52nd Annual Meeting
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Pennsylvania Convention Center
Philadelphia, Pennsylvania

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EDUCATIONAL COURSE TU-A-BRB-1

Physics and Dosimetry of SBRT

Part III: Planning Case Studies

3 of the AAPM SBRT sessions

- HOW do we and some others do SBRT?
  - Tuesday 730 am, “Physics and Dosimetry of SBRT”, moderator M Miften, Educational Session
- WHY did we reach this place?
  - Tuesday 130 pm, “Establishing an SBRT Program”, moderator S Benedict, Practical Medical Physics
- WHAT have we accomplished so far?
  - Wednesday 130 pm, “Stereotactic Body Radiotherapy (SBRT): Technical and Clinical Considerations”, moderator I Chetty, Therapy Symposium

Spectrum of applications of SBRT

- Intensified treatment to a primary cancer
  - Stage I lung cancer
  - Primary HCC
  - Pancreas cancer
  - Prostate cancer
- Palliation/control for challenging sites of recurrence
  - Spinal
  - Retroperitoneal
  - Previously irradiated volumes
- Adjuvant systemic cytoreductive therapy
  - “Radical” treatment for isolated liver, lung, spine, and other oligometastases

Top to Bottom:

HOW do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer

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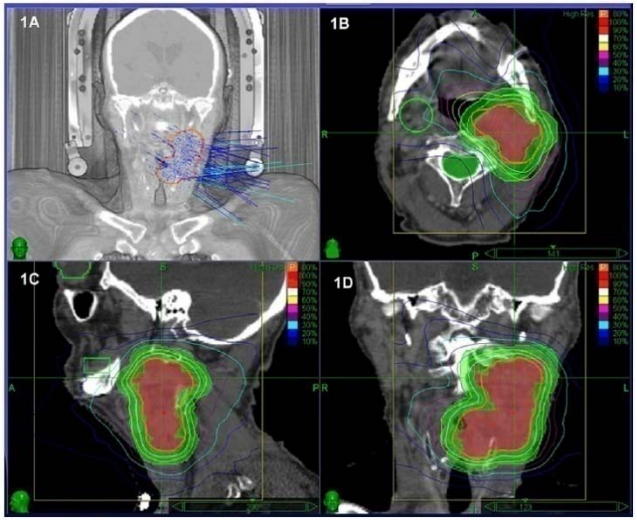
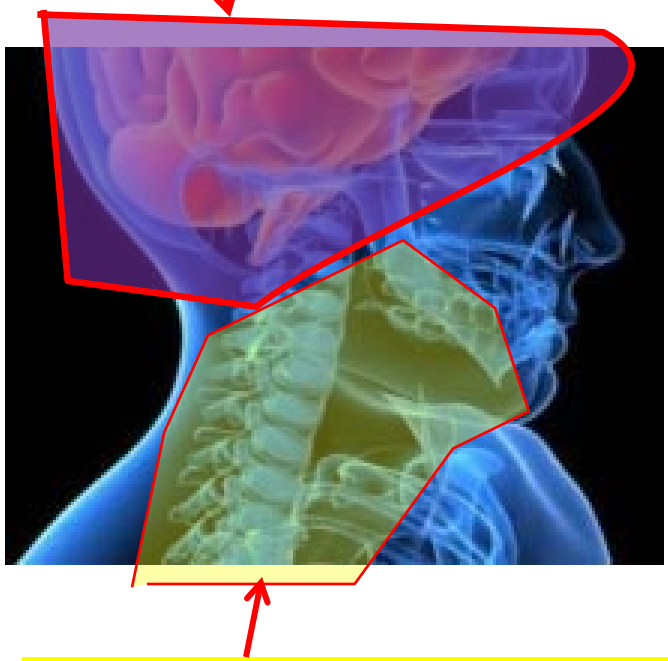


Heron et al, IJROBP 2009

CPT code semantics

- SBRT term can be used for fractionated brain tumor SRS for the MD pro fee
  - But the delivery code is SRS
- SRS is the term used for primary OR BOOST treatment to base of skull region tumors
- SBRT describes <u>an entire course of treatment</u>, not a boost phase of treatment

Delivery code = SRS
MD pro fee = SRS if 1 fxn,
SBRT for 2-5 fractions
Can be boost



Delivery code = SBRT
MD pro fee = SBRT if 1-5 fxns
Complete course, not boost

Pittsburgh H&N SBRT

Rgiawe et al, AJCO 2010

•Previously established normal tissue dose limits in Phase I study

- For Spinal cord:
  - 8 Gy in 1 fraction
  - 12 Gy in 2 fractions
- 9 Gy for the brainstem
- 20 Gy for the brain
- 10 Gy for the retina, optic nerves, and chiasm
- 6 Gy for the lens of the eye
- 20 Gy for the carotid artery
- 20 Gy for the esophagus and larynx.

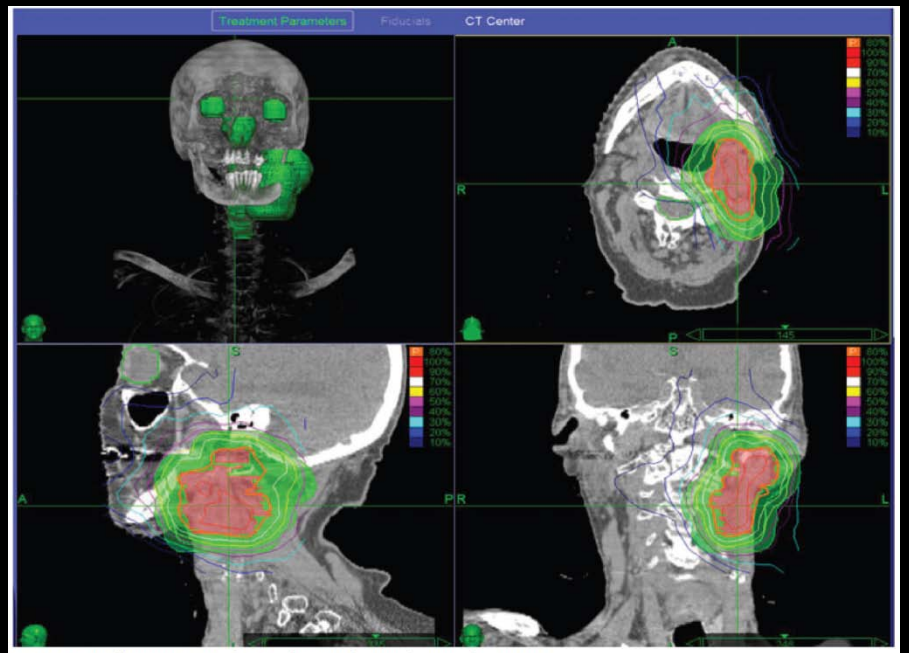
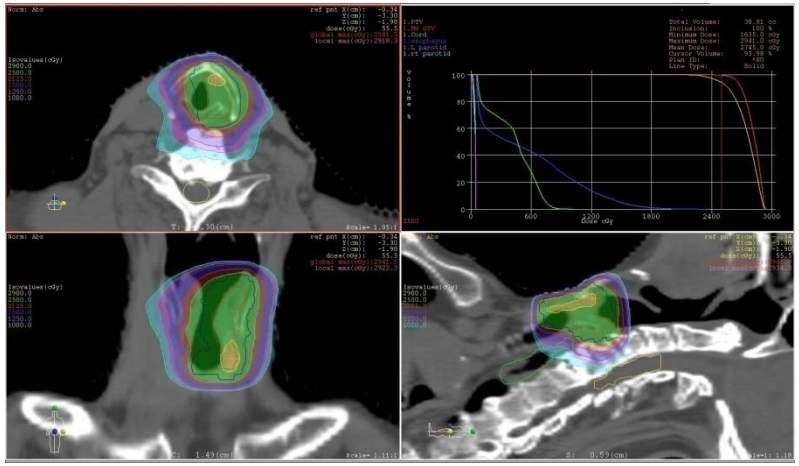


FIGURE 1. An illustrative case of SBRT planning for oropharyngeal recurrence.

- Immobilization via thermoplastic mask
- Treatment given every other day

Sample HN SBRT case, UCH

- 81 yo M with T3 N0 M0 SCC of the L true vocal cord. Pt with prior T1a SCC of L true vocal cord treated to 70 Gy/35 fractions in 11/2000.
- Plan: 25 Gy/5 fxns with cetuximab
- PTV (38.81cc): 94% volume gets 25 Gy
  - max=2941 cGy
  - min=1635 cGy
  - mean=2745 cGy
- GTV (12.11cc): 99.5% volume gets 25 Gy
  - max=2941 cGy
  - min=2345cGy
  - mean=2813 cGy
- cord: 1% max=830 cGy @ approx C5-C6
  - max=1028 cGy
  - mean=413cGy
- Esophagus: V15=0.59cc, max=2353 cGy,min=49 cGy,mean=551 cGy
- FOLLOWUP 7 mos:
  - NED on exam and PET



Immobilization alternatives

Top to Bottom:
HOW do we and some others do SBRT?

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  - And lung metastases
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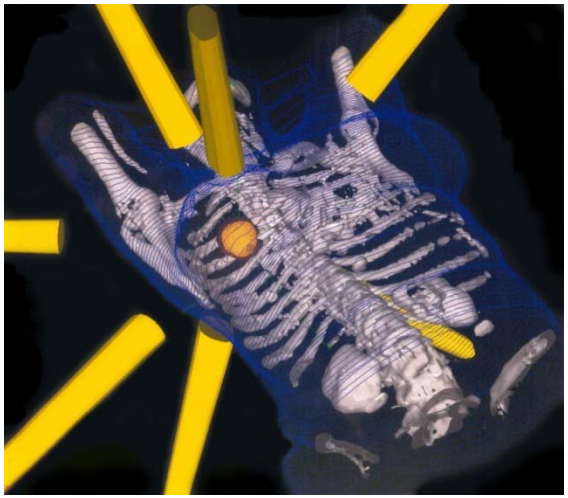
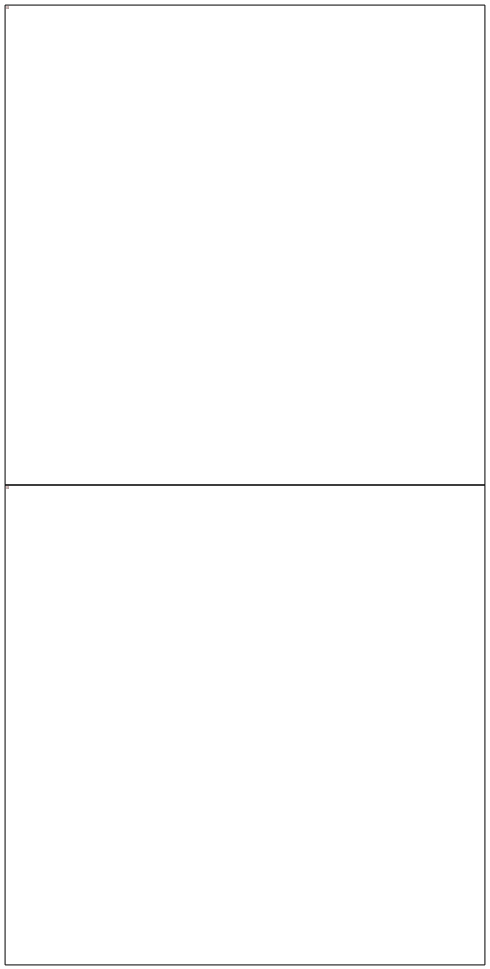
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer



The technical necessities for SBRT

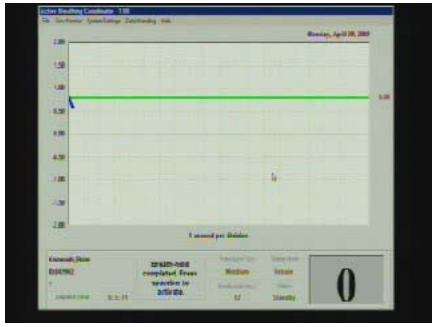
- Immobilization
  - Needs to be comfortable since treatments sometimes lengthy
- Image guidance
  - Need to relocalize target prior to each treatment
  - Removes need for rigid body frame
- Breathing motion management
  - Passive
    - Margin-based
  - Active
    - Abdominal compression
    - Controlled breath-hold
    - Gated beam-on devices

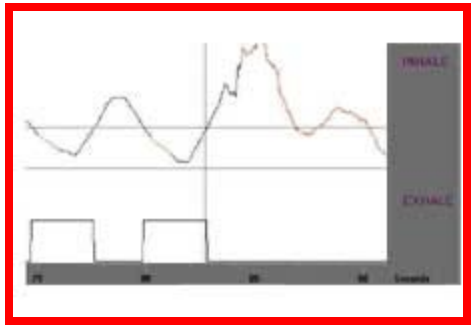


cineMRI courtesy of Dr. Paul Read, Univ. of Virginia

Respiratory control for SBRT

- Abdominal compression
  - Forces shallow breathing
- Controlled breath-hold
  - Stabilizes tumor within the respiratory cycle
  - Can be device-assisted
- Tumor tracking
  - Implanted fiducials
- Gated beam-on devices
  - Treatment only given when tumor located within the beam
  - Respiratory tracing used





