

SBRT for the lung cancer : who and when to refer

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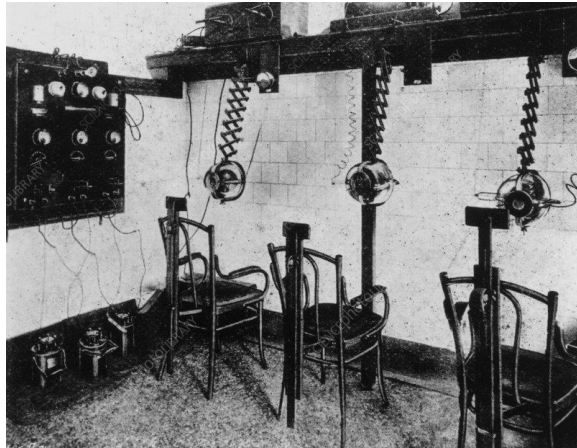
1. Background
2. Challenging situations for lung SBRT
 - Large tumor (>5cm)
 - Central and Ultracentral
 - ILD, COPD
 - Re-irradiation
 - Oligometastatic lung cancer
3. Conclusions

Background

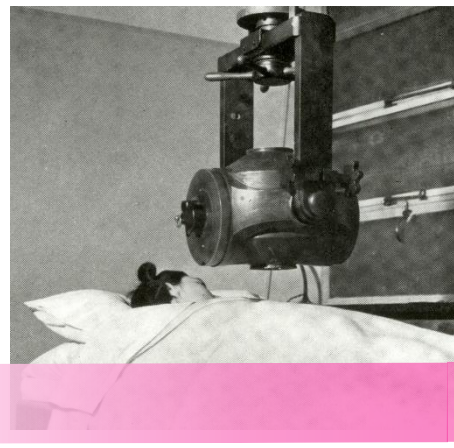
Radiotherapy



1895
Roentgen's wife



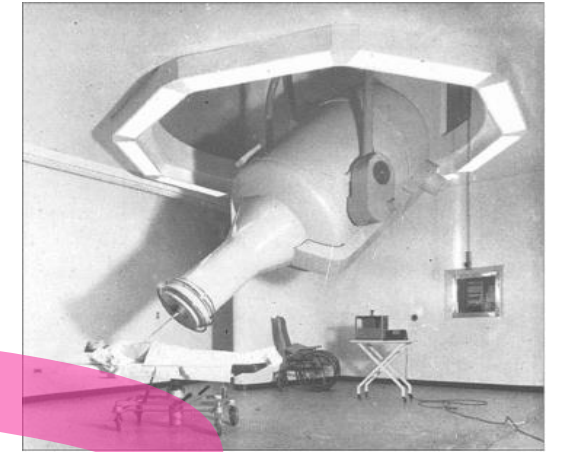
1903
Roentgen therapy



1918 Radium



1950s Electron

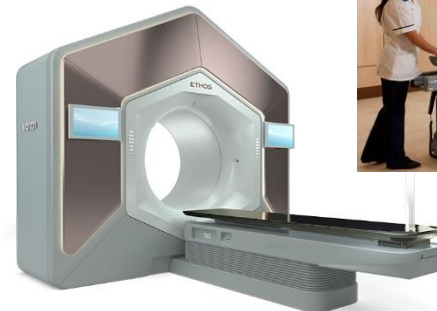


1960s first linear accelerator

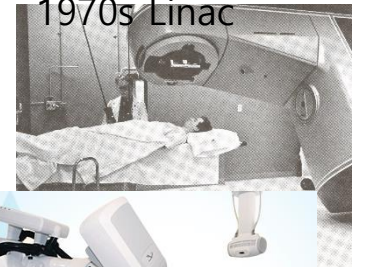
2010s Heavy ion therapy



Daily Adopt



1970s Linac

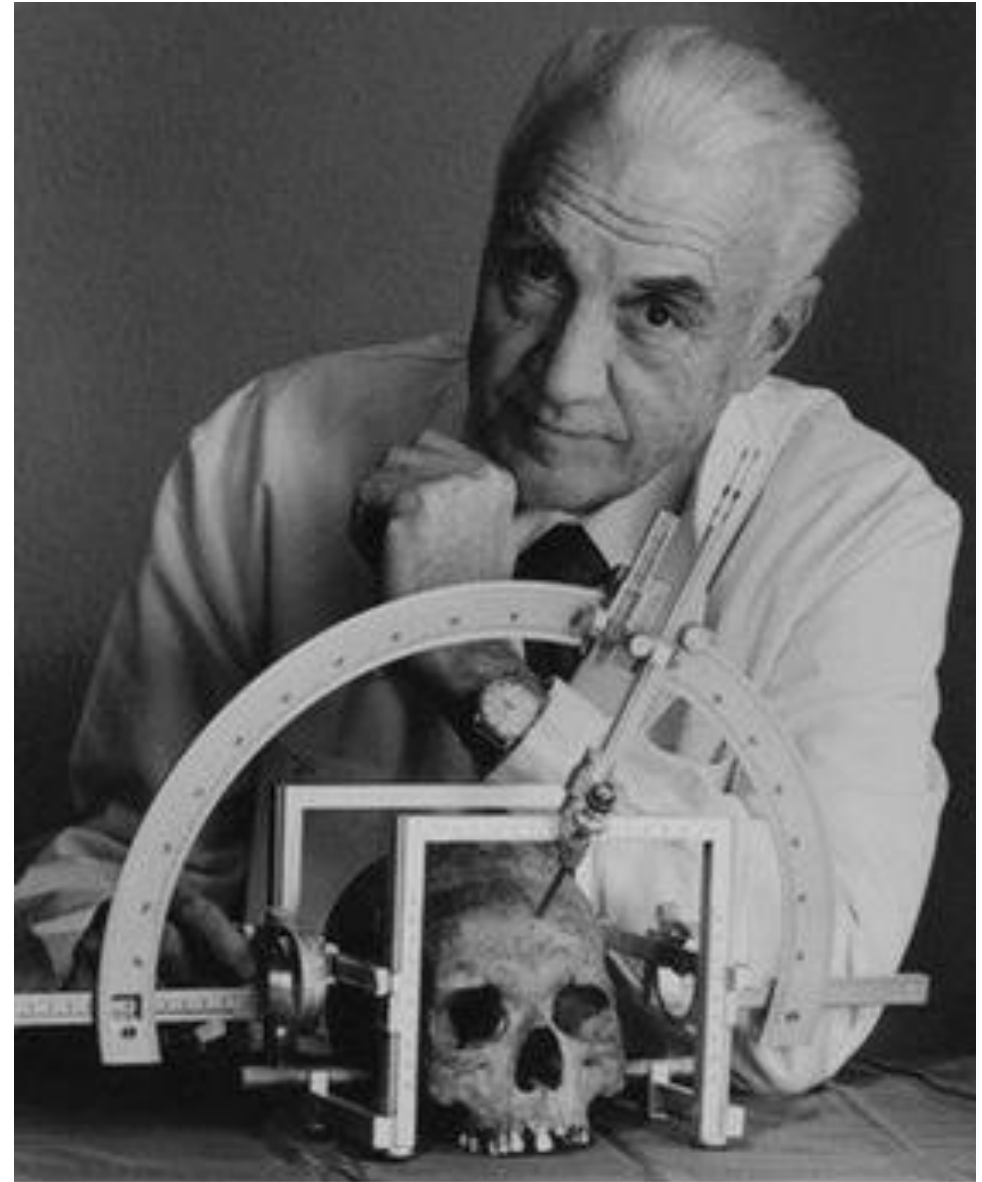


Definition

- **Stereotactic body radiotherapy (SBRT)**, also referred to as **stereotactic ablative radiotherapy (SABR)**, is defined as the delivery of **high ablative doses** with extreme precision to a targeted area, typically administered in **one to five fractions**.

