Important Aspects of Plan Evaluation in Stereotactic Body Radiation Therapy (SBRT)

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What we plan to cover ?

- General aspects of plan evaluation in SBRT.

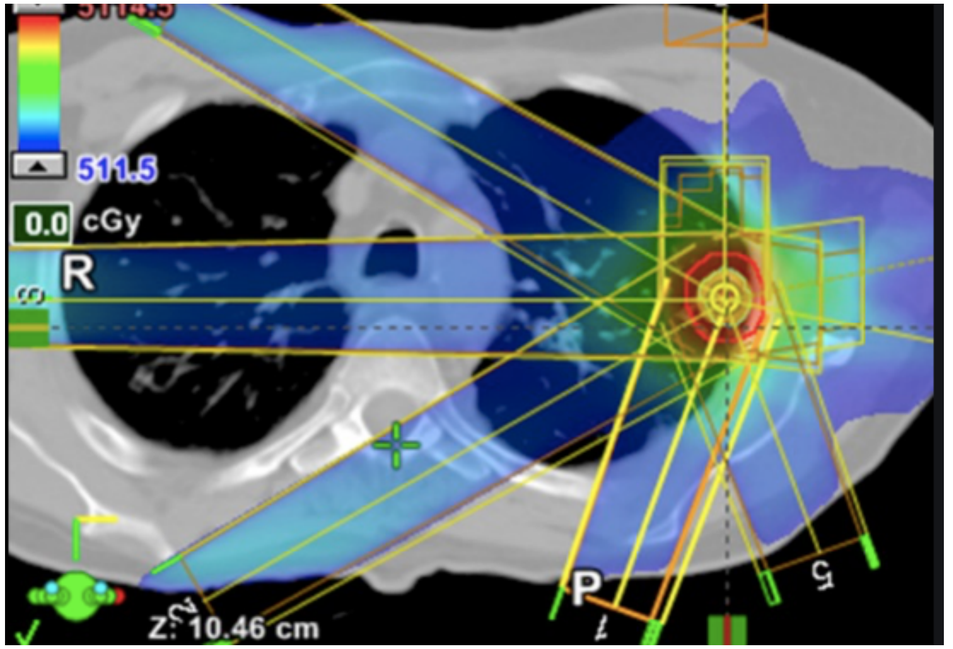
- We will specifically see plan evaluation in 3 subsites and discuss.

    1. Lung
    2. Liver
    3. Spine

Definition of SBRT

- An external beam radiation therapy method used to very precisely deliver a high dose of radiation to an extracranial target within the body, using either a single dose or a small number of fractions.

- SBRT combines multiple finely collimated radiation beams and stereotaxy (3D target localization). The multiple radiation beams intersect to deliver an accurate, high dose of radiation to a carefully defined location.



ACR & ASTRO Definition:American College of Radiology (ACR). Practice guideline for the performance of stereotactic body radiation therapy. Reston VA: American College of Radiology (ACR); 2009. p. 8

Basics of SBRT

SBRT began as an extension of SRS and shares some of the same characteristics.

- Dose heterogeneity inside the tumor.
- Sharp dose gradient outside the tumor.
- Highly effective patient immobilization.
- Use of many beams.

Basics of SBRT

- The goal of SBRT treatment is to “ablate” tissues within the PTV
- These tissues are not considered at risk for complications.
- The main objective of the plan is to minimize the volume of those normal tissues outside PTV receiving high dose per fraction.
- Dose more than 5Gy (Range: 5 Gy to 34 Gy per fraction)
- Number of fractions less than or equal to 5
- Safe delivery is of utmost importance due to high fractional dose and small number of fractions.

Evaluating the SBRT Plan

Dose Volume Histogram - Is a valuable tool – but not enough.

- Prescription Dose
- Prescription isodose
- Prescription Isodose Surface Coverage
- High Dose Spillage (Conformity Index)
- Intermediate Dose Spillage

  1. Location (D 2cm) 2. Volume (R50%)

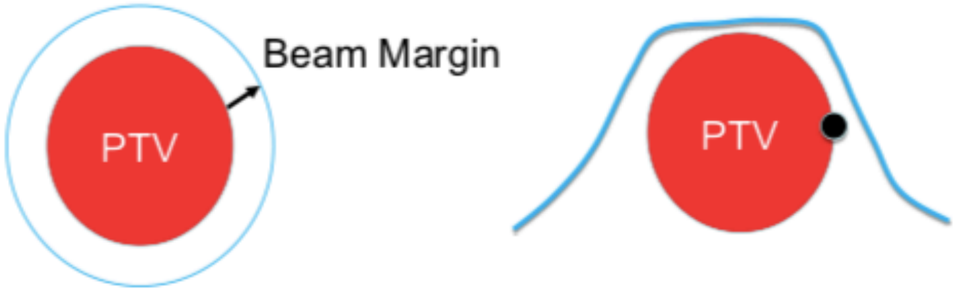
- Normal Tissue Constraints

Evaluating the SBRT Plan - Prescription Dose

- The Prescription dose depends on the Site, Size and location of lesions.
- The treatment plan should be normalized such that 100% corresponds to the center of mass of the PTV.
- This point will typically also correspond (but is not required to correspond) to the isocenter of the treatment beams.
- Dose inhomogeneity inside the PTV is considered acceptable and not considered a priority in plan design with maximum dose some times will be more than 125%, upto 160%.

Basics of plan evaluation: SBRT

If beam margin is close to beam penumbra (5-6 mm)→
Homogeneous PTV dose, Maximum dose about 110% of Prescription Dose (PD).
Dose fall off outside PTV is slow



If beam margin is much less than beam penumbra (0-2 mm) →
Inhomogeneous PTV dose, Maximum dose ~ 125% or more of PD.
Dose fall off outside PTV is fast

Image used from : SBRT Treatment Planning: Practical Considerations
Linda Hong, Ph.D. Montefiore Medical Center Albert Einstein College of Medicine Bronx, New York

Evaluating the SBRT Plan - Prescription Dose

Peripheral Lung Tumors: Dose fractionation:	25–34 Gy × 1 fraction 18 Gy×3 fractions 12 Gy×4 fractions 10 Gy×5 fractions
Central Lung Tumors : Dose fractionation:	10 Gy × 5 fractions
Lung Metastasis: Dose fractionation:	26 Gy × 1 fraction 30 - 37.5 Gy×3 fractions 48 Gy×4 fractions 40-60 Gy×5 fractions

