase between adjacent couch positions

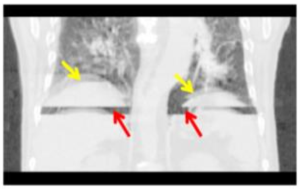

FIG. 1. Examples of misalignment artifacts and motion-blurring artifacts. Upper arrows show misalignment artifacts resulting from mismatches in respiratory phase between adjacent couch positions. The diaphragm is imaged as two disconnected parts. Lower arrows show motion-blurring artifacts. The edges 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

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Amplitude binning is better than phase binning

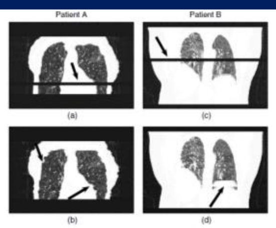

Figure 12. Coronal lung images for patient A (figures 12(a) and (b)) at bin 35% ± 5%, and patient B (figures 12(c) and (d)) at bin 65% ± 5%. Top images show a case of amplitude binning, while the bottom images show phase binning at the same respective bins. Note the missing slices near the bottom of 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.

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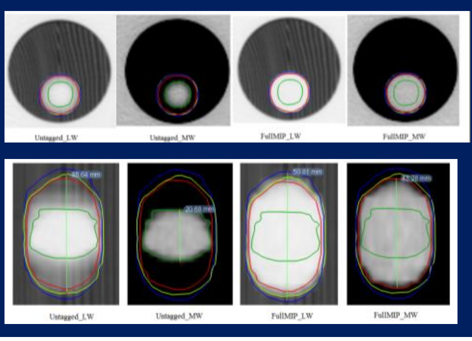
W/L Matters



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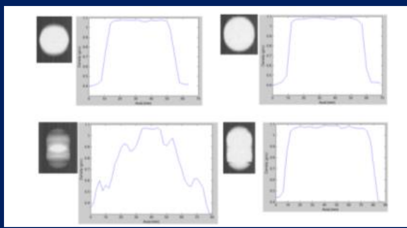
Effects of motion amplitude and tumor diameter



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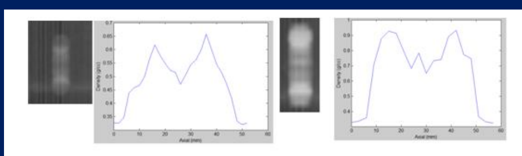
Effects of motion amplitude and tumor diameter



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

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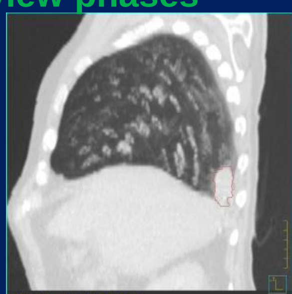
MIPs can be problematic Helpful to review phases

- 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



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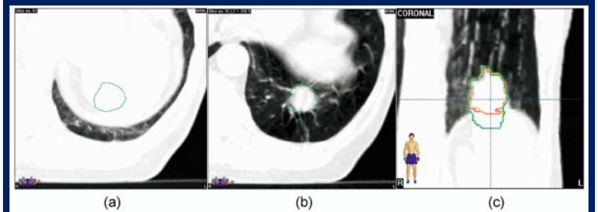
Tumor adjacent to diaphragm



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

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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

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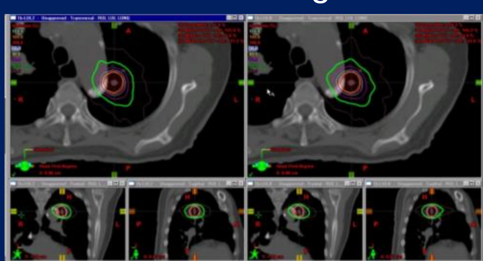
FFF VMAT for lung SBRT



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

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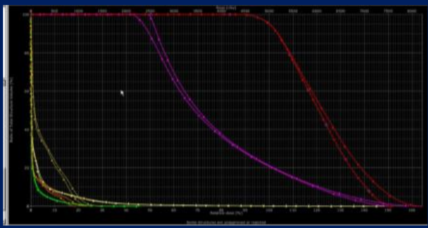
FFF VMAT for lung SBRT



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

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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).

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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%**)

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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).

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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%).