“Stereotactic”

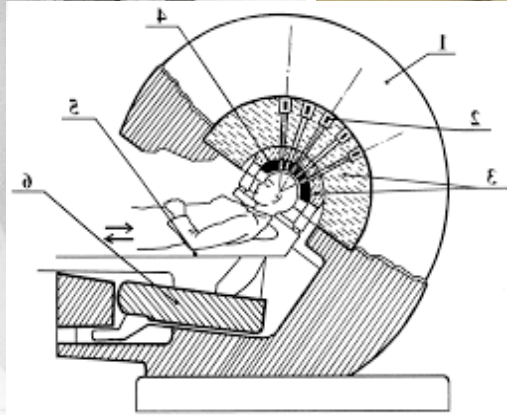
The Leksell Stereotactic System
1951



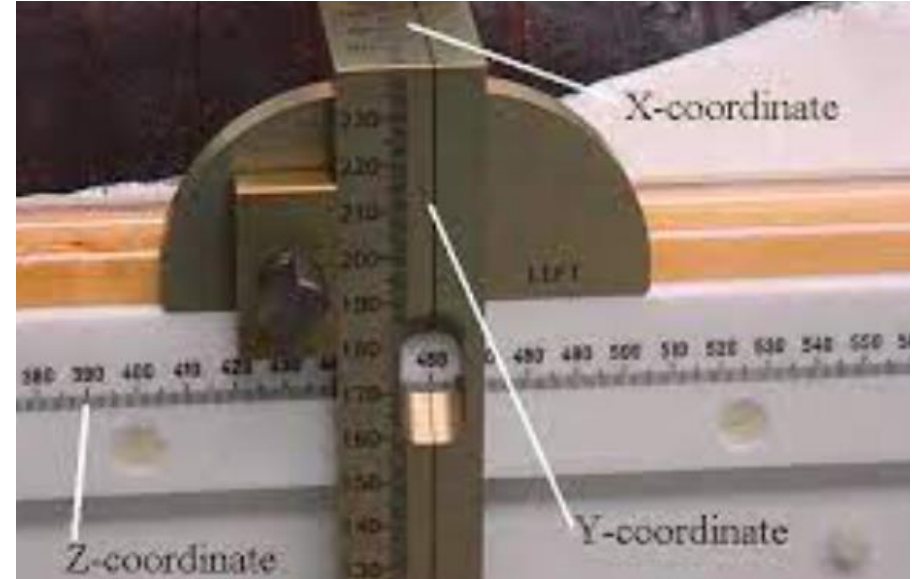
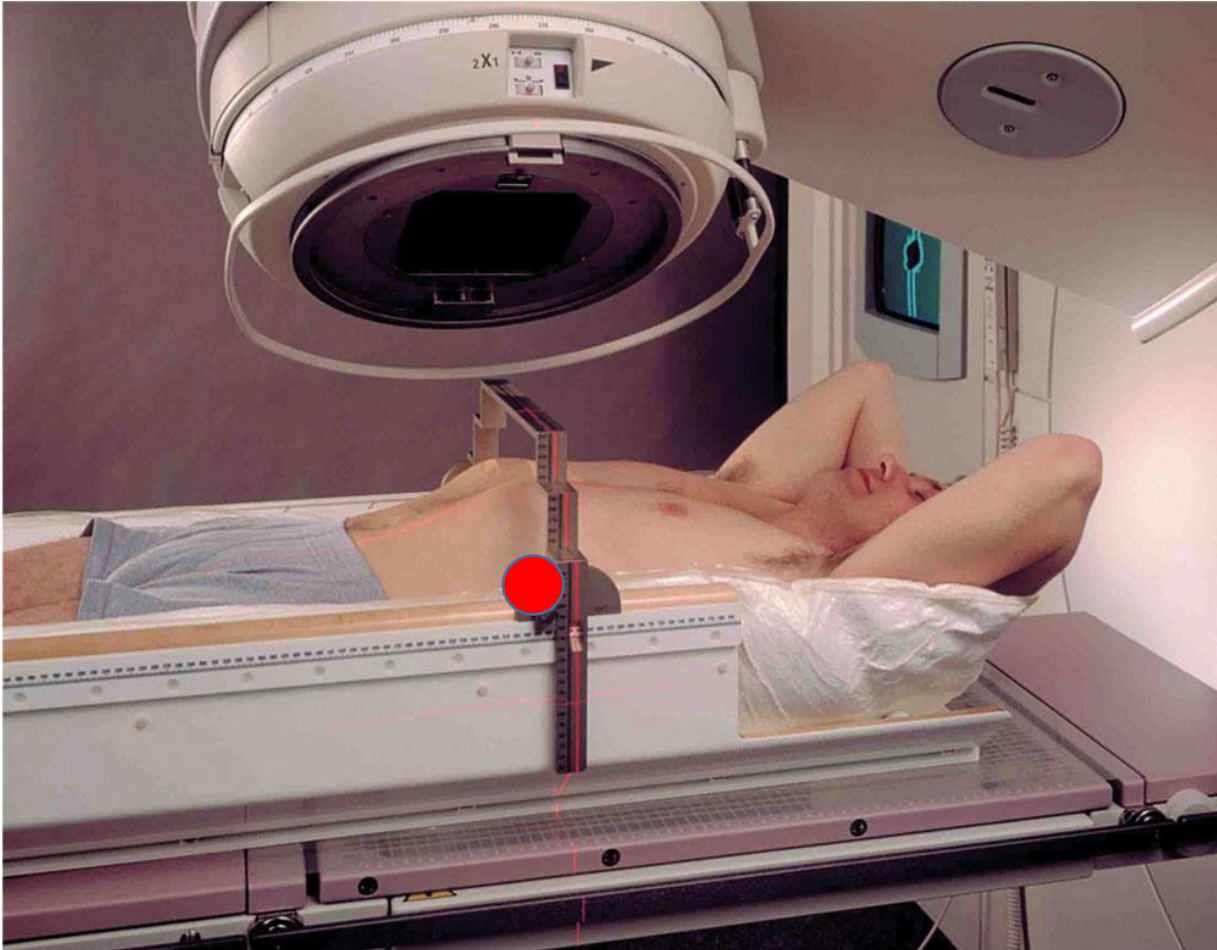
“Stereotatic” Radiosurgery (SRS)



Gamma knife Radiosurgery (1968)