Table 7.3 Selected studies of SBRT treated NSCLC patients

Study	Patients	Treatment	LC/OS	Notes
Onishi et al. JRS-SBRTSG (IJROBP 2013)	2226 patients stage I NSCLC	32–70 Gy in 3–12 fractions, median BED 107 Gy (range 58–150 Gy)	3 years LC/OS 85 %/72 % 3 years LPFS 87 % T1, 72 % T2 3 years OS 75 % BED ≥ 100 Gy vs. 63 % BED < 100 Gy (p < 0.01)	2.9 % grade ≥3
Grills et al. Multi-institutional (JTO 2012)	482 patients (505 tumors) T1-3N0 NSCLC, 87 % medically inoperable	20–64 Gy in 1–15 fractions, median 54 Gy in 3 fractions	2 years LC/OS 94 %/60 %, LC 96 % BED ≥ 105 vs. 85 % BED < 105 (p < 0.001)	7 % grade ≥2 pneumonitis 3 % rib fracture
Shibamoto et al. Japan (IJROBP 2013, Cancer 2011)	180 patients stage I NSCLC (120 medically inoperable, 60 operable)	Volume-adapted 44 Gy in 4 fractions <1.5 cm, 48 Gy in 4 fractions 1.5–3.0 cm, 52 Gy in 4 fractions >3.0 cm	3 years LC/OS 83 %/69 %, OS 74 % operable vs. 59 % inoperable, LC 86 % ≤3 cm vs. 73 % >3 cm 5 years LC/OS 82 %/68 %	13 % grade ≥2 pneumonitis
Uematsu et al. Japan (IJROBP 2001)	50 patients T1-T2N0 NSCLC (21 medically inoperable, 29 operable)	50–60 Gy in 5–10 fractions (18 patients received 40–60 Gy in 20–33 fractions prior to SBRT)	3 years LC/OS 94 %/66 % (86 % OS in medically operable subgroup)	4 % rib fracture
Badiyan et al. Wash U. (RO 2013)	120 patients (early-stage NSCLC and AIS)	54 Gy in 3 fractions	3 years LC/OS 100 %/35 % AIS, 86 %/47 % NSCLC	Not reported
Bradley et al. Wash U. (IJROBP 2010)	91 patients stage I/II NSCLC, medically inoperable	Peripheral tumors 54 Gy in 3 fractions, central tumors 45 Gy in 5 fractions	2 years LC/OS 86 %/70 %	3 % grade 2 pneumonitis 4 % rib fracture 1 % brachial plexopathy
Palma et al. VUMC (IJROBP 2012)	176 patients stage I NSCLC, severe COPD	60 Gy in 3–5 fractions	3 years LC/OS 89 %/47 %	3 % grade 3
Chang et al. MDACC (RO 2012)	130 patients stage I NSCLC	50 Gy in 4 fractions	2 years LC/OS 98 %/78 %	12 % grade 2–3 pneumonitis
Griffioen et al. VUMC (RO 2013)	62 patients with multiple synchronous primary early-stage NSCLC	54–60 Gy in 3–8 fractions	2 years LC/OS 84 %/56 %	4.8 % grade 3

Table 7.4 Selected studies of SBRT for metastatic lung lesions

Study	Patients	Treatment	LC/OS	Toxicity
Singh et al. Rochester (J Thorac Dis 2014)	34 patients with 1–5 metastatic lesions	40–60 Gy in 5 fractions	2 years LC/OS 88 %/44 %	No grade ≥2
Johnson et al. UCSF (Oncology 2014)	90 patients with central tumors (72 with metastatic lesions)	50 Gy in 5 fractions	2 years LC/OS 82 %/32 % metastatic subgroup	4 % ≥ grade 3
Baschnagel et al. Wash University (Clin Oncol 2013)	32 patients with 1–3 metastatic lesions	48–60 Gy in 4–5 fractions	2 years LC/OS 92 %/76 %	16 % grade 3 no grade ≥4
Hamamoto et al. Japan (JJCO 2009)	62 patients (10 with metastatic lesions, 52 with stage I NSCLC)	48 Gy in 4 fractions	2 years LC/OS 25 %/86 % in metastatic subgroup (vs. 88 %/96 % in primary NSCLC patients, p < 0.0001)	Not reported
Norihisa et al. Japan (IJROBP 2008)	34 patients with 1–2 metastatic lesions	48 Gy in 4 fractions, 60 Gy in 5 fractions	2 years LC/OS 90 %/84 %	12 % grade 2 3 % grade 3
Wulf et al. Germany (IJROBP 2004)	61 patients (41 with metastatic lesions, 20 with stage I-II NSCLC)	30–37.5 Gy in 3 fractions, 26 Gy in 1 fraction	1 year LC/OS 80 %/85 % metastatic subgroup	3 % grade 2 no grade ≥3

Evaluating the SBRT Plan - Prescription Dose

Liver:

Based on location and underlying liver function.

Peripheral: 23–30 Gy in 1 fraction,
27.5–60 Gy in 3–6 fractions.

Central: 40 Gy in 5 fractions.

Prospective Trials for SBRT for Primary Liver Malignancies.

Study	Institution	Year	Design	No. of Patients	Histology	CP Class	Tumor Size	Dose (Gy) Range	No. of Fractions
Bujold et al[15]	Princess Margaret Hospital, Canada	2013	Phase I/II	102	HCC: 102	A	1.4-23.1 cm	24-54	6
Tse et al[4]	Princess Margaret Hospital, Canada	2008	Phase I	41	HCC: 31 IHC: 10	A	9-1913 mL	24-54	6
Mendez-Romero et al[11]	Erasmus MC, The Netherlands	2006	Phase I/II	8	HCC: 8	A/B	0.5-7.2 cm	25-37.5	3-5
Kang et al[14]	KIRMS, Korea	2012	Phase II	47	HCC: 47	A/B	1.3-8 cm	42-60	3
Cardenes et al[12]	Indiana University, Indianapolis, Indiana	2010	Phase I	17	HCC: 17	A/B	≤6 cm cumulative	36-48	3-4
Kim et al[19]	Yonsei University College of Medicine, Korea	2016	Phase I	18	HCC: 18	A/B	≤6 cm cumulative	36-60	4
Price et al[13]	Indiana University, Indianapolis, Indiana	2012	Phase I/II	26	HCC: 26	A/B	20.8-252.9 mL	24-48	3-5
Goodman et al[20]	Stanford University, Stanford, California	2010	Phase I	29	HCC: 2 IHC: 5 METS: 22		<5 cm	18-30	1

Evaluating the SBRT Plan - Prescription Dose

Spine :

- Limited disease in patients without prior radiation: 16–24 Gy in 1 fraction.
- Multi-segment disease without prior radiation: 20–27 Gy in 2–3 fractions.
- Multi-segment disease in previously irradiated field: 20–25 Gy in 5 fractions.

Evaluating the SBRT Plan - Prescription Isodose

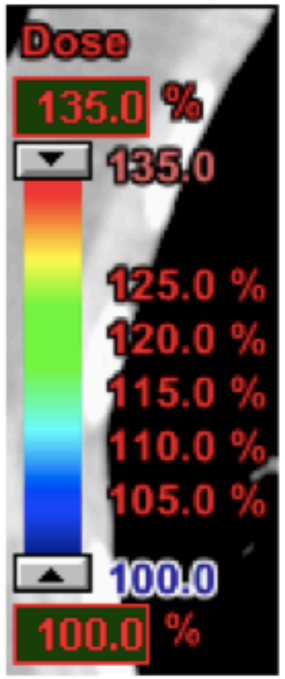
- The prescription isodose chosen is not 95 - 100 % like in conventional RT.
- The isodose surface chosen must be ≥ 60% and < 90% of the maximum dose.
- This is mainly done to achieve steep dose fall off and to spare adjoining normal structures.

Evaluating the SBRT Plan - Prescription Isodose

- The prescription isodose surface will be chosen such that 95% of the target volume (PTV) is conformally covered by the prescription isodose surface (PTV V95%RX = 100%) and 99% of the target volume (PTV) receives a minimum of 90% of the prescription dose (PTV V90%RX > 99%).

- Also depends on location and the tolerance of surrounding normal structures.

