AAPM Spring Clinical Meeting 2015
Treatment Planning Fundamentals: Lung Cancer

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Disclosure

My department receives research support from:

- NIH/NCI
- Varian Medical Systems
- Philips HealthCare

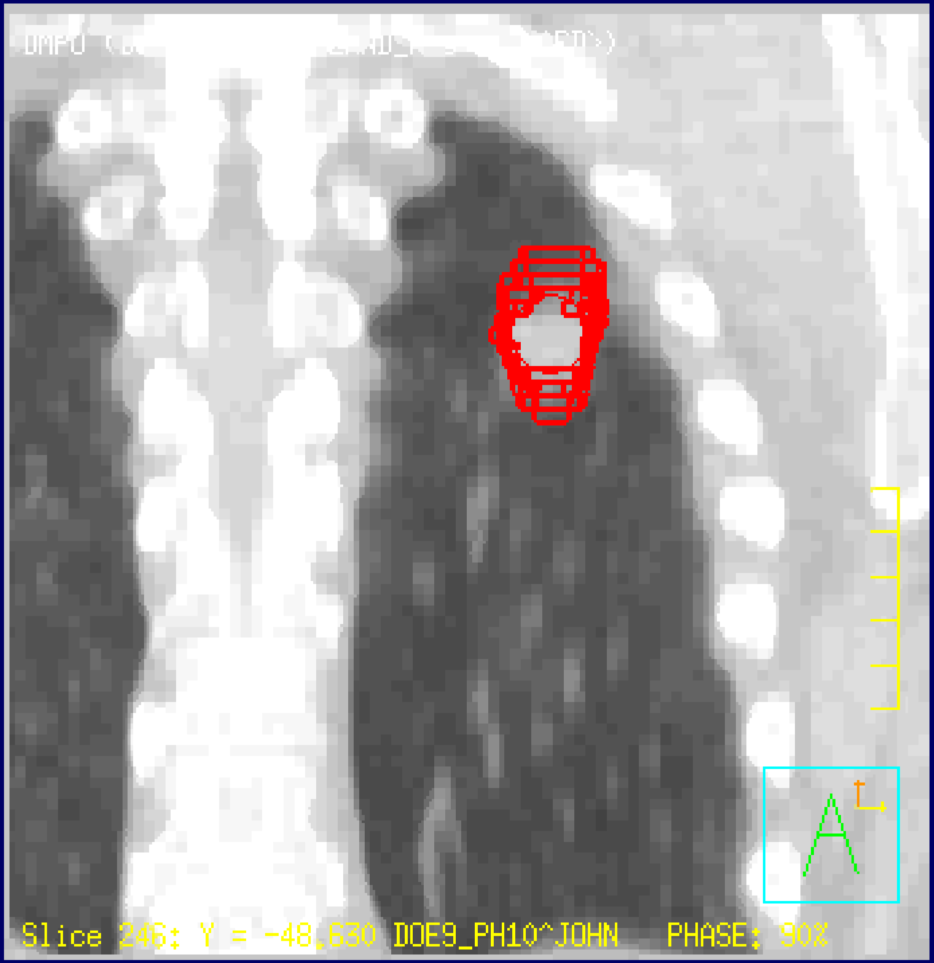
Learning Objectives/Outline

To review the fundamentals of treatment planning for lung tumors, including motion management and margin assessment, planning strategies, the physics of lung dose calculations, and the interplay effect

Managing motion and forming planning margins

Motion Mitigation in Planning: 4D CT

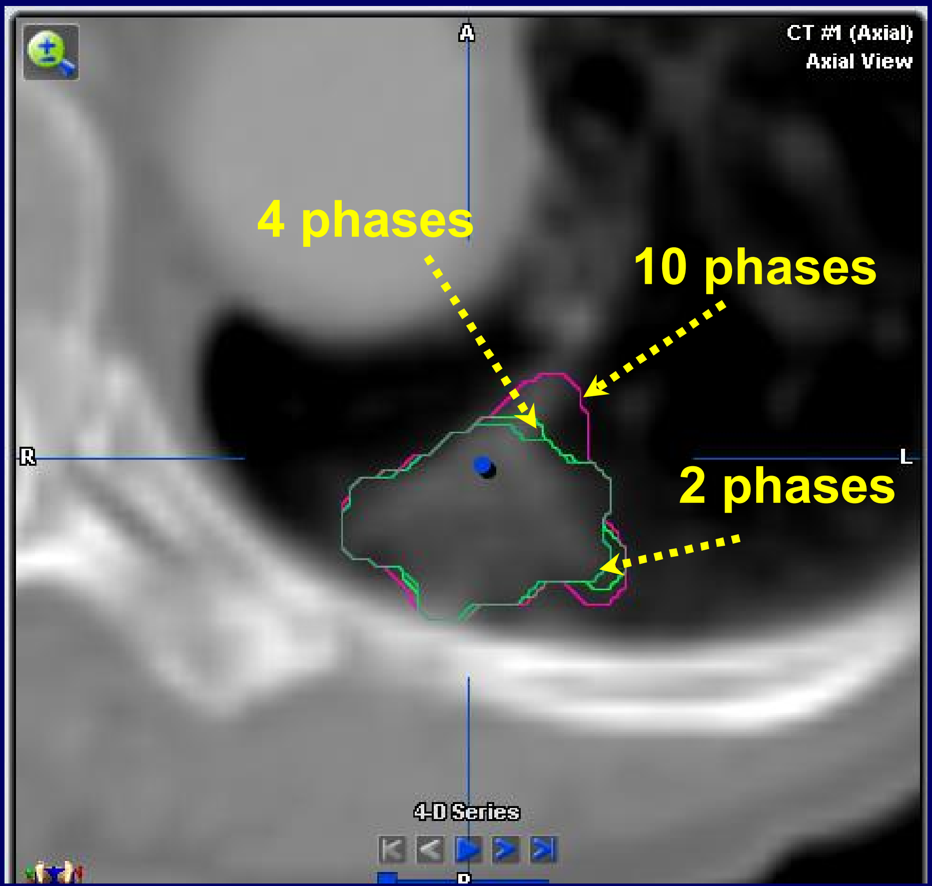
ICRU Report No. 62 – Internal Target Volume (ITV) accounts for variations in size, shape, and position of the CTV *during treatment*



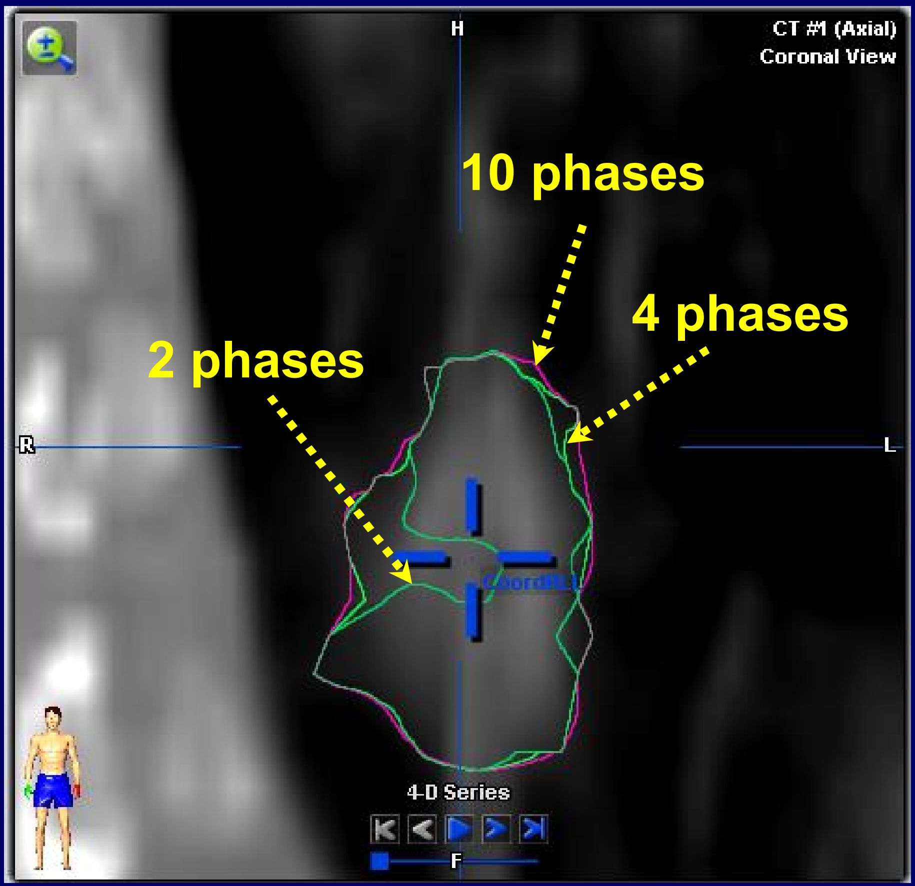
Courtesy:
Carri Glide-Hurst
HFHS

The number of datasets used to create the ITV will impact the planning margin

Axial view



Coronal view



Does abdominal compression help reduce motion?

Heinzerling et al, IJROBP 70(5):1571–1578, 2008

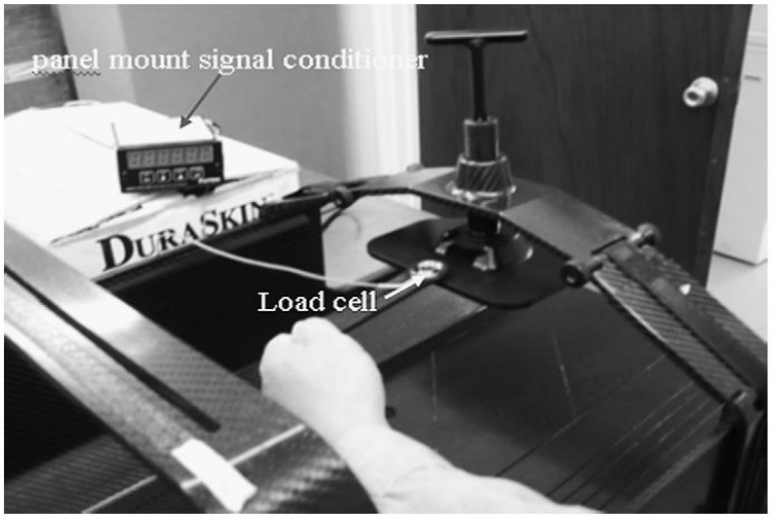


Fig. 1. Stereotactic body radiation therapy frame showing load cell and panel mount signal conditioner.

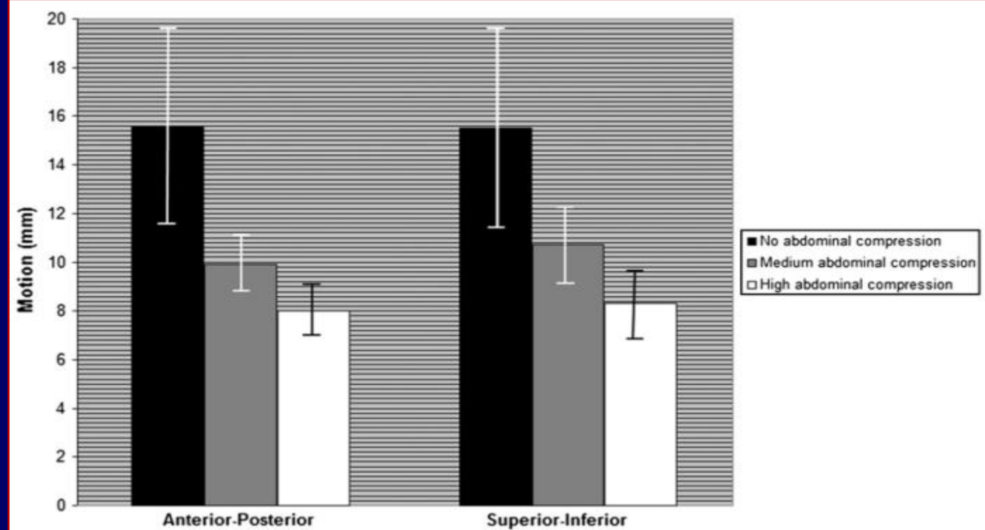


Fig. 3. Motion of diaphragm at varying levels of abdominal compression.

<u>Note</u>: *high compression force* approx 90N, or approx 22 pounds, reduced diaphragm sup-inf motion from approx. 15 mm to 8 mm on average – *S/I motion reduced to less than 1 cm in most cases.*

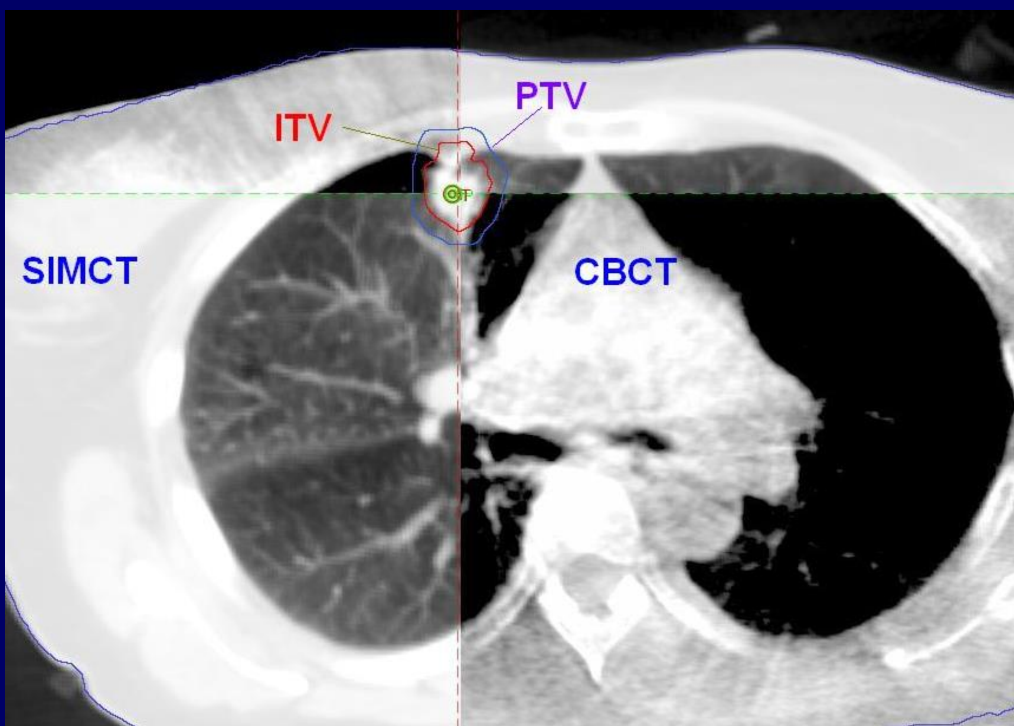
Margins: what is being done in the field?