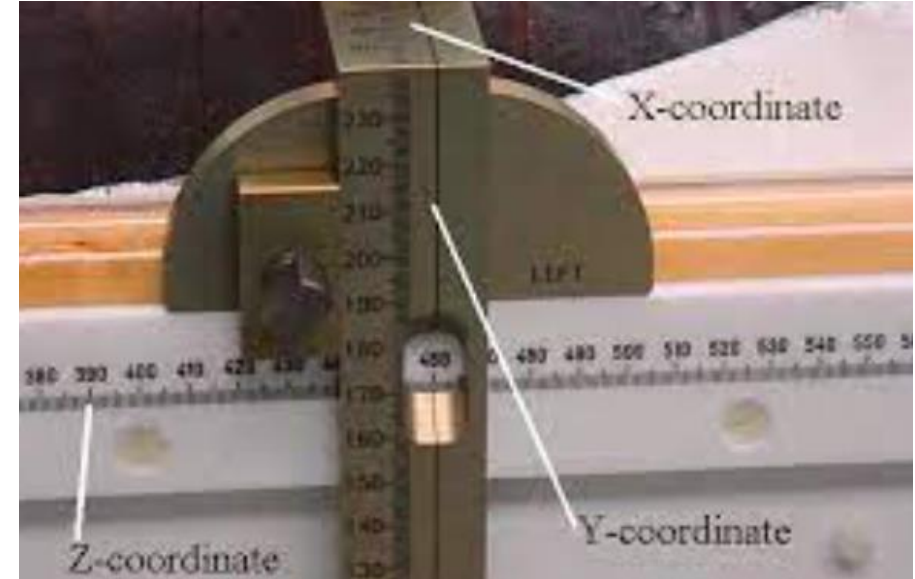
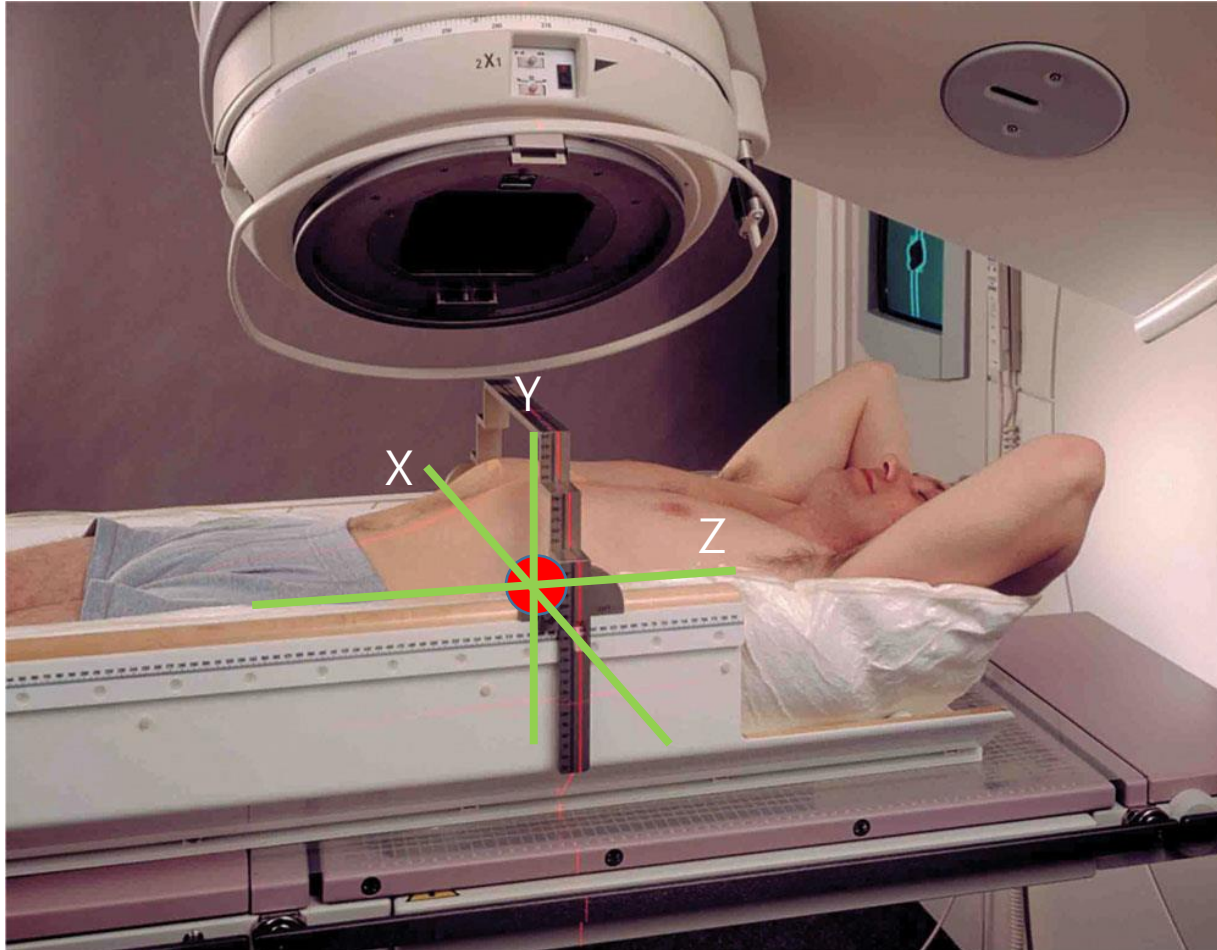
Extracranial SRS (with "stereotatic body" frame)



Stereotactic high dose fraction radiation therapy of extracranial tumors

Blomgren H et al. Acta Oncol 34:861-870, 1995

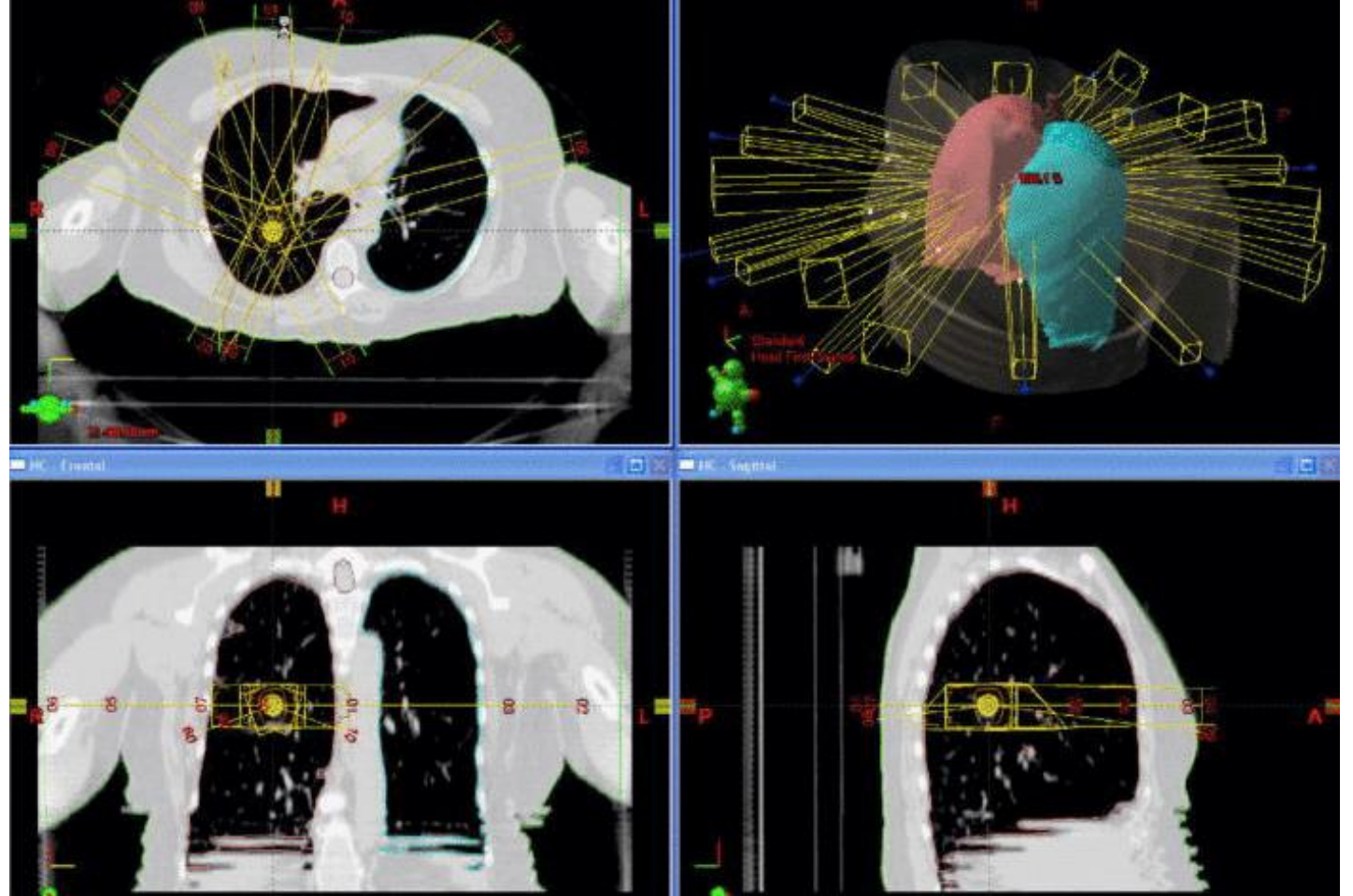
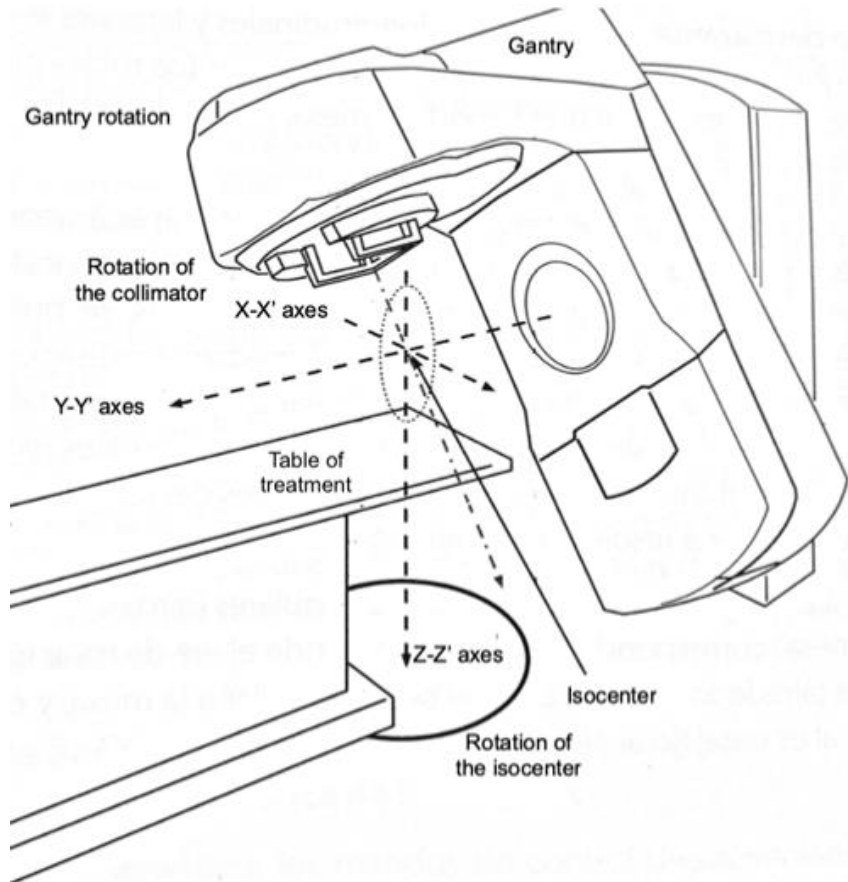
Extracranial SRS (with "stereotatic body" frame)