Prescription Isodose Surface Coverage:



PD = 100% = 20 Gy/fx x 3

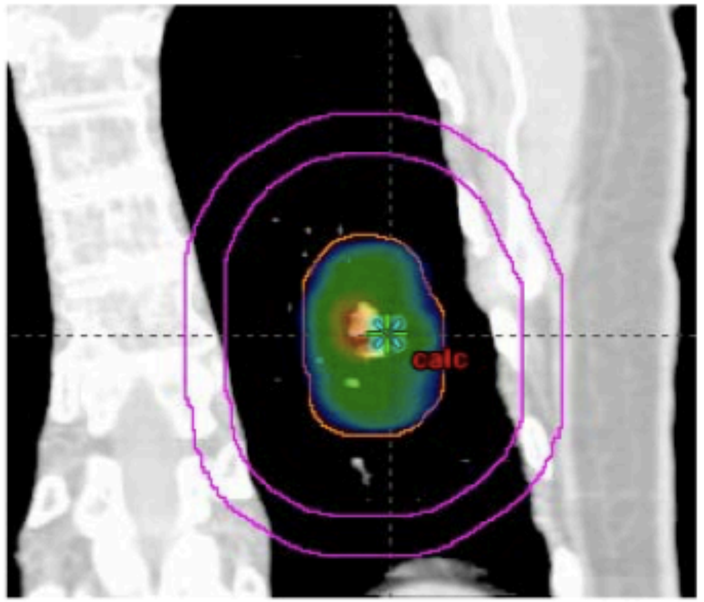
PTV V100 = 95%

PTV V100 = 95%

100% PD and Above

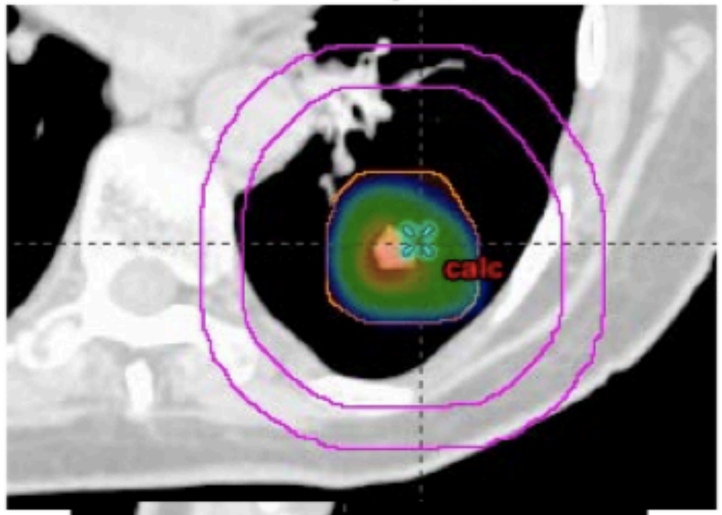
PTV

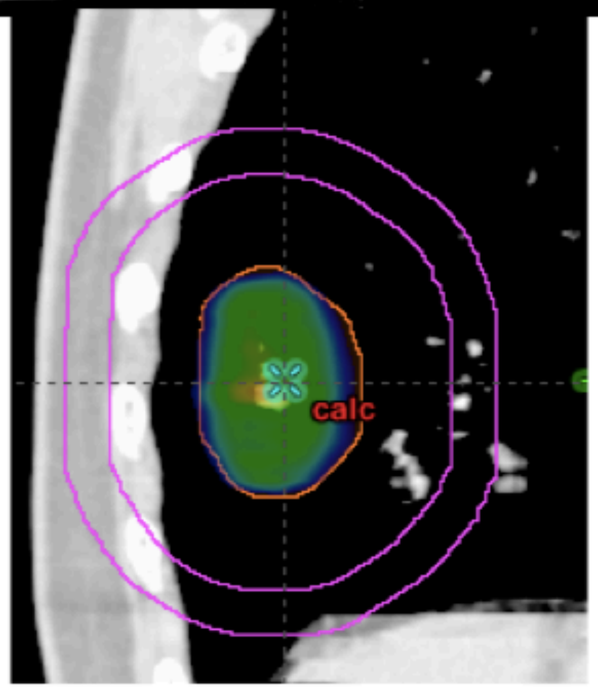
2cm-3cm ring



Cor

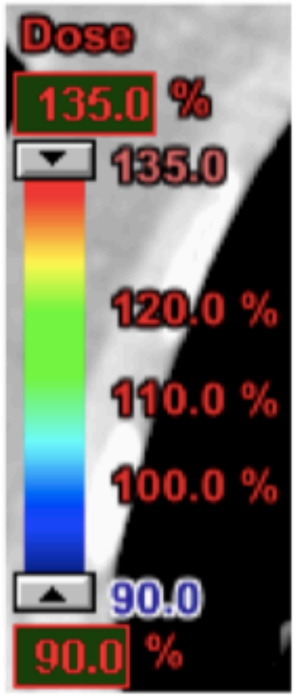
CAX





Sag

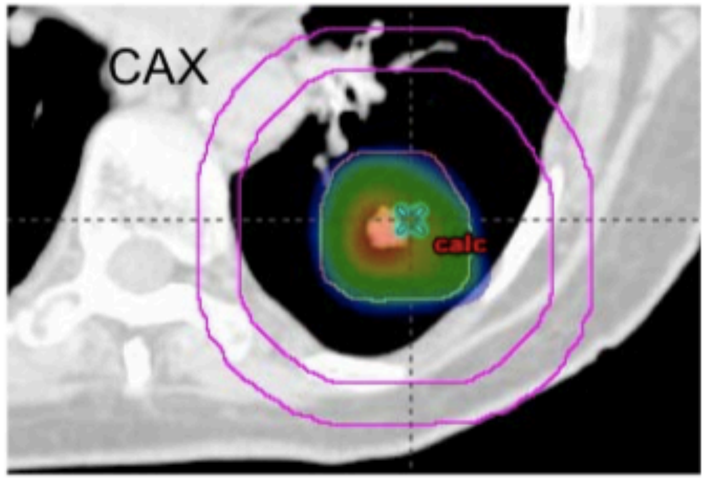
Prescription Isodose Surface Coverage:



PD = 100% = 20 Gy/fx x 3

PTV V90% > 99%

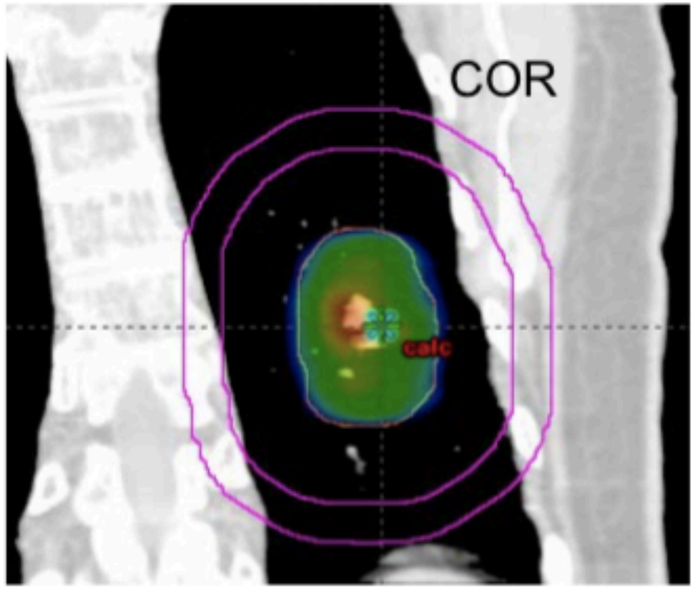
Here PTV V90% = 100%

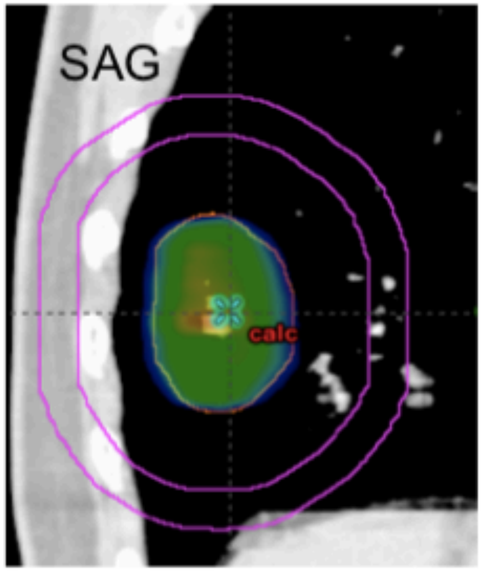


90% PD and Above

PTV

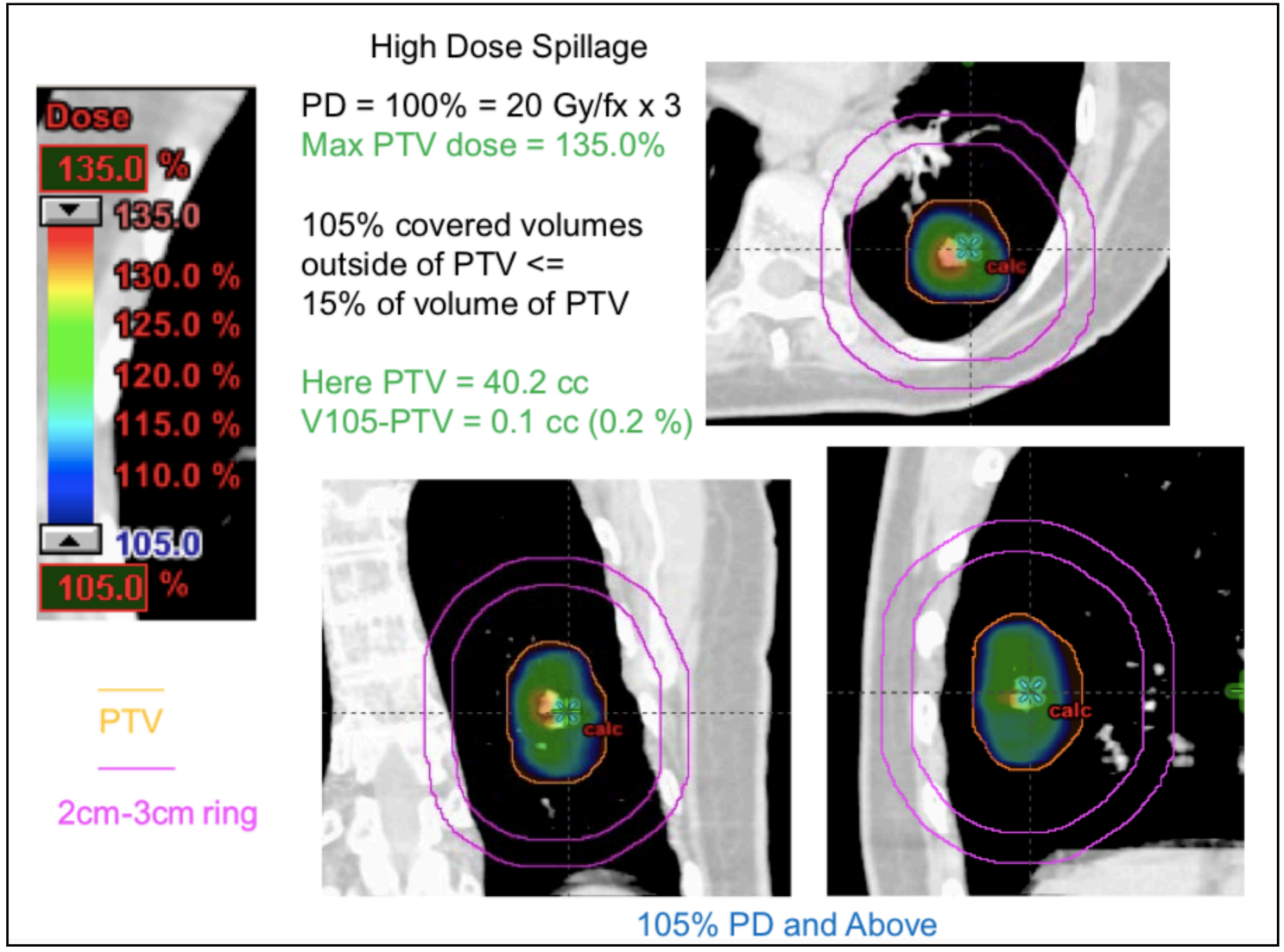
2cm-3cm ring



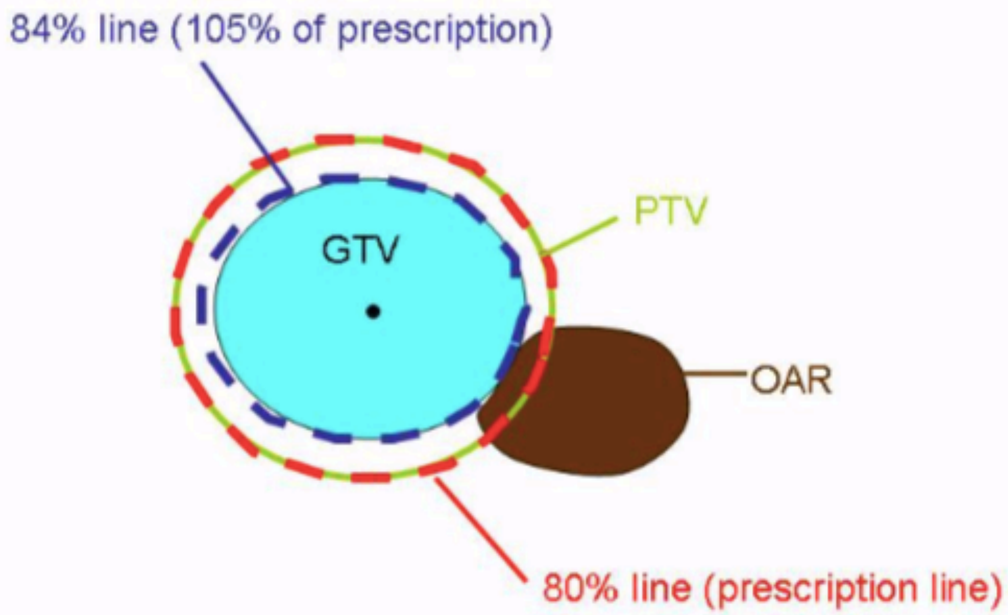


Evaluating the SBRT Plan - High Dose Spillage

The cumulative volume of all tissue outside the PTV receiving a dose > 105% of prescription dose should be no more than 15% of the PTV volume.



Summarising:

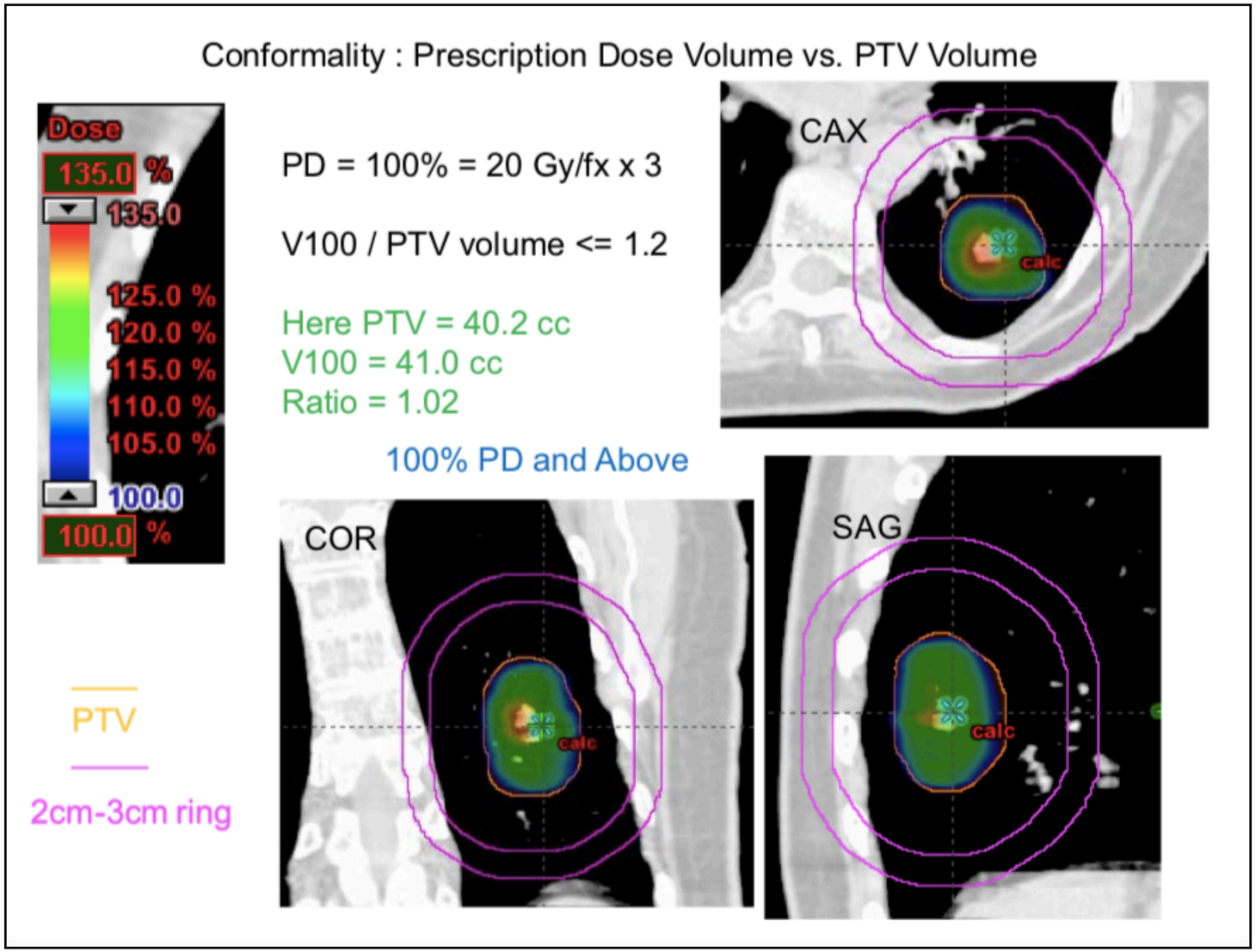


1. Prescription dose 50 Gy
2. Prescription isodose 80%
3. 105% of prescription dose 52.5 Gy (corresponds to 84% isodose line)
4. Maximum dose (normalization) at isocenter is 62.5 Gy

Image used from :RTOG 0813

Evaluating the SBRT Plan -Conformity Index

- Ratio of Prescription Isodose Volume / PTV Volume < 1.2



(ICRU 50/62)

Evaluating the SBRT Plan -Intermediate Dose Spillage

LOCATION

- The maximum total dose over all fractions in Gray (Gy) to any point 2 cm or greater away from the PTV in any direction must be no greater than D2CM, depends on PTV volume.
- Used to evaluate the dose fall off 2 cm in all directions from the PTV, usually 50 % of prescribed dose.

VOLUME

- R50 - Ratio of 50% Prescription Isodose Volume / PTV Volume < 3.0-3.9.
- The value is dependent on the PTV diameter

.

Table 1: Conformality of Prescribed Dose for Calculations Based on Deposition of Photon Beam Energy in Heterogeneous Tissue

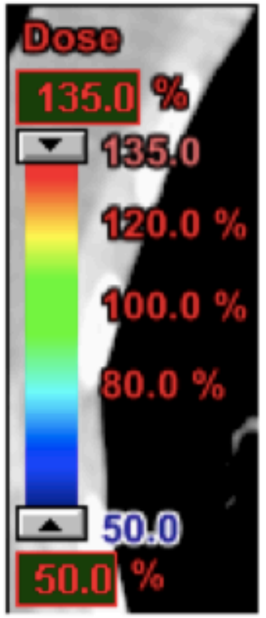
PTV Volume (cc)	Ratio of Prescription Isodose Volume to the PTV Volume		Ratio of 50% Prescription Isodose Volume to the PTV Volume, $R_{50\%}$		Maximum Dose (in % of dose prescribed) @ 2 cm from PTV in Any Direction, D_{2cm} (Gy)		Percent of Lung Receiving 20 Gy Total or More, V_{20} (%)	
	Deviation		Deviation		Deviation		Deviation	
	None	Minor	None	Minor	None	Minor	None	Minor
1.8	<1.2	<1.5	<5.9	<7.5	<50.0	<57.0	<10	<15
3.8	<1.2	.<1.5	<5.5	<6.5	<50.0	<57.0	<10	<15
7.4	<1.2	<1.5	<5.1	<6.0	<50.0	<58.0	<10	<15
13.2	<1.2	<1.5	<4.7	<5.8	<50.0	<58.0	<10	<15
22.0	<1.2	<1.5	<4.5	<5.5	<54.0	<63.0	<10	<15
34.0	<1.2	<1.5	<4.3	<5.3	<58.0	<68.0	<10	<15
50.0	<1.2	<1.5	<4.0	<5.0	<62.0	<77.0	<10	<15
70.0	<1.2	<1.5	<3.5	<4.8	<66.0	<86.0	<10	<15
95.0	<1.2	<1.5	<3.3	<4.4	<70.0	<89.0	<10	<15
126.0	<1.2	<1.5	<3.1	<4.0	<73.0	>91.0	<10	<15
163.0	<1.2	<1.5	<2.9	<3.7	<77.0	>94.0	<10	<15

Note 1: For values of PTV dimension or volume not specified, linear interpolation between table entries is required.

Note 2: Protocol deviations greater than listed here as “minor” will be classified as “major” for protocol compliance (see Section 6.7).

(RTOG 0813 and 0915 lung protocols)

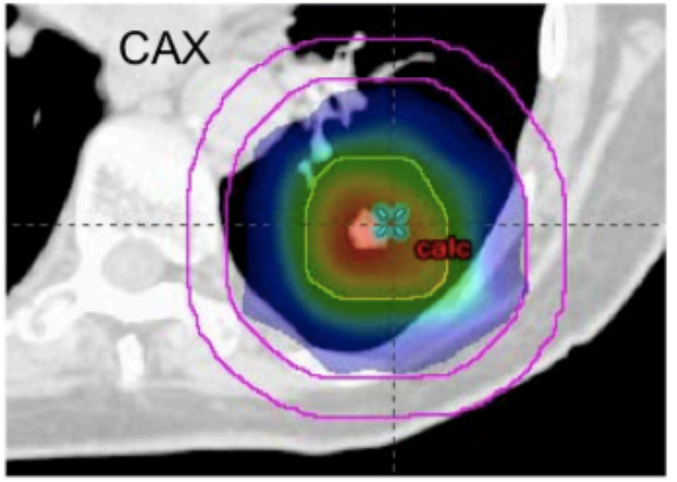
Intermediate Dose Spillage: $R_{50\%}$ and D_{2cm}



For PTV = 40.2 cc
$R_{50\%}$ <= 4.2; D_{2cm} = 59.6%

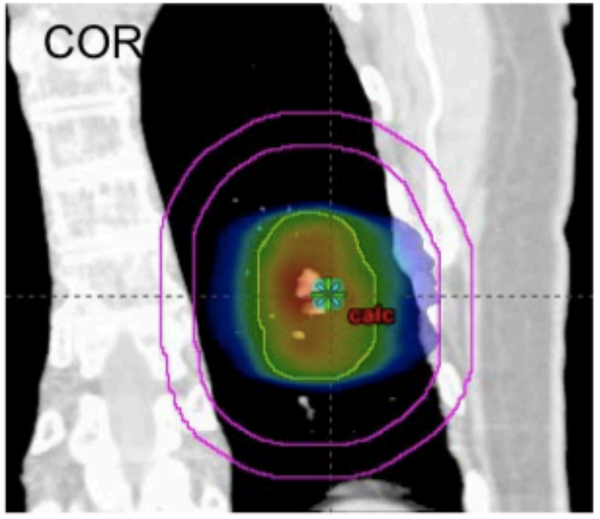
Here V50% = 169.5 cc
$R_{50\%}$ = 4.2
D_{2cm} = 52.6%

