On the use of 4DCT derived composite CT images in treatment planning of SBRT for lung tumors

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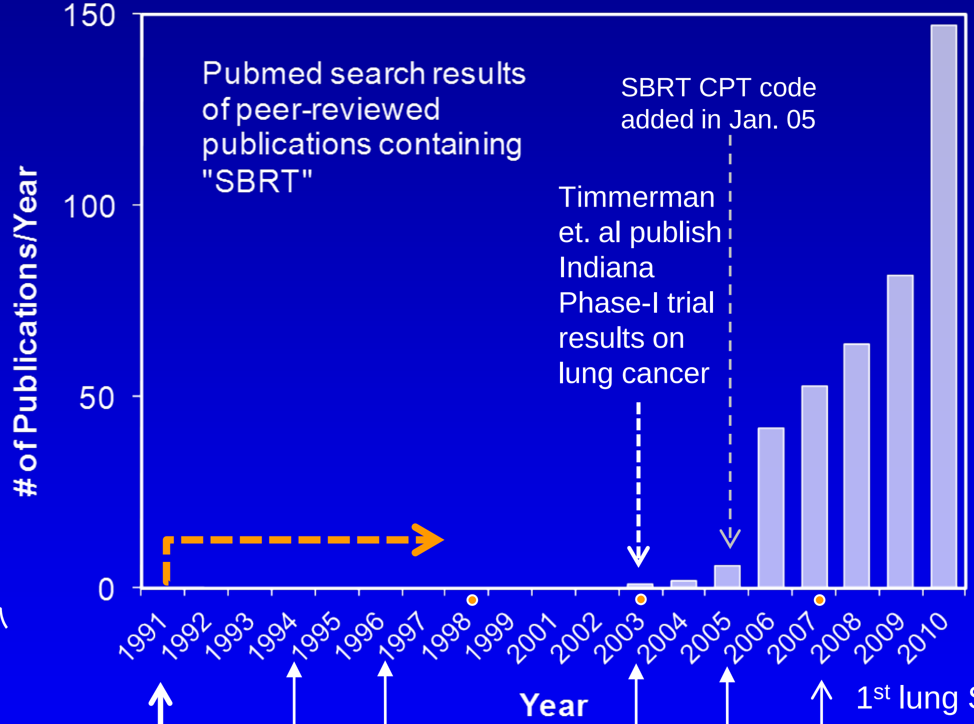
The Emergence of SBRT

- Gauged by the yearly publications containing “SBRT”:



3-year results of RTOG 0236 trial for medically inoperable patients with early stage NSCLC (Timmerman et. al, JAMA 2010):

- LC: 97.6%
- OS: 55.8%
- Moderate morbidity

“First significant change in 50 years for these patients”
– R. Timmerman, 51st ASTRO annual meeting, 2009

1987 IMRT Concept

Peacock IMRT

DMLC IMRT

Elekta XVI CBCT

Varian OBI CBCT

1st lung SBRT patient at Yale treated on Sept. 5, 2007

Started by I. Lax and H Blomgren of Karolinska University Hospital and Institute under the name “Extracranial stereotactic radiation therapy” (1,965 tumors treated between 1991 and 2003)

ACS Statistics on Lung Cancer

- Represents ~15% of all cancer diagnoses
- Accounts for ~28% of all cancer deaths

➡ More Americans die each year from lung cancer than from breast, prostate and colorectal cancers combined

New diagnosis and mortality in 2009:

- ~220,250 new cases
- ~159,390 die from lung cancer

➡ > 70% of patients diagnosed with lung cancer will eventually die from lung cancer

Treatments for Early Stage Lung Cancer

Standard Tx

Surgical resection

5-year survival rates:
~ 60-70% for stage I
(T1-2, N0) NSCLC

Medically inoperable

e.g., due to:

- emphysema
- heart disease
- diabetics

Conventional RT
(45 - 66 Gy with 1.8 or 2 Gy per fraction)

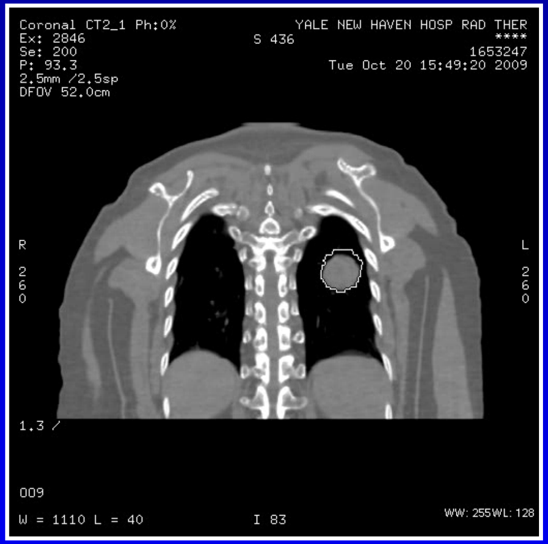
Observation without specific cancer therapy