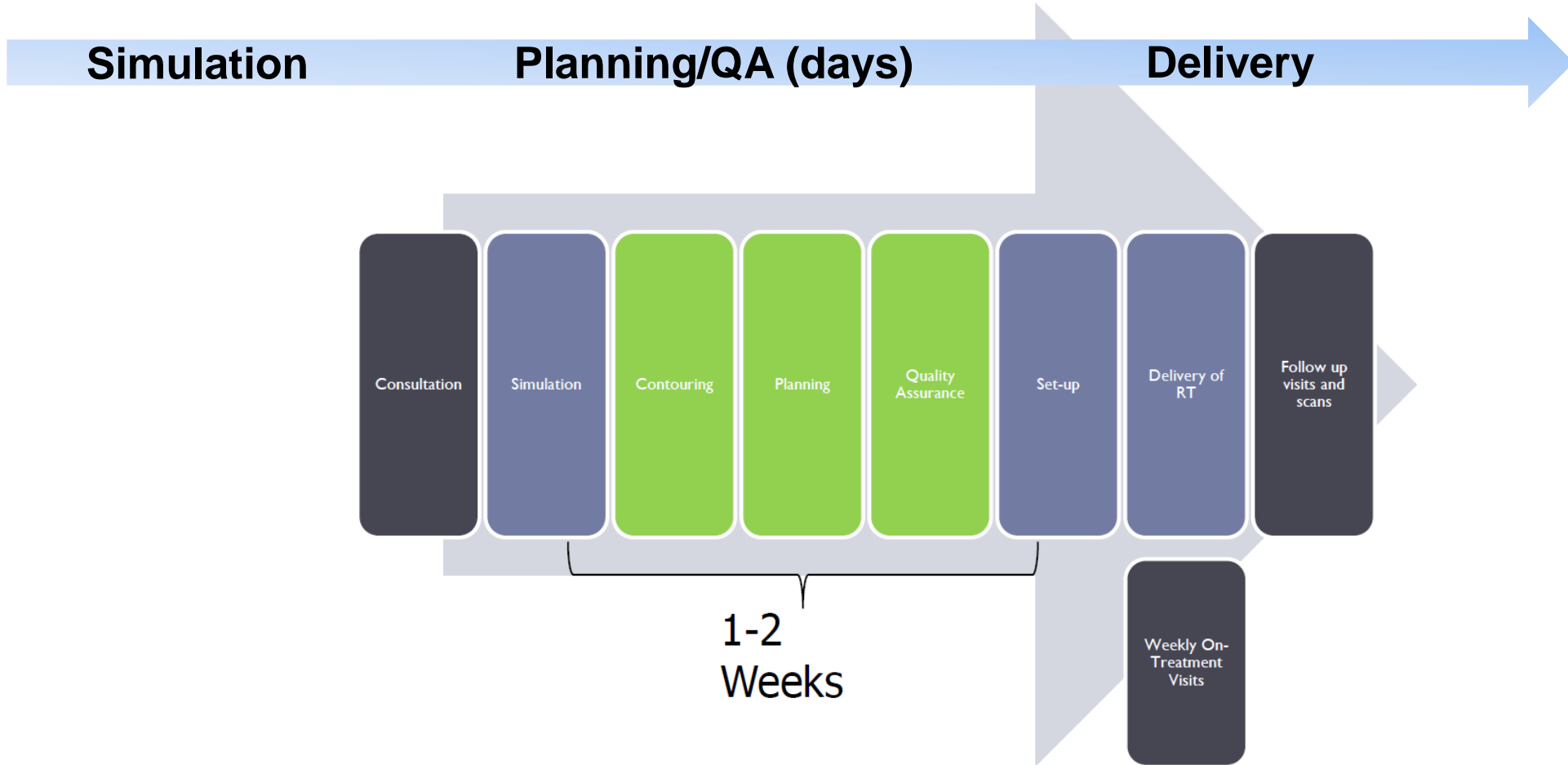
Stereotactic high dose fraction radiation therapy of extracranial tumors