Quantitative analysis of abdominal pressure relative to breathing motion

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

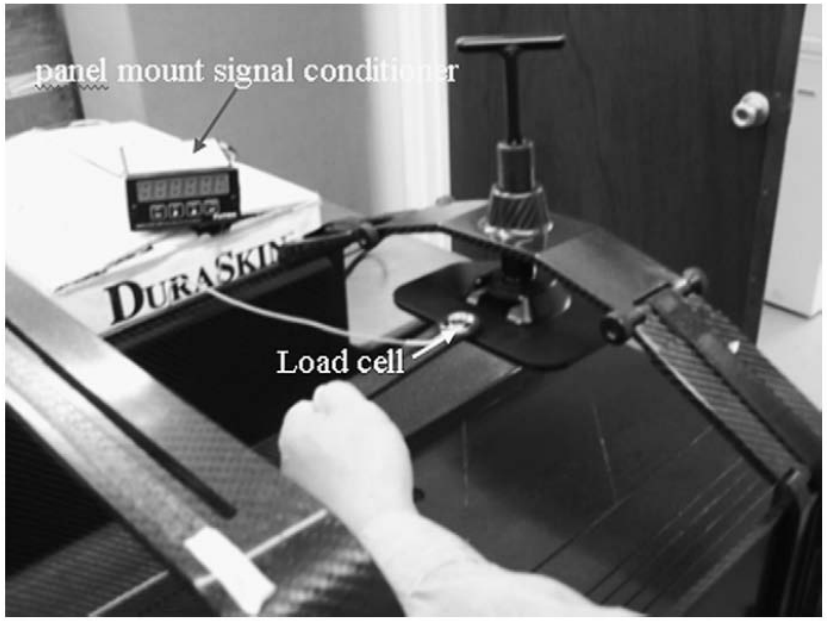


Fig. 1. Stereotactic body radiation therapy frame showing load cell and panel mount signal conditioner.

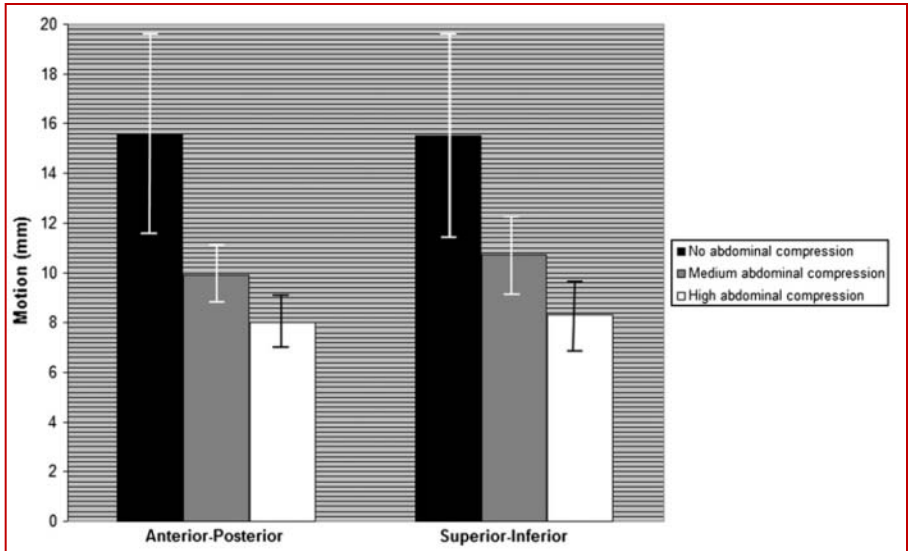


Fig. 3. Motion of diaphragm at varying levels of abdominal compression.

Note: high compression force approx 90N, or approx 22 pounds, reduced diaphragm sup-inf motion from approx 15mm to 8 mm on average

4D CT simulation *note: belt higher than for liver*

Liver case

Comparison of the 2 lung SBRT chest/rib toxicity studies

Dunlap, IJROBP 2009

U Virginia & U Colorado

- 60 patients, minimum point dose 20 Gy in 3-5 fractions to chest wall
- Endpoint: severe pain (narcotics) or rib fracture
- DVHs analyzed:
  - Chest wall = all tissue (bone and soft tissue) peripheral to lung

Pettersson, Radiother Oncol 2009

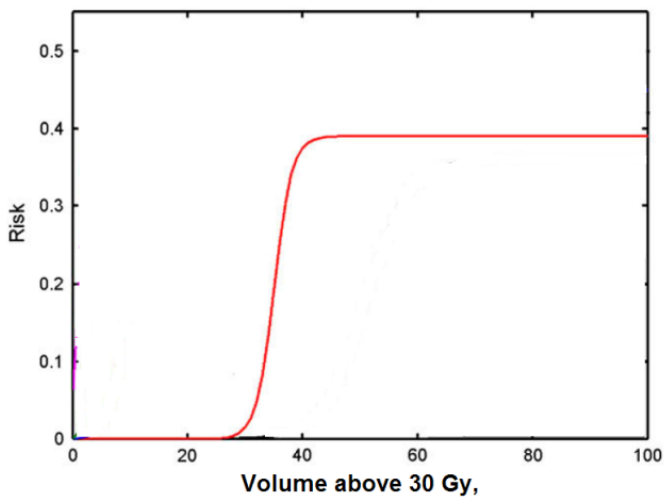
Sahlgrenska U, Sweden

- 81 ribs in 26 patients,minimum point dose 21 Gy/3 fractions received
- Endpoint: rib fracture on CT
- DVHs analyzed
  - Ribs receiving >21 Gy contoured without margin for setup errors

Common finding: absolute volume predictive parameters

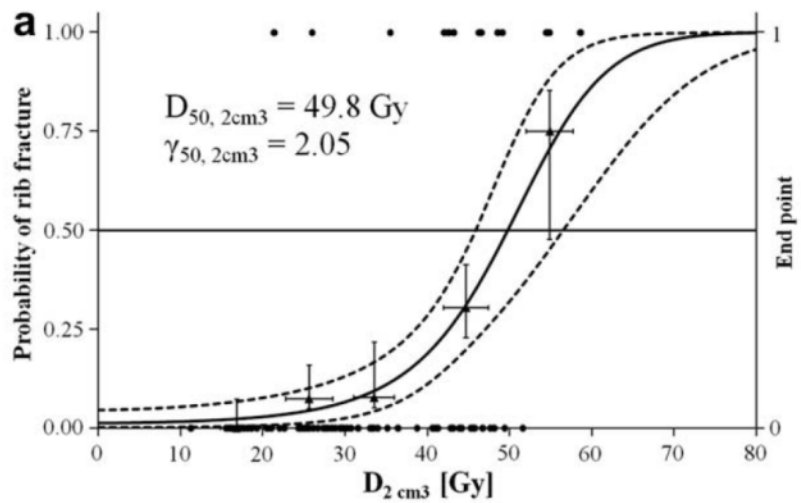
Dunlap et al:

Keep absolute V30 < 30 cc



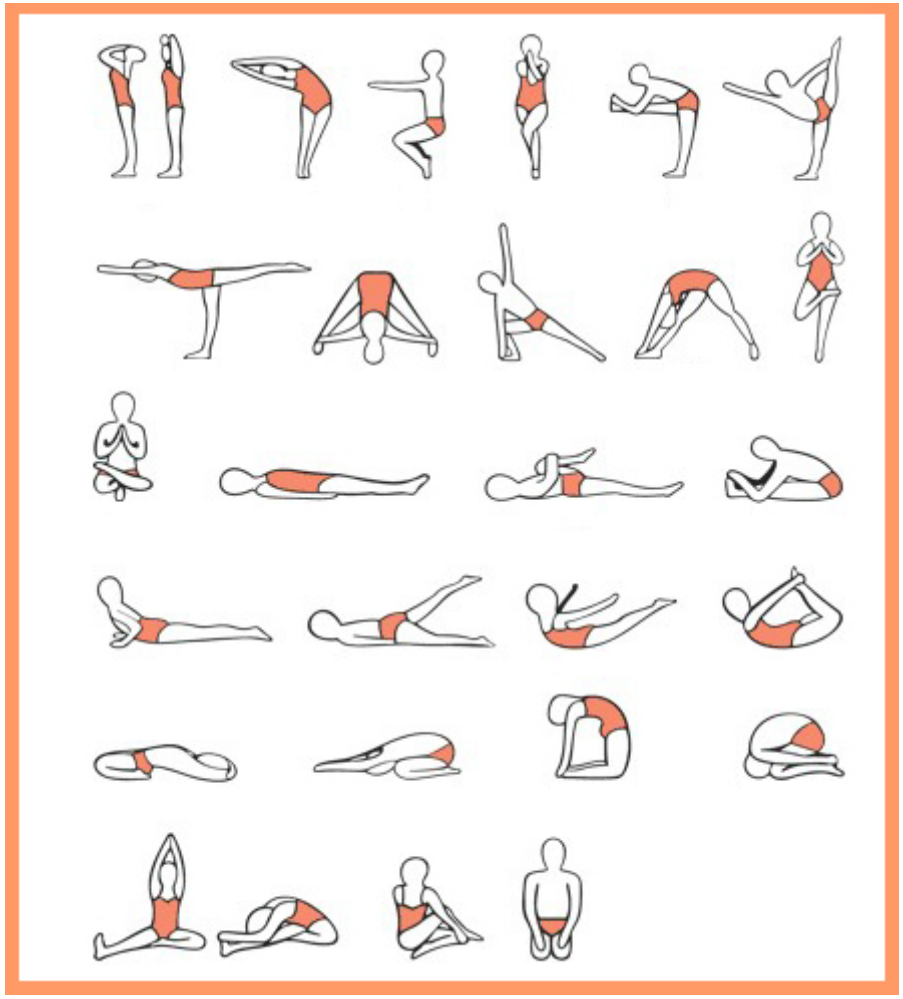
Petterssen et al:

Keep D_{2cc} as low as possible



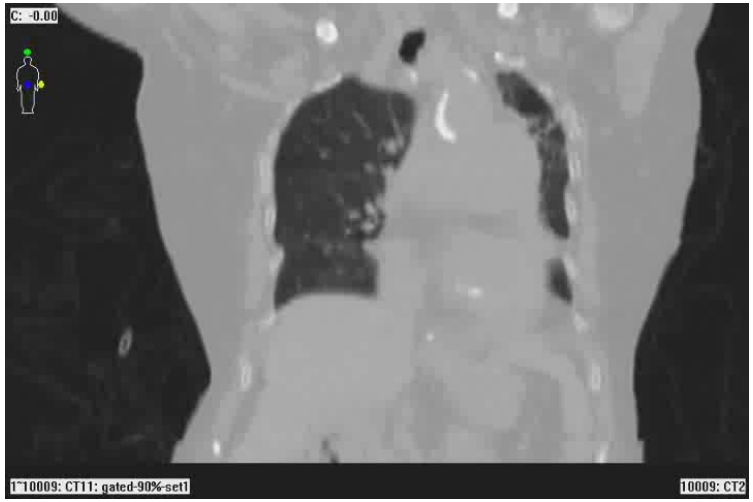
Solving irregular breathing:

