Respiratory Gated and Four-Dimensional Tumor Tracking Radiotherapy

P Keall[1,2], S Vedam[2,3] and M Murphy[2]
[1]Stanford University
[2]Virginia Commonwealth University
[3]UT MD Anderson Cancer Center

Potential conflicts-of-interest

- I am PI of a sponsored research agreement between Stanford University and Varian Medical Systems

Educational objectives

- Understand the rationale for accounting for respiratory motion during imaging, treatment planning and radiation delivery
- Learn about respiratory gated radiotherapy and 4D tumor tracking radiotherapy
- Understand the advantages and disadvantages of respiratory gated and tumor tracking radiotherapy

Overview

- Effects of poor motion management
- Clinical rationale for improved motion management
- Target position monitoring systems
- Uses of target position information
- Summary

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Measurement of respiratory motion

Site	Technique					
	CT	MR	Fluoroscopy	Ultrasound	Nuc. imaging	EPID
Pancreas				Suramo[68] Bryan[69]		
Liver		Korin[73]		Suramo[68] Davies[66]	Weiss[84] Harauz[85]	
Kidney				Suramo[68] Davies[66]		
Diaphragm	Giraud[72]	Korin[73]	Wade[74] Ford[81] Minohara[77]	Davies[66]		
Prostate			Malone[75]			
Lung	Ross[70] Hanley[71] Shimizu[46] Essapen[172] Stevens[37] Sixel[87] Grills[88]		Kubo[30] Ekberg[20] Shirato[178] Murphy[78] Chen[79] Engelsman[22] Barnes[80] Shimizu[47] Murphy[82] Seppenwoolde[18] Ozhasoglu[83]			Erridge[86]
Breast						Van Tienhoven[29]

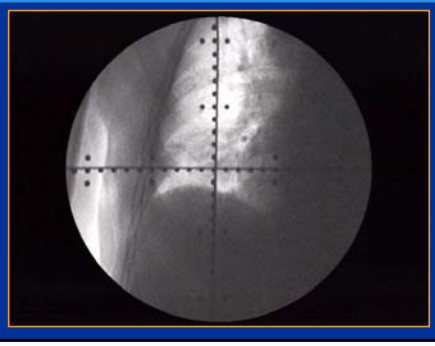
Measurement of lung tumor motion

Observer	Direction		
	IS	AP	LR
Ross[70]: Upper lobe	-	1 (0 - 5)	1 (0 - 3)
Middle lobe	-	0	9 (0 - 16)
Lower lobe	-	1 (0 - 4)	10.5 (0 - 13)
Chen[79]	(0 - 50)	-	-
Barnes[80]: Lower lobe	18.7 (0 – 32)	-	-
Middle, upper lobe	7.5 (2 - 11)	-	-
Shimizu[43]	-	6.4 (2 - 24)	-
Hanley[71]	12 (2 – 20)	5 (0 - 13)	1 (0 - 1)
Engelsman[22]: Middle, upper	(2 - 6)	-	-
Lower lobe	(2 - 9)	-	-
Seppenwoolde[18]	5.8 (0 - 25)	2.5 (0 - 8)	1.5 (0 - 3)
Murphy[42]	7 (2 - 15)	-	-
Ekberg[20]	3.9 (0 - 12)	2.4 (0 - 5)	2.4 (0 - 5)
Erridge[90]	12.5 (6 – 34)	9.4 (5 – 22)	7.3 (3 – 12)
Stevens[57]	4.5 (0 – 22)	-	-
Sixel[87]	(0 – 13)	(0 – 5)	(0 – 4)
Grills[10]	(2 – 30)	(0 – 10)	(0 – 6)