Blomgren H et al. Acta Oncol 34:861-870, 1995

Stereotatic body radiotherapy



Timeline of lung SBRT



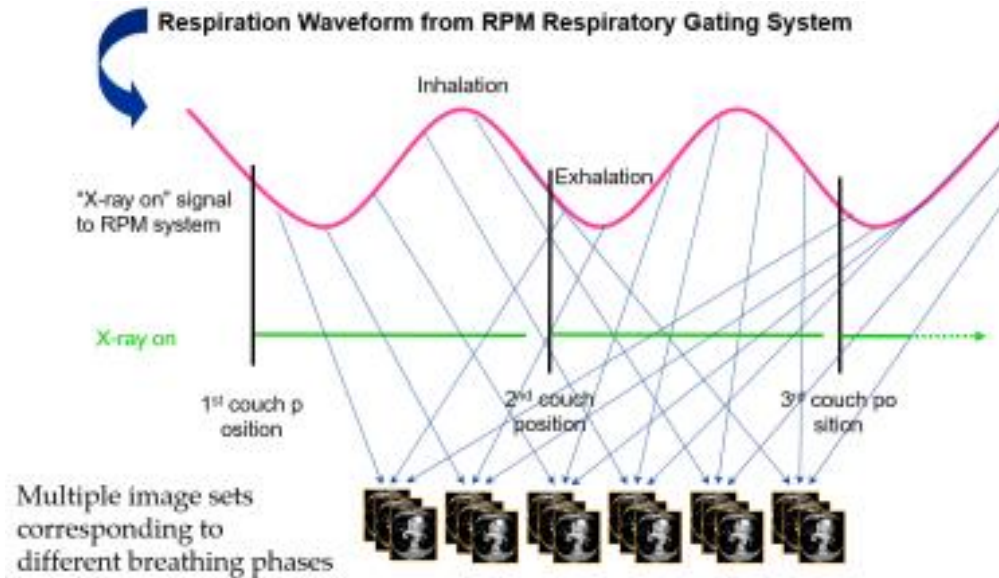
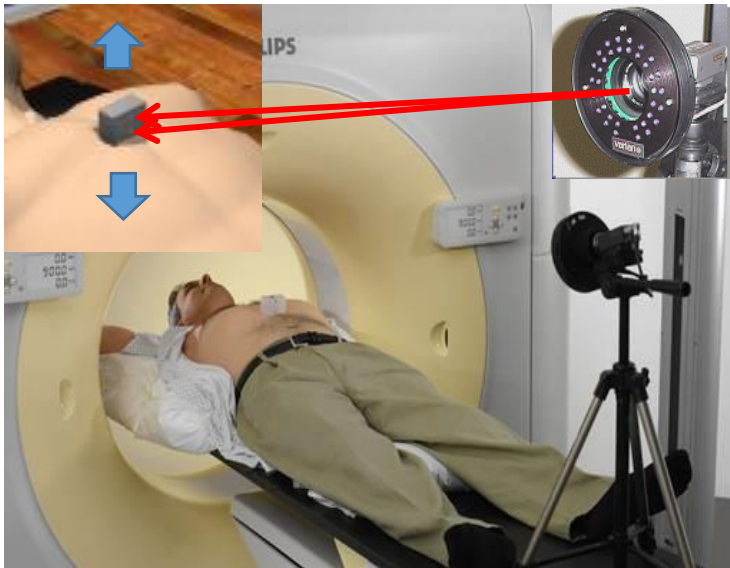
Timeline of lung SBRT

Simulation

Planning

Delivery

4D CT



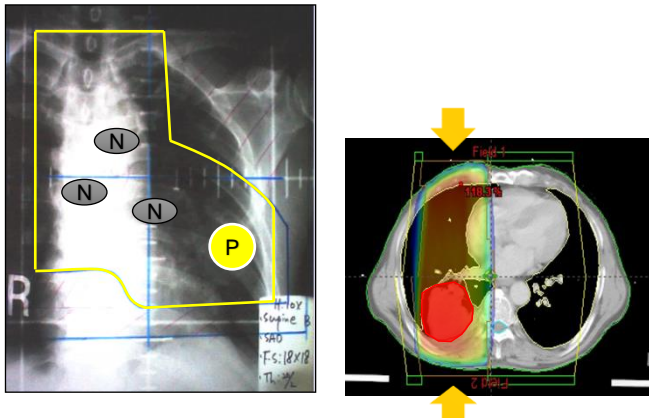
Timeline of lung SBRT

Simulation

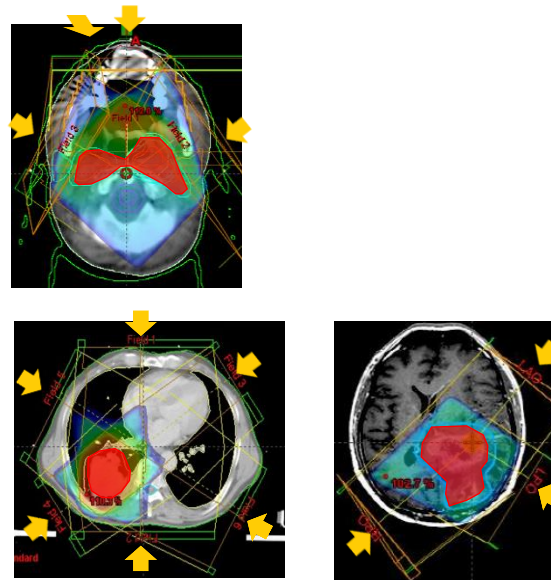
Planning

Delivery

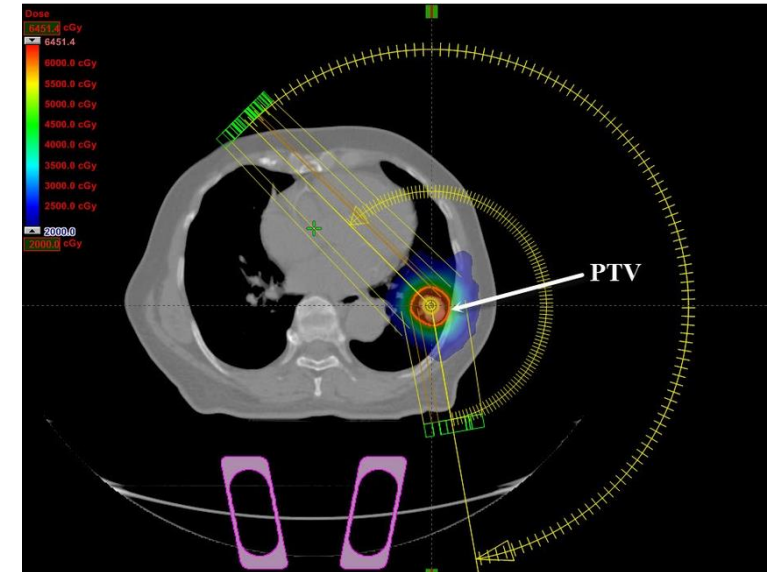
2D-RT (2-dimensional RT)



3D-CRT (3D-Conformal RT)



VMAT



Timeline of lung SBRT

Simulation

Planning/QA

Delivery



SGRT (Surface guide): set up

IGRT (Image guide)

Respiratory management

- Gating
- Breath hold

Timeline of lung SBRT

Simulation

Planning/QA

Delivery

SGRT (Surface guide): set up



Richards, Jane
29/07/1983, IM45982

Left Breast DIBH

SGRT Free Breath Surface

FB

VRT _{cm}	-0.13	
LNG _{cm}	-0.07	
LAT _{cm}	-0.03	
MAG _{cm}	0.16	
RTN [°]	0.4	
ROLL [°]	-0.6	
PITCH [°]	-2.0	

Reference Treatment Couch 0.0° Send to Couch Beam Control OFF

Coaching Surface Deformation Video

alignrt | 22.4 fps | MonitoringState | Field Status | 1656.57 MB | System Status | 13/09/2022 13:21

Timeline of lung SBRT

Simulation

Planning/QA

Delivery

SGRT (Surface guide): set up

IGRT (Image guide)

Respiratory management

- Gating
- Breath hold



CBCT
(conebeam)
(4D CBCT)