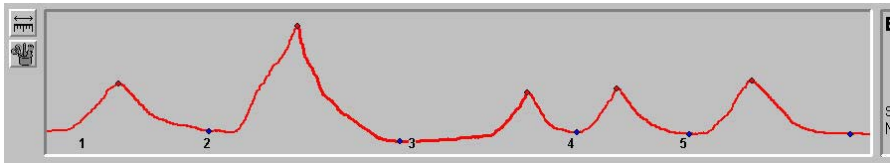
pranayama breathing

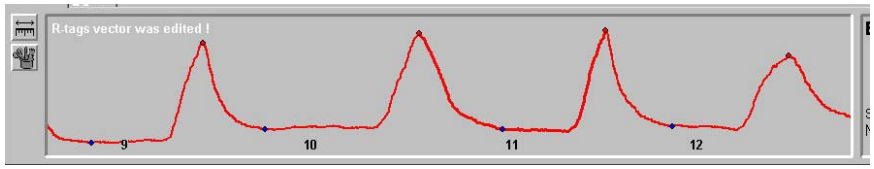


Free breathing

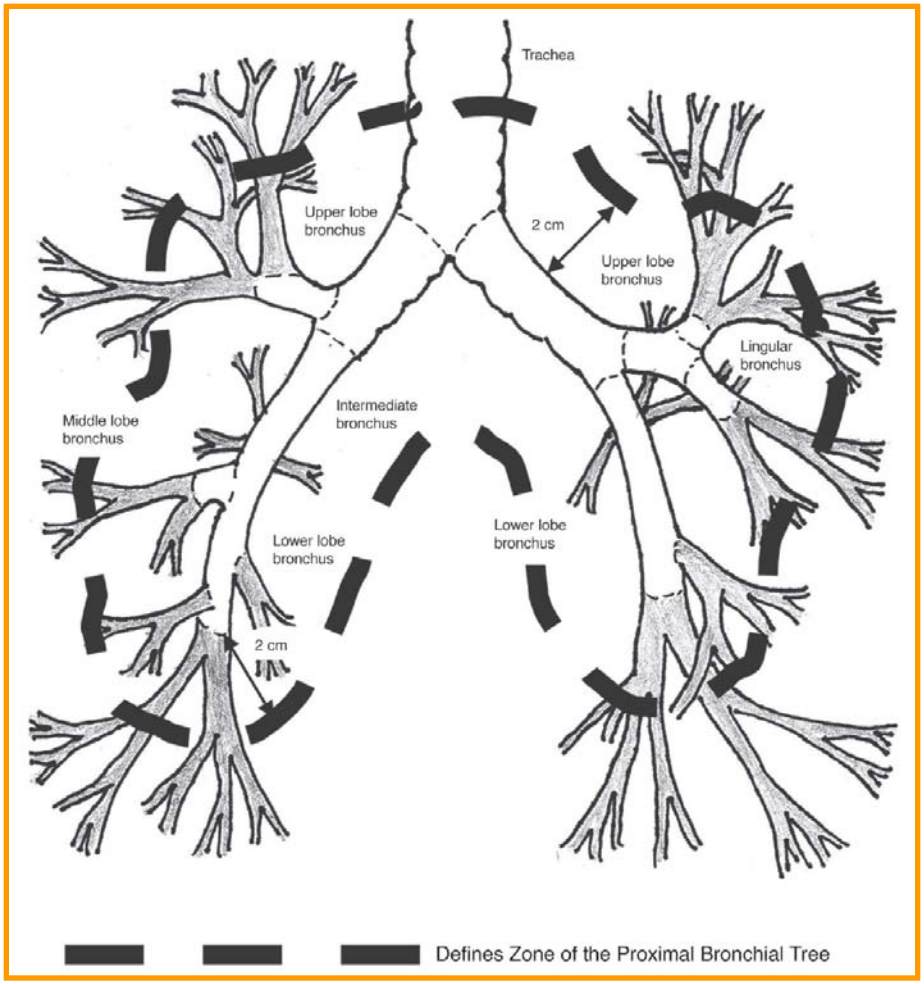
Pranayama breathing

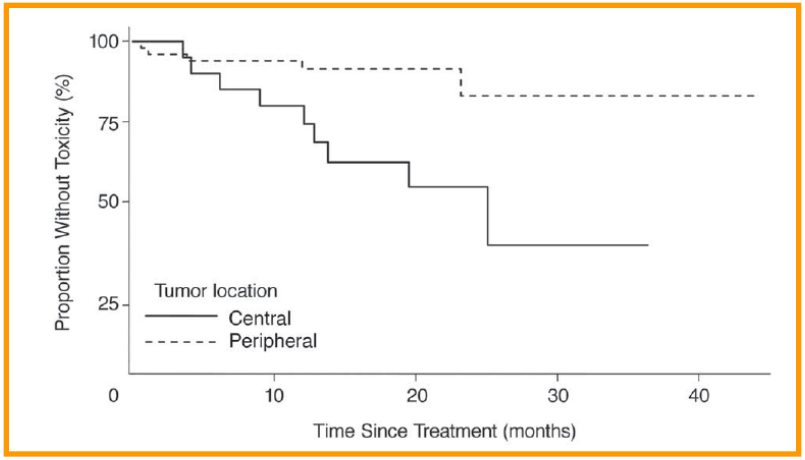






Cautionary note:
Possible problems near the proximal airways





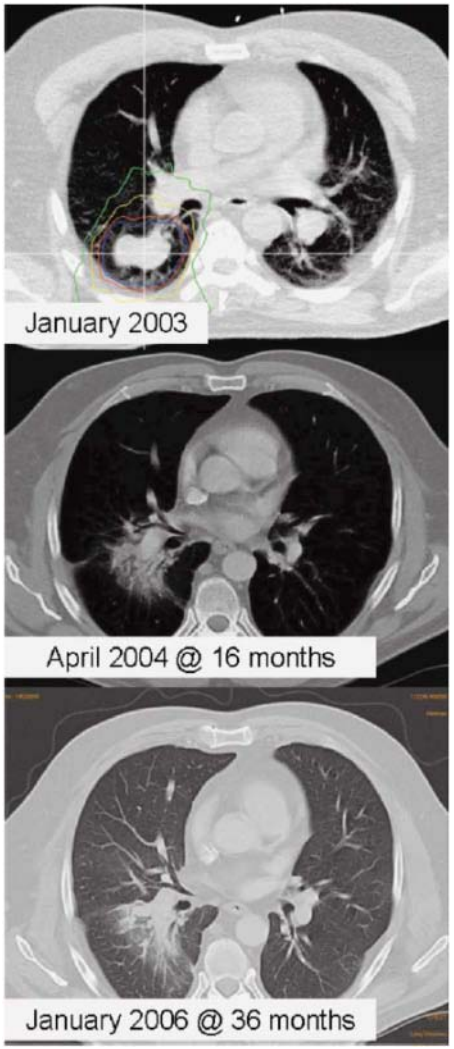
Freedom from grade 3-5 toxicity

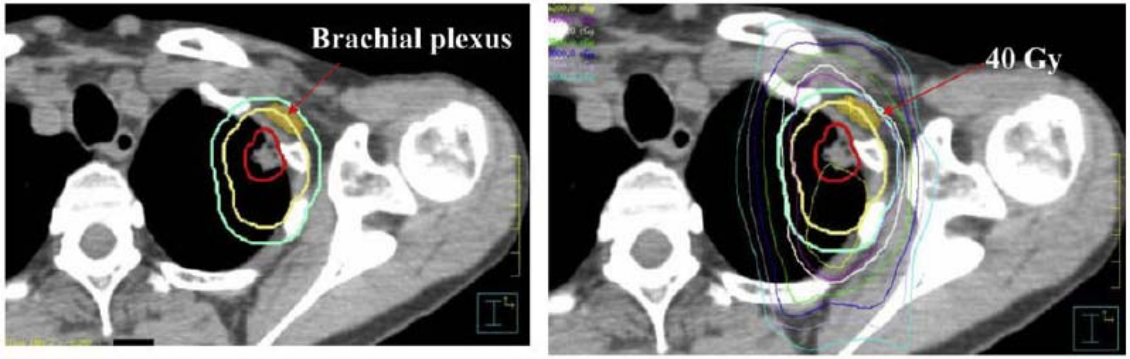
2 responses to the IU proximal airway report

Chang et al, IJROBP 2008; 72(4) 967–971

- UT-SA experience (above)
  - n=9; dose = 3x12 Gy
  - No serious toxicity
    - Median f/u 11 mos (range, 3-42)
- MD Anderson experience
  - N = 27; dose = 4x10-12.5 Gy
  - No serious lung toxicity
    - Median f/u 17 mos (range, 6-40)
    - 1 brachial plexopathy (>40 Gy/4 fxns)

BELOW: from Joyner et al, Acta Oncol 2006; 45: 802-807

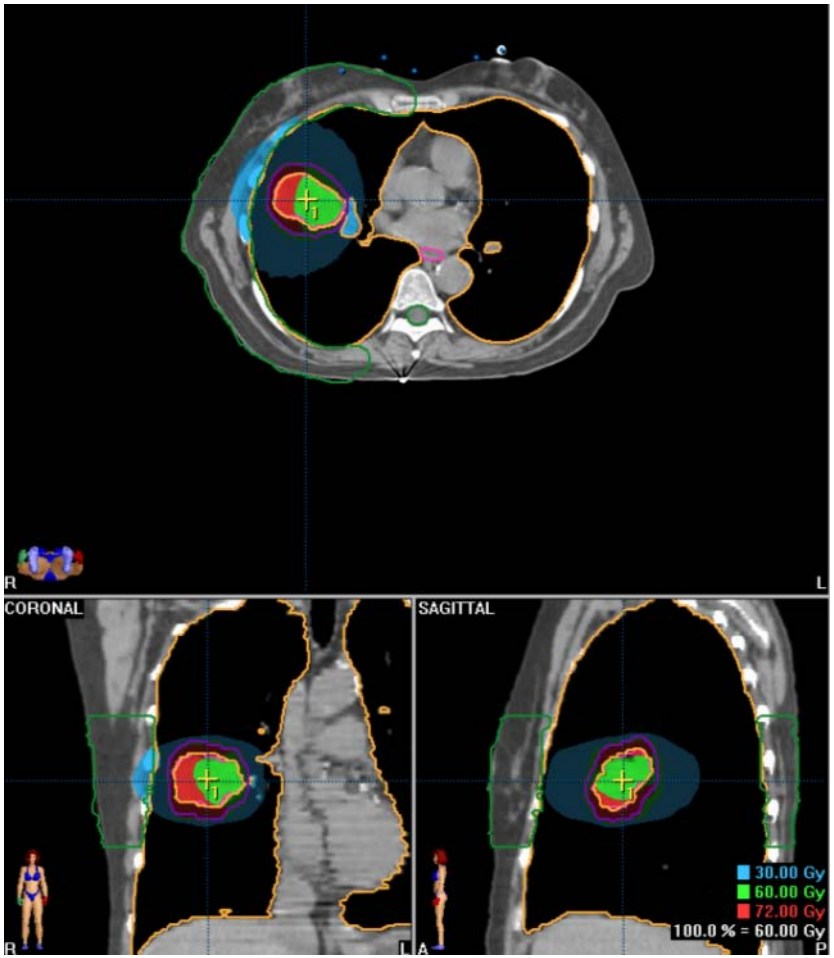




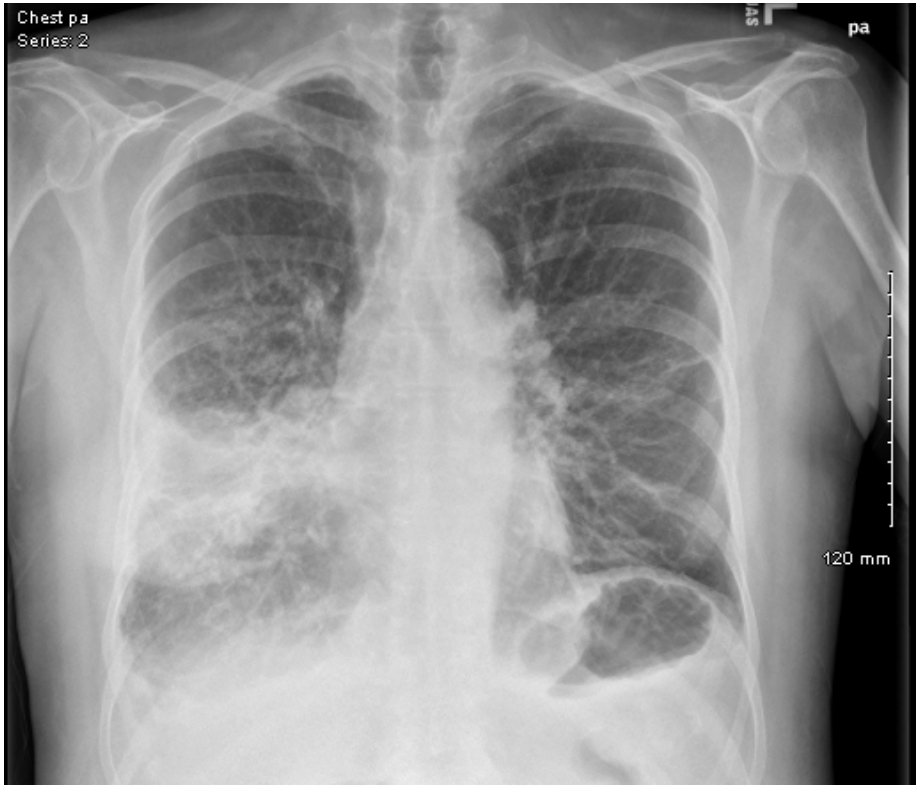
LEFT: from Chang et al, IJROBP 2008; 72(4) 967–971

Another example case

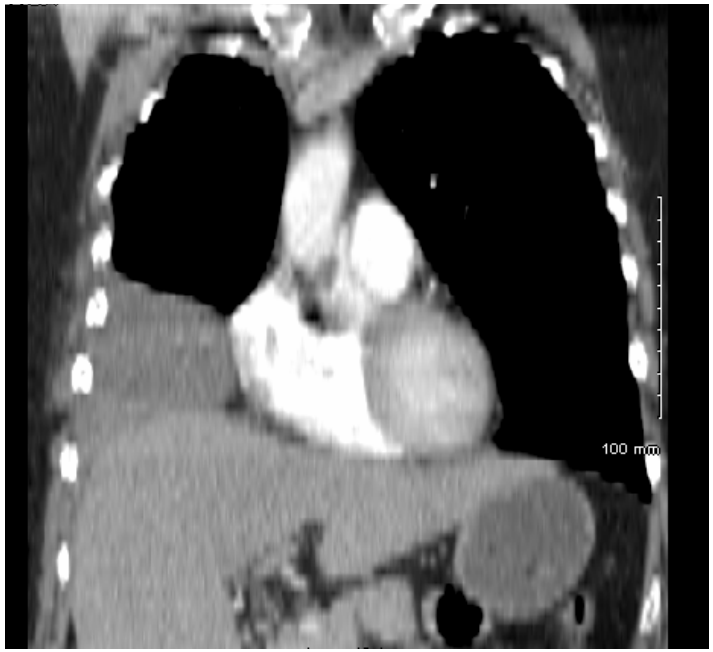
- Aug, 2008:
  - 59yo F with h/o metastatic NSCLC s/p surgery/WBRT 1 year ago
  - only current site of disease = 5cm mass in rt mid lung.
  - plan: SBRT to rt lung mass