Institution	*ITV*	*CTV (mm)*	*PTV (mm)*
A	$GTV_1 \cup GTV_2 \cup \ldots GTV_{10}$	ITV + 5	CTV + 5 (IGRT) CTV + 10 (no IGRT)
B	GTV from MIP	ITV	SBRT: ITV + 5 STD Fx: ITV + 10
C	$GTV_1 \cup GTV_2 \cup \ldots GTV_4$	SBRT: ITV STD Fx (no 4D): GTV + 10 STD Fx (4D): ITV + 5	CTV + 6 (IGRT) CTV + 5 (no IGRT) CTV + 10 (no IGRT)
D	GTV from MIP or expected percentiles (gating)	SBRT: ITV STD Fx: ITV + 5	CTV + 5 (IGRT) CTV + 7 (no IGRT)

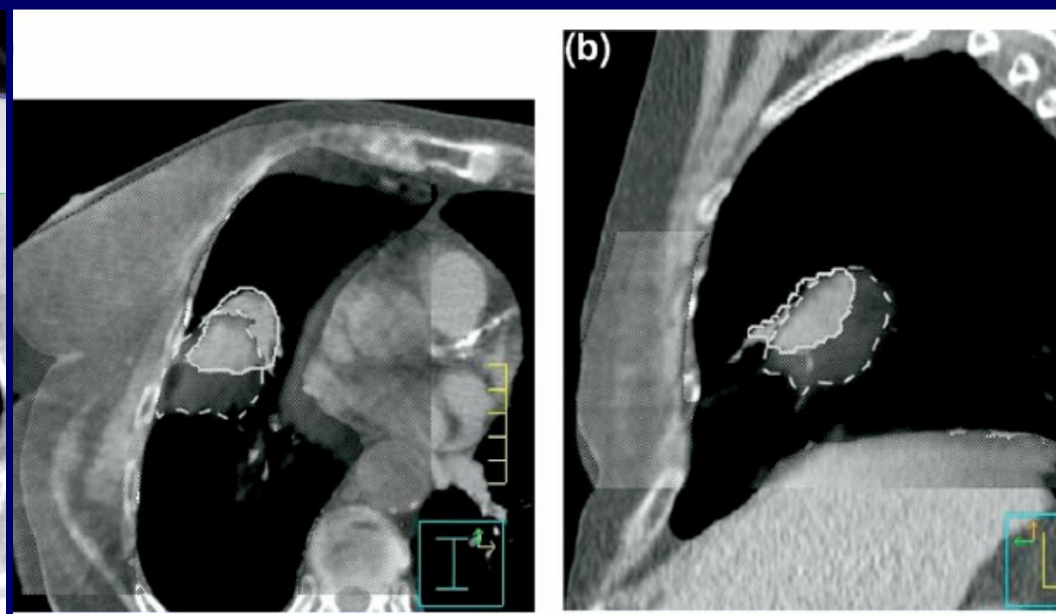
Adapted from “Lung Panel”, Kestin *et al.* ASTRO State of the Art Meeting, 2011

Soft-tissue visualization with CBCT

Planning CT/CBCT alignment



Correction of systematic shifts



Purdie *et al.* (PMH)
Red Journal ’07

Daily CBCT reduces margins for locally advanced lung CA

Less-than-daily CBCT-based IG protocols incurred $\geq$ 5mm residual setup errors in 20–43% of fractions; daily IG reduced this to 6% (n=100) [Higgins *et al.* (PMH) Red Journal, 2011]

Table 5. Population-based setup margins using van Herk margin recipe ($2.5\Sigma + 0.7\sigma$)

	Population-based setup margins (mm)		
Imaging protocol	ML	CC	AP
No IG	6	8	6
First 5-day IG	7	9	6
Weekly IG	5	7	5
Alternate day IG	4	5	5
[redacted]			

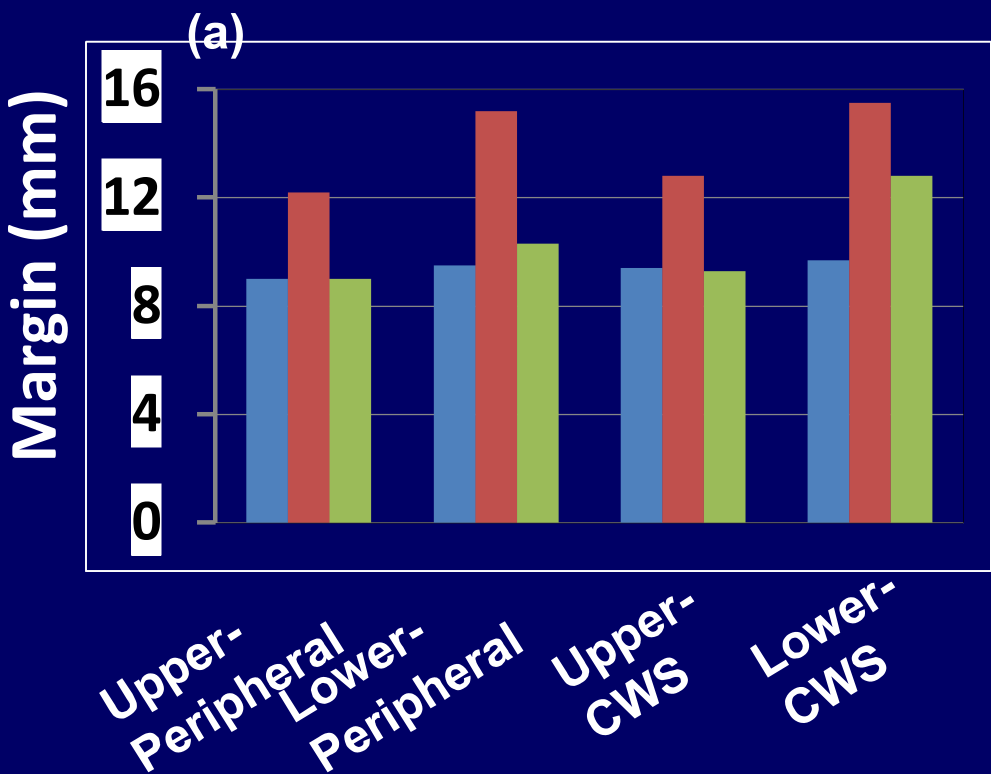
Higgins *et al.* Red Journal, 2011

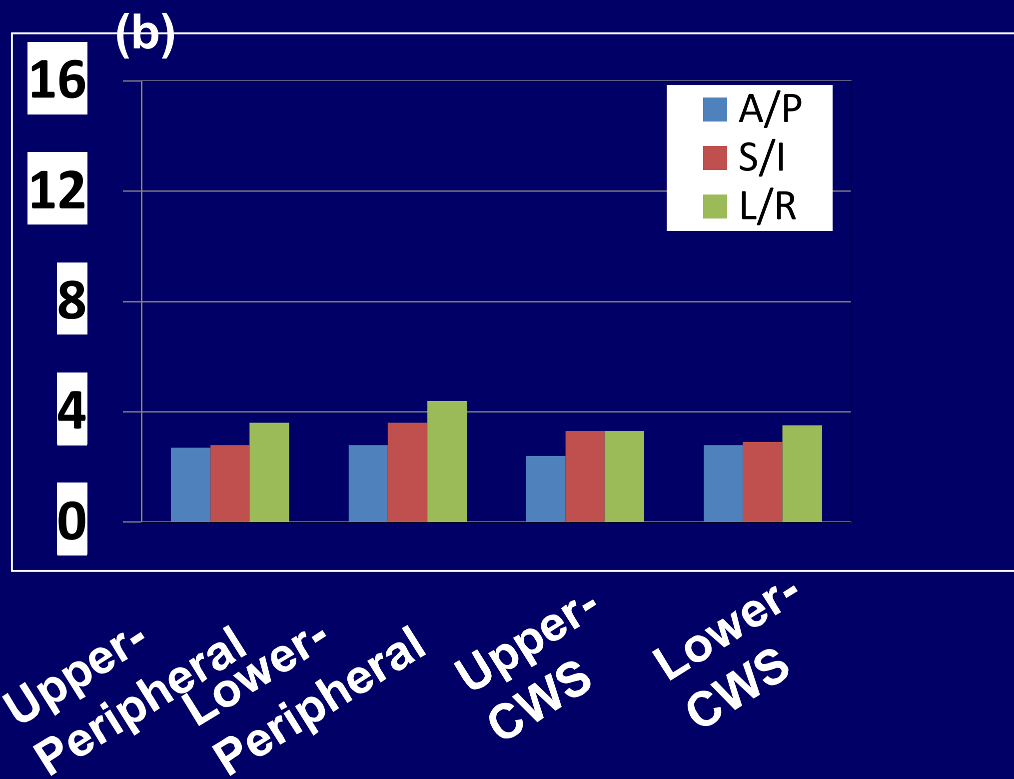
Daily CBCT reduces margins for SABR/SBRT

(a) margins needed if localization was based on the skin tattoos

N = 150

(b) margins needed based on residual errors after CBCT alignment





Courtesy: E. Mayyas, PhD: Henry Ford Hospital

SAM's Question No. 1

1. According to an article by Higgins et al. on the use CBCT imaging for localizing advanced stage lung tumors, which of the following statements is True?

A. With CBCT imaging for only the first 5-days of treatment, margins were reduced to less than 5 mm.
B. With weekly CBCT imaging, margins were reduced to less than 5 mm.
C. With daily CBCT imaging, margins were reduced to less than 5 mm.
D. With alternate day CBCT imaging, margins were reduced to less than 5 mm.
E. With no CBCT imaging margins were less than 3 mm.

SAM's Question No. 1

According to an article by Higgins et al. on the use CBCT imaging for localizing advanced stage lung tumors, which of the following statements is True?

20% 1. With CBCT imaging for only the first 5-days of treatment, margins were reduced to less than 5 mm.

20% 2. With weekly CBCT imaging, margins were reduced to less than 5 mm.

20% 3. With daily CBCT imaging, margins were reduced to less than 5 mm.

20% 4. With alternate day CBCT imaging, margins were reduced to less than 5 mm.

20% 5. With no CBCT imaging margins were less than 3 mm.

SAM's Question No. 1: Answer

Answer: 3 - With daily CBCT imaging, margins were reduced to less than 5 mm.

Ref: Higgins *et al.* "F Effect of Image-Guidance Frequency on Geometric Accuracy and Setup Margins in Radiotherapy for Locally Advanced Lung Cancer", Int J Radiat Oncol Biol Phys: 80:1330ï 1337, 2011.

Planning the Treatment

Lung SBRT planning: General Guidelines

Appropriate planning margins and treatment planning techniques following nationally accepted guidelines e.g. RTOG/NRG 0236, 0813, 0915

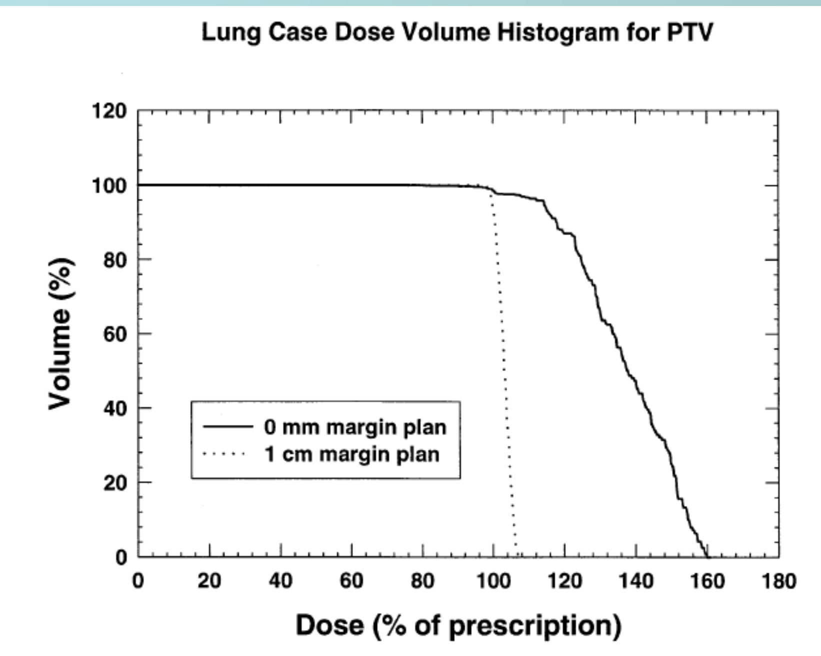
Planning guidelines:

Use as many beams as possible – greater number of beams results in better target dose conformity and dose fall-off away from the target. Typically use 7 or more beams. More beams = less skin toxicity

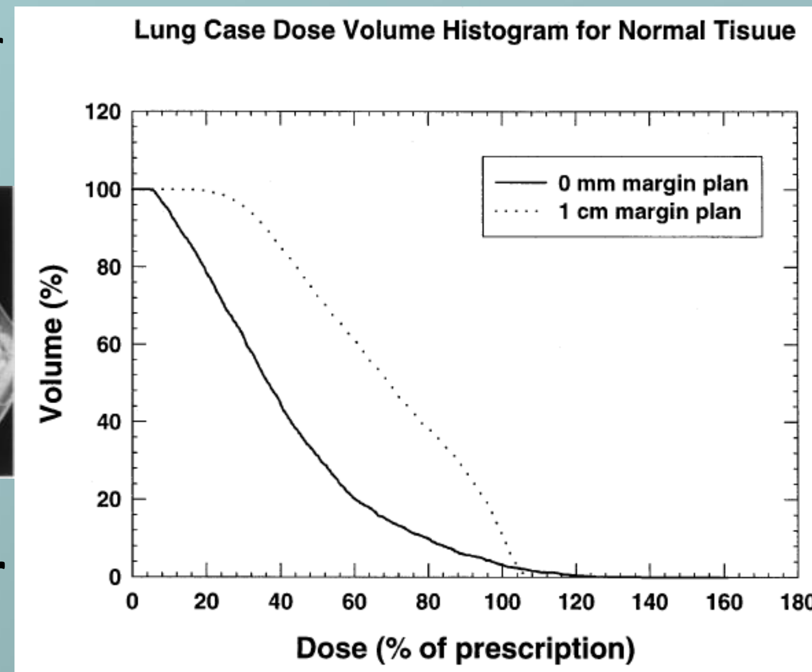
Include non-coplanar beam angles

Use “smart” beam angle selection

The block (BEV) margin for SBRT: small or none



7 non-coplanar beams



Hotter hotspot in tumor with 0 mm BEV margin v larger margin

Steeper dose falloff in lung

Lower NTCP

Margin (mm)	Lung case NTCP (%)
10	46
5	13
2.5	9
0.0	5

IJROBP 1999

PHYSICS CONTRIBUTION

DETERMINING THE OPTIMAL BLOCK MARGIN ON THE PLANNING TARGET VOLUME FOR EXTRACRANIAL STEREOTACTIC RADIOTHERAPY

Robert M. Cardinale, M.D., Qiuwen Wu, Ph.D., Stanley H. Benedict, Ph.D., Brian D. Kavanagh, M.D., Edward Bump, B.A., and Radhe Mohan, Ph.D.