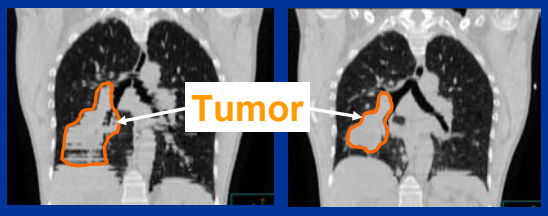
Measurement of other sites

Site	Observer	Breathing mode	
		Shallow	Deep
Pancreas	Suramo[68]	20 (10 - 30)	43 (20 - 80)
	Bryan[69]	20 (0 - 35)	-
Liver	Weiss[84]	13 +/- 5	-
	Harauz[85]	14	-
	Suramo[68]	25 (10 - 40)	55 (30 - 80)
	Davies[66]	10 (5 - 17)	37 (21 - 57)
Kidney	Suramo[68]	19 (10 - 40)	40 (20 - 70)
	Davies[66]	11 (5 - 16)	-
Diaphragm	Wade[74]	17	101
	Korin[73]	13	39
	Davies[66]	12 (7 - 28)	43 (25 - 57)
	Weiss[84]	13 +/- 5	-
	Giraud[72]	-	35 (3 - 95)
	Ford[81]	20 (13 - 31)	-

The tumor moves with time



Distorted images, incorrect anatomical positions, volumes or shapes



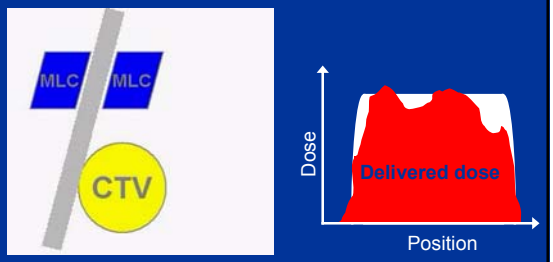
Conventional With 4D imaging

Treatment Planning: Large margins are added to the clinical target volume

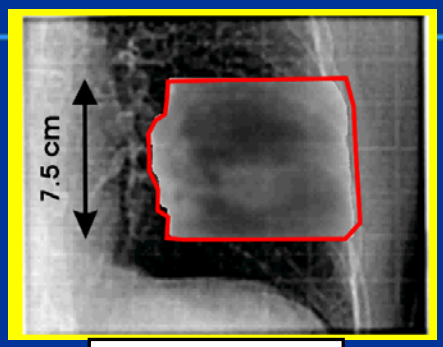
- Increases normal tissue dose and limits target dose

Conventional Account for motion

IMRT Delivery: Interplay between anatomy and MLC leaf motion leads to motion artifacts

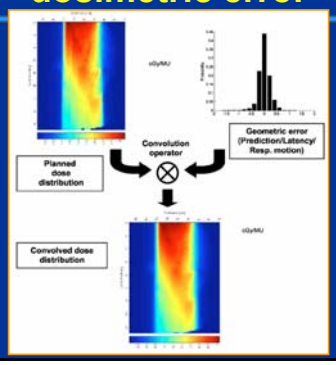


Motion during treatment

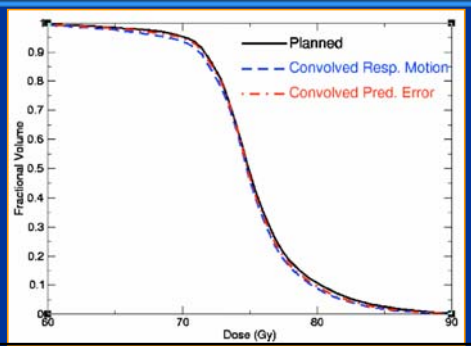


Courtesy Slobodan Devic

Geometric error translates to dosimetric error



Geometric error translates to dosimetric error



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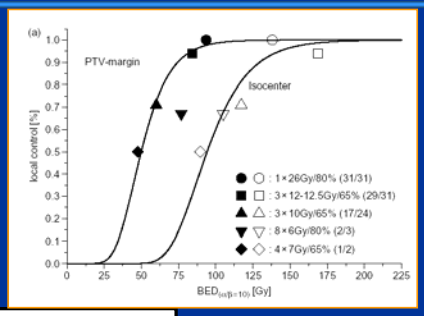
Clinical rationale