One year later: cough, dyspnea



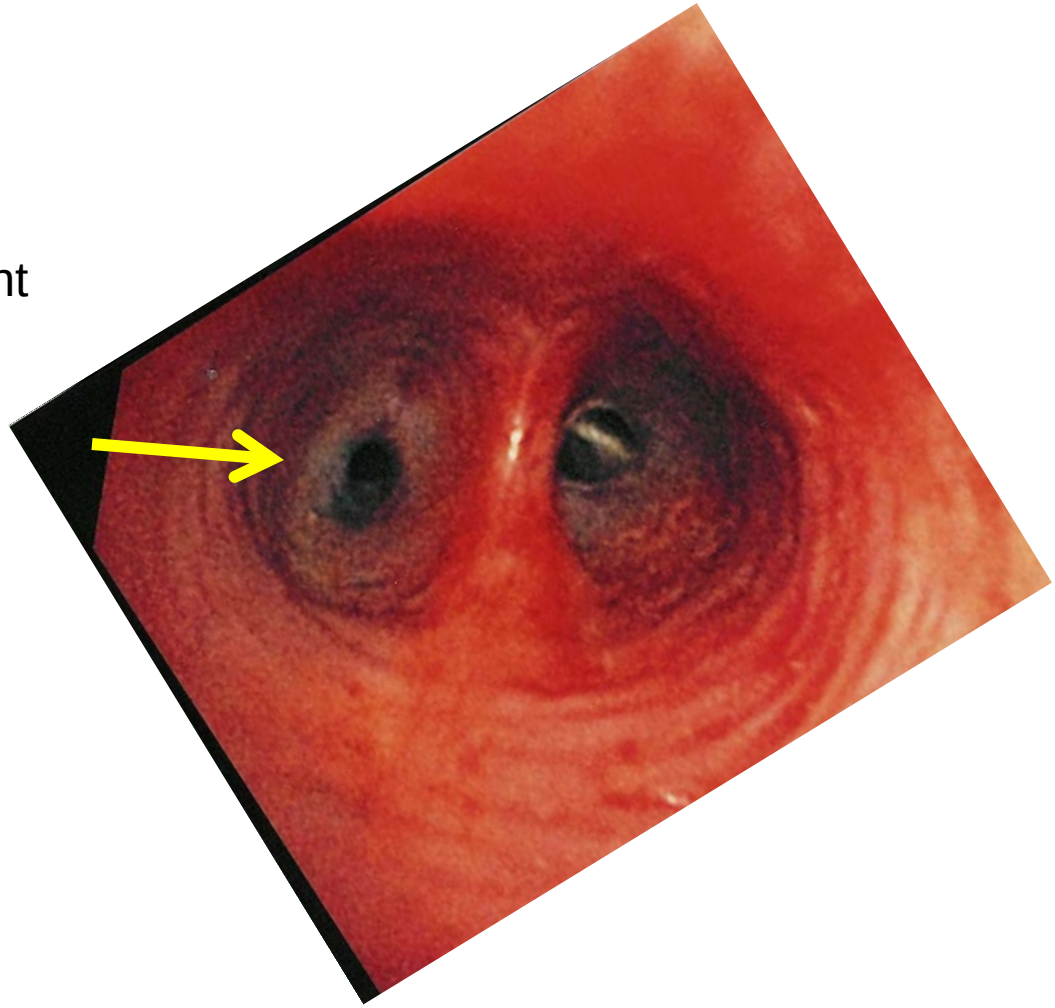
Chest x-ray



Coronal reconstruction, CT scan

Bronchoscopy:
mucus plug cleared from RML bronchus

Lateral segment
RML bronchus:
Narrow but patent
after clearing



This can also happen after *hyper*-fractionated RT
Miller et al, IJROBP 61: 64-69, 2005

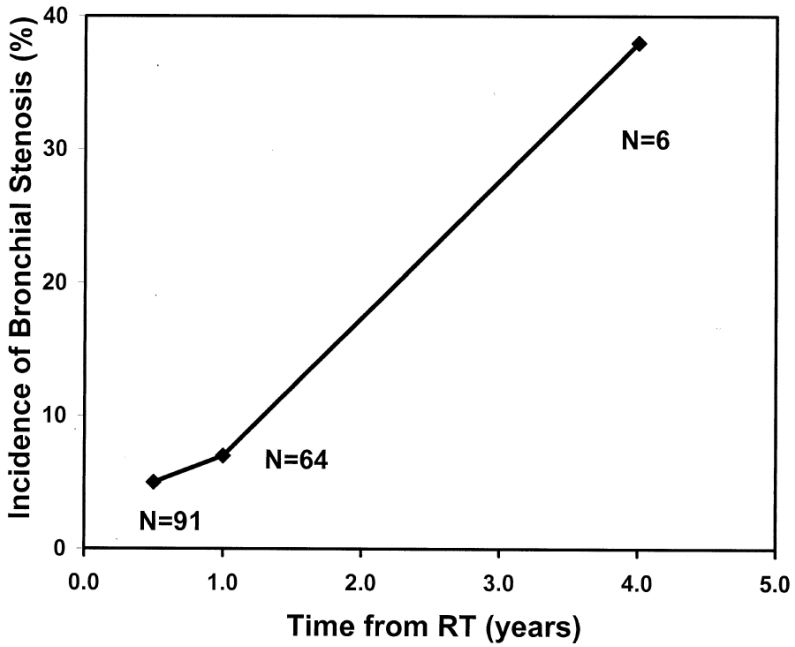
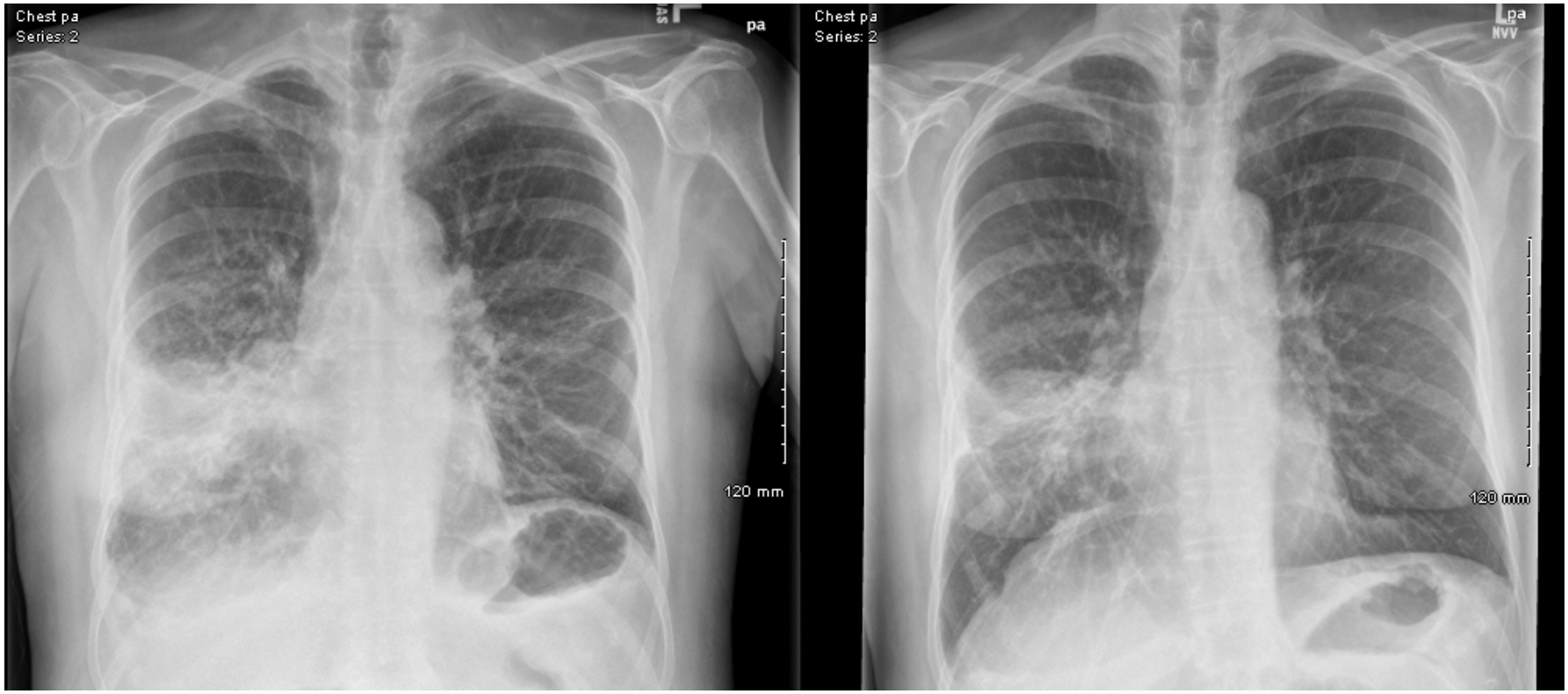


Table 2. Dose–response data for incidence of bronchial stenosis

Study	Treatment	Dose (Gy)	Rate of bronchial stenosis (%)*
Current	b.i.d. EBRT	74	4 (3/67)
Current	b.i.d. EBRT	80	5 (1/20)
Current	b.i.d. EBRT	86	25 (4/16)
Hayakawa *et al.* (14)	q.d. EBRT	80	80 (4/5)
Speiser and Spratling (13)	q.d. EBRT + endobronchial HDR 60 + 22.5–30 HDR		9 (6/68)

Abbreviations: b.i.d. = twice daily; EBRT = external beam radiation therapy; q.d. = once daily; HDR = high-dose-rate brachytherapy.
* Patient numbers in parentheses.

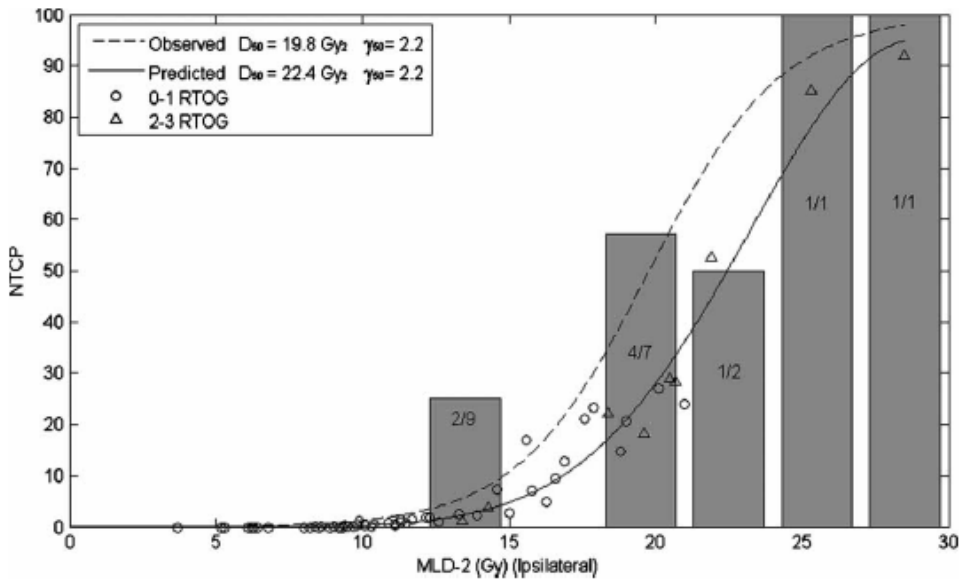
Pre- and post-bronch to clear mucus plug