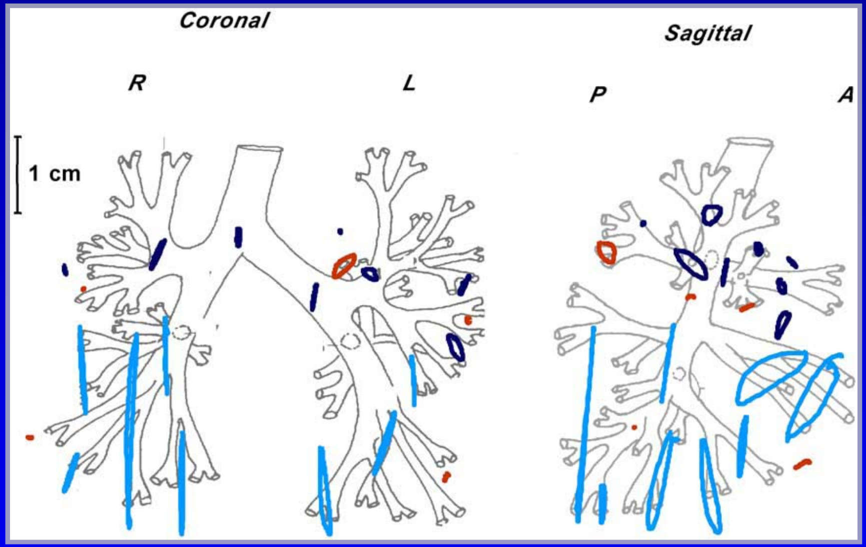
Outcomes are not ideal with either approach:

- 2-year survival < 40% with either approach
- RT: local control ~ 30-40%
- RT: 5-year survival ~ 10-30%

Physical Challenges in Lung RT

- Thoracic anatomy
- Large tissue heterogeneity
- Respiration-induced target and organ motions





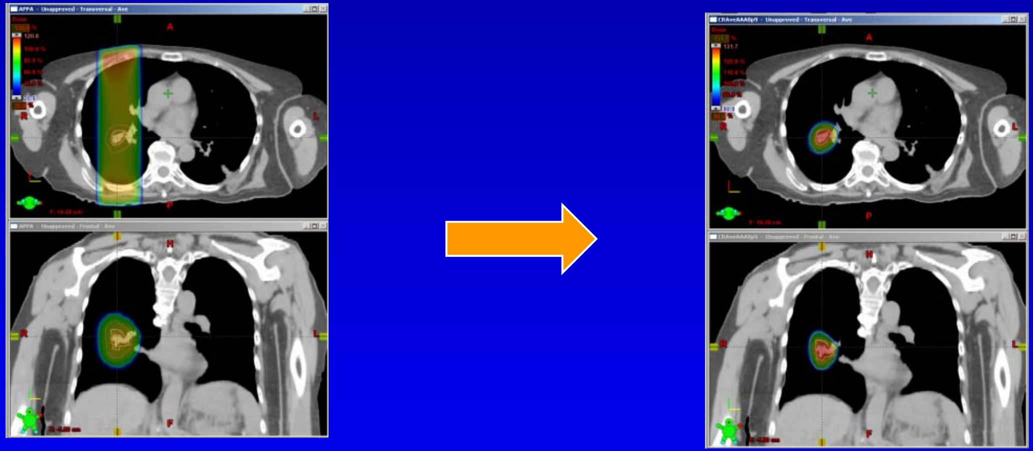
- 50% of lung tumors move >5 mm during treatment
- Unfixed tumors in lower lobe can move >10 mm
- Tumor motion largest in cranial-caudal direction but not one-dimensional

H. Shirato, Y. Seppenwoolde, et. el, “Intrafractional Tumor Motion: Lung and Liver”, *Seminars in Radiation Oncology*, Vol **14**, No 1 (January), 2004: pp 10-18

SBRT for Lung Tumors

Aims to deliver a significantly larger dose, in a few fractions (e.g. 1-5), to enable destruction of tumor cells without causing excessive damage to normal tissues through:

- Highly conformal dose distribution with sharp dose falloff



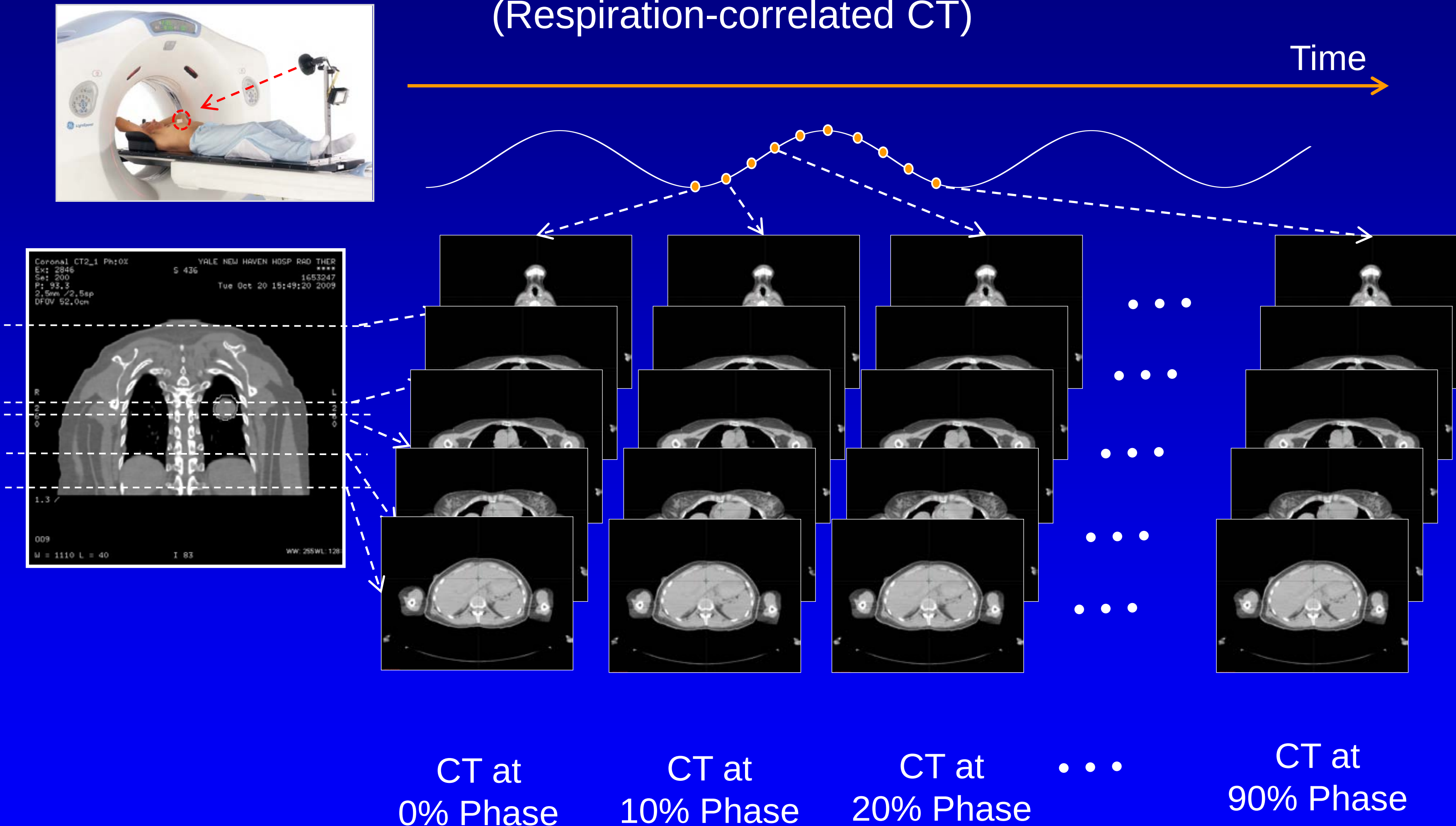
- Precise targeting
- Active management / reduction of organ motions

Motion Reduction & Management

- **Motion reduction:**
  - Breath hold
  - Abdominal compression
    (used early on by Lax and Blomgren at Karolinska Institute to keep motion with ± 5mm)
  - Gated RT: Active breathing control (ABC) or free breathing
- **Motion management:**
  - Real-time tumor tracking and dose delivery
    (novel method, still under research and development)
  - Mid-ventilation targeting under free breathing
    (studied by and used in The Netherlands Cancer Institute)