Note: relative (not absolute) NTCP values

Courtesy: Brian Kavanagh, MD

SAM's Question No. 2

2. For a SBRT treatment plan, the optimal distance from the PTV to MLC edge for most cases will be:

A. 0 mm
B. 5 mm
C. 10 mm
D. At the edge of the CTV
E. At the edge of the ITV

SAM's Question No. 2

For a SBRT treatment plan, the optimal distance from the PTV to MLC edge for most cases will be:

0% 1. 0 mm

0% 2. 5 mm

0% 3. 10 mm

0% 4. At the edge of the CTV

0% 5. At the edge of the ITV

SAM's Question No. 2: Answer

Answer: 1. ï 0 mm

Ref: Videtic *et al*. RTOG 0915 (NCCTG N0927) "A randomized phase II study comparing 2 stereotactic body radiation therapy (SBRT) schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer."
(http://www.rtog.org/ClinicalTrials/) (2009)

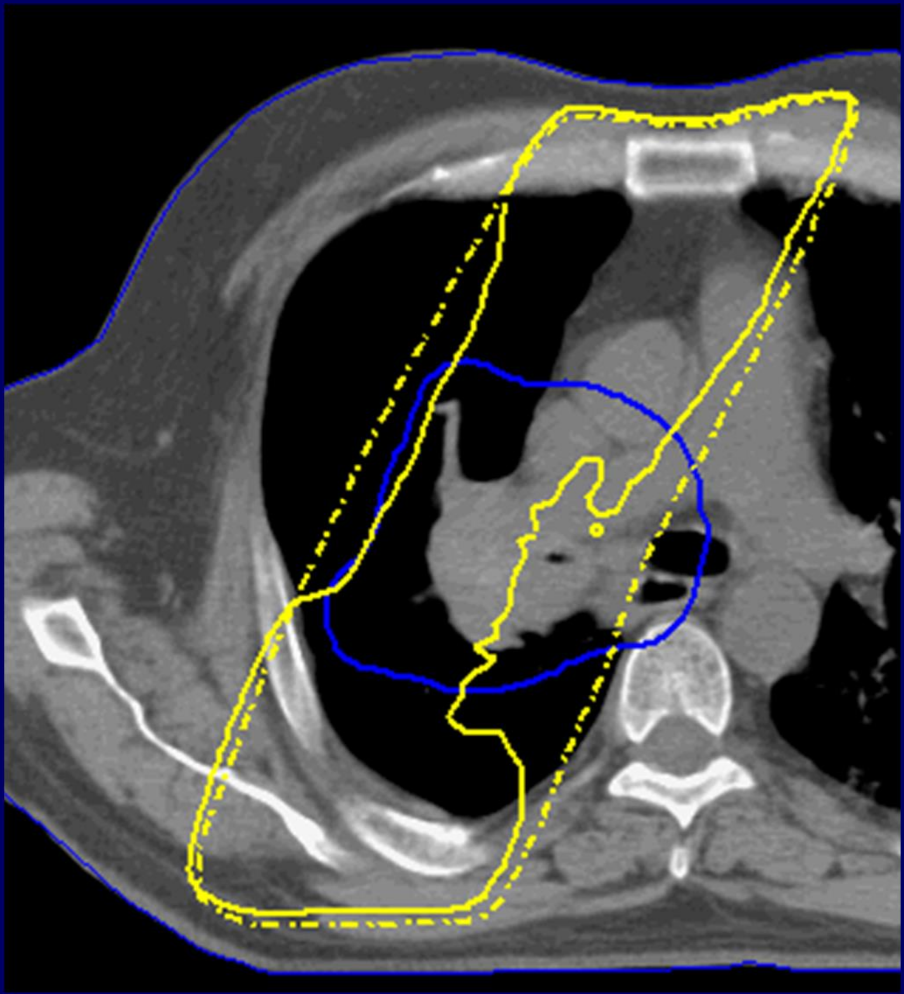
Lung SABR planning: what dose algorithm should be used?

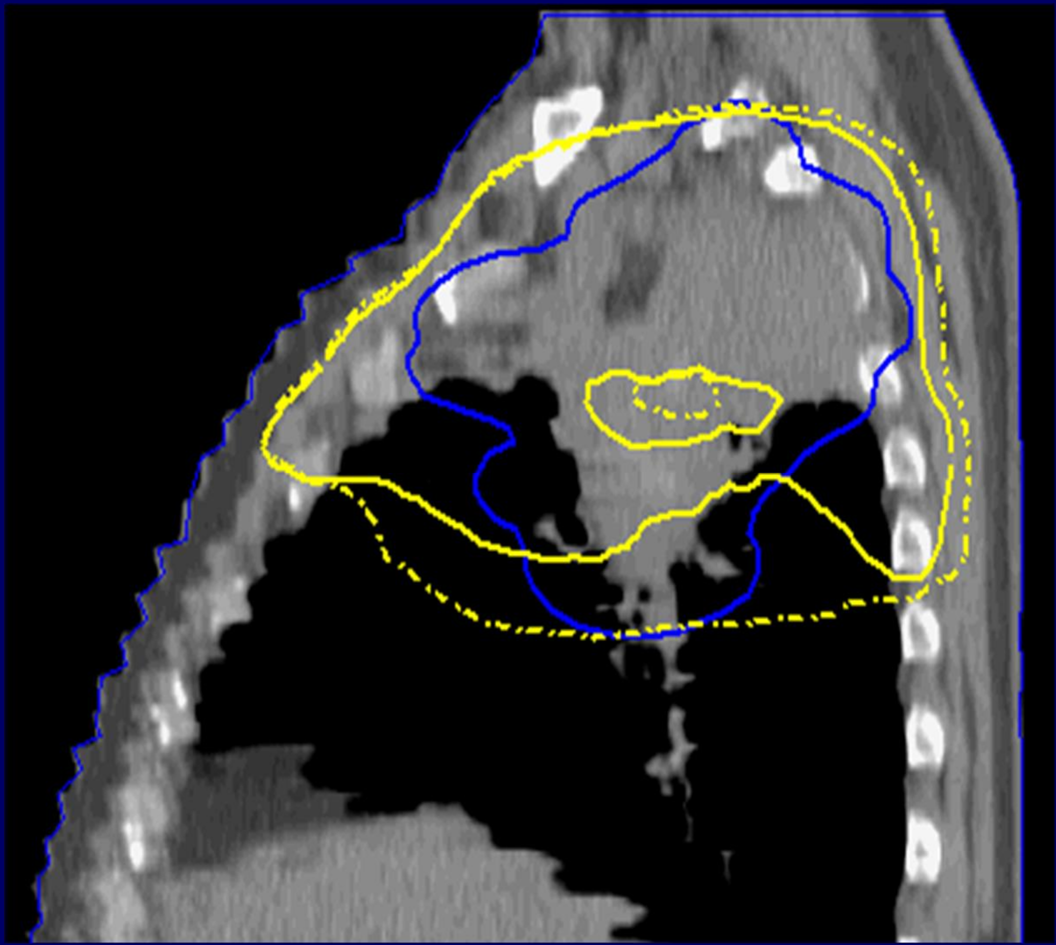
Recommendation of AAPM TG Report No. 101 (Benedict et al Med Phys 37: 2010)…..Algorithms accounting for 3D scatter (e.g. convolution/superposition) perform adequately in most situations, including (in many cases) under circumstances where there is a loss of e' equilibrium such as lung/tissue interface or tumor margin in lung medium. Algorithms accounting for better transport, e.g. Monte Carlo are preferred for the most demanding situations, e.g. small, "island-like" tumors. *Pencil beam algorithms are not recommended….*

Minimum field size (3.5 cm) and energy (low X) constraints: RTOG 0236, 0813, 0915

Advanced stage disease: underdosage of the PTV

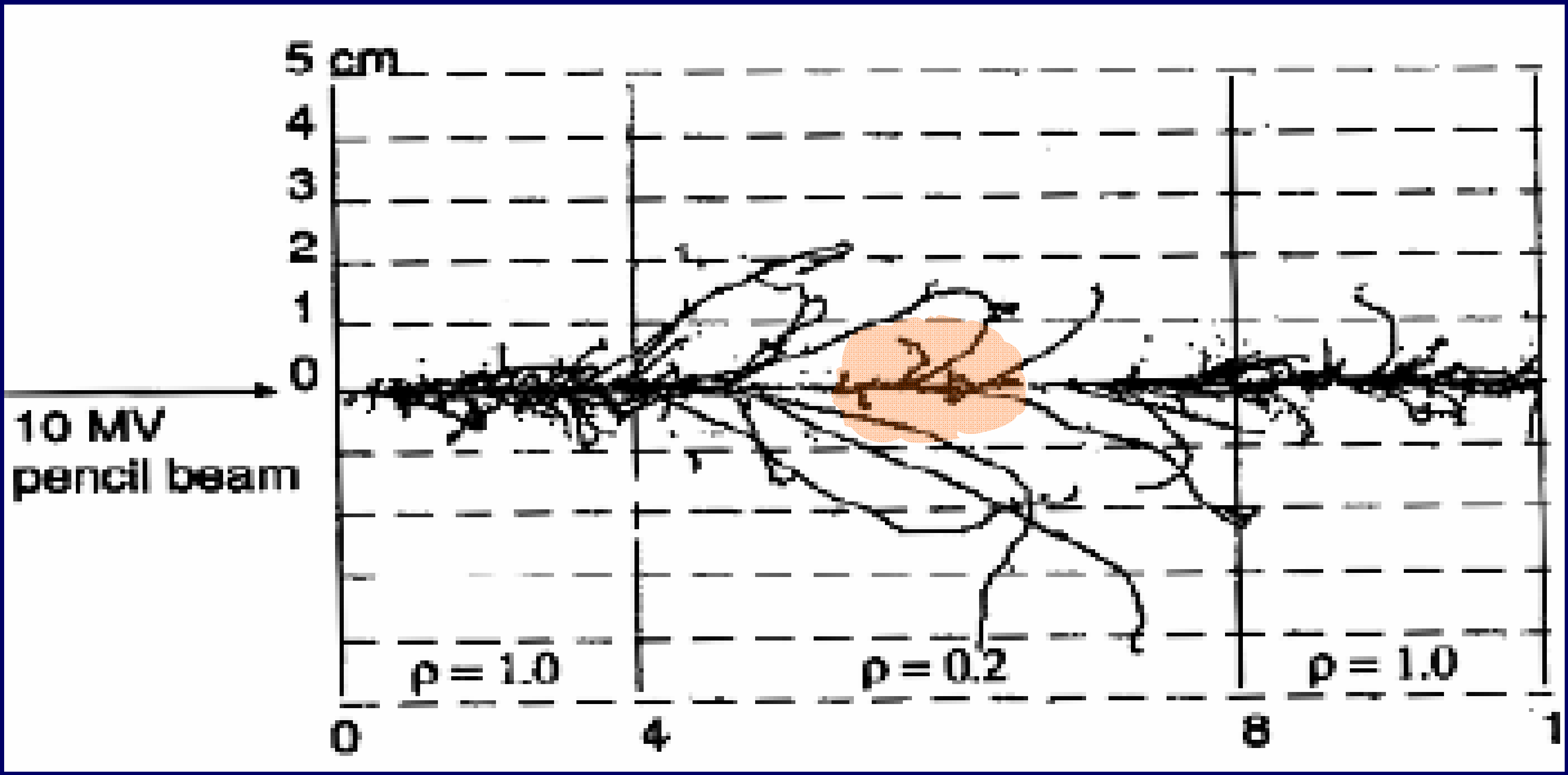
Comparison of the 100% IDLs, Pencil beam (dashed) and MC (solid)