Radiation Pneumonitis

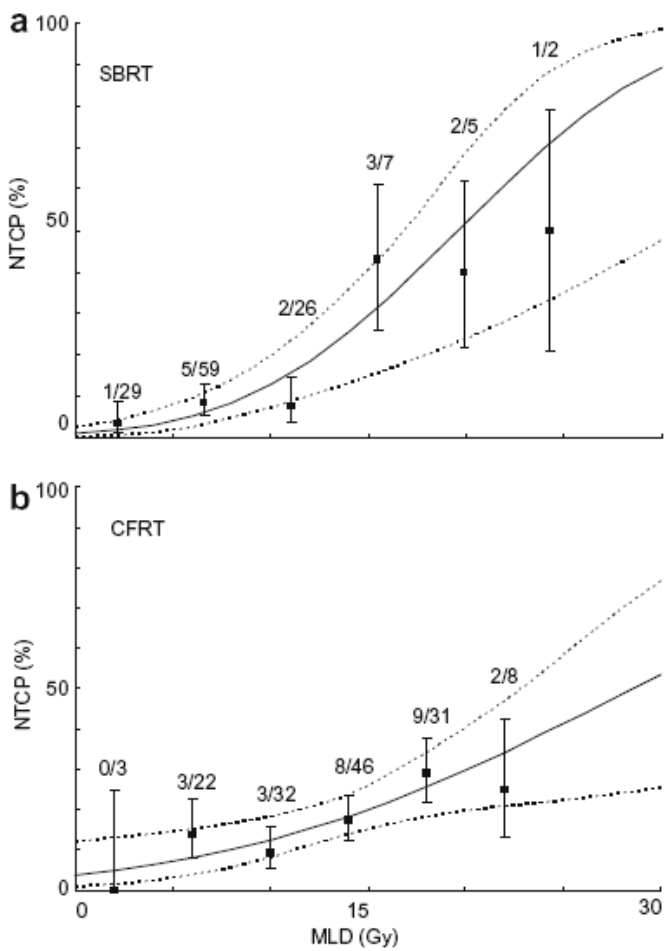
Ricardi et al, Acat Oncol 2009

- 63 patients
  - 9/63 Grade 2+ RP
- Correlated with MLD_2
  - No toxicity when MLD_2 ≤ 12 Gy
- Median 4.8 months



Radiation Pneumonitis

Borst et al,Radiother Oncol 2009



- 128 patient treated with SBRT
- 10.9% pneumonitis
- Correlated to MLD_2

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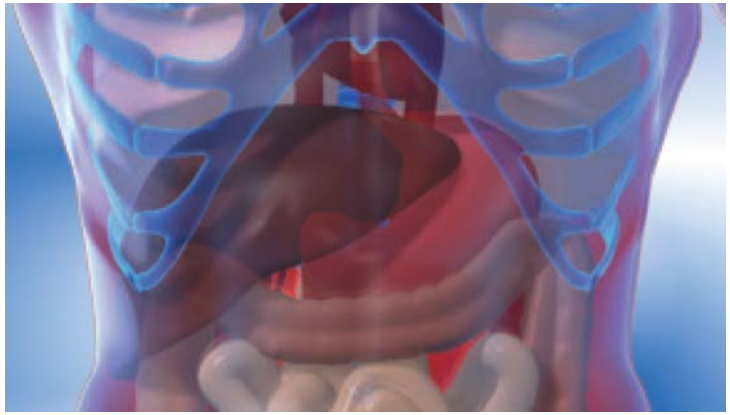


A DOSIMETRIC MODEL OF DUODENAL TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PANCREATIC CANCER

Murphy et al, IJROBP, in press

- 73 pts
  - No prior RT
  - Unresectable
  - Not recurrent after Whipple
- 25 Gy single fraction
  - PTV = GTV + 2 to 3mm
  - duodenum constraints:
    - 5% < 22.5 Gy
    - 50% <12.5 Gy
    - the 50% isodose line shouldnot reach the distal wall of the duodenal lumen on any CT image

A DOSIMETRIC MODEL OF DUODENAL TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PANCREATIC CANCER

Murphy et al, IJROBP, in press

- Only 6/73 grade 3+ duodenal toxicity
- Numerous individual predictors significant on univariate
- NTCP also significant (not shown)

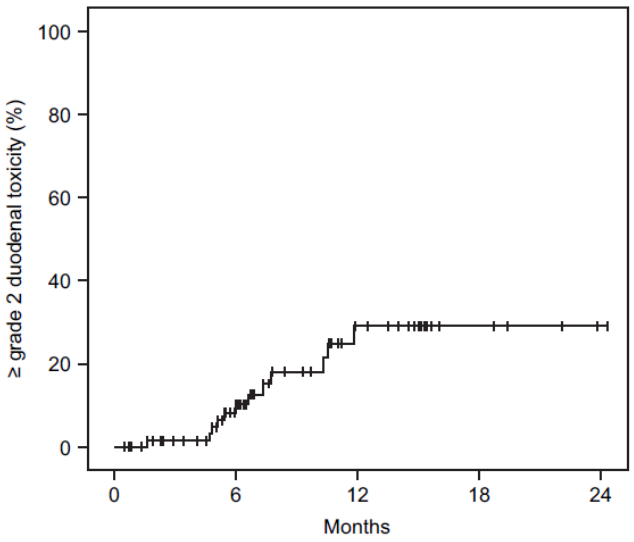


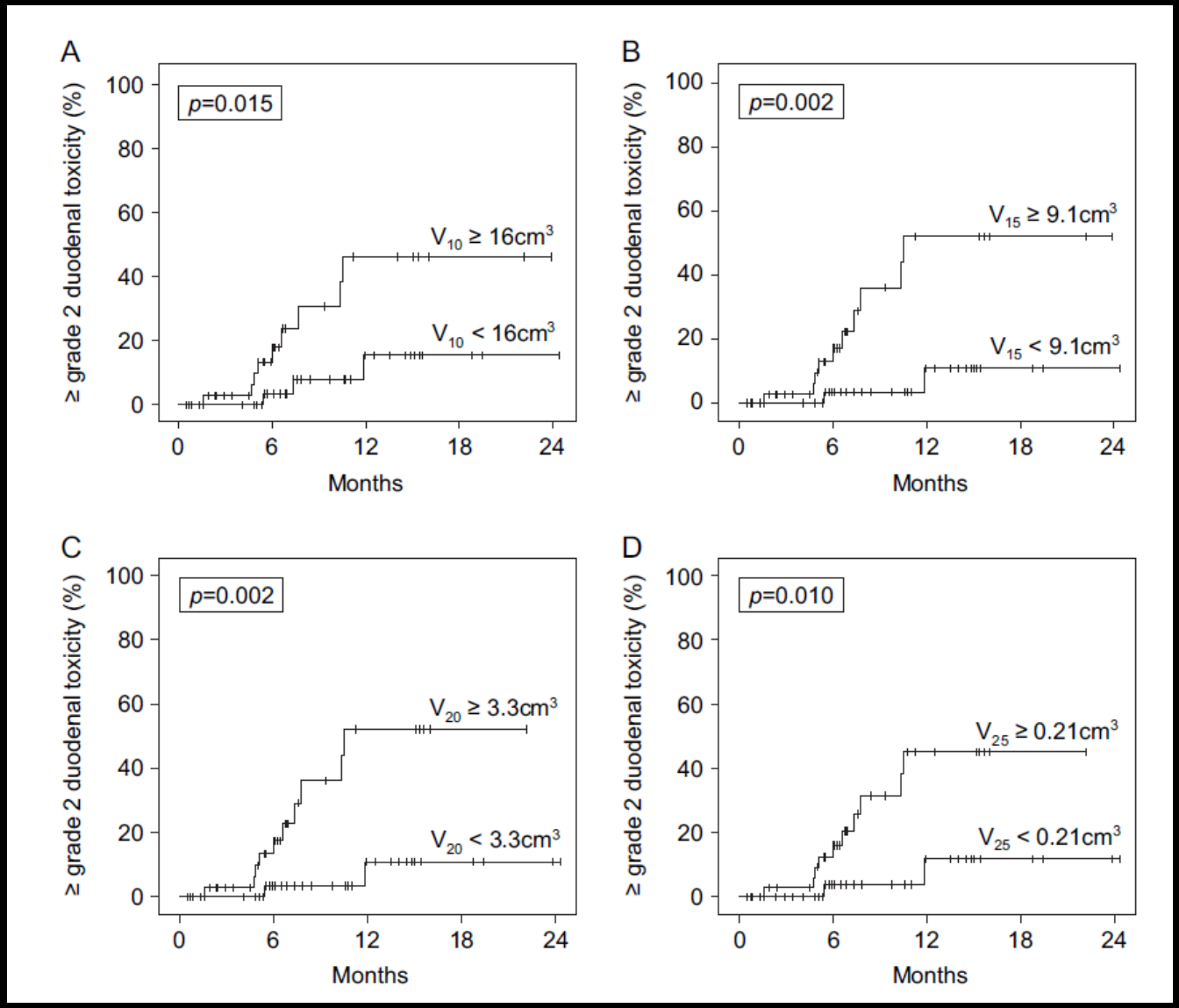
Fig. 1. Duodenal toxicity.

Table 3. Univariate analysis of dosimetric endpoints

Variable*	Cutoff†	Incidence of Grade 2–4 duodenal toxicity (%)‡	Log-rank p value
V5			
	<25 cm^3	28	0.39
	≥25 cm^3	31	
V10			
	<16 cm^3	15	0.015
	≥16 cm^3	46	
V15			
	<9.1 cm^3	11	0.002
	≥9.1 cm^3	52	
V20			
	<3.3 cm^3	11	0.002
	≥3.3 cm^3	52	
V25			
	<0.21 cm^3	12	0.010
	≥0.21 cm^3	45	

* V5 refers to the volume of duodenum receiving 5 Gy.
† Cutoff refers to the median value.
‡ Actuarial incidence at 12 months.

Murphy et al, continued



Pancreas SBRT v conventional RT

Stanford, IJROBP 2010

- Primary unresectable
- 25 Gy/1 fxn
- 84% GEM-based chemo
- Toxicity:
  - 8% (6/73) G3-4 duodenal toxicity
  - Other toxicities not stated

RTOG, *JAMA. 2008;299(9):1019-1026*

- Adjuvant post-op, GTR
- 50.4 Gy/28 with 5FU
- GEM or 5FU neo and adj
- Toxicity:
  - **58% total *non-hematologic* toxicity G3-4**
    - Diarrhea
    - Stomatitis
    - Other GI
    - etc

Other sources of guidance for SBRT normal tissue dose constraints

- Selected RTOG SBRT studies
- QUANTEC papers—very limited SBRT, mostly conventional
  - Liver
    - Pan et al, IJROBP 76(3) Suppl: S94–S100, 2010
  - Kidney
    - Dawson et al, IJROBP 76(3) Suppl: S94–S100, 2010
  - Stomach and small bowel
    - Kavanagh et al, IJROBP 76(3) Suppl: S94–S100, 2010
- Timmerman RD. Sem Rad Onc 18(4): 215-222, 2008
  - Mostly unvalidated but well considered estimates for 1, 3, and 5 fractions

ELSEVIER
Seminars in RADIATION ONCOLOGY
Volume 18, Number 4 October 2008

An Overview of Hypofractionation and Introduction to This Issue of *Seminars in Radiation Oncology*

Timmerman RD.
Sem Rad Onc 18(4): 215-222, 2008
3 fraction dose guidelines

Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint (≥Grade 3)
THREE-FRACTION TREATMENT				
Optic pathway	<0.2	15 (5 Gy/fx)	19.5 (6.5 Gy/fx)	Neuritis
Cochlea			20 (6.67 Gy/fx)	Hearing loss
Brainstem	<1	18 (6 Gy/fx)	23 (7.67 Gy/fx)	Cranial neuropathy
Spinal cord	<0.25	18 (6 Gy/fx)	22 (7.33 Gy/fx)	Myelitis
	<1.2	11.1 (3.7 Gy/fx)		
Cauda equina	<5	21.9 (7.3 Gy/fx)	24 (8 Gy/fx)	Neuritis
Sacral plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Esophagus*	<5	21 (7 Gy/fx)	27 (9 Gy/fx)	Stenosis/fistula
Ipsilateral brachial plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Heart/pericardium	<15	24 (8 Gy/fx)	30 (10 Gy/fx)	Pericarditis
Great vessels	<10	39 (13 Gy/fx)	45 (15 Gy/fx)	Aneurysm
Trachea and ipsilateral bronchus*	<4	15 (5 Gy/fx)	30 (10 Gy/fx)	Stenosis/fistula
Skin	<10	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Stomach	<10	21 (7 Gy/fx)	24 (8 Gy/fx)	Ulceration/fistula
Duodenum*	<5	15 (5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Jejunum/ileum*	<5	16.2 (5.4 Gy/fx)	27 (9 Gy/fx)	Enteritis/obstruction
Colon*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Colitis/fistula
Rectum*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Proctitis/fistula
Bladder wall	<15	15 (5 Gy/fx)	30 (10 Gy/fx)	Cystitis/fistula
Penile bulb	<3	21.9 (7.3 Gy/fx)	42 (14 Gy/fx)	Impotence
Femoral heads (right and left)	<10	21.9 (7.3 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	18.6 (6.2 Gy/fx)		Malignant hypertension

Parallel Tissue	Critical Volume (mL)	Critical Volume Dose Max (Gy)	Endpoint (≥Grade 3)
Lung (right and left)	1,500	10.5 (3.5 Gy/fx)	Basic lung function
Lung (right and left)	1,000	11.4 (3.8 Gy/fx)	Pneumonitis
Liver	700	17.1 (5.7 Gy/fx)	Basic liver function
Renal cortex (right and left)	200	14.4 (4.8 Gy/fx)	Basic renal function