4DCT

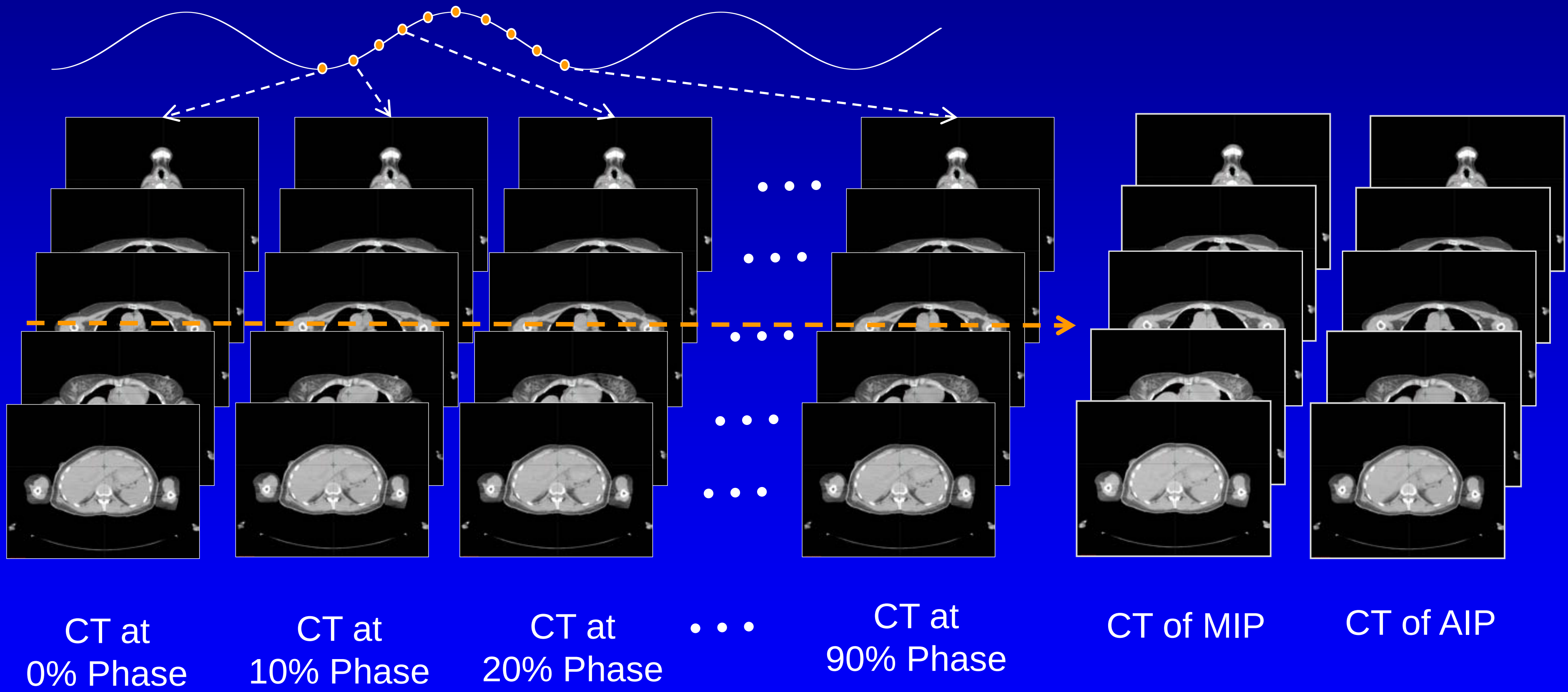
(Respiration-correlated CT)



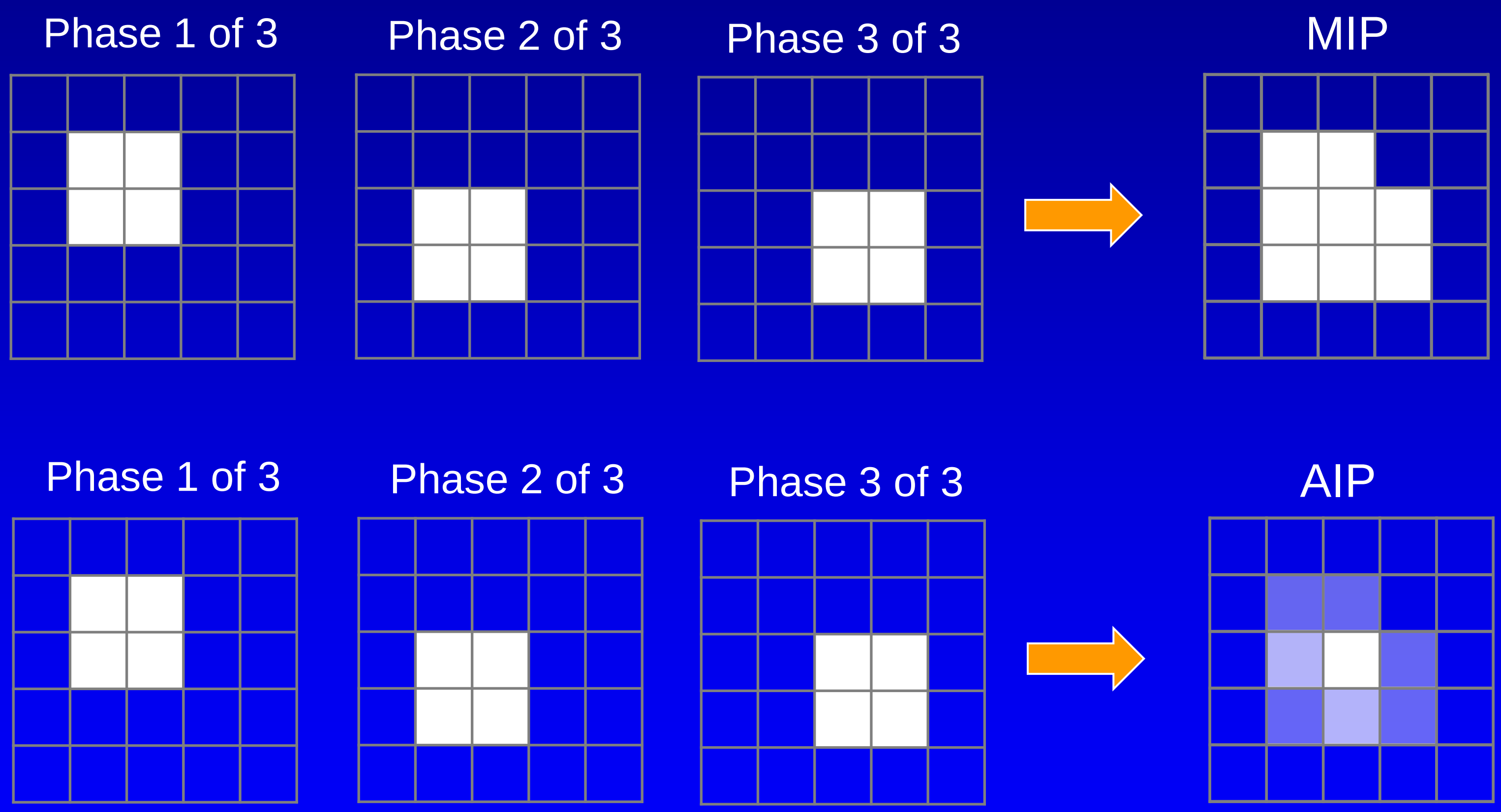
Enabling technology – 4DCT: Description of 4DCT first appeared in 2003 in publication form