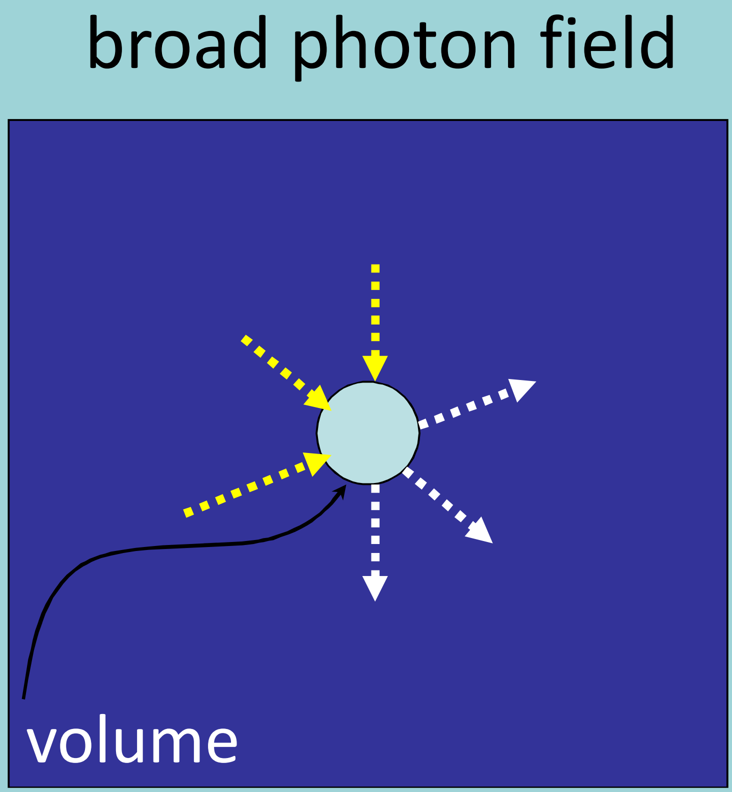
Data from UMPLan, University of Michigan

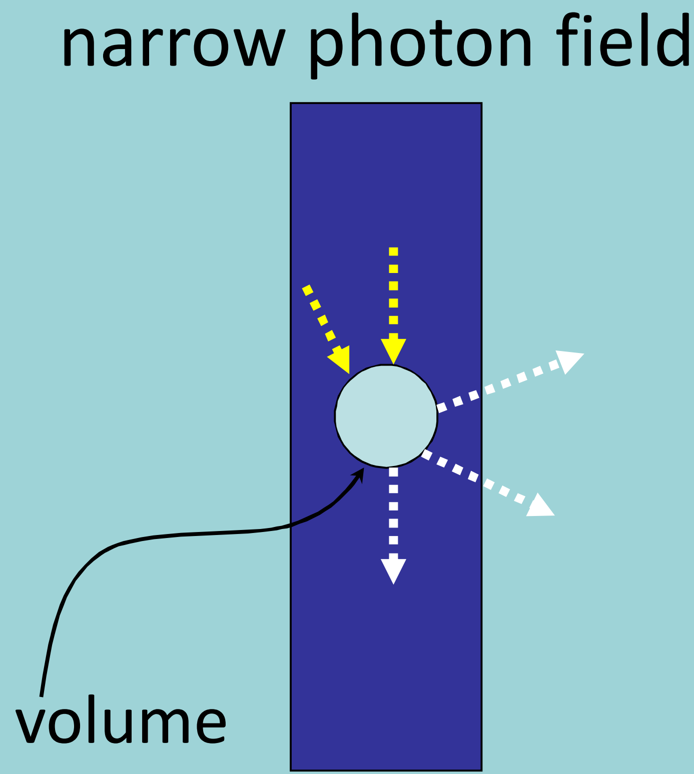
Lateral Scattering of electrons in low density lung tissue carries energy/dose away from the tumor



Monte Carlo simulation, 10 MV pencil beam

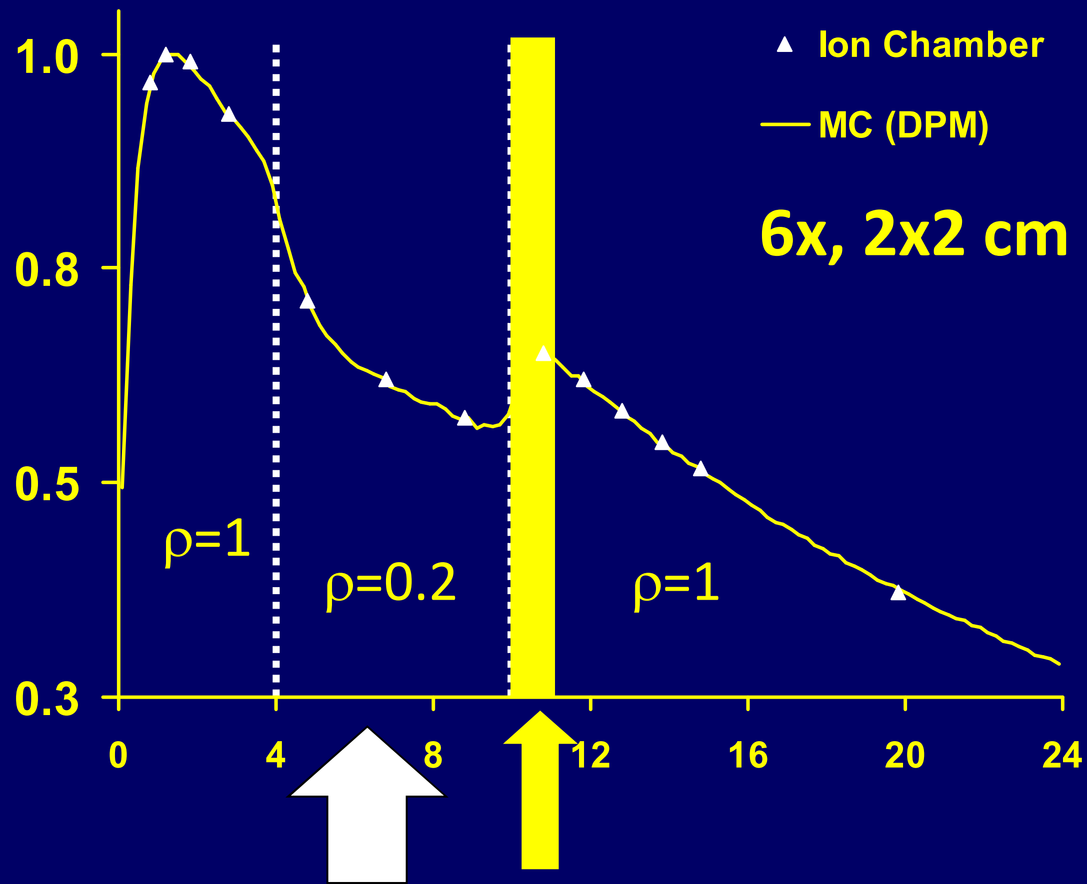
Small Field Dosimetry: Loss of charged particle equilibrium (CPE)





In narrow field, CPE is lost and dose reduction can be severe

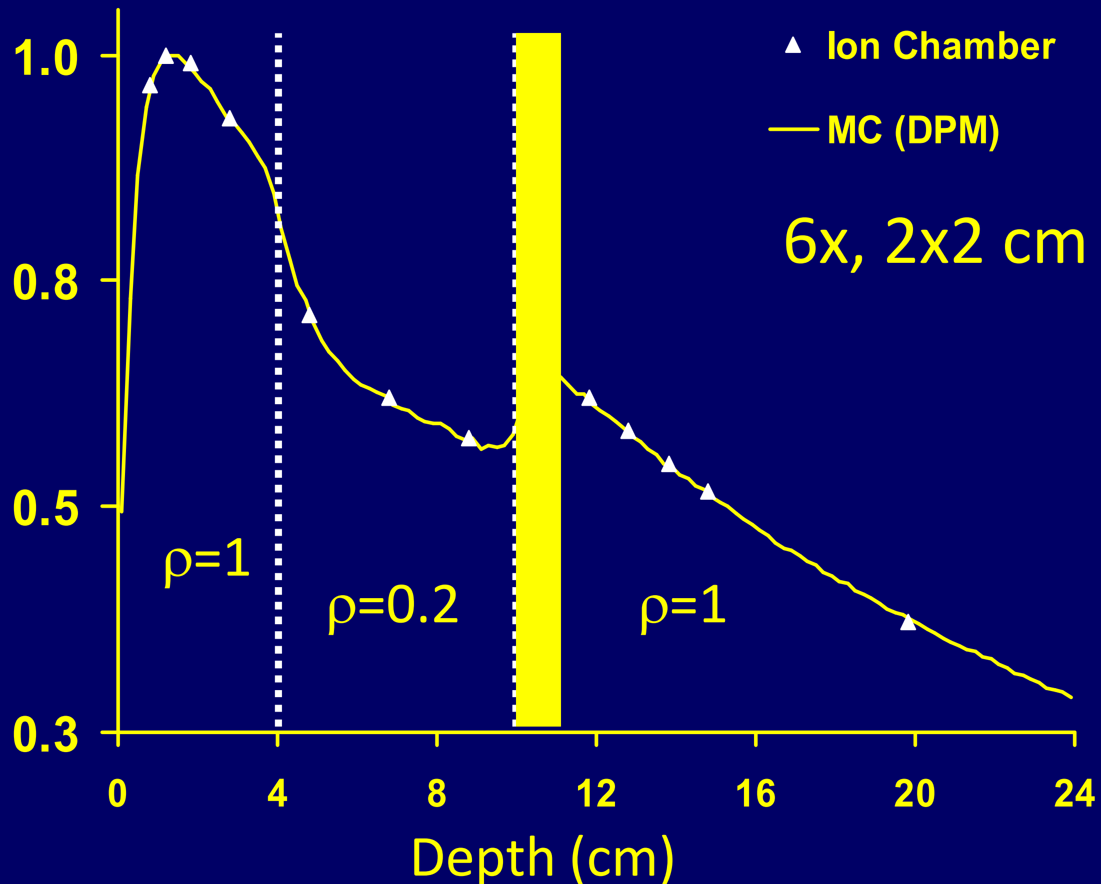
Small field central axis depth dose: slab phantom

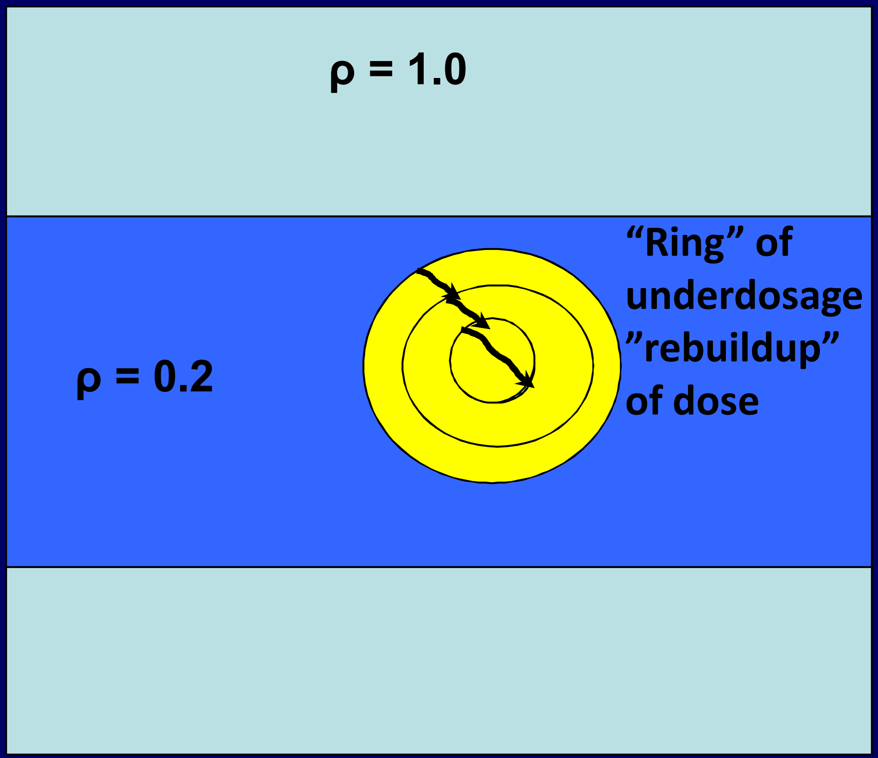


“Build down effect” – severe dose reduction caused by scattering of electrons into the lung tissue

Dose builds up in the tumor resulting in underdosage at tumor periphery.