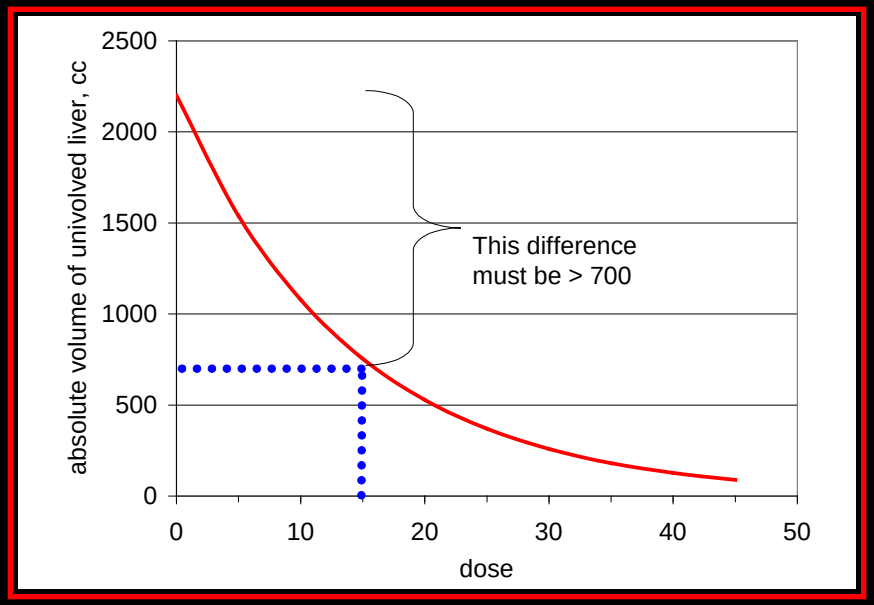
Colorado Phase I/II Liver SBRT Trial,

Schefter et al, IJROBP 62:1371-78, 2005

Methods

- Standard 3+3 Phase I design
- Starting dose, 12 Gy x 3 = 36 Gy total
- Safe escalation to pre-selected maximum dose
  - 20 Gy x 3 = 60 Gy

- Critical volume model
  - At least 700 cc normal liver received < 15 Gy cumulative



Mostly Unvalidated Normal Tissue Dose Constraints for SBRT

Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint (≥Grade 3)
THREE-FRACTION TREATMENT				
Optic pathway	<0.2	15 (5 Gy/fx)	19.5 (6.5 Gy/fx)	Neuritis
Cochlea			20 (6.67 Gy/fx)	Hearing loss
Brainstem	<1	18 (6 Gy/fx)	23 (7.67 Gy/fx)	Cranial neuropathy
Spinal cord	<0.25	18 (6 Gy/fx)	22 (7.33 Gy/fx)	Myelitis
	<1.2	11.1 (3.7 Gy/fx)		
Cauda equina	<5	21.9 (7.3 Gy/fx)	24 (8 Gy/fx)	Neuritis
Sacral plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Esophagus*	<5	21 (7 Gy/fx)	27 (9 Gy/fx)	Stenosis/fistula
Ipsilateral brachial plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Heart/pericardium	<15	24 (8 Gy/fx)	30 (10 Gy/fx)	Pericarditis
Great vessels	<10	39 (13 Gy/fx)	45 (15 Gy/fx)	Aneurysm
Trachea and ipsilateral bronchus*	<4	15 (5 Gy/fx)	30 (10 Gy/fx)	Stenosis/fistula
Skin	<10	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Stomach	<10	21 (7 Gy/fx)	24 (8 Gy/fx)	Ulceration/fistula
Duodenum*	<5	15 (5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Jejunum/ileum*	<5	16.2 (5.4 Gy/fx)	27 (9 Gy/fx)	Enteritis/obstruction
Colon*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Colitis/fistula
Rectum*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Proctitis/fistula
Bladder wall	<15	15 (5 Gy/fx)	30 (10 Gy/fx)	Cystitis/fistula
Penile bulb	<3	21.9 (7.3 Gy/fx)	42 (14 Gy/fx)	Impotence
Femoral heads (right and left)	<10	21.9 (7.3 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	18.6 (6.2 Gy/fx)		Malignant hypertension

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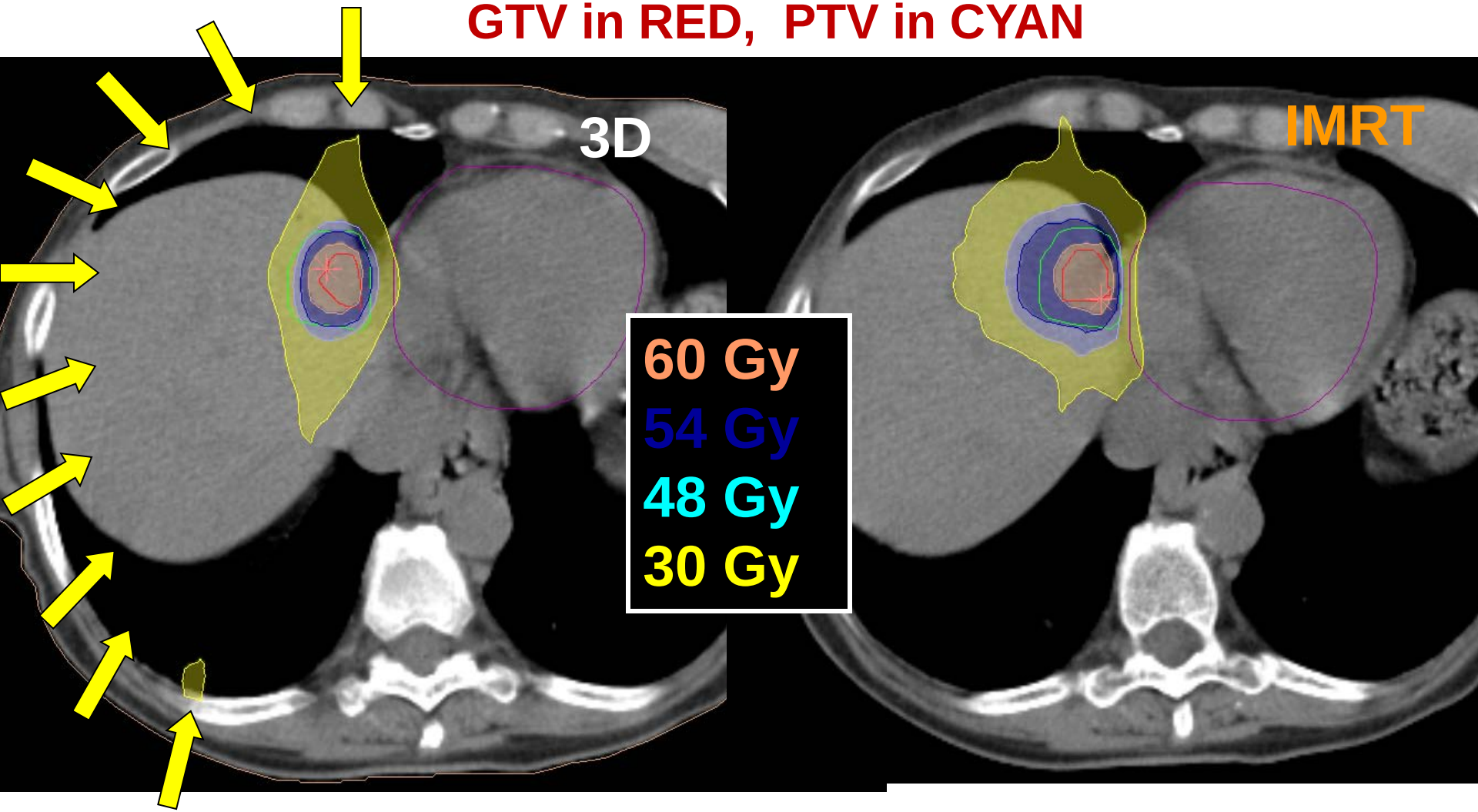
Timmerman RD. Sem Rad Onc. 18(4) :215-222, 2008

Liver Case: 3DCRT vs. IMRT

Prescription Dose: 54 Gy to PTV in 3 Fxs

GTV in RED, PTV in CYAN



Both plans use 10 coplanar fields

UC Liver SBRT Phase II Results, Toxicity
No RILD, no Gr 4-5 toxicity of any kind
1 case of grade III soft tissue toxicity

What not to do:
Insufficient number of fields

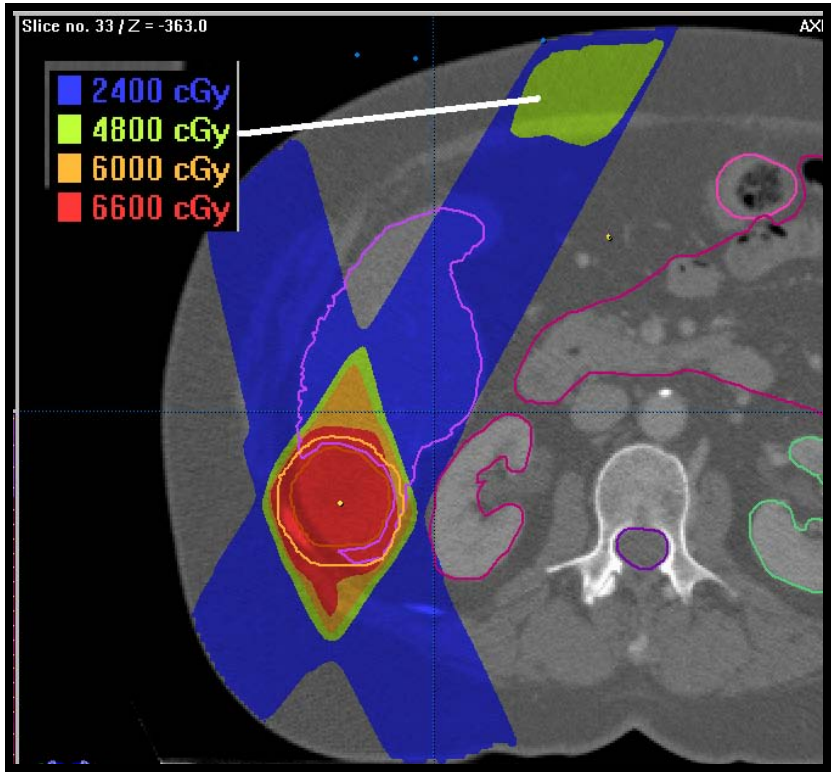
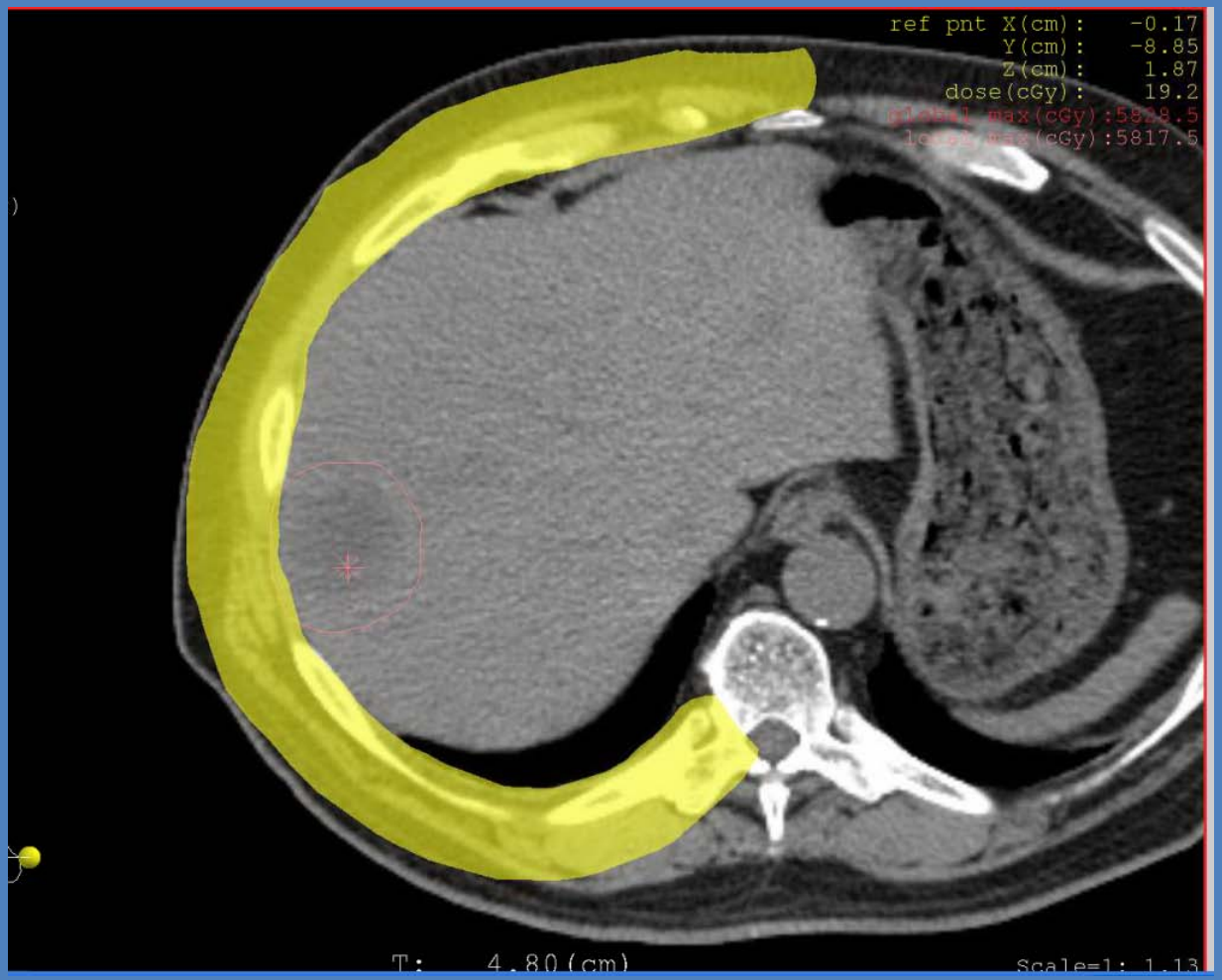