Timeline of lung SBRT

Simulation

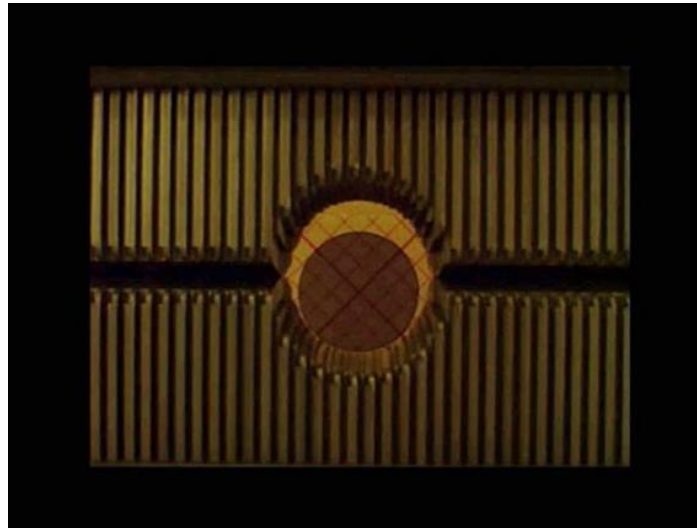
Planning/QA

Delivery

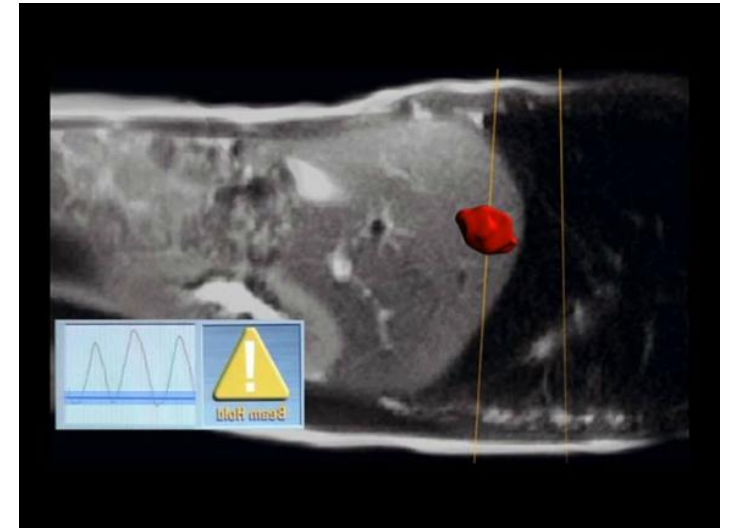
SGRT (Surface guide): set up
IGRT (Image guide)

Respiratory management

- Gating
- Breath hold



No gating



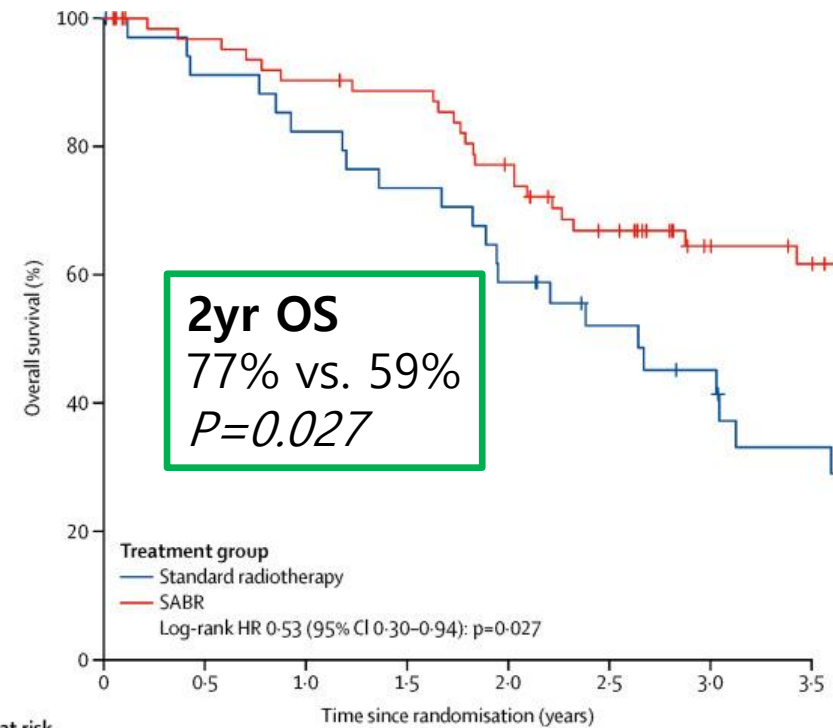
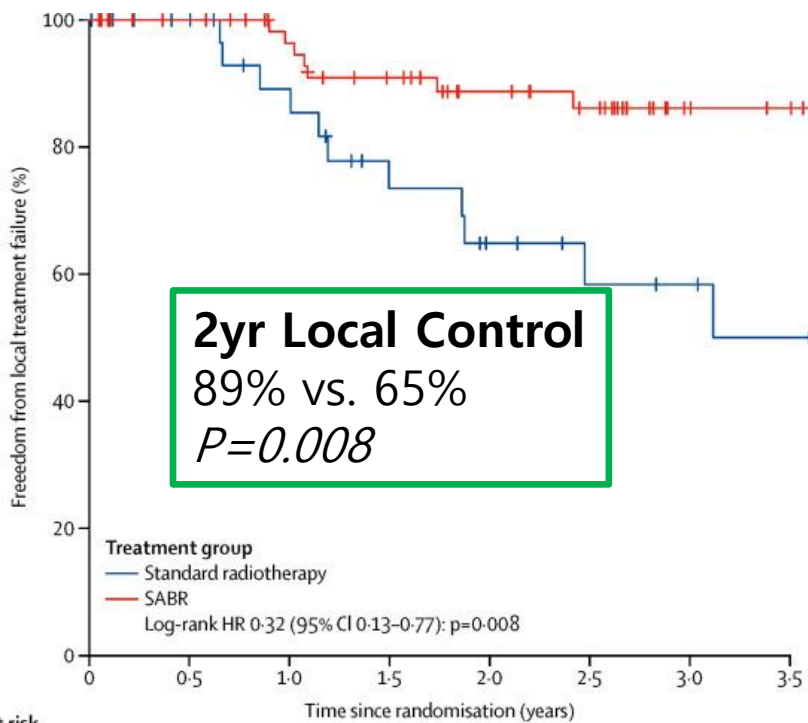
Gated RT

SBRT: early stage, medically inoperable lung cancer

Year	Reference	Design	N	LC	OS	Toxicity
2006	Timmerman et al	Phase II	70	2y 95%	2y 54.7%	
2010	RTOG 0236	Phase II	55	3y 97.6% 5y 92.7%	3y 55.8% 5y 40%	G3/4: 16.4% (9 of 55)
2018	RTOG 0618	Phase II	26	4y 96%	4y 56%	G3 AEs: 7.7% No G4/G5 AEs
2019	RTOG 0915	Phase II	84	34 Gy, 5y 89.4% 48 Gy, 5y 93.2%	34 Gy, 5y 29.6% 48 Gy, 5y 41.1%	34 Gy, G3 or higher: 2.6% 48 Gy, G3 or higher: 11.1%

SBRT vs. conventional RT (daily 2 Gy)