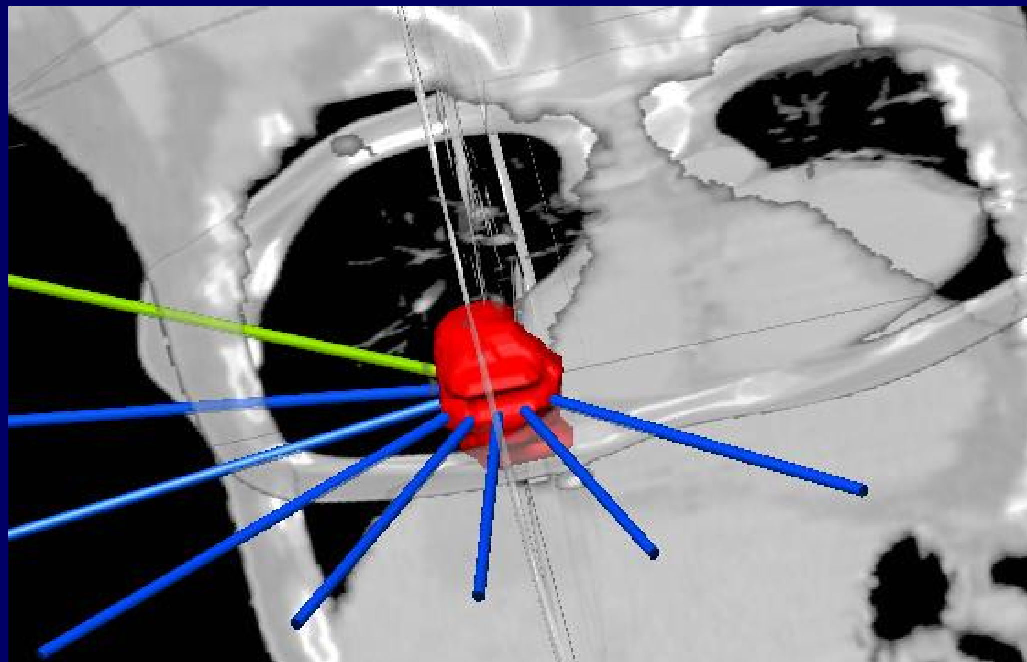
Implications for "island" tumors





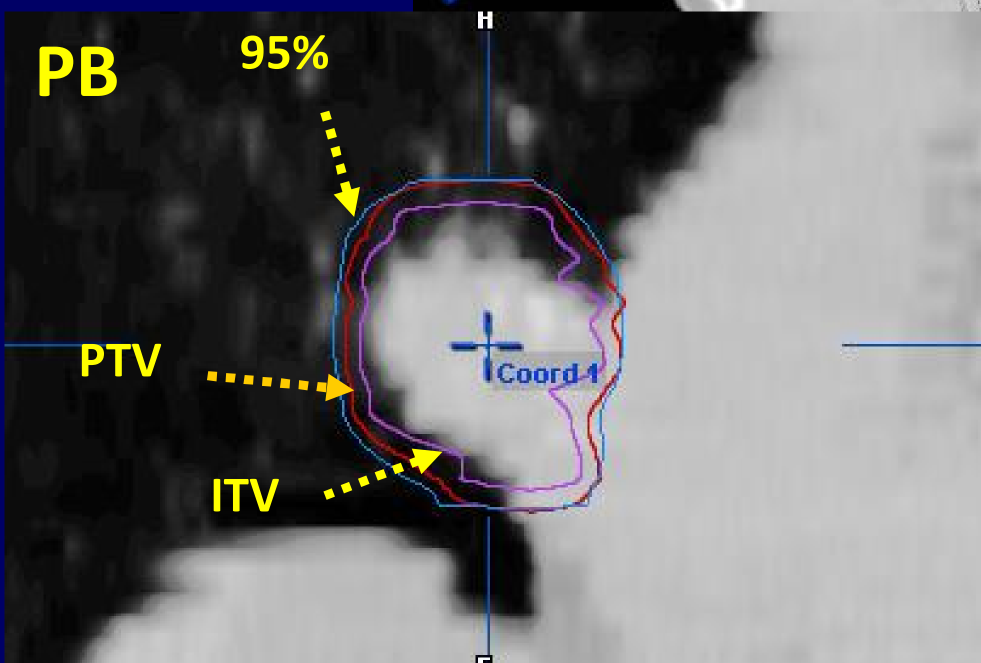
"Ring" of underdosage gets larger for smaller tumors (as the tumor size approaches the electron range)

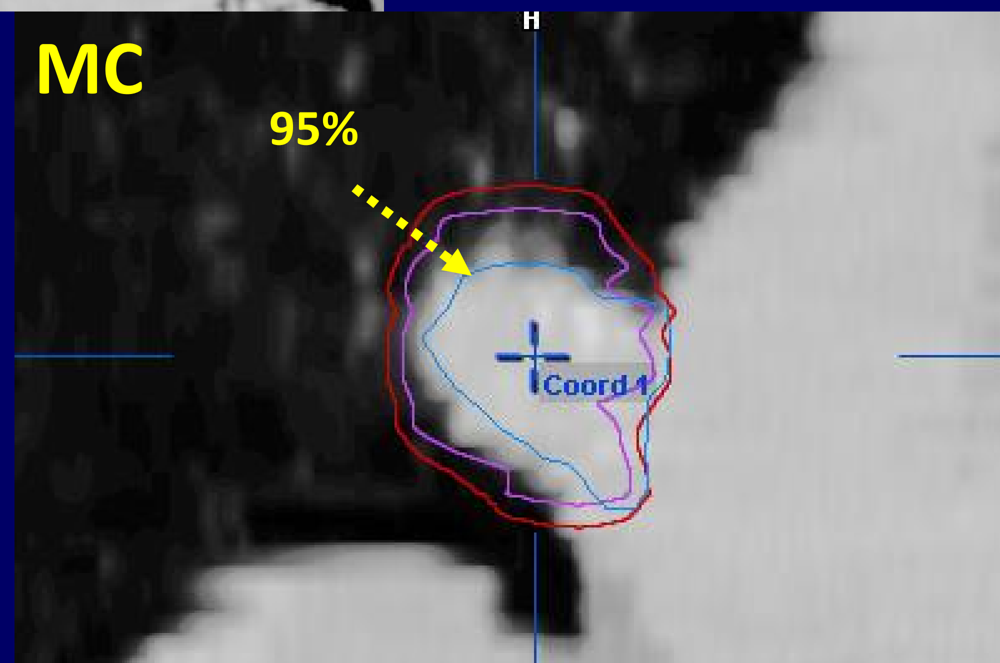
Lung SBRT dose calcs



PTV diam. = 5.2 cm

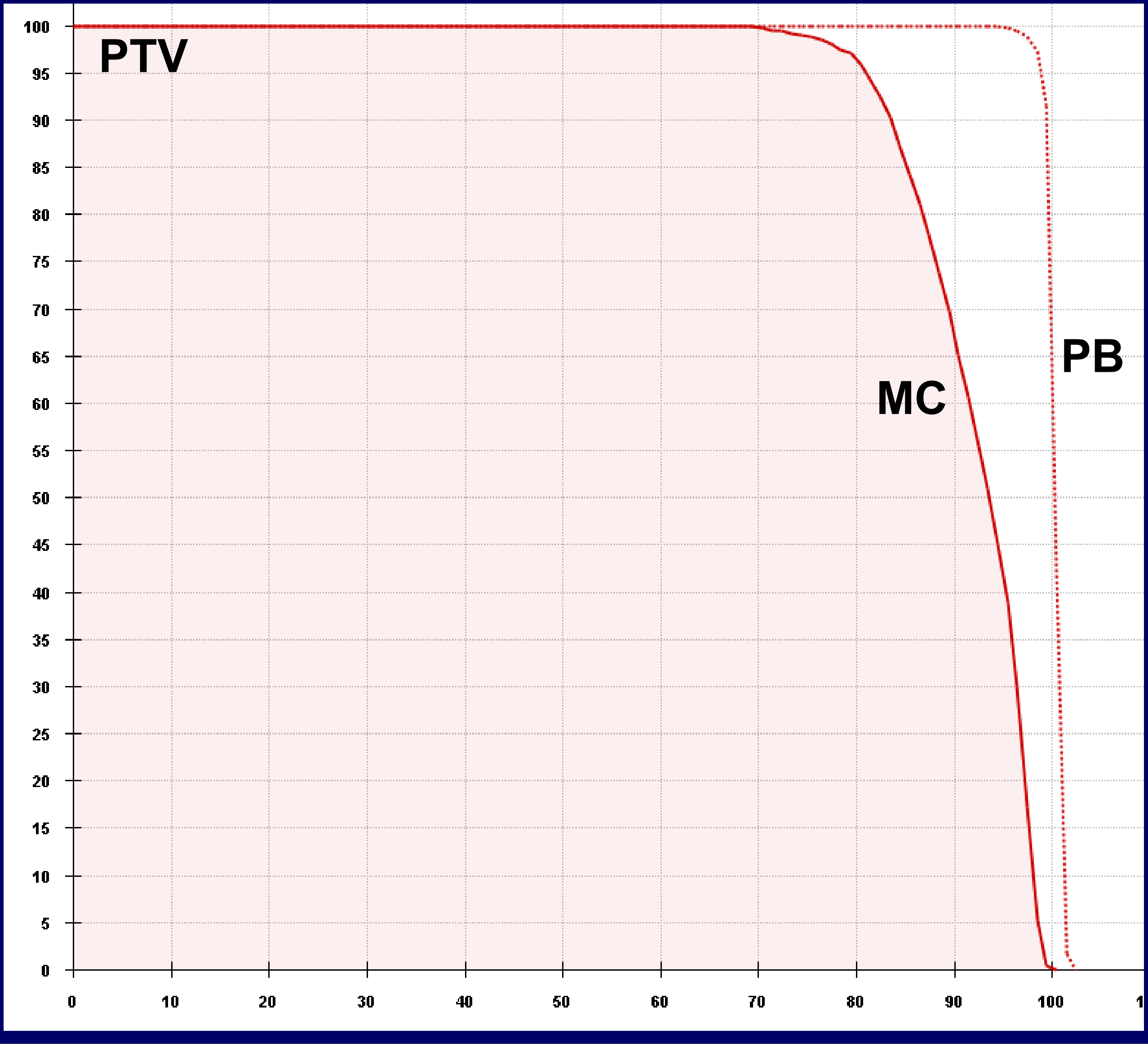
PTV vol. = 41.0 cc





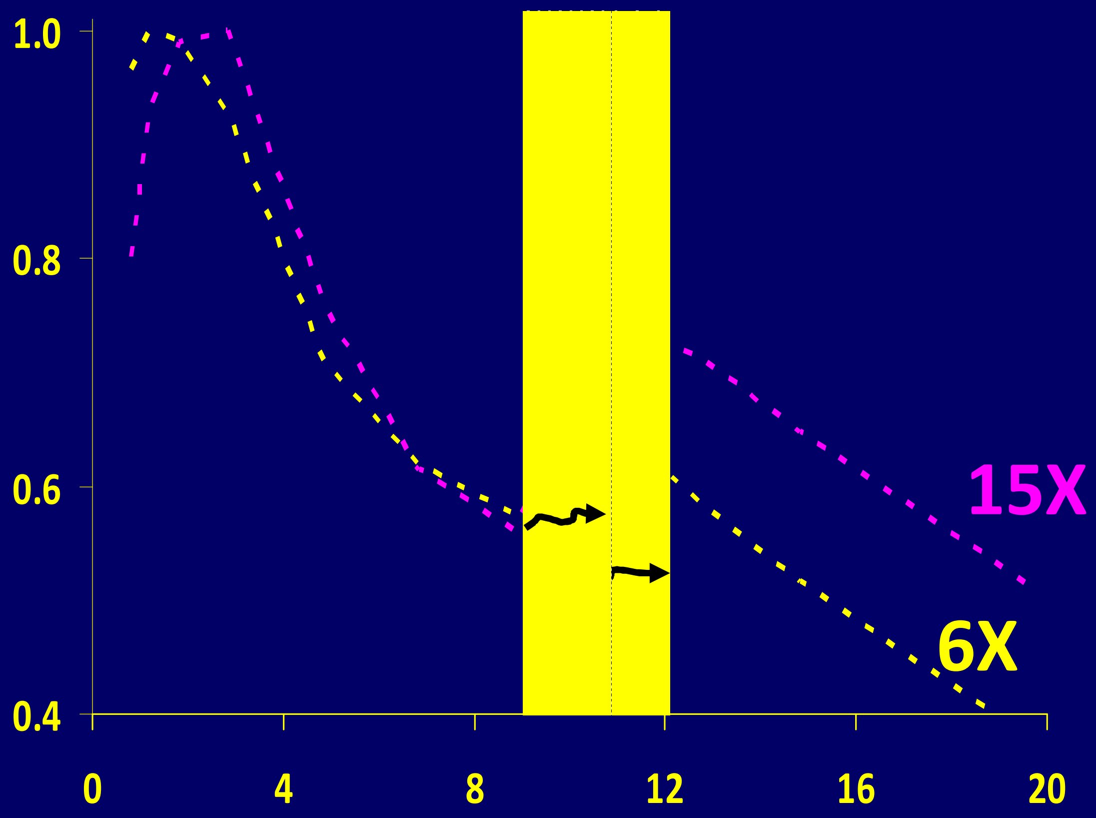
Dose Volume Histograms (DVHs)