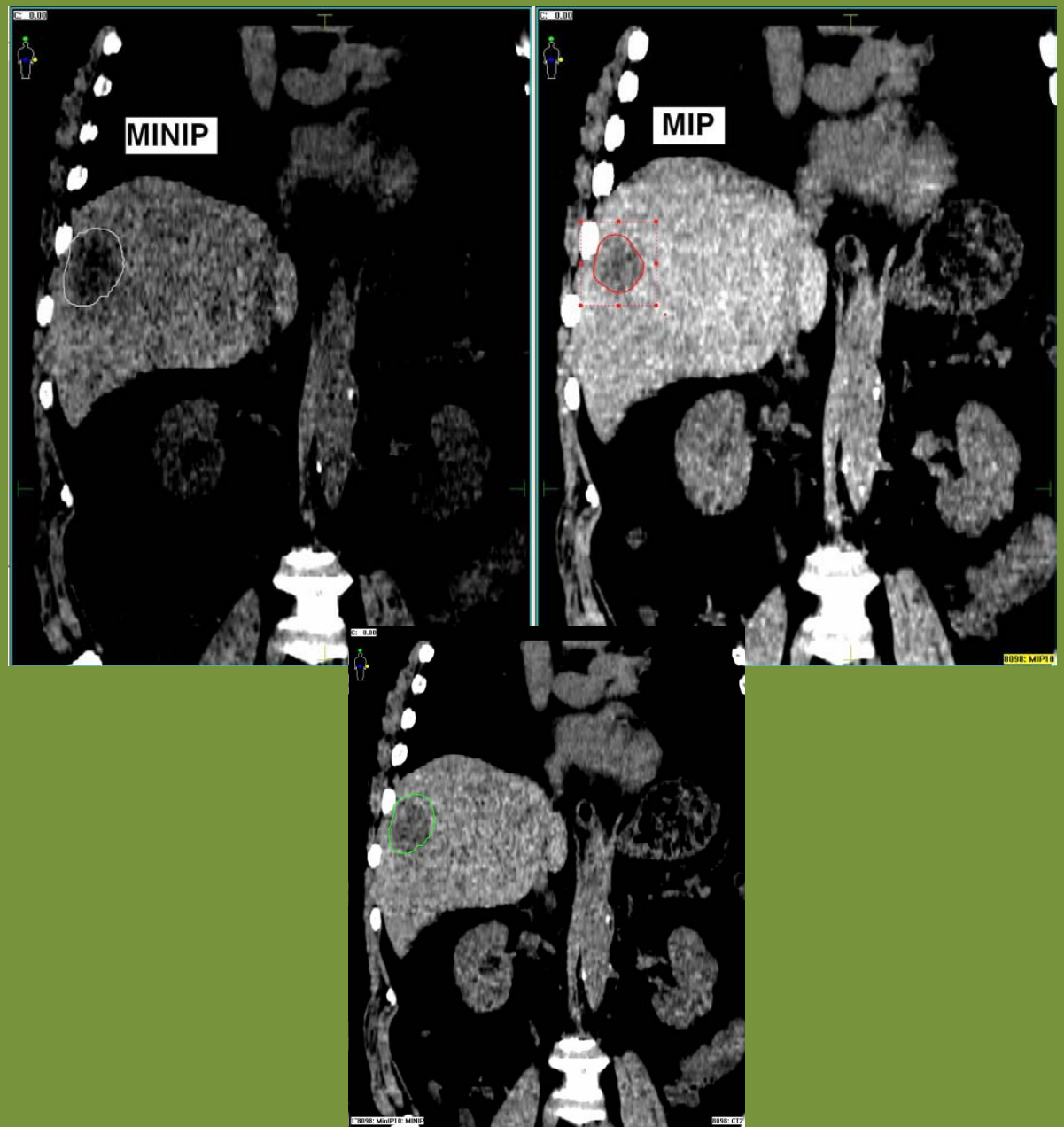
Photo taken 8 mos after SBRT
At last followup 17 post-SBRT, lesion controlled.
Necrosis is slowly healing.

Chest wall contouring



Note:
In this case we accepted a slightly high chest wall V30 of 44 cc.
The pain syndrome reported had typical onset 7 mos post-SBRT and lasted approx 4 mos.
Most pt recovered to zero pain level.
Thus, an important consideration but should be judged relative to overall clinical goal.

MINIP vs MIP: a few comments

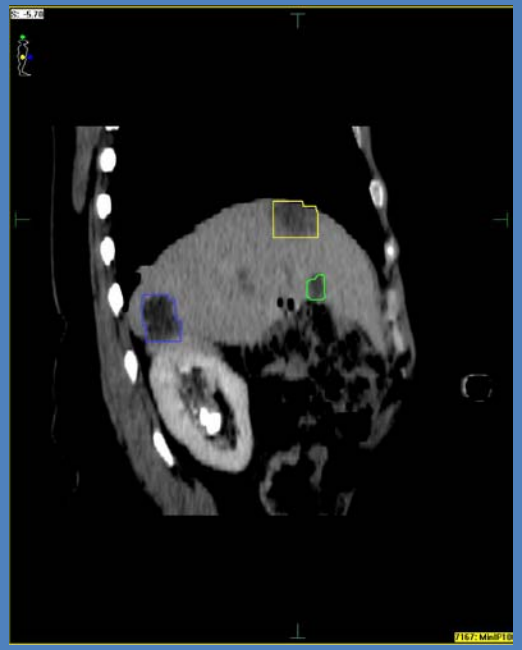


Notice one obvious difference between MINIP and MIP is the volume of liver projected, since the lower density adjacent tissues that move with respiration provide the minimum HU voxels.

We generally use ITV+5mm margin for lung and liver

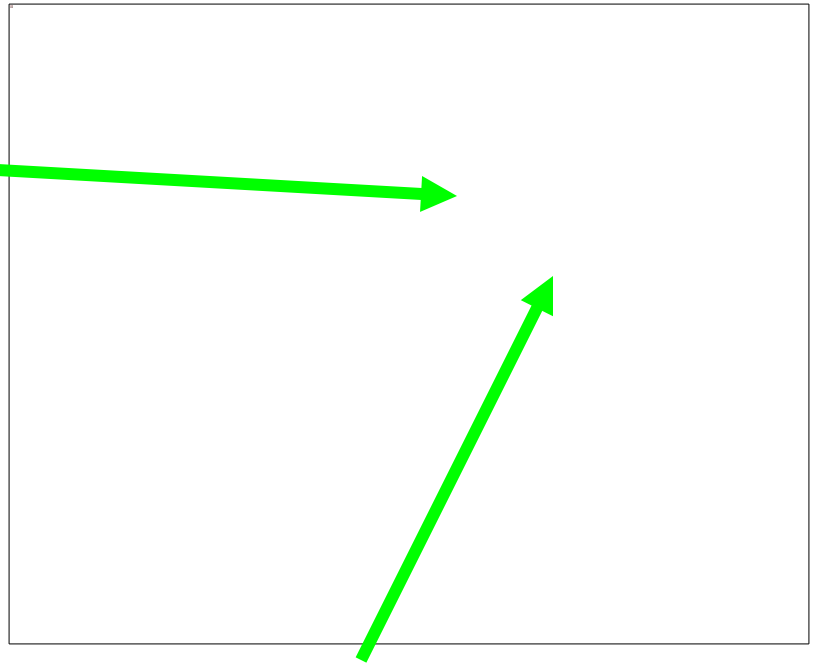
MIP usually helpful for lung ITV

MINIP often helpful for liver ITV, but be careful with lesion near the dome



MINIP (above) helpful to show ITV for 2 of the three lesions, but 4D CT cine view (right) shows actual motion of dome lesion outside of MINIP-based ITV.

Non-protocol patient:
max pt to stomach >10 Gy/fxn



Pale, denuded mucosa; progressed to ulceration but eventually healed in approx 3 mos

Sometimes you just can't do 3 fractions and keep max GI point dose to <10 Gy/fractions

Yes, that is a liver metastasis—unusual anatomy! Stomach, not small bowel, adjacent

Stomach V40 = 2.25 cc
"4/40 rule" = keep total GI tract volume >40 Gy to <4cc

Top to Bottom:
HOW do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer

Range of applied cord constraints

Institution	Dose Constraint
MSKCC	14 Gy Dmax
UPMC	10 Gy Dmax
HENRY FORD	V10Gy $\leq$ 10%
MDACC	12 Gy Dmax TO 0.1 CC
PMH	12 Gy Dmax TO THECAL SAC OR CORD + 2mm
CLEVELAND CLINIC	14Gy Dmax AND V10Gy $\leq$10%
STANFORD	14 Gy Dmax, V12Gy $\leq$ 0.3 CC, V10Gy $\leq$ 0.5 CC V8Gy $\leq$ 1 CC
DALLAS	14 Gy Dmax, V10Gy $\leq$ 0.35CC, V8Gy $\leq$ 1.2CC

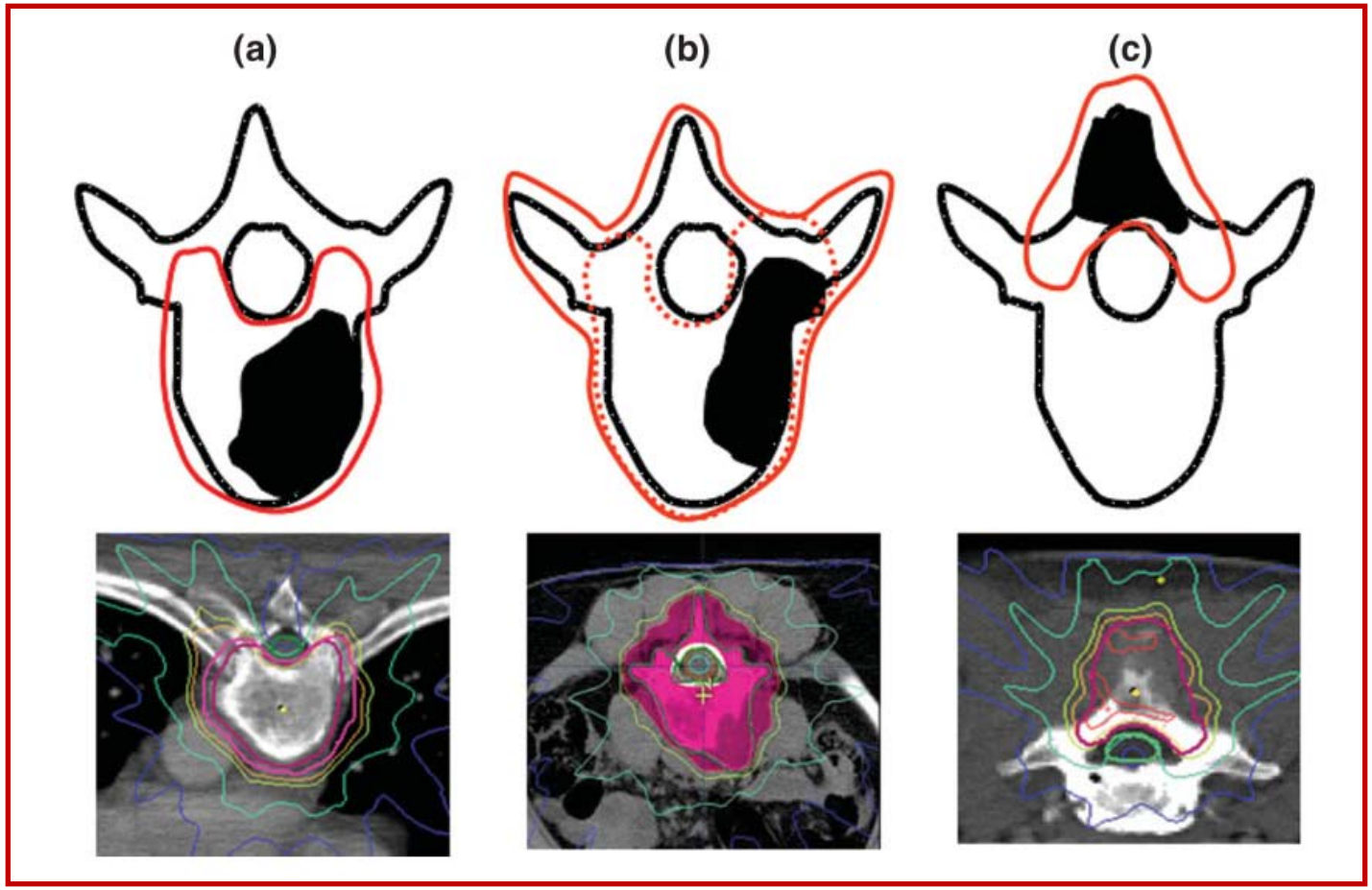
Yosh Yamada, MSKCC, from ASTRO IGRT mtg, 2009