- TROG 09.02 CHISEL (phase III, RCT)
- T1-2a, medically inoperable



60 Gy in a different way

2 Gy x 30 fractions 15 Gy x 4 fractions

60 Gy

60 Gy

Total dose

72 Gy

150 Gy

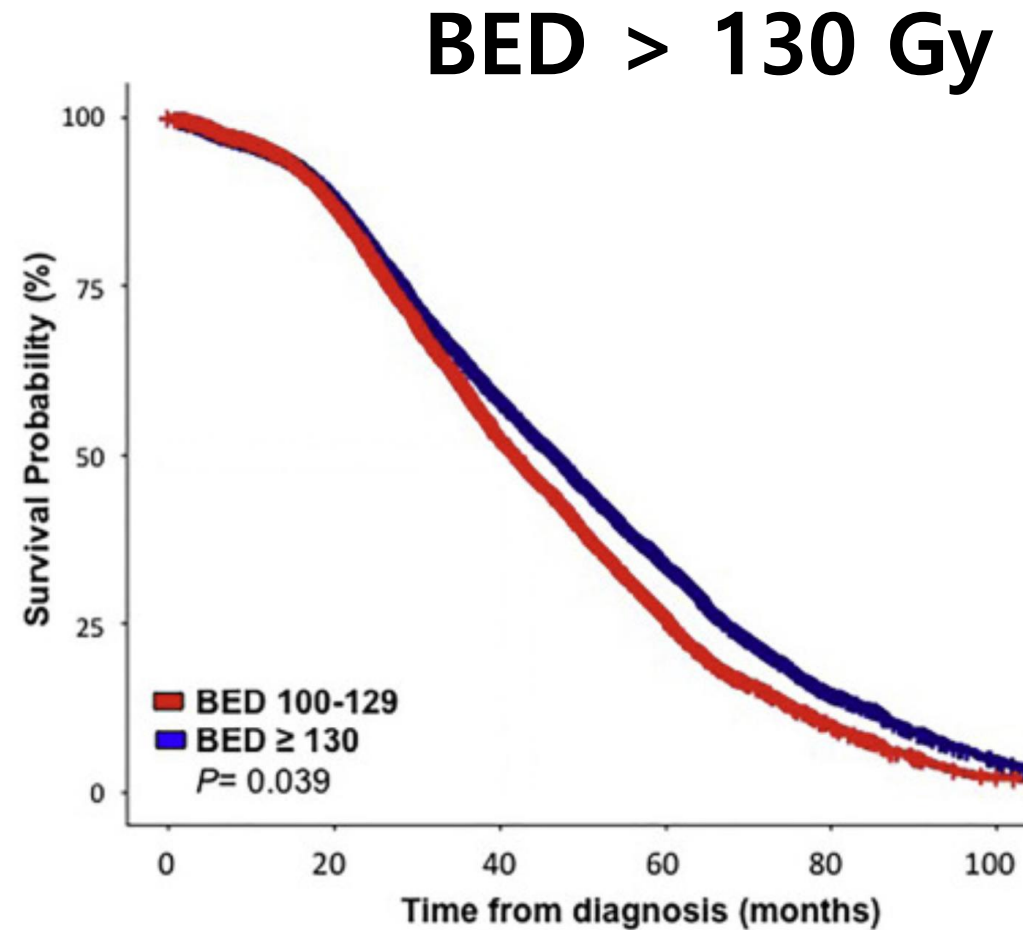
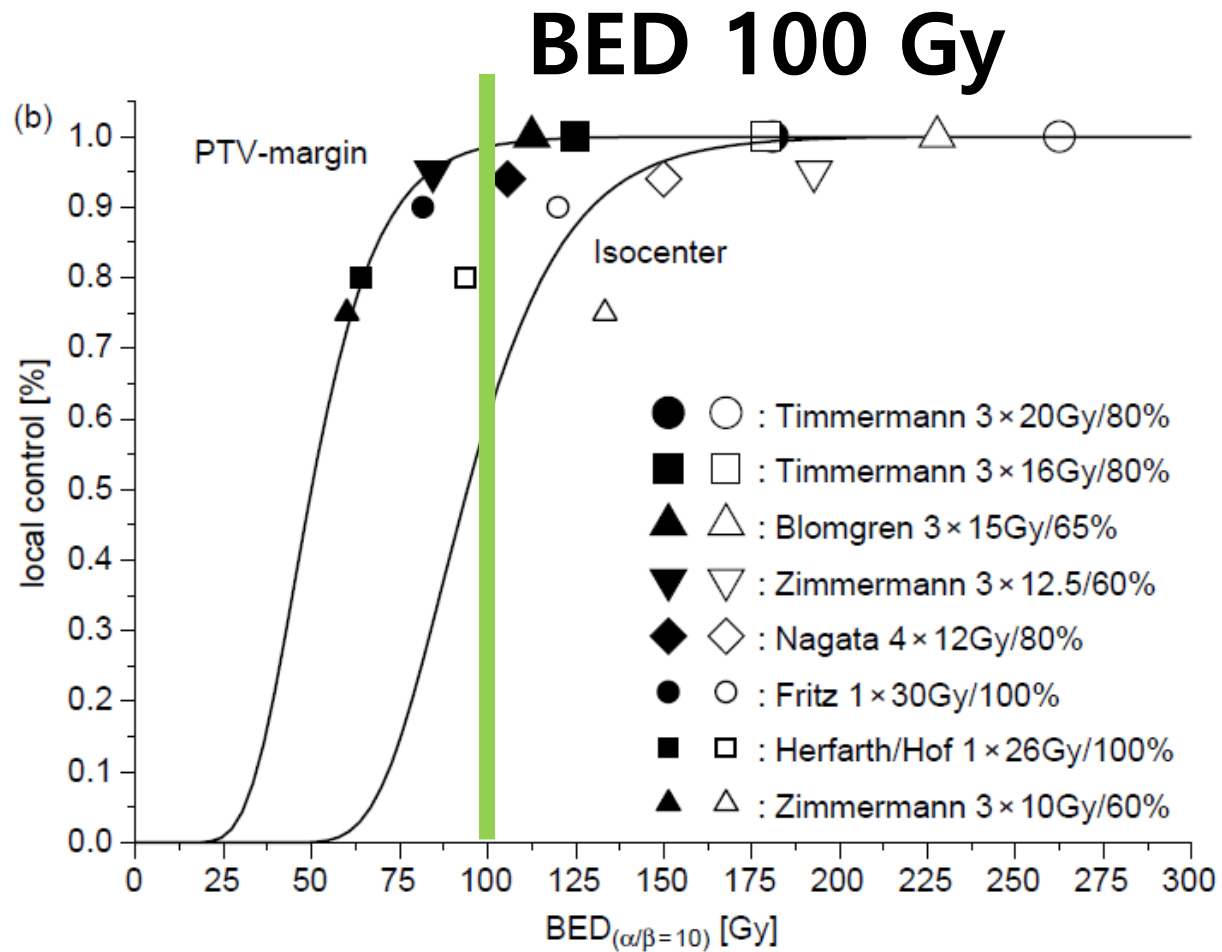
Biological effective dose (BED₁₀)

94.3 Gy

317.1 Gy

Biological effective dose (BED_{3.5})

SBRT BED



Summary

SBRT defined as

- Ablation dose, **BED > 100 Gy**
- 1-5 fractions
- Precision delivery
 - 4DCT, IGRT, respiratory management

SBRT for inoperable early stage lung cancer

→ > 90% local control (2yr, 3yr)

Role of SBRT in Challenging situations

1. Central and Ultracentral tumors
2. Large tumor (>5cm)
3. ILD, COPD
4. Re-irradiation
5. Oligometastatic lung cancer

Role of SBRT in Challenging situations

Clinical Management Considerations

- Majority of patients:
- Frail elderly patients, inoperable state, operable but high risk
- **SBRT** vs. conventional RT, surgery, chemotherapy or observation
- **Tumor location is the primary determinant of toxicity.**
Organ at risks (OARs), Dose constraints

Case 1.