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

- 7% 1. Maximum intensity projection image (MIP)
- 20% 2. MIP image and the phase images of inhalation phases
- 10% 3. Time average (untagged) image
- 30% 4. 3DCT image with no time information
- 27% 5. Minimum intensity projection image

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

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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

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

10%	1. 3DCT image which carries a snap shot of the tumor position
7%	2. Maximum intensity projection image (MIP)
23%	3. Minimum intensity projection image (Minip)
30%	4. Time average (untagged) image
20%	5. CBCT image

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- 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)

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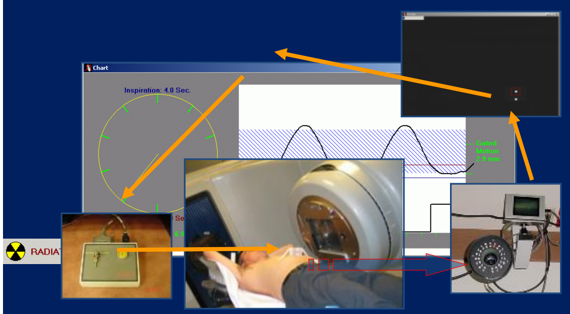
Gated Radiotherapy



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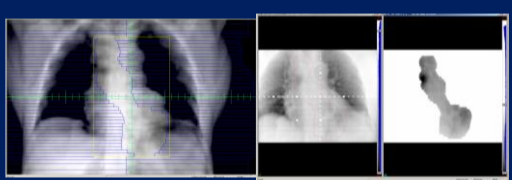
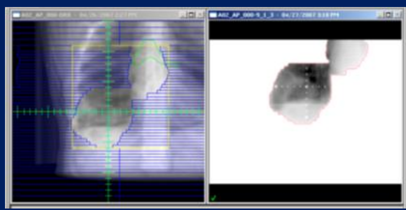
To ensure an Accurate Externally Gated Treatment, QA steps

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



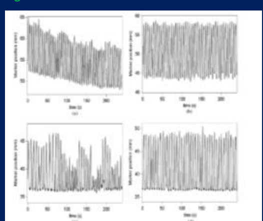
To ensure an Accurate Externally Gated Treatment, QA steps

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

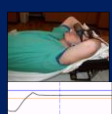


To Ensure an Accurate Externally Gated Treatment, QA Steps Continued…

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.

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

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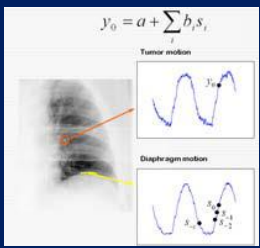
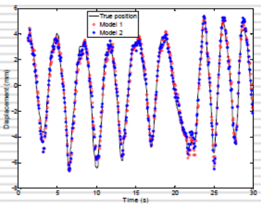
Diaphragm as an internal surrogate





Mean error ~ 1 mm

Maximum error (e95) ~ 2 mm

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

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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

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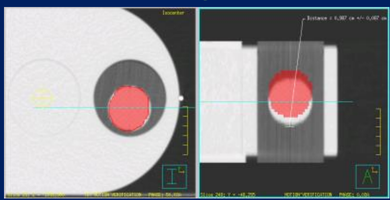
4DCT scan QA

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

Annual QA – 4DCT



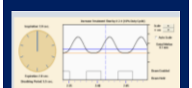
Measurement Setup:
Set the motion range 10 mm –SI of Quasar phantom and image using 4DCT (slice thickness: 0.2 cm) synchronized with RPM.

9.87 mm (0.13 mm deviation)

Annual QA – Treatment with gating

Annual QA – Temporal accuracy of phase/amplitude gating TG 142

	period	gating time (s)	diff (ms)
motion phantom	5.4	2.48	
imaging		2.55	-60
RPM		2.50	20



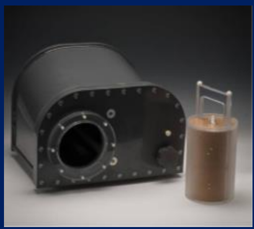
TG-142 tolerance: 100 ms of expected

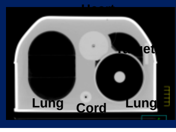
Measurement Setup:
Using OmniPro IMRT software, set 20 ms/ frame (50Hz) and measure the images synchronized with RPM measurement.
RPM signal has a time resolution 33ms/frame (30 Hz)