The easy part for spinal targets: motion is not a major problem

cineMRI courtesy Dr Paul Read, U of Virginia

Spinal Target volumes, from "Partial Volume Tolerance of the Spinal Cord and Complications of Single-Dose Radiosurgery"

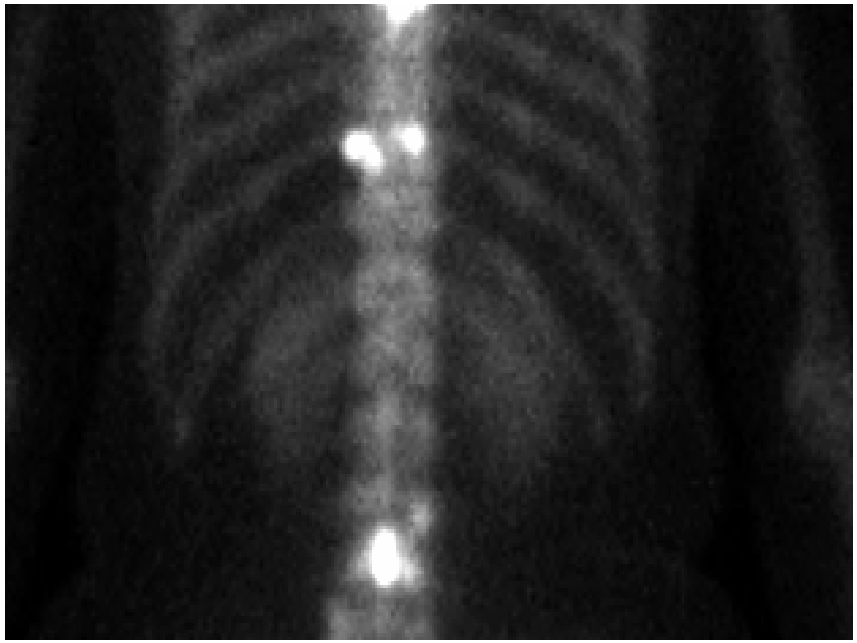
Ryu et al, Cancer, 2007



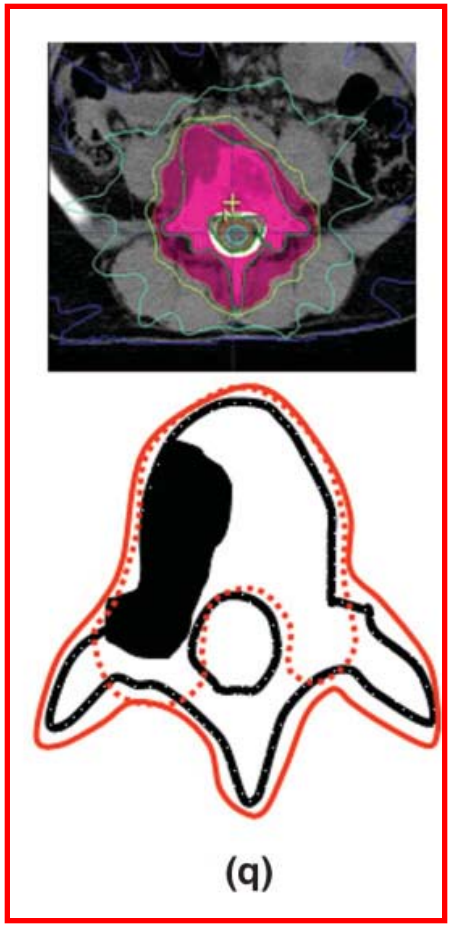
- Cord drawn 6mm above and below target
- Major constraint: no more than 10% of cord receives dose above 10 Gy
- Only 1 observed cord complication among 177 pts

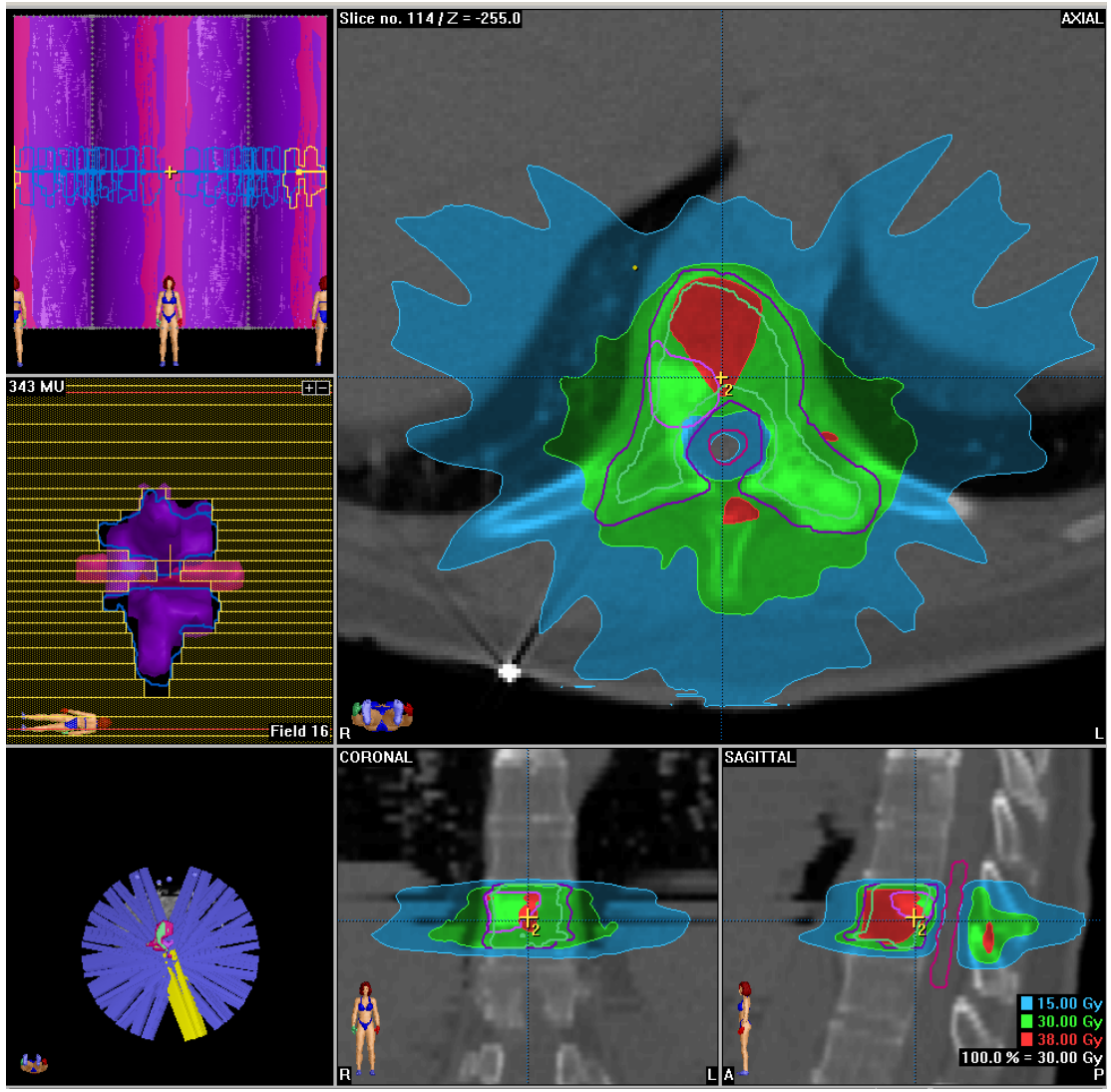
Sample case: 60 y/o F

- 5/04 T1N2M0 NSCLC
  - Adjuvant chemo (gem/carbo)
- 5/05 bone mets
  - Erlotinib started 9/05
- Mid-2006
  - spine SRS T7,sacrum
  - Brain SRS 3 lesion
- Early 2007
  - SRS to another brain met
- Late 2007
  - SRS to 2 other brain mets
- Early 2008
  - Progressing spine lesions at T10, L3



Target volume and plan





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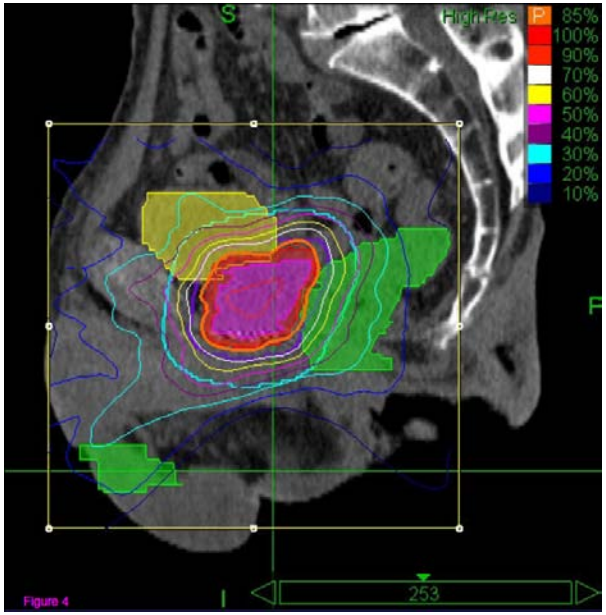
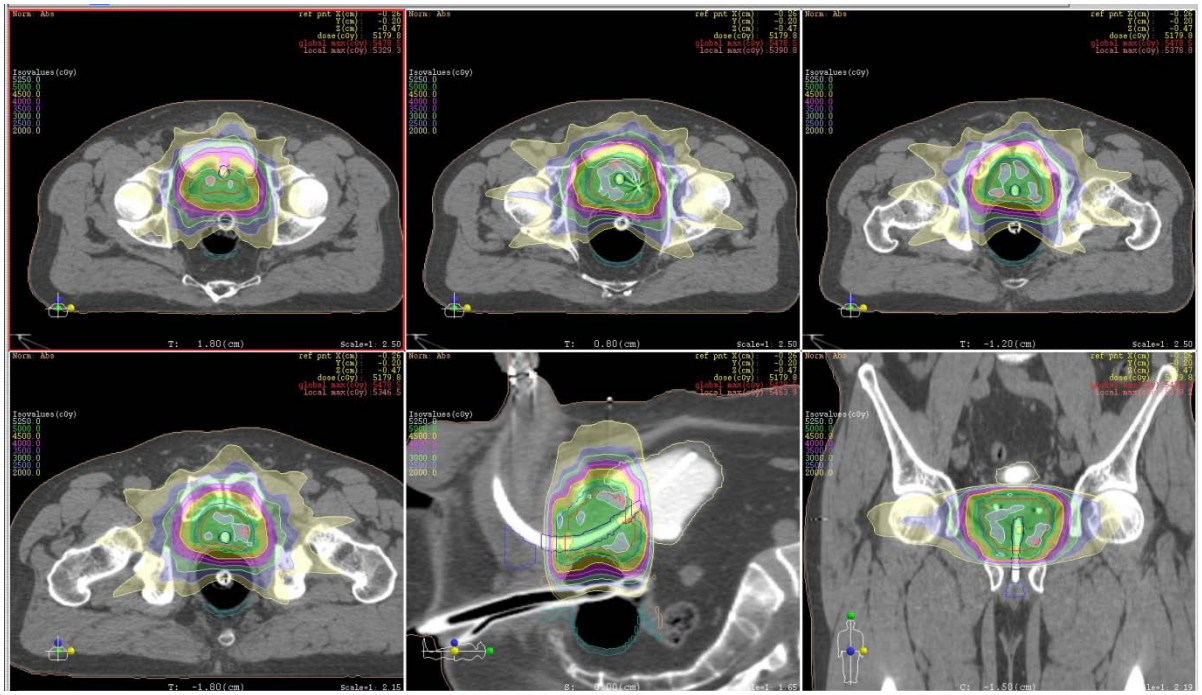
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer

From Katz et al, BMC Urology 2010
7.25 Gy x 5 F
Note: caution with testis dose using CK system





Multi-institutional trial
First UC patients
10 Gy x 5F
Note: balloon placed to displace rectum and take advantage of reduced backscatter dose

Thanks for your attention!