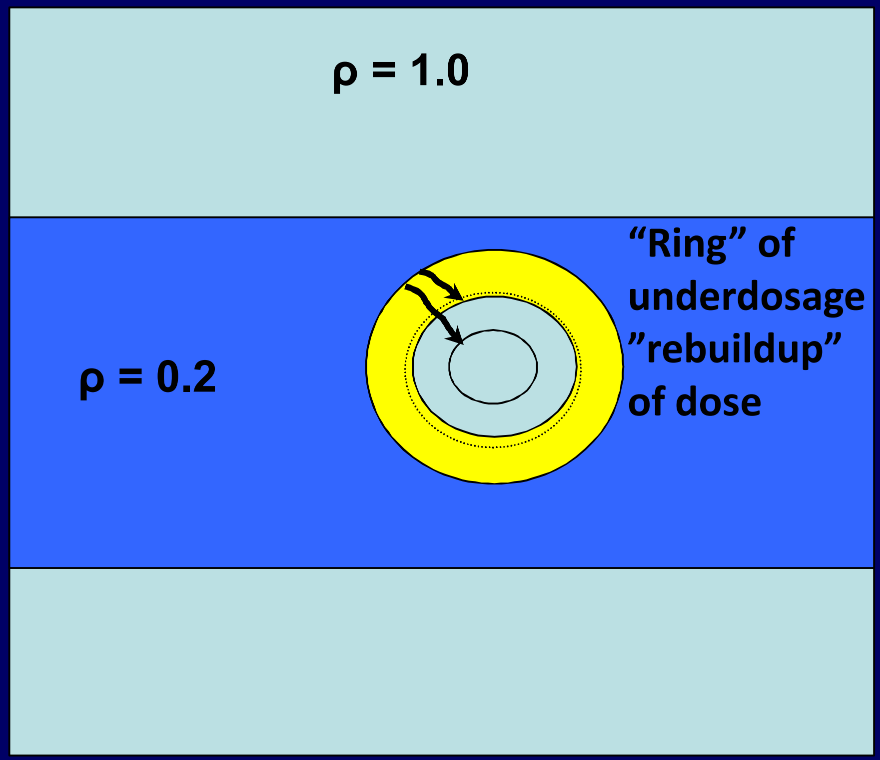
PTV diam. = 5.2 cm; PTV Vol. = 41.0 cc



The Energy Effect

Ion chamber measurements: 2x2

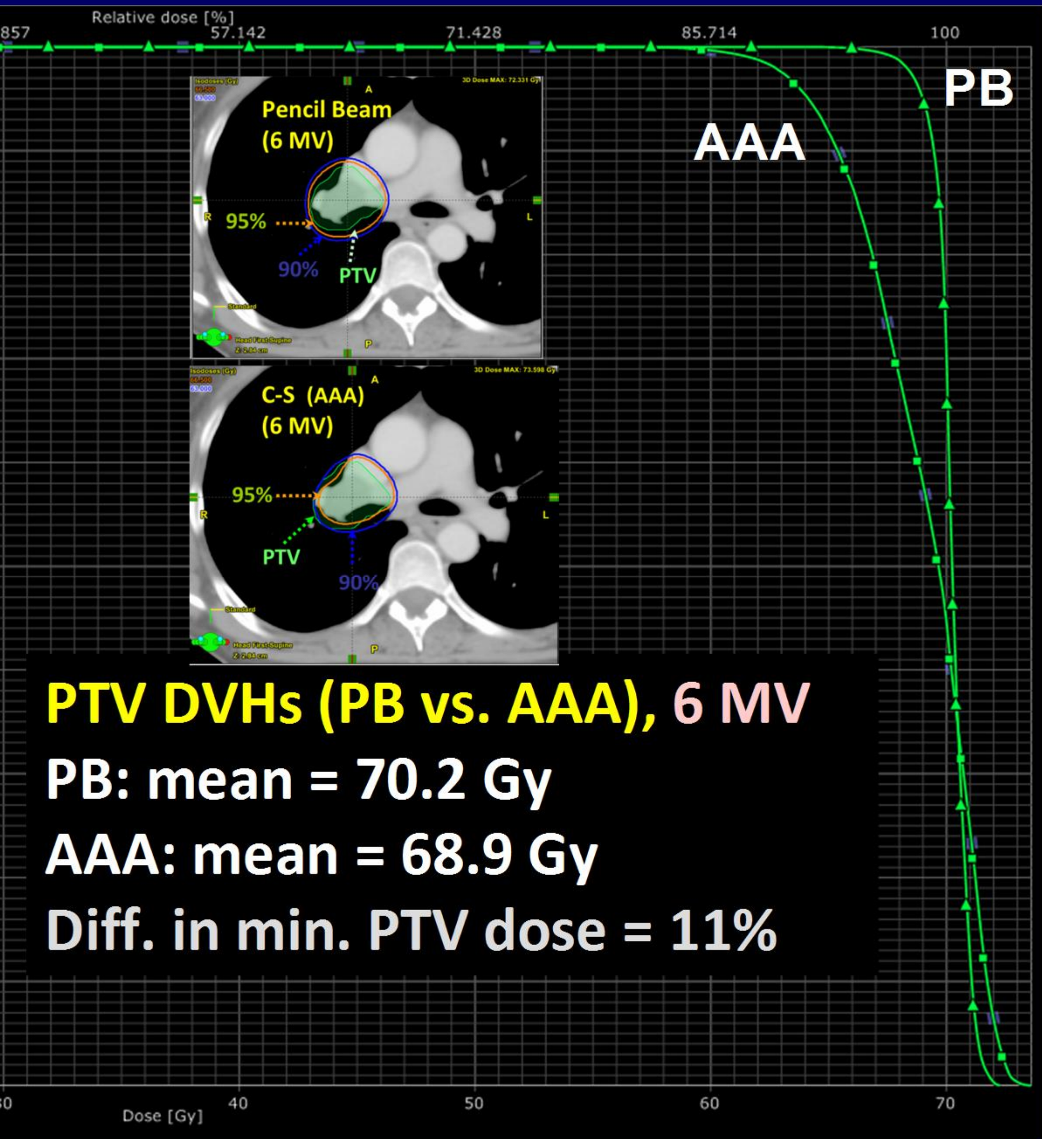




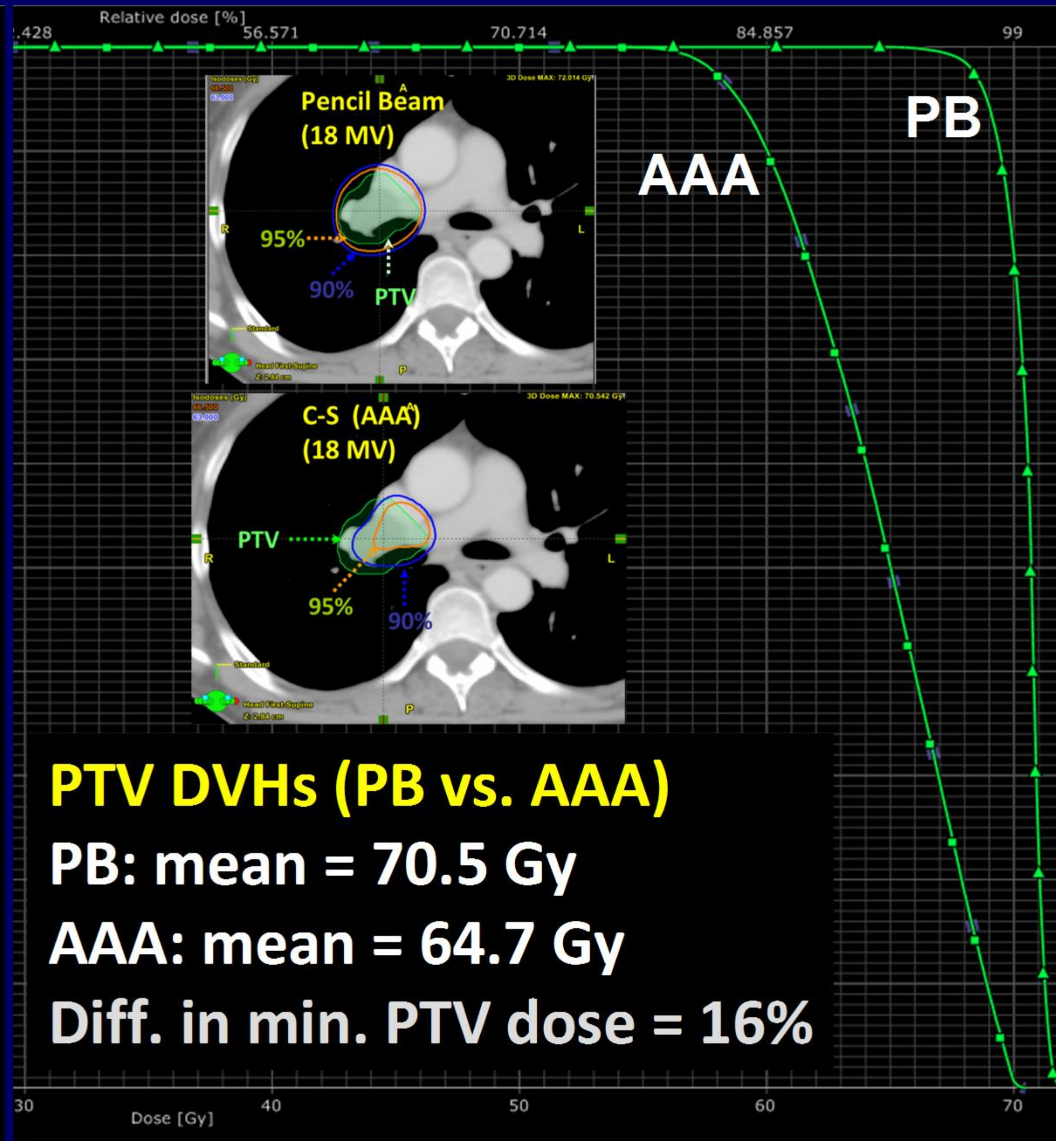
“Ring” of underdosage gets larger with beam energy due to the increased electron range

The Energy Effect

6X



18X



Lung SBRT dose algorithm comparison

135 patients planned w/ 1D-pencil beam (1D-EPL, iPlan) retrospectively replanned using 3D-EPL (Eclispe), AAA (Eclipse), CCC (Pinnacle), Acuros (Eclipse), MC (iPlan)

D95 (of the PTV evaluated relative to 1D-EPL (D95 = 100%) : 12 Gy x 4 Fractions

Location	FS (cm)	3D-EPL_D95	AAA_D95	CCC_D95	Acuros_D95	MC_D95
	3≤FS<5	95.1±2.1	80.2±4.3	80.0±6.0	76.6±6.9	79.7±5.9
Lung-island	5≤FS<7	95.7±1.9	83.0±4.3	82.7±5.4	80.0±5.9	83.0±5.1
N=39	7≤FS<10	92.8±0.3	84.5±0.8	85.3±0.7	83.5±1.2	85.7±1.4
	3≤FS<5	94.8±1.8	83.2±5.5	83.3±6.4	81.7±6.9	83.5±5.9
Lung-central	5≤FS<7	95.3±2.1	86.1±5.8	86.8±6.5	85.0±7.1	86.8±6.1
N=52	7≤FS<10	95.4±1.1	90.7±3.7	90.9±3.9	89.8±3.9	91.3±4.0

Comprehensive investigation of dose calculation accuracy for lung stereotactic ablative radiation (SABR): Effects of tumor size and location and clinical recommendations

S Devpura *et al* 2014 *J. Phys.: Conf. Ser.* 489 012007

SAM's Question No. 3

3. For the treatment of small lung tumors located peripherally using SBRT, which dose algorithm will result in a significant underdosage of the tumor relative to the tumor dose prescription:

A. Convolution
B. Superposition/Convolution
C. Monte Carlo
D. Acuros
E. Pencil Beam

SAM's Question No. 3

For the treatment of small lung tumors located peripherally using SBRT, which dose algorithm will result in a significant underdosage of the tumor relative to the tumor dose prescription:

0% **1. Convolution**

0% **2. Superposition/Convolution**

0% **3. Monte Carlo**

0% **4. Acuros**

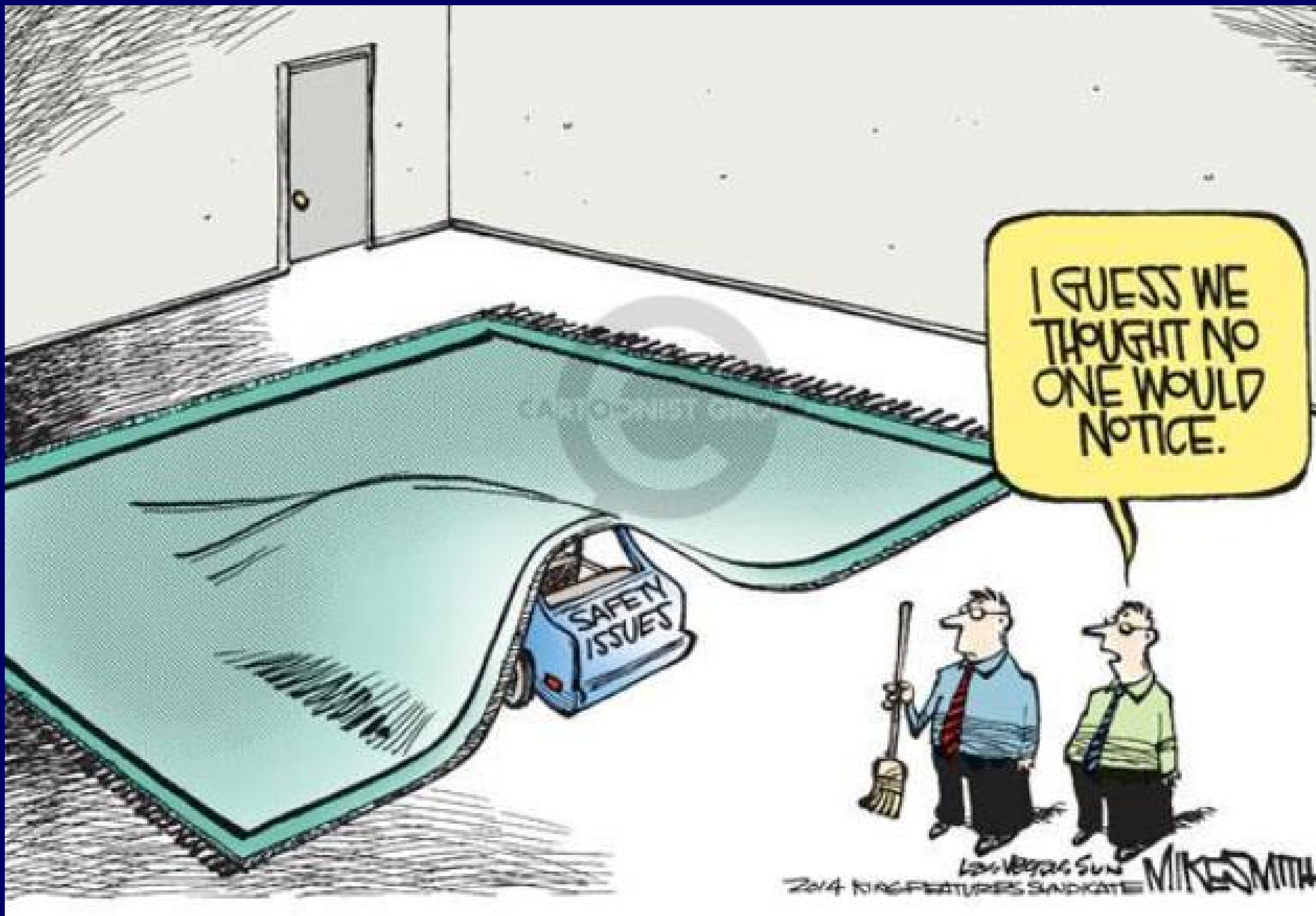
0% **5. Pencil Beam**

SAM’s Question No. 3: Answer

Answer: 5 ï Pencil Beam algorithm

Ref: Benedict, *et al*. " Stereotactic body radiation therapy: The report of AAPM Task Group 101", Med Phys 37, 4078-4101 (2011).