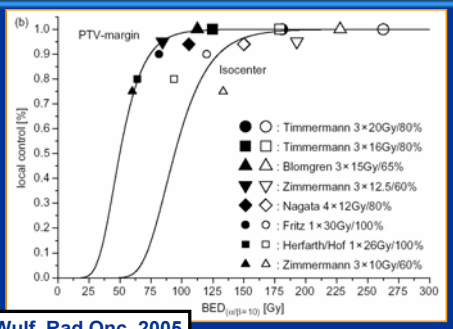
- An RTOG retrospective analysis of 1290 NSCLC patients demonstrates that every 10-Gy increase in BED results in an 18% decrease in the risk of death
- Martel *et al*. estimate that 85 Gy is needed to achieve 50% local progression-free survival at 30 months
- The cost of dose escalation is normal tissue toxicity, which has been shown to be dose dependent for lung, heart, esophagus and bronchus

Improved targeting will allow improved tumor control



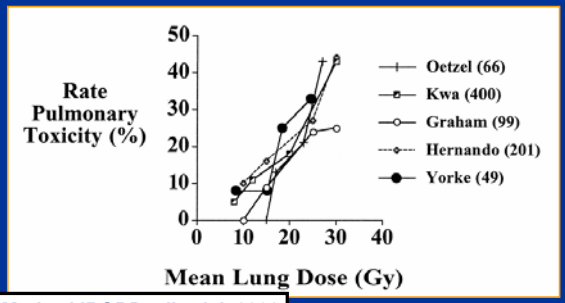
Wulf, Rad Onc, 2005

Improved targeting will allow improved tumor control



Wulf, Rad Onc, 2005

Improved targeting will allow reduced treatment toxicity



Marks, IJROBP editorial, 2002

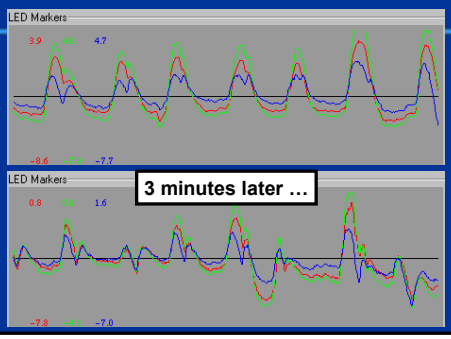
Clinical rationale

- Simultaneously increase tumor dose and reduce normal tissue dose?
  - Increase treatment accuracy
- Other methods
  - Improve dose calculation accuracy
  - Improve IMRT
  - Increase degrees of freedom in delivery
  - Normal tissue displacement
  - Particles
  - Synergistic biologic modifiers
  - …

Clinical rationale

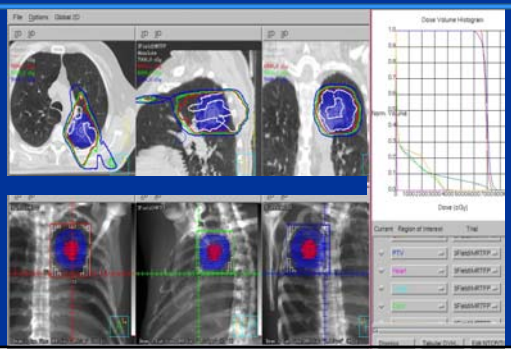
- The skeletal, respiratory, GU, GI and cardiac systems cause tumor motion
- The magnitude of motion is variable and unpredictable

Respiratory variability

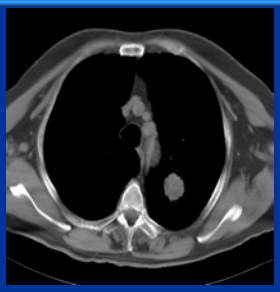


Courtesy Sonja Dieterich, Georgetown University

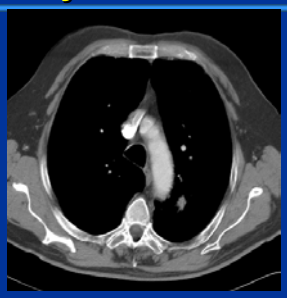
Case study: T1 NSCLC; non-operative due to COPD



Case study: Gated IMRT 70Gy in 2Gy/fx



Prior to gated IMRT



3 wks after 70 Gy gated IMRT

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Respiration signals

- External
  - Optical
  - Spirometer
  - Strain gauge
  - Nasal thermistor
  - Pressure sensors
  - …
- Internal
  - Fluoroscopy
  - EPID
  - Indoor GPS
  - EM
  - MRI
  - US
  - …