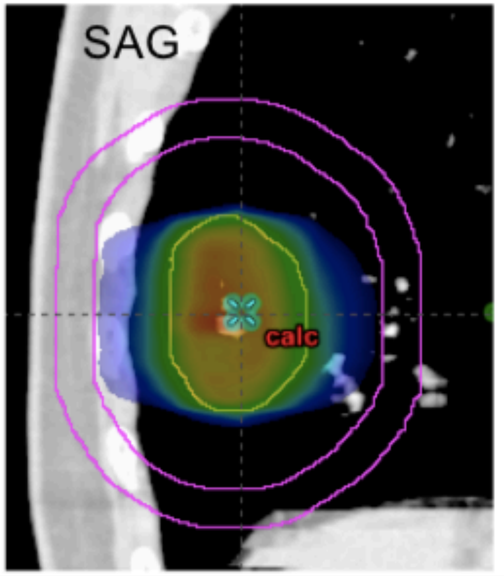
50% PD and Above

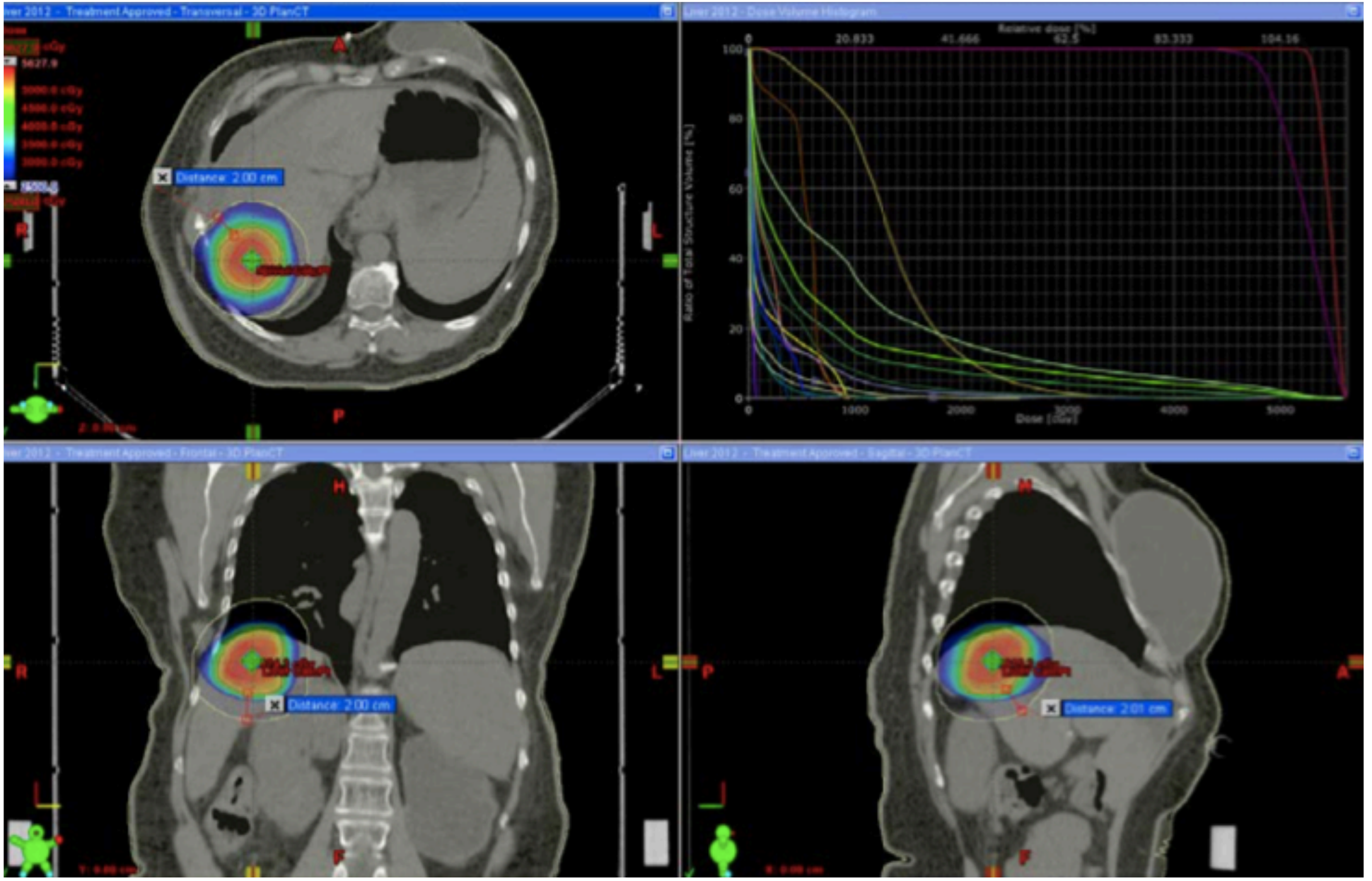


PTV

2cm-3cm ring






Liver 2012 - Treatment Approved - Transversal - 3D PlanCT
Distance: 2.00 cm
Liver 2012 - Dose Volume Histogram
Relative dose [%]
Ratio of Total Structure Volume [%]
Dose [cGy]
Liver 2012 - Treatment Approved - Frontal - 3D PlanCT
Distance: 2.00 cm
Liver 2012 - Treatment Approved - Sagittal - 3D PlanCT
Distance: 2.01 cm

Evaluating the SBRT Plan - Normal Constraints (LUNG)

Table 2

Serial Tissue	Volume	Volume Max (Gy)	Max Point Dose (Gy)	Avoidance Endpoint
Spinal Cord	<0.25 cc <0.5 cc	22.5 Gy (4.5 Gy/fx) 13.5 Gy (2.7 Gy/fx)	30 Gy (6 Gy/fx)	myelitis
Ipsilateral Brachial Plexus	<3 cc	30 Gy (6 Gy/fx)	32 Gy (6.4 Gy/fx)	neuropathy
Skin	<10 cc	30 Gy (6 Gy/fx)	32 Gy (6.4 Gy/fx)	ulceration
Parallel Tissue	**Critical Volume**	**Critical Volume Dose Max (Gy)**		**Avoidance Endpoint**
Lung (Right & Left)	1500 cc	12.5 Gy (2.5 Gy/fx)		Basic Lung Function
Lung (Right & Left)	1000 cc	13.5 Gy (2.7 Gy/fx)		Pneumonitis

Table 3

Serial Tissue*	Volume	Volume Max (Gy)	Max Point Dose (Gy)	Avoidance Endpoint
Esophagus, non-adjacent wall	<5 cc	27.5 Gy (5.5 Gy/fx)	105% of PTV prescription	stenosis/fistula
Heart/Pericardium	<15 cc	32 Gy (6.4 Gy/fx)	105% of PTV prescription	pericarditis
Great vessels, non-adjacent wall	<10 cc	47 Gy (9.4 Gy/fx)	105% of PTV prescription	aneurysm
Trachea and ipsilateral bronchus, non-adjacent wall	<4 cc	18 Gy (3.6 Gy/fx)	105% of PTV prescription	stenosis/fistula

Dose Constraints from RTOG 0813

Evaluating the SBRT Plan - Normal Constraints (Liver)