Practical Issues: *Understanding the details*



http://www.theeditorialcartoons.com/

Lung Cancer Treatment Planning: Practical Issues
How many phases should be used for definition of the ITV in the 4D-CT?

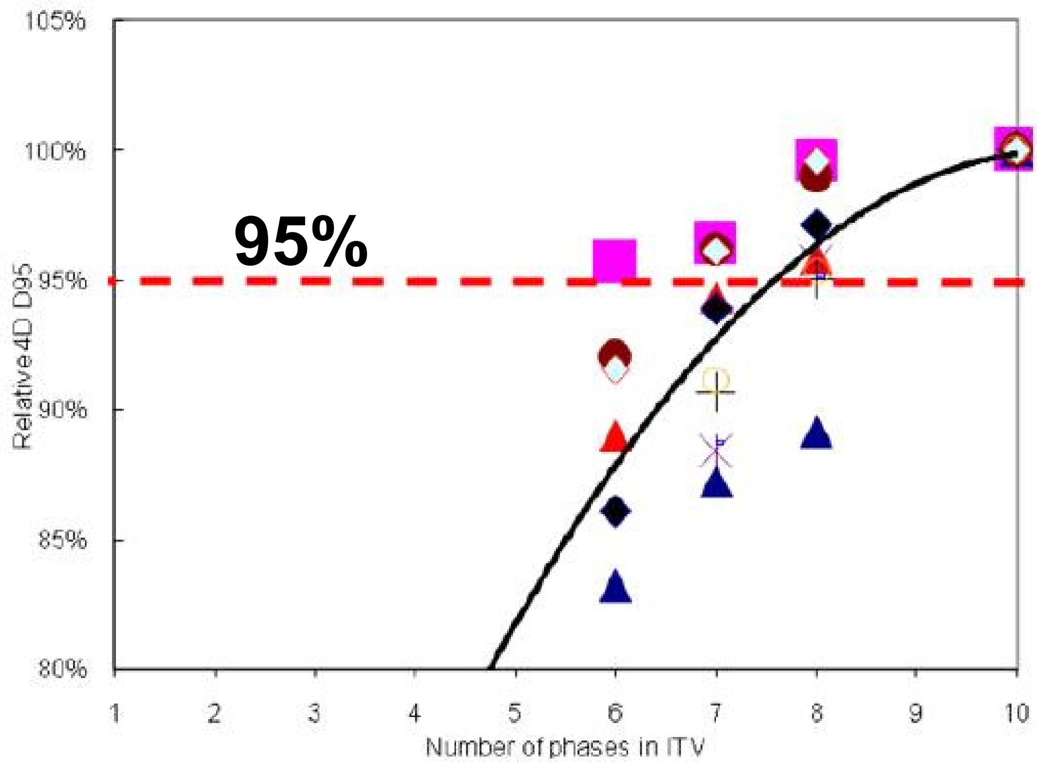


FIG. 2. D_{95} value as a function of the number of phases in the 4D CT image set used to calculate the ITV. All values were taken from 4D dose calculations and were normalized to the D_{95} for N = 10 (i.e., normalized to current clinical practice). Each marker type is for a different patient. The solid line is the average.

Yakoumakis…and Court: JACMP: 13(6), 2012

Which phase is the most accurate for planning?

Table shows diffs in cGy and % between AVE-CT and full 4D plan (10 phases using deformable dose accumulation – phantom study)

	Dose discrepancy (cGy)				
S-I Amplitude (cm)	GTV_{Min}	GTV_{Mean}	GTV D_{99}	GTV D_1	MLD
2	0.27 (0.30%)	0.35 (0.37%)	0.80 (0.88%)	0.45 (0.47%)	0.25 (0.25%)
3	0.56 (0.63%)	0.55 (0.58%)	0.70 (0.77%)	0.70 (0.73%)	0.39 (1.01%)
4	1.74 (1.99%)	0.29 (0.31%)	1.20 (1.34%)	0.60 (0.63%)	0.39 (1.01%)
2.7 cm diaphragm-tumor distance	0.81 (0.89%)	0.03 (0.03%)	0.75 (0.82%)	0.10 (0.10%)	0.22 (0.58%)
4.7 cm diaphragm-tumor distance	0.19 (0.22%)	0.21 (0.23%)	0.40 (0.44%)	0.45 (0.47%)	0.63 (1.61%)

Glide-Hurst *et al*: Med Phys:35: 5269 (2008)

What is the difference between the free-breathing (FB), average (AIP) and MIP-based CT datasets?

PTV doses (Gy) and abs. V20 (cc) averaged over 20 lung SBRT patients

PTV doses in Gy

D_{mean}	FB	50.3
	MIP	50.9
	AIP	50.4
D95	FB	47.3
	MIP	48.1
	AIP	47.5

Abs V20 in CC

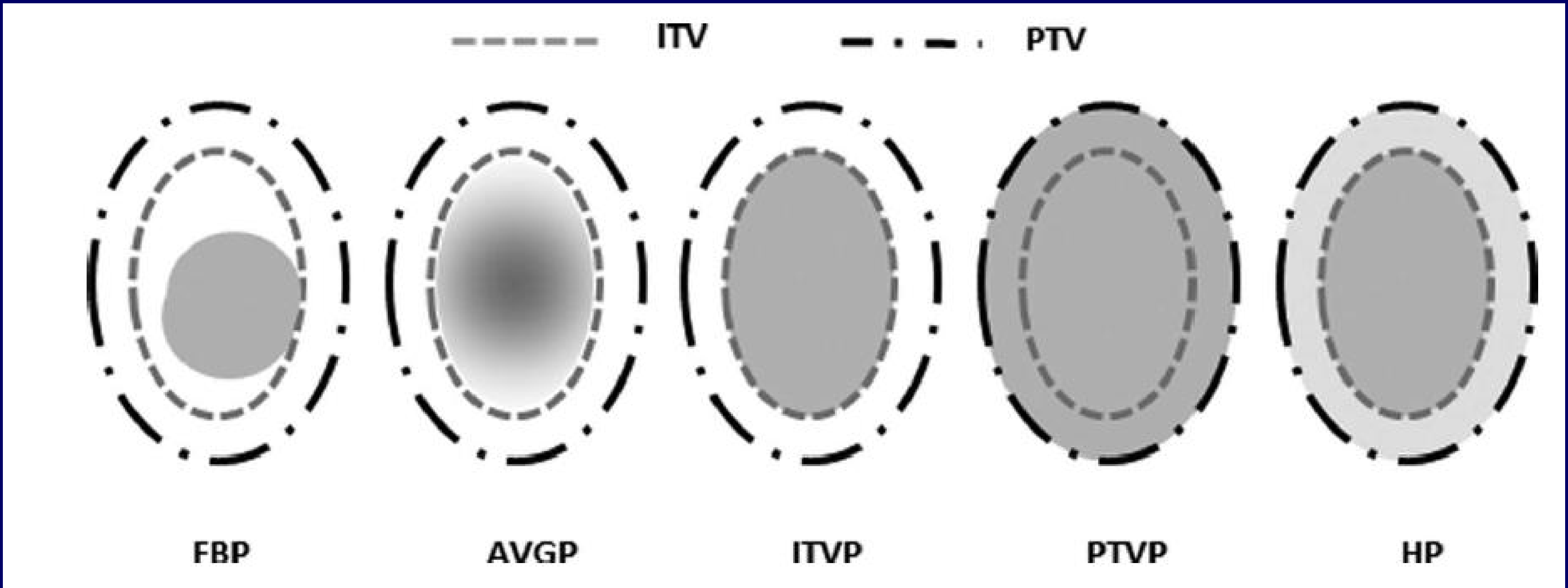
Abs. V20	FB	167.7
	MIP	160.1
	AIP	167.7

- Dose characteristics are similar
- AIP has less artifact than FB
- AIP (ave. CT) is most favorable

Tian…and F-F Yin: Med Phys: 39:2754 (2012)

What difference do density overrides make?

Different methods for overriding the densities compared with no density override (free breathing and average datasets)



Wiant…and Sintay: Med Phys: 41:081707 (2014)

What difference do density overrides make?

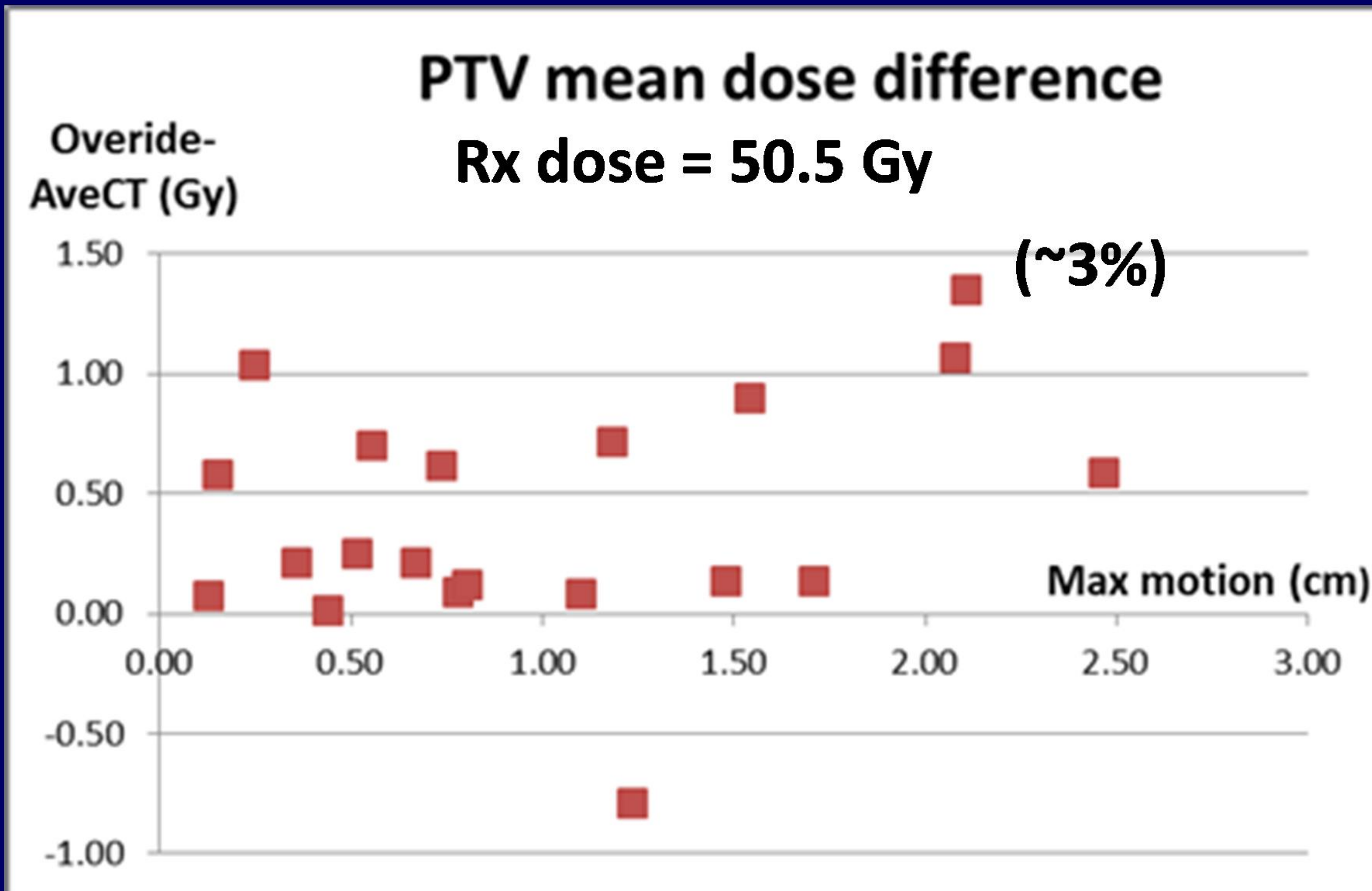
Comparison for 5 lung SBRT patients treated with VMAT

Case	Plan type	ITV (cm^3)	GTV motion (cm)	% PTV coverage	CI plan	Mean dose plan (Gy)	Max dose plan (Gy)	Mean dose 4DCT (Gy)
1	FBP	9.7	1.3	95.0	1.04	12.0	12.9	12.0 ± 0.0
	AVGP			95.4	0.99	11.5	12.1	11.6 ± 0.1
	PTVP			96.5	1.00	11.7	12.4	11.4 ± 0.0
	HP			95.8	0.99	11.7	12.4	11.4 ± 0.0
2	FBP	10.4	1.5	97.3	1.07	11.9	13.5	11.9 ± 0.1
	AVGP			97.3	1.06	11.9	13.2	12.0 ± 0.1
	PTVP			97.6	1.07	12.1	13.9	11.7 ± 0.1
	HP			97.3	1.06	11.9	13.1	11.6 ± 0.1
3	FBP	57.9	3.4	95.7	0.97	11.6	12.5	11.5 ± 0.2
	AVGP			95.0	0.97	11.3	12.1	11.3 ± 0.1
	PTVP			95.6	0.97	11.7	12.5	11.4 ± 0.2
	HP			96.2	0.98	11.7	12.8	11.5 ± 0.2

Wiant…and Sintay: Med Phys: 41:081707 (2014)

Density overrides: 20 SBRT lung patients:

PTV density override (1.0 g/cc) *vs* no override (AveCT)



Courtesy: Cindy Qin (Henry Ford Hospital)

To Gate or Not to Gate?