Annual QA – Treatment with gating TG 142

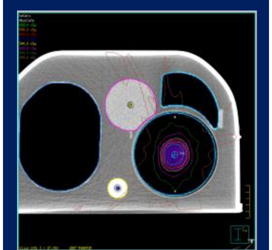
Depth Measured	Beam Energy	Electrometer Readings	Average Reading	Corrected Readings	Nominal Value	Percent Difference	Percent Difference with gating
Cube (5.0cm)	6 MV	17.54 17.54	17.54	18.02	17.71	1.8	
Cube (10.0cm)	Energy Reading	13.15	'Ratio =	0.750	0.753	-0.4	
Cube (5.0cm)	15 MV	19.31 19.30	19.31	19.83	19.56	1.4	
Cube (10.0cm)	Energy Reading	15.40	Ratio =	0.798	0.799	-0.2	
Cube (5.0cm)	6 MV **Gating**	17.55 17.54	17.55	18.03	17.71	1.8	output 0.0 energy
Cube (10.0cm)	Energy Reading	13.16	'Ratio =	0.750	0.753	-0.4	0.0
Cube (5.0cm)	15 MV **Gating**	19.28 19.30	19.29	19.82	19.56	1.3	output 0.1 energy
Cube (10.0cm)	Energy Reading	15.42	Ratio =	0.799	0.799	0.0	-0.2

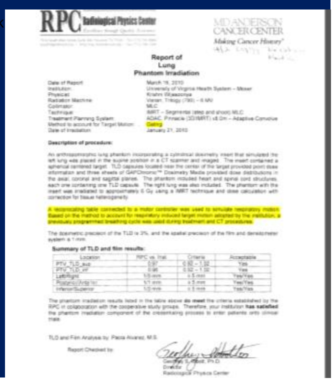
RPC Lung Phantom





RPC Lung Motion Phantom Benchmark





RPC Radiological Physics Center

MD ANDERSON CANCER CENTER
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Report of Lung Phantom Irradiation

Date of Report:	March 19, 2010
Institution:	University of Virginia Health System – Moser
Physicist:	Krishni Wijesooriya
Radiation Machine:	Varian, Trilogy (790) – 6 MV
Collimator:	MLC
Technique:	IMRT – Segmental (step and shoot) MLC
Treatment Planning System:	ADAC, Pinnacle (3D/IMRT) v8.0m – Adaptive Convolve
Method to account for Target Motion:	Gating
Date of Irradiation:	January 21, 2010

Description of procedure:

An anthropomorphic lung phantom incorporating a cylindrical dosimetry insert that simulated the left lung was placed in the supine position in a CT scanner and imaged. The insert contained a spherical centered target. TLD capsules located near the center of the target provided point dose information and three sheets of GAFChromic™ Dosimetry Media provided dose distributions in the axial, coronal and sagittal planes. The phantom included heart and spinal cord structures, each one containing one TLD capsule. The right lung was also included. The phantom with the insert was irradiated to approximately 6 Gy using a IMRT technique and dose calculation with correction for tissue heterogeneity.

A reciprocating table connected to a motor controller was used to simulate respiratory motion. Based on the method to account for respiratory induced target motion adopted by the institution, a previously programmed breathing cycle was used during treatment and CT procedures.

The dosimetric precision of the TLD is 3%, and the spatial precision of the film and densitometer system is 1 mm.

Summary of TLD and film results:

Location	RPC vs. Inst.	Criteria	Acceptable
PTV_TLD_sup	0.97	0.92 – 1.02	Yes
PTV_TLD_inf	0.96	0.92 – 1.02	Yes
Left/Right	[illegible]	± 5 mm	Yes/Yes
Posterior/Anterior	[illegible]	± 5 mm	Yes/Yes
Inferior/Superior	[illegible]	± 5 mm	Yes/Yes

The phantom irradiation results listed in the table above **do meet** the criteria established by the RPC in collaboration with the cooperative study groups. Therefore, your institution **has satisfied** the phantom irradiation component of the credentialing process to enter patients onto clinical trials.

TLD and Film Analysis by: Paola Alvarez, M.S.

Report Checked by:

Geoffrey S. Ibbott, Ph.D.
Director
Radiological Physics Center

Department of Radiation Oncology

University of Virginia Health System

Prior to establishing a lung SBRT program in your clinic, how do you verify the accuracy of motion management program in your clinic?

- 20% 1. Perform an end to end QA requesting a RPC motion phantom for lung or Quasar motion phantom with lung density material
- 27% 2. Perform end to end QA using your IBA matrixx system
- 27% 3. Perform end to end QA using your Delta4 device
- 13% 4. Perform end to end Qa using your annual scanning system
- 10% 5. Meaure the energy of the machine with and without gating

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Answer: 1

References:

- • TG 101
- • Timmerman R. et al. "Accreditation and quality assurance for radiation therapy oncology group: Multi clinical trials using stereotactic body radiation therapy in lung cancer", Acta oncologica, 45:779-786 (2006)

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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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Acknowledgements

- Thanks to University of Virginia Dept. of Radiation Oncology!