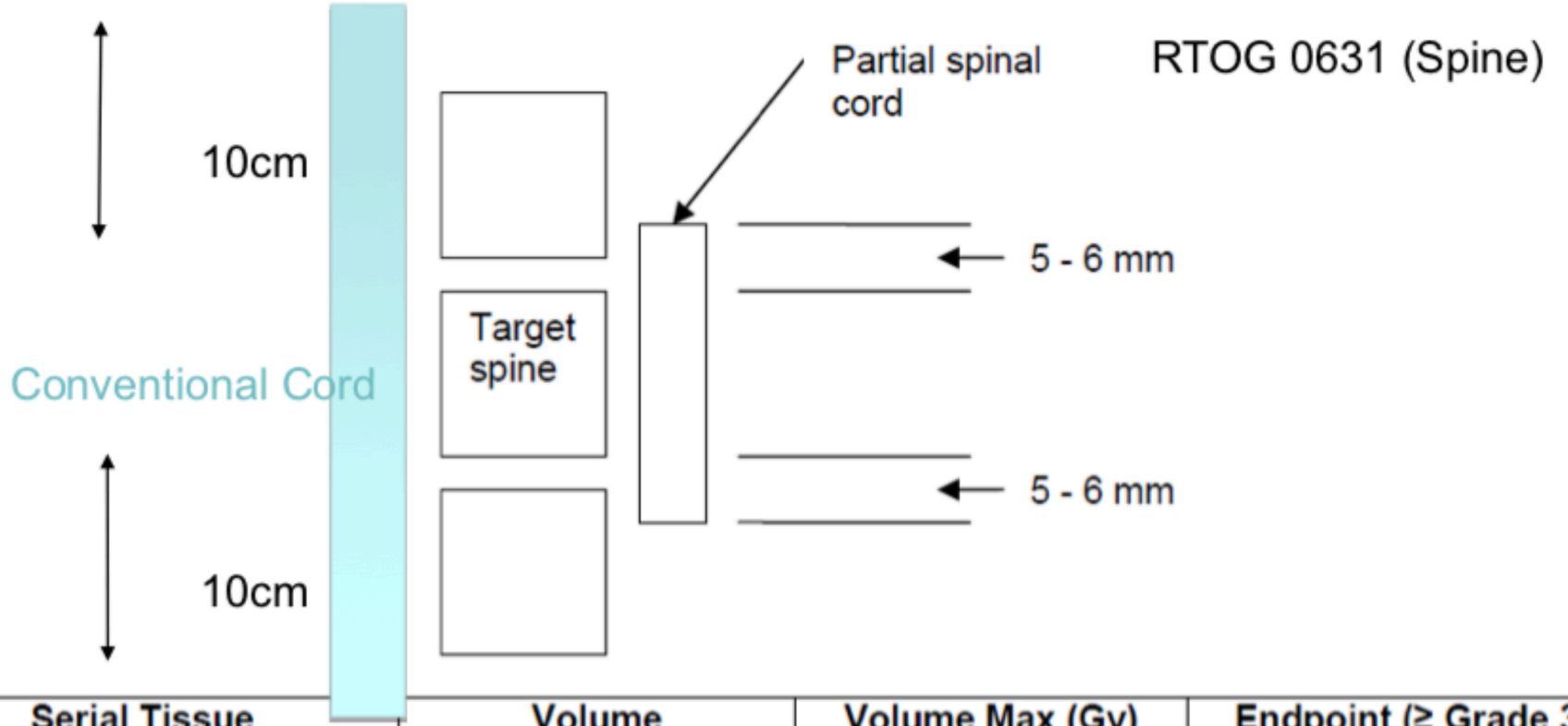
Dose Constraints for SBRT.[a]

Organ at Risk	Max Dose Constraint	Volume Dose Constraint
Liver minus all GTVs		>700 cc and V10 Gy < 70%
Esophagus	32 Gy to 0.5 cc	
Stomach	30 Gy to 0.5 cc	
Spinal cord + 5 mm	25 Gy to 0.5 cc	
Kidneys, bilateral		Mean dose < 10 Gy
Duodenum	30 Gy to 0.5 cc	
Small bowel	30 Gy to 0.5 cc	
Large bowel	32 Gy to 0.5 cc	
Heart	<30 Gy to 30 cc	
Great vessels	<60 Gy to 0.5 cc	
Chest wall	<50 Gy to 0.5 cc	
Skin (external)	<32 Gy to 0.5 cc	
Gallbladder	<55 Gy to 0.5 cc	
Common bile duct	<50 Gy to 0.5 cc	

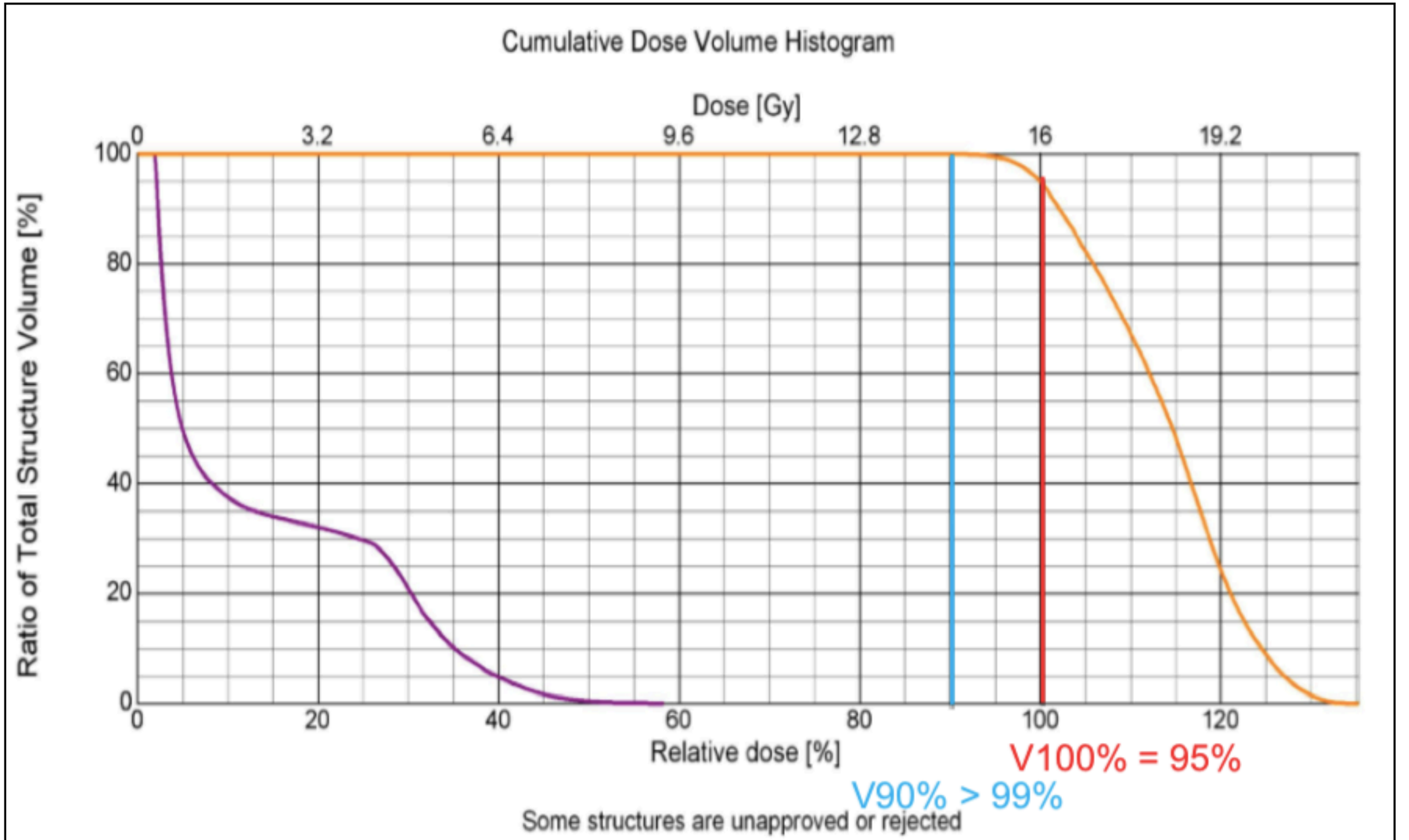
Abbreviations: GTV, gross tumor volume; SBRT, stereotactic body radiotherapy.

[a] Constraints adapted from RTOG 1112 protocol for a 5-fraction regimen.