Surrogate choices

Surrogate	The good	The bad
External respiration signal	Real time	Limited dimensionality, no positional information, variable tumor correlation
Implanted markers	Real time	Limited dimensionality, migration, invasive
4D CT	Large dimensionality	Not real time
MRI/US	Large dimensionality, real time	Not yet commercially available

Surrogate vs. tumor motion

$$\mathbf{R}(t) = \mathbf{S} + \mathbf{I} + \mathbf{M}\left[\mathbf{T}(t + \Delta\theta)\right] + \boldsymbol{\varepsilon}(t)$$

$\mathbf{R}(t)$ = motion signal at time t
$\mathbf{S}$ = set-up error
$\mathbf{I}$ = internal motion
$\mathbf{M}$ = motion ratio (surrogate/tumor)
$\mathbf{T}(t)$ = tumor motion
$\Delta\theta$ = phase difference
$\boldsymbol{\varepsilon}(t)$ = error term

Organ/respiratory signal correlation

Organ/source	Respiratory signal	N patients (measurements)	Correlation range	Phase shift	Source
Diaphragm SI fluoroscopy	Abdominal displacement	5 (60)	0.82-0.95	Not observed	Vedam *et al.*[91]
Tumor and diaphragm, fluoroscopy	Abdominal displacement	43	0.41-0.94	Short delays observed	Ahn *et al.*[102]
Tumor, SI fluoroscopy	Spirometry & abdominal displacement	11 (23)	0.39-0.99	-0.65 – 0.5 s	Hoisak *et al.*[103]
Tumor, 3D biplane radiography	Abdominal displacement	26	Respiratory waveform cycle agreed with SI and AP tumor motion	Principally within 0-0.3 s existence of > 1.0 s	Tsunashima *et al.*[104]
Lung vessels, cine MRI	Abdominal displacement	4	SI 0.87 ± 0.23, AP 0.44 ± 0.27	-	Koch *et al.*[105]
Lung tumor, respiration correlated CT	Abdominal displacement	9 where tumor SI motion > 5 mm	0.74-0.98	<1 s 4 pts <0.5 s 5 pts	Mageras *et al.*[99]
Lung tumor, SI respiration correlated CT	Diaphragm position	12	0.73-0.96	<1 s 4 pts <0.5 s 5 pts	Mageras *et al.*[99]

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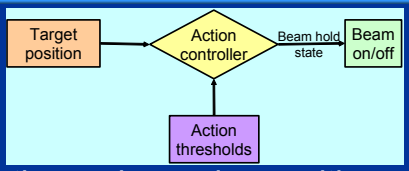
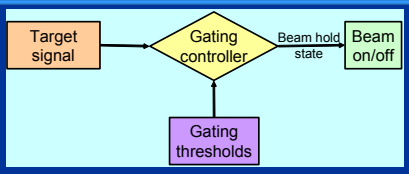
Action threshold



- Continuously receive position information
- Beam on if position < threshold
- Beam hold if position > threshold

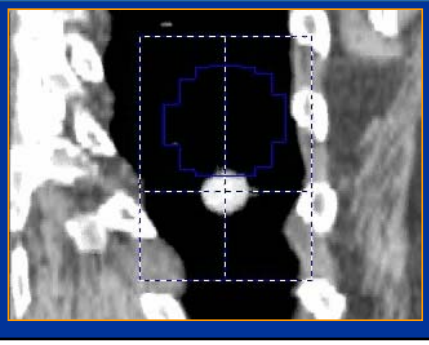
Respiratory gating

Gated control

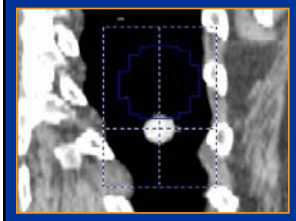


- Similar to action threshold but applicable to periodic motion
- Continuously receive position information
- Beam on if position < threshold
- Beam hold if position > threshold