4DCT-Derived Composite CT

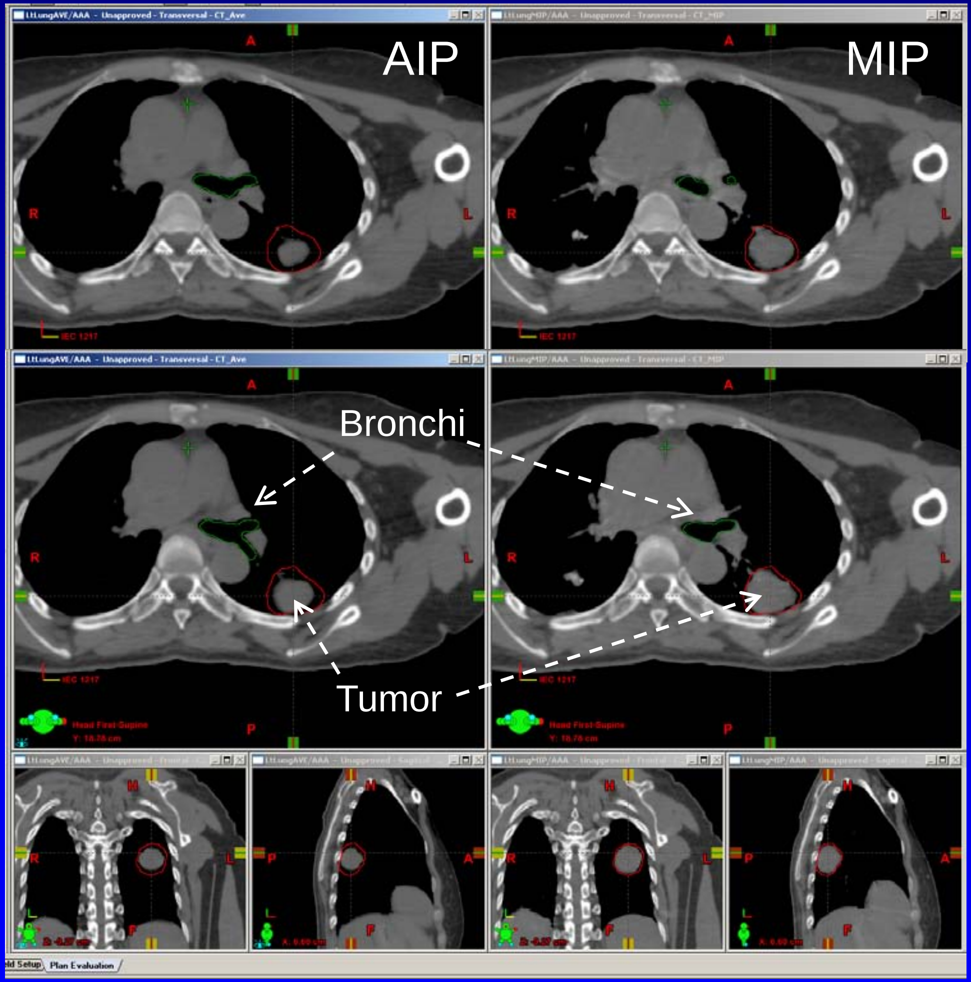
- Maximum intensity projection (MIP) & average intensity projection (AIP)



4DCT-Derived Composite CT



Impact on Organ Delineation



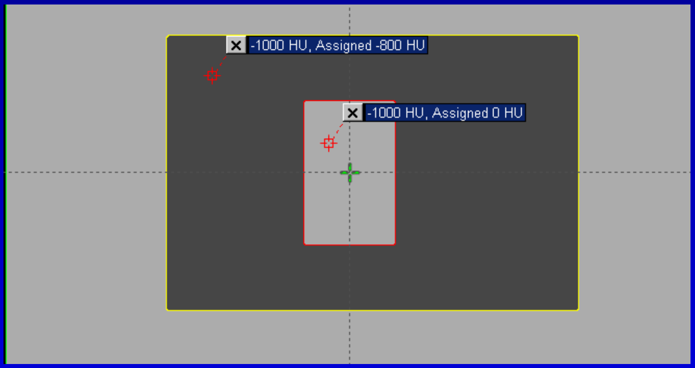
- The shape and volume of moving structures can be different on AIP- and MIP-CT, dependent on the motion magnitude