Figure 3: Diagram of Defining Partial Spinal Cord Volume

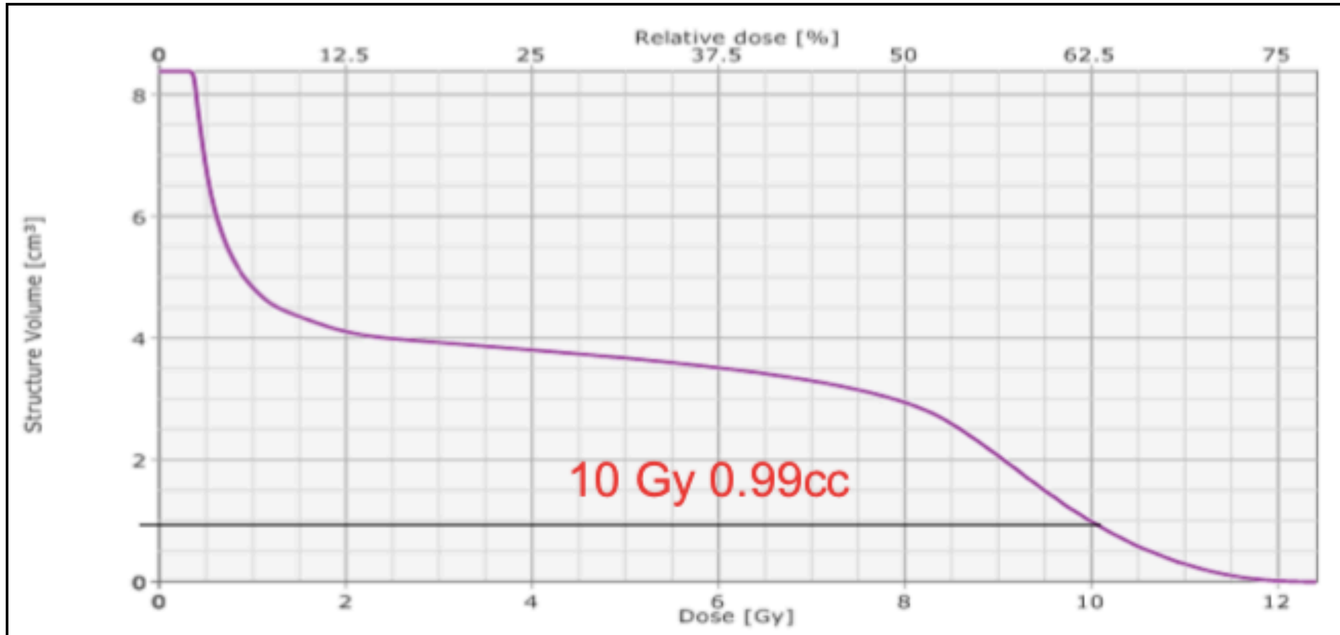


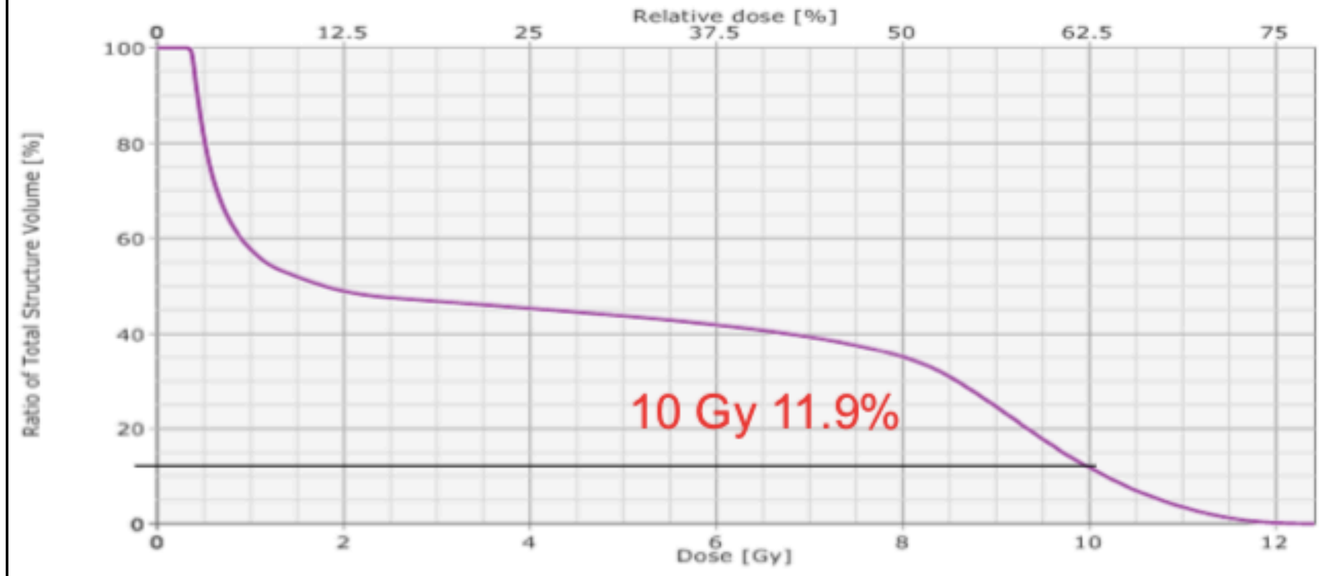
Serial Tissue	Volume	Volume Max (Gy)	Endpoint (≥ Grade 3)
Spinal Cord	Less than or equal to 0.35cc	10 Gy	myelitis
AND			
Spinal Cord	Less than or equal to 10% of the partial spinal cord	10 Gy	myelitis
AND			
Spinal Cord	Less than or equal to 0.03cc	14 Gy	myelitis
Cauda Equina	<0.03 cc <5 cc	16 Gy 14 Gy	Max point dose neuritis



Structure	Structure Status	Coverage [%/%]	Volume	Min Dose	Max Dose	Mean Dose	Modal Dose	Median Dose	Std Dev
RTOG-F-CORD	Unapproved	100.0 / 100.0	8.4 cm³	1.8 %	58.3 %	13.7 %	2.1 %	5.0 %	14.0 %
RTOG-PTV	Unapproved	100.0 / 100.0	19.1 cm³	88.3 %	135.3 %	113.8 %	116.3 %	114.6 %	8.3 %

Cord: Max point dose 9.33 Gy





RTOG 0631 Criteria:

10 Gy covers <= 0.35cc
AND
10 Gy covers <= 10%
AND
14 Gy covers <= 0.03cc
(Montefiore
Max point dose 14Gy)

Max point cord dose:
12.4 Gy

Plan Evaluation SBRT :Conclusion

- Prescription dose : Depends on site, size and location.
- Prescription isodose chosen: 95% PTV conformally covered by 100% prescription isodose and 99% PTV receives a minimum of 90% of the prescription dose.
- Conformality Index : Ideally < 1.2 and R 50 should be < 3.0-3.9 (PTV Volume dependent)
- Dose Spillage:

A. The cumulative volume of all tissue outside the PTV receiving a dose > 105% of prescription dose should be no more than 15% of the PTV volume.

B. Dose at 2 cms beyond PTV to be below 50% of prescribed dose (PTV Volume dependent)

- Dose constraints to normal structures to be adhered as stated in RTOG protocols or AAPM task group 101 guidelines.
- All above points have to be satisfied in the plan evaluation for the plan to be accepted.

References:

- RTOG 0631 Spine SBRT Protocol.
- RTOG 0813 and 0915 SBRT Lung Protocol.
- RTOG 0438 and 1112 SBRT Liver Protocol.
- AAPM TG Report 101 – Stereotactic Body Radiation TherapyImage used from : SBRT Treatment Planning: Practical Considerations
- SBRT treatment planning: Practical Considerations AAPM, Hong,. Montefiore Medical Center Albert Einstein College of Medicine Bronx, New York.
- RajniA.Sethi, IgorJ.Barani DavidA.Larson. MackRoach,III.Handbook of Evidence-Based Stereotactic Radiosurgery and Stereotactic Body Radiotherapy.Springer International Publishing Switzerland 2016

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- THANK YOU