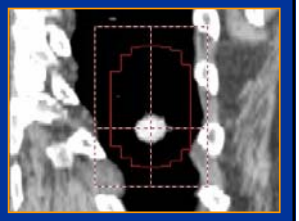
Respiratory gated treatment



Respiratory gated treatment



Motion inclusive treatment



RPM system components

IR Reflective marker block

Markers reflect IR light making them appear as bright areas on CCD camera images

Video distribution amplifier

Amplify video signals

IR Illuminator

Infra-red light source

CCD Camera

Obtains real-time images of IR reflective marker block motion

Junction Box

Power supply source and routing center for signals

In room View Finder

Ensure markers are within field of view of CCD camera

Gating switch box

Enable/Disable gated treatments at Linac

Motion tracking

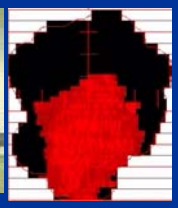
Dynamic motion compensation

- Open loop- move beam
  - Robotic control of the linear accelerator (clinically available)
  - Block motion (used clinically at one center)
  - DMLC (proof of principle but not clinical)
- Closed loop- move patient
  - Couch motion (proof of principle but not clinical)

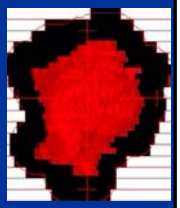
Couch tracking

Courtesy Warren D'Souza
University of Maryland

Schematic



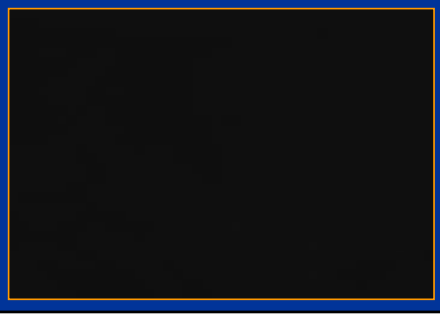
No tracking



Tracking

Beam tracking

Courtesy Accuray



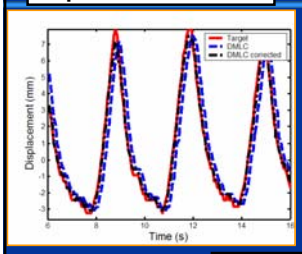
Block tracking

DMLC tracking (CRT)

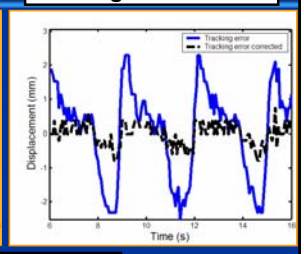
DMLC tracking (IMRT)

Tracking patient-derived motion

Displacement vs. time

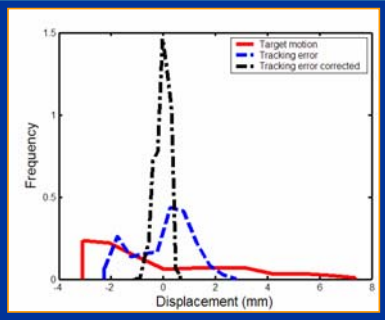


Tracking error vs. time

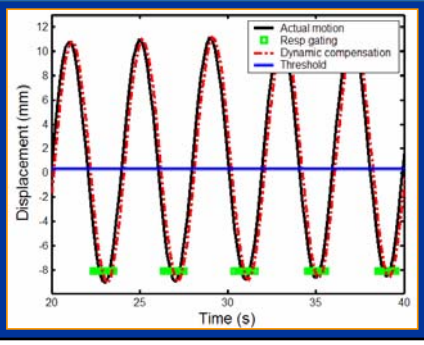


—Target
—Beam
—Beam (RT corr)

PDF of corrected and uncorrected motion



Comparison of motion compensation methods



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- Position monitoring devices provide useful information
- This information can be used in several ways
- A targeted radiotherapy control system can minimize geometric error
- Geometric errors translate to dosimetric errors
- Engineering and implementation issues remain

Integrated position monitoring and targeted radiotherapy systems

can

- Significantly reduce systematic and random treatment errors
- Reduce set-up time
- Reduce operator error

Integrated position monitoring and targeted radiotherapy systems

are limited by

- Accuracy of position monitoring system
- Relationship of surrogate to target
  - Deformation
  - Rotation
  - Migration
  - Anatomic and physiologic changes
- Tracking of normal anatomy

Radiotherapy challenge?

Courtesy Steve Jiang
Massachusetts General Hospital