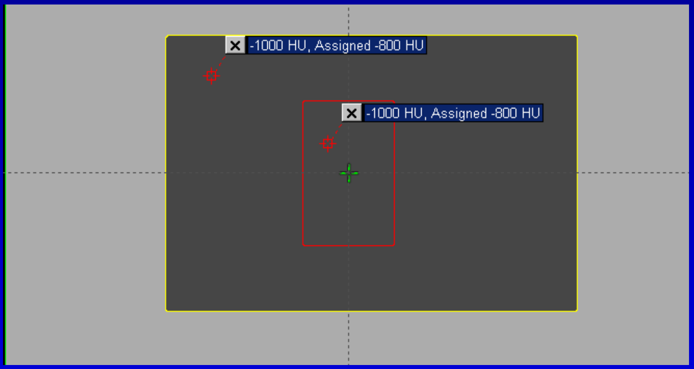
Impact on Dose-Volume Evaluation

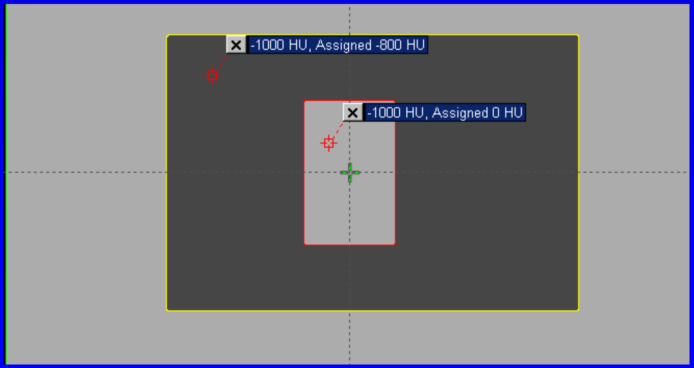
A two phase model:

Target in field 50% of time

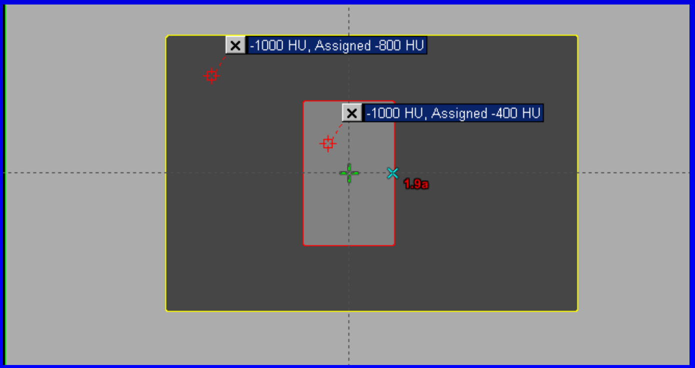
Target out of field 50% of time







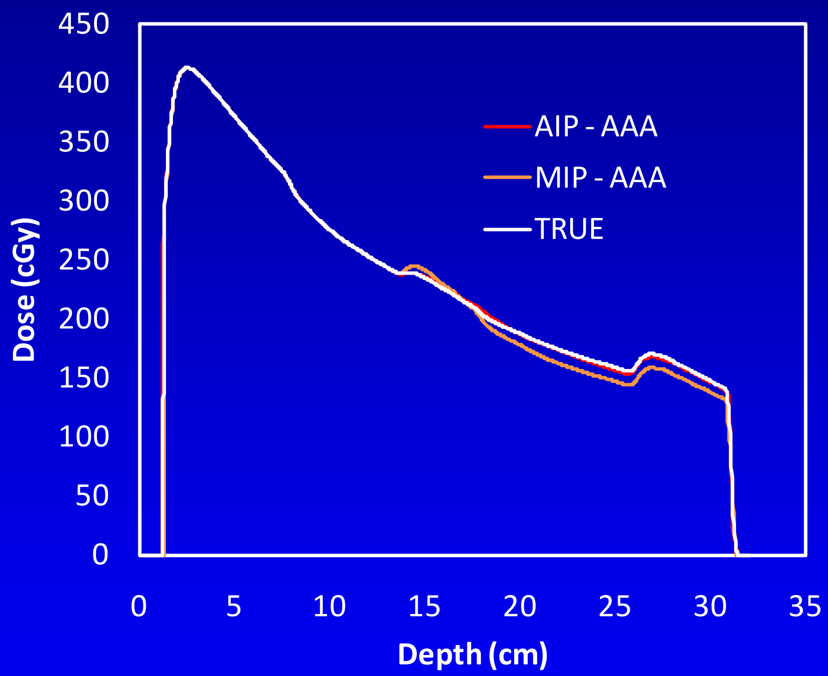
MIP

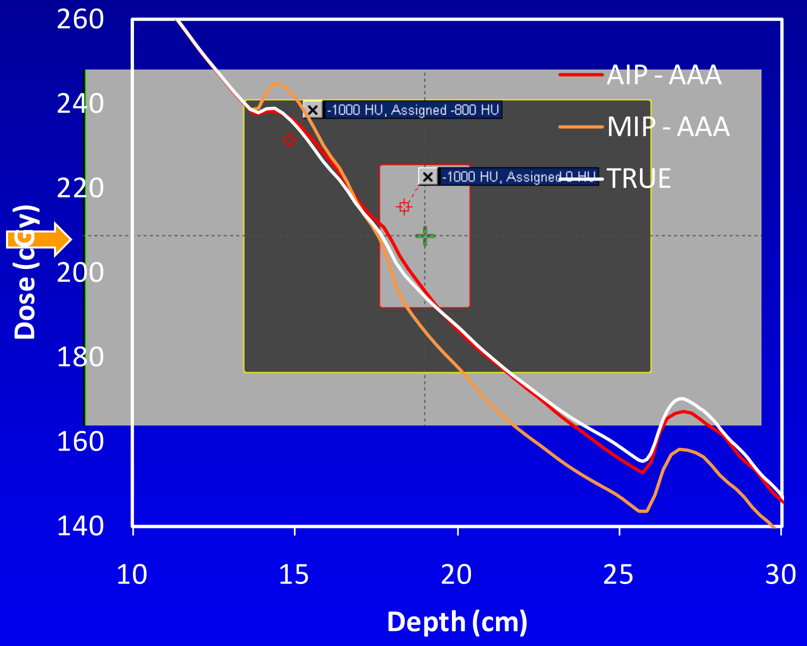


AIP

Impact on Dose-Volume Evaluation

Dose profile along the central axis:



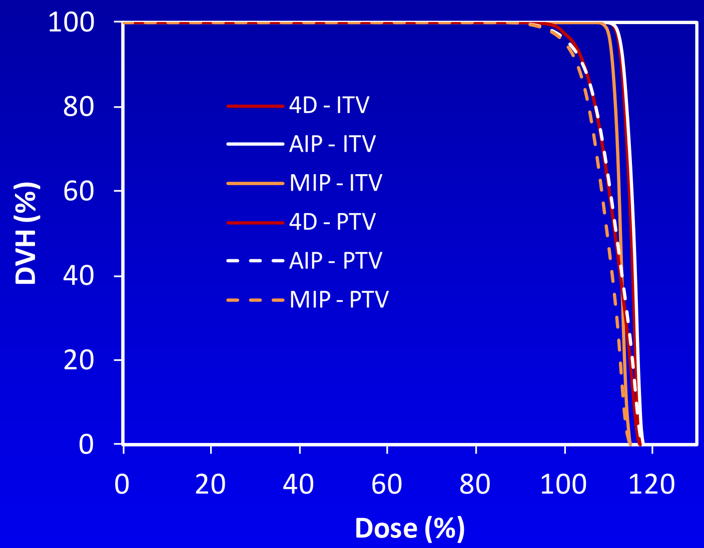


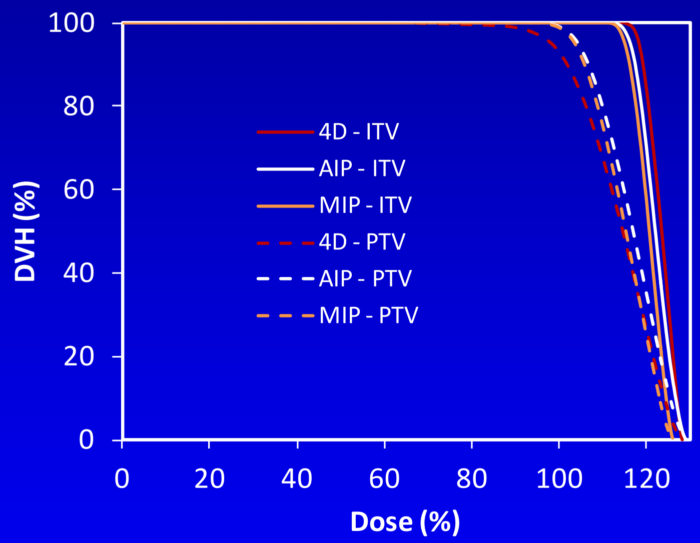
- Dose calculated with AIP is closer to actual
- However, AIP cannot fully reproduce the build-up and build-down effects at target interface, resulting in some differences
- Dose calculated with MIP has larger difference from actual

Impact on Dose-Volume Evaluation

Patient data - target volumes:

- Sample DVHs:





Impact on Dose-Volume Evaluation

- Dose statistics for target volumes:

ITV - D_{99} (%)			Relative Error(%)		ITV - D_{90} (%)			Relative Error(%)	
AIP	MIP	4D	AIP	MIP	AIP	MIP	4D	AIP	MIP
118.8	120.9	117.3	1.3	3.1	121.8	123.3	121.7	0.1	1.3
114.1	113.1	116.7	-2.2	-3.0	117.2	115.9	119.2	-1.6	-2.7
111.6	109.3	111.3	0.3	-1.8	113.4	110.9	112.9	0.4	-1.8
112.0	115.6	115.1	-2.7	0.4	117.9	120.0	119.4	-1.3	0.5
115.7	116.2	115.9	-0.2	0.3	118.1	118.2	118.1	0.0	0.1
98.8	100.3	94.3	4.8	6.4	104.1	106.9	104.6	-0.5	2.2