78/M

No lymphadenopathy
Medically inoperable

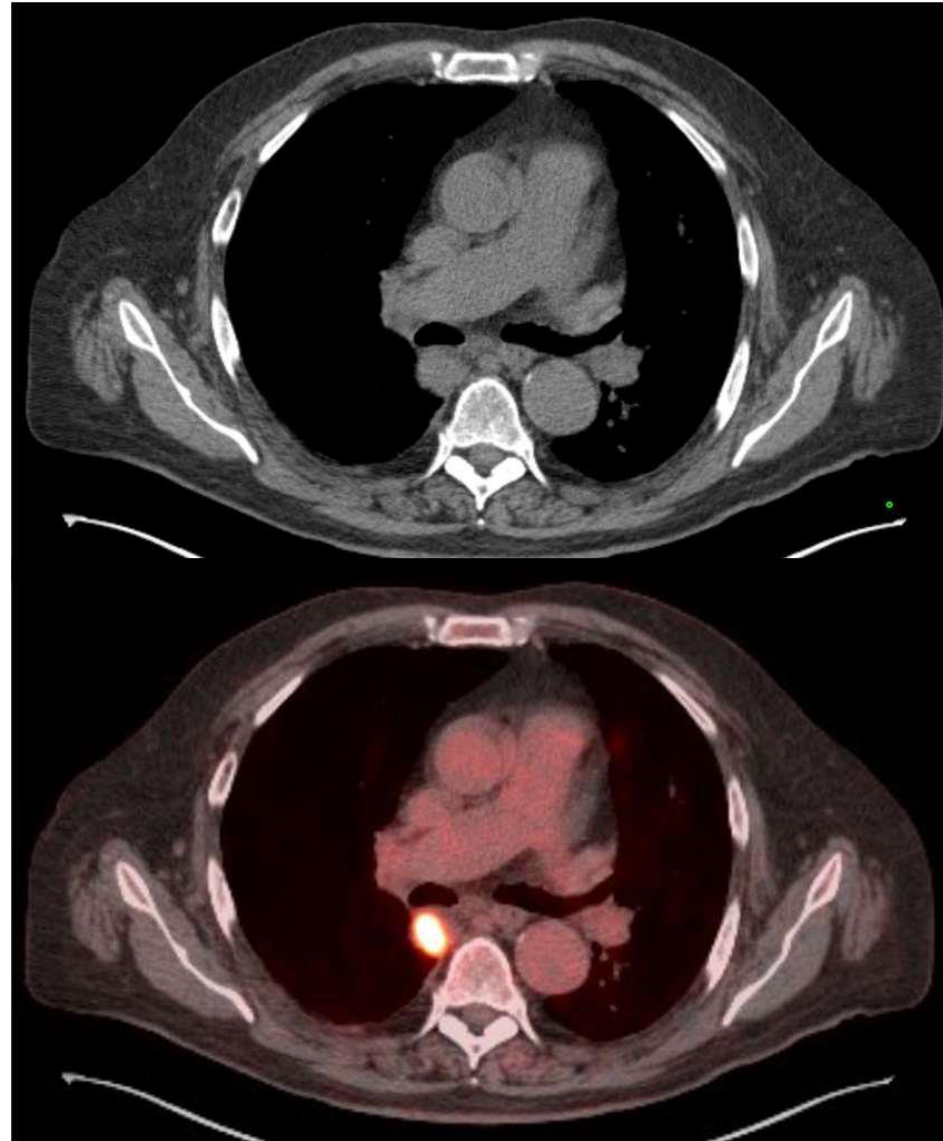
Organ at risk (OAR)

Lung

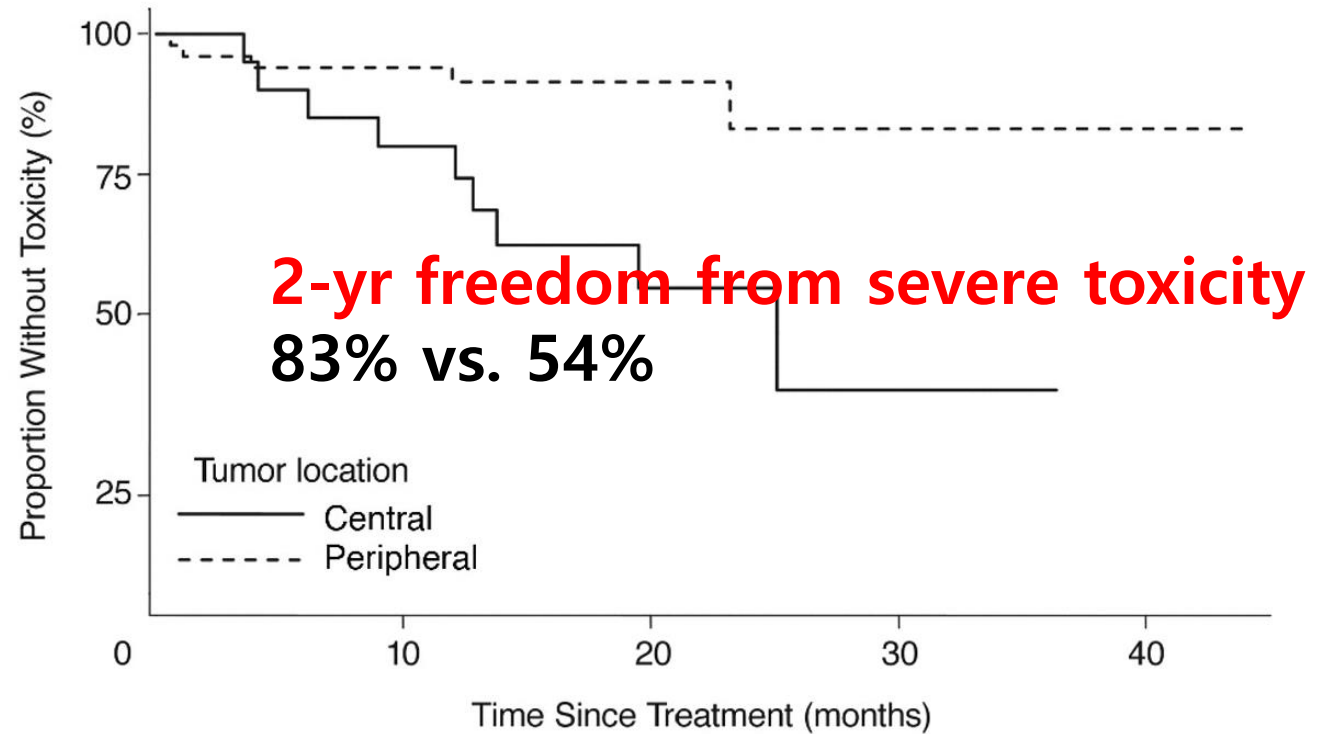
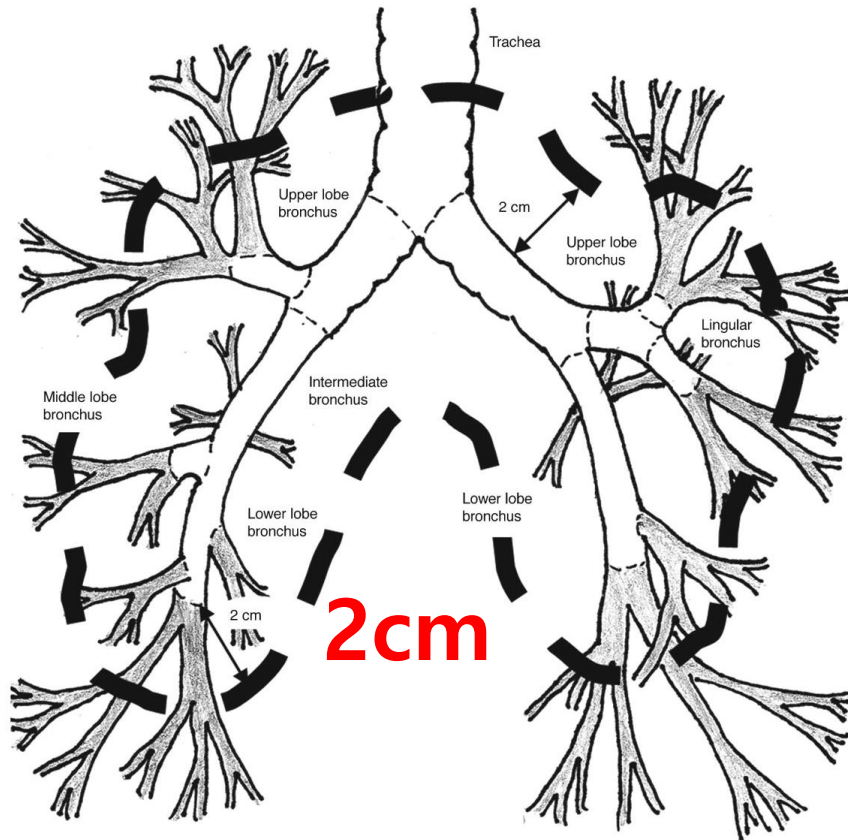
Proximal bronchial tree

Esophagus

Spinal cord