Decisions should be made based on clinically relevant dosimetric endpoints

Å N=150 lung SBRT patients

Å 18 Gyx3; 12 Gyx4; 10 Gyx5

Å Plans optimized for same target coverage

Å PTV (ITV) margin = ITV+ 5 mm

Å Gated margin = GTV+5 mm

Å MLD, V20, V5 converted to EQ2Gy

Courtesy: J. Kim *et al* submitted to *PRO*
(Henry Ford Hospital)

Mean Lung Dose _EQD2 (Gy); (18 Gy x 3)

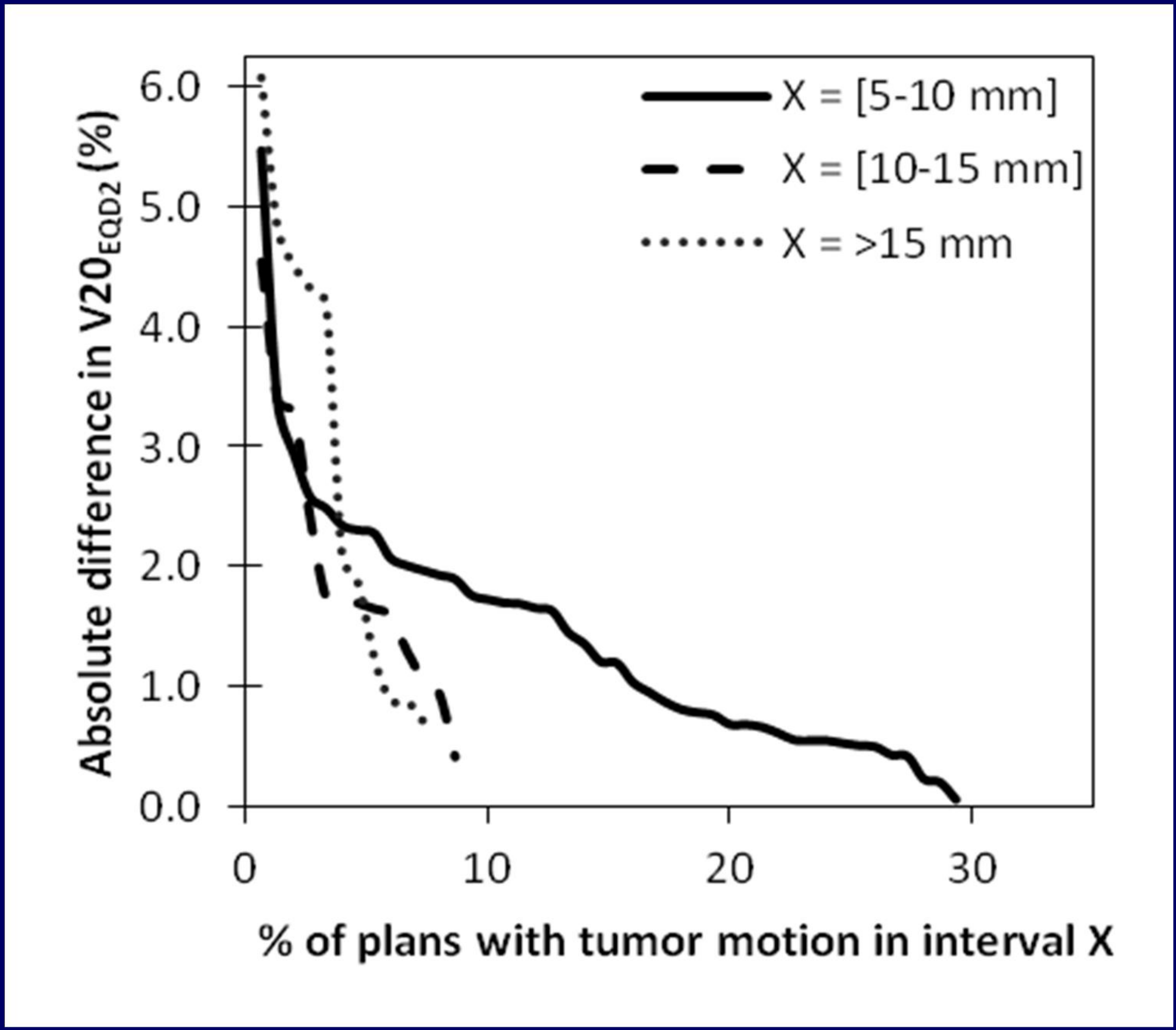
	Gated (Gy)	ITV (Gy)	Diff. (Gy)
Peripheral (Lung Wall) (N=57)	6.3 ± 3.2 (13.4)	7.2 ± 3.8 (15.7)	0.9 ± 1.1 (max=5.4; ITV=14.9)
Peripheral (Island) (N=57)	6.5 ± 2.8 (13.6)	7.9 ± 3.3 (15.5)	1.4 ± 1.2 (max=4.8; ITV=8.9)
Central (N=36)	8.5 ± 4.0 (20.4)	9.5± 4.6 (24.4; 4.0)	1.0 ± 1.2 (max=5.4; ITV=15.4)

V20 % differences less than 1.5% on average with a maximum V20 of 26.1% (ITV plan)

12 Gy x 4 and 10 Gy x 5 dosing schemes showed smaller MLD and V20 differences

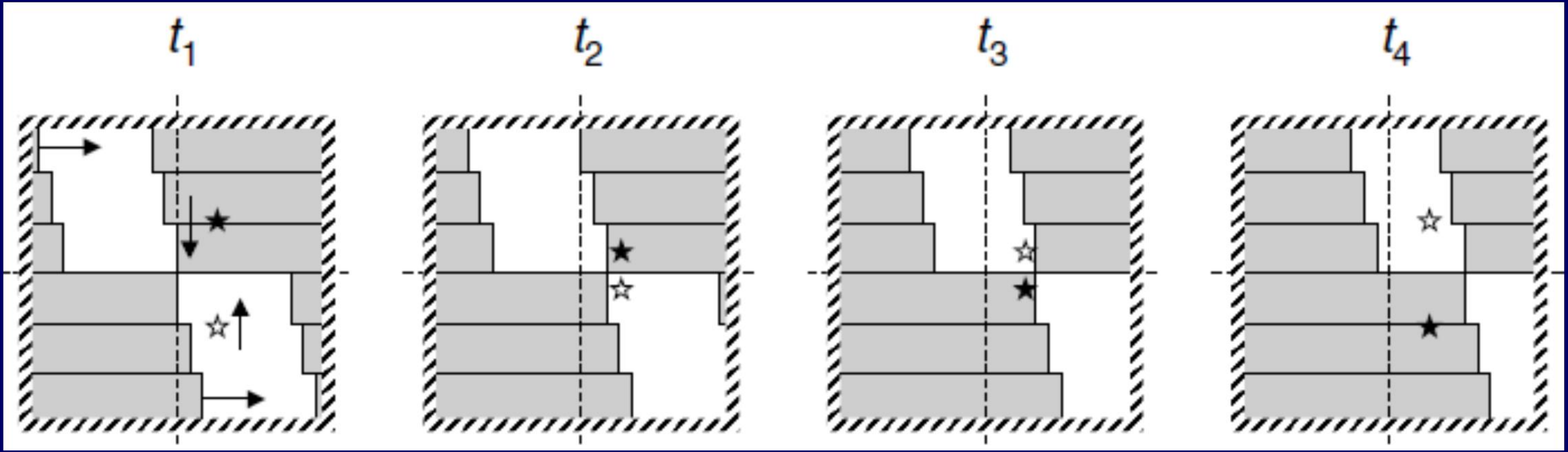
Low dose comparison, V5 values were within 1-2% for ITV and Gated plans

Difference between ITV and Gating (V20) for different motion amplitudes



The Interplay Effect

Describes the interaction between organ motion and MLC leaf motion.



From Bortfeld *et al.* Physics in Medicine and Biology: 47, 2002

Interplay effect in IMRT is generally small (~1%) especially for highly fractionated treatments

Evaluation of the interplay effect when using RapidArc to treat targets moving in the craniocaudal or right-left direction

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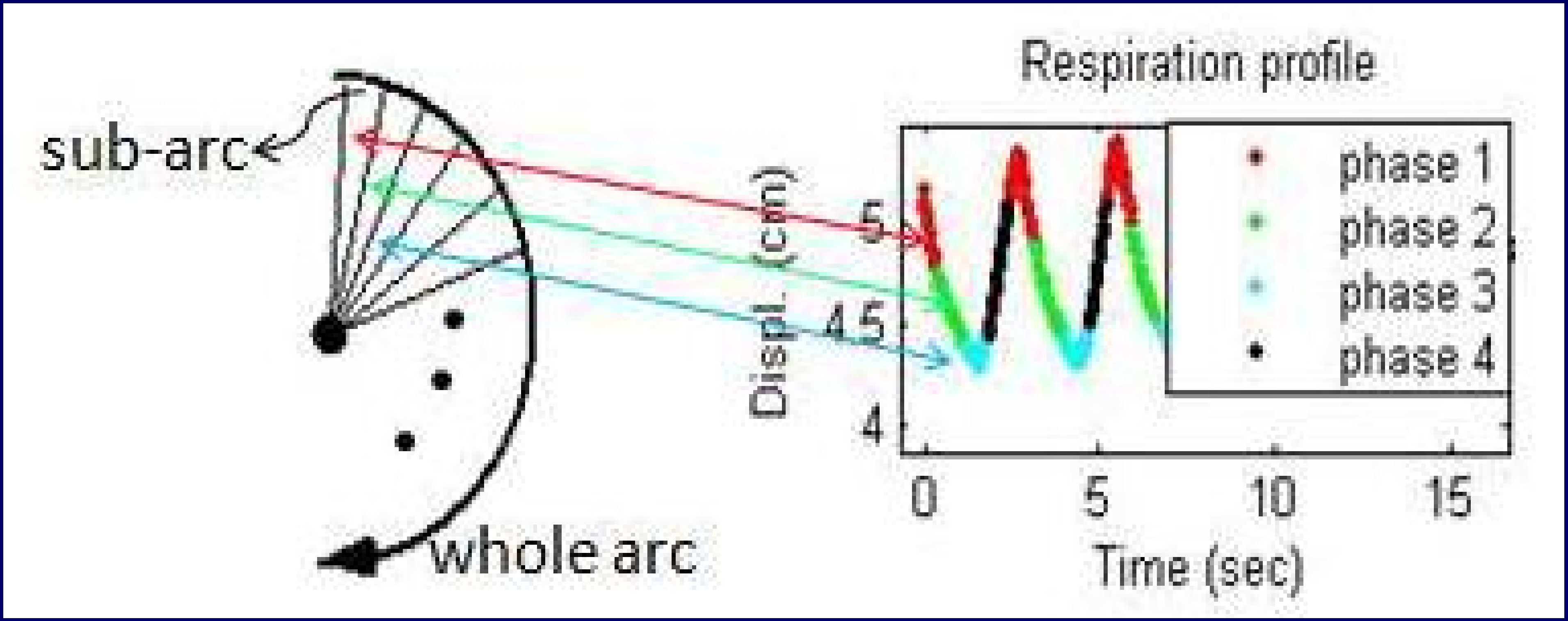
Med. Phys. 37 (1), January 2010

"The percentage of pixels for which the daily dose error could be larger than 5% increased with increasing plan complexity field MU, but was less **than 15% for all plans if the motion was 1 cm or less. For 2 cm motion, the dose error could be larger than 5% for 40% of pixels**, but was less than 5% for more than 80% of pixels for MU550, and was less than 10% for 99% of all pixels."

"The interplay effect increases with plan complexity, and with target magnitude and period. It may average out after many fractions."

Dosimetric Impact of the Interplay Effect on VMAT/RapidArc Lung Cancer Treatment Using SABR



Courtesy: Haisen Li *et al.* (Henry Ford Hospital)

Dosimetric Impact of the Interplay Effect on VMAT and IMRT

Patient No.		1	2	3
Tumor location and motion amplitude in SI, AP, RL (cm)		RLL	LLL	RLL
		1.3, 0.4, 0.2	1.0, 0.5, 0.7	0.7, 0.5, 0.3
	RA			
	IMRT			
% decrease in ITV mean dose	RA	-0.1	0.0	1.9
	IMRT	-0.5	-0.2	2.3

Patient No.		4	5	6
Tumor location and motion amplitude in SI, AP, RL (cm)		RLL	LLL	RML
		1.0, 0.0, 0.0	1.2, 0.4, 0.1	0.8, 0.7, 0.5
	RA			
	IMRT			
% decrease in ITV mean dose	RA	-0.8	0.6	-0.2
	IMRT	0.8	0.6	-0.2

Considerations: VMAT/RapidArc Interplay

<u>**Is dependent on:**</u>

Direction of major tumor motion relative to that of MLC motion

Amplitude of motion

Complexity of intensity modulation

Tends to average out over multiple fractions

Is similar for IMRT and VMAT – tradeoff between number of beam angles and level of modulation

SAM's Question No. 4

4. Which of the following statements regarding the interplay effect is True?

A. It is independent of the modulation complexity.
B. It is independent of the direction of major tumor motion in relation to the MLC motion.
C. It is independent of the amplitude of motion.
D. It is much larger for VMAT than for IMRT
E. It tends to average out over many fractions.

SAM's Question No. 4

Which of the following statements regarding the interplay effect is True?

20% 1. It is independent of the modulation complexity.

20% 2. It is independent of the direction of major tumor motion in relation to the MLC motion.

20% 3. It is independent of the amplitude of motion.

20% 4. It is much larger for VMAT than for IMRT

20% 5. It tends to average out over many fractions.

SAM's Question No. 4: Answer

Answer: 5 ï It tends to average out over many fractions

Ref: Court, *et al*. " Evaluation of the interplay effect when using RapidArc to treat targets moving in the craniocaudal or right-left direction", Med Phys 37, 4-11 (2010).

Summary

4D simulation helps create appropriate planning margins for motion – care must be taken in defining the target; no. of datasets, and the phase used for planning are important factors

Daily volumetric imaging (CBCT) helps reduce margins and provides institutional experience on tailoring of margins

Convolution/superposition or MC-based methods should be used for lung cancer treatment planning – avoid pencil beam algorithms

Pay attention to interplay effects for IMRT and VMAT motion when amplitude is large (> 1.5 cm) and modulation is high

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Thank You