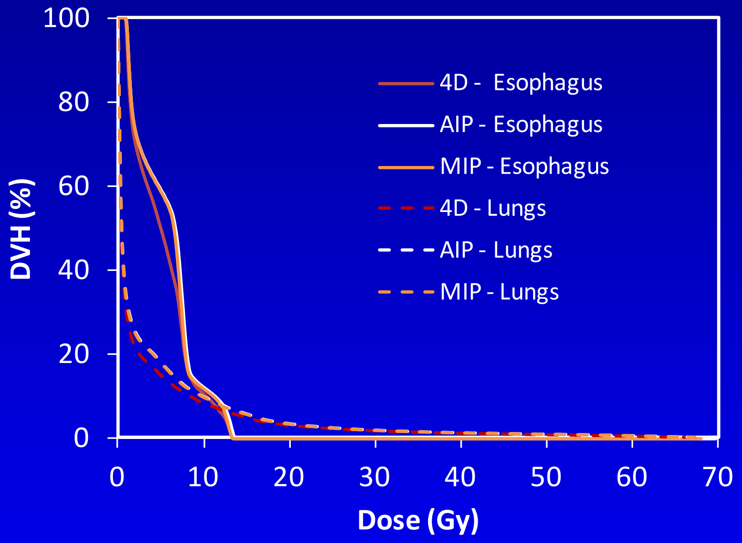
PTV - D_{99} (%)			Relative Error(%)		PTV - D_{90} (%)			Relative Error(%)	
AIP	MIP	4D	AIP	MIP	AIP	MIP	4D	AIP	MIP
99.6	120.9	117.3	-15.1	3.1	105.7	107.9	99.0	6.8	9.0
99.8	99.3	88.9	12.3	11.7	106.5	105.6	101.9	4.5	3.6
94.8	94.2	98.2	-3.5	-4.1	104.3	102.9	104.5	-0.2	-1.5
93.5	95.9	94.3	-0.8	1.8	102.9	104.8	104.7	-1.8	0.1
98.4	99.1	98.3	0.1	0.8	105.9	106.2	106.6	-0.7	-0.4
85.5	88.0	65.5	30.5	34.4	92.5	95.9	87.8	5.4	9.3

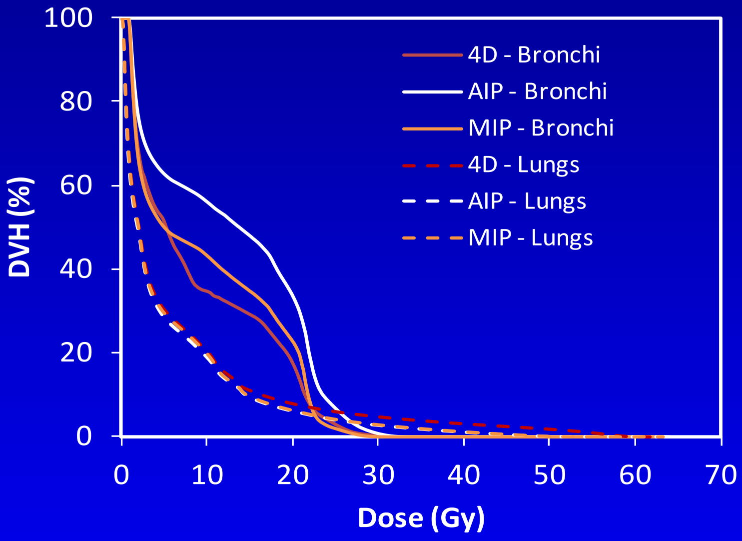
- Larger dose errors were observed in PTV as expected
- Compared with using AIP, doses near the periphery of ITV were overestimated (up to 7.4%) while doses in the central portion were underestimated (up to 2%) when using MIP.

Impact on Dose-Volume Evaluation

Patient data - moving normal organs:

- Sample DVHs:





- Depends on the proximity to target volume and the magnitude of motion
- Effects are small in most cases (e.g. the left chart above)
- For a bronchi close to ITV, dose-volume overestimation by up to 10 Gy in dose and 20% in volume were observed when using enclosed-volume contoured on AIP (e.g. the right chart above).

On the Use of 4DCT-Derived CT

- AIP and MIP provide a convenient interim solution to lung SBRT planning in absence of true 4D planning capability
- Planning based on AIP and MIP could introduce variable dose uncertainties depending on the location and the magnitude of respiration-induced motion of involved anatomic structures
- Dose calculated using AIP is generally closer to that of 4D reference than using MIP
- Volumes delineated on MIP are larger than actual for structures with HU > 0
- Volumes enclosed by hollow structures (with HU <0) are larger when delineated on AIP and smaller when delineated on MIP
- Further deviation in dose can occur when patient's breathing pattern deviate from that in 4DCT scan
- 4D planning with controlled breathing motion is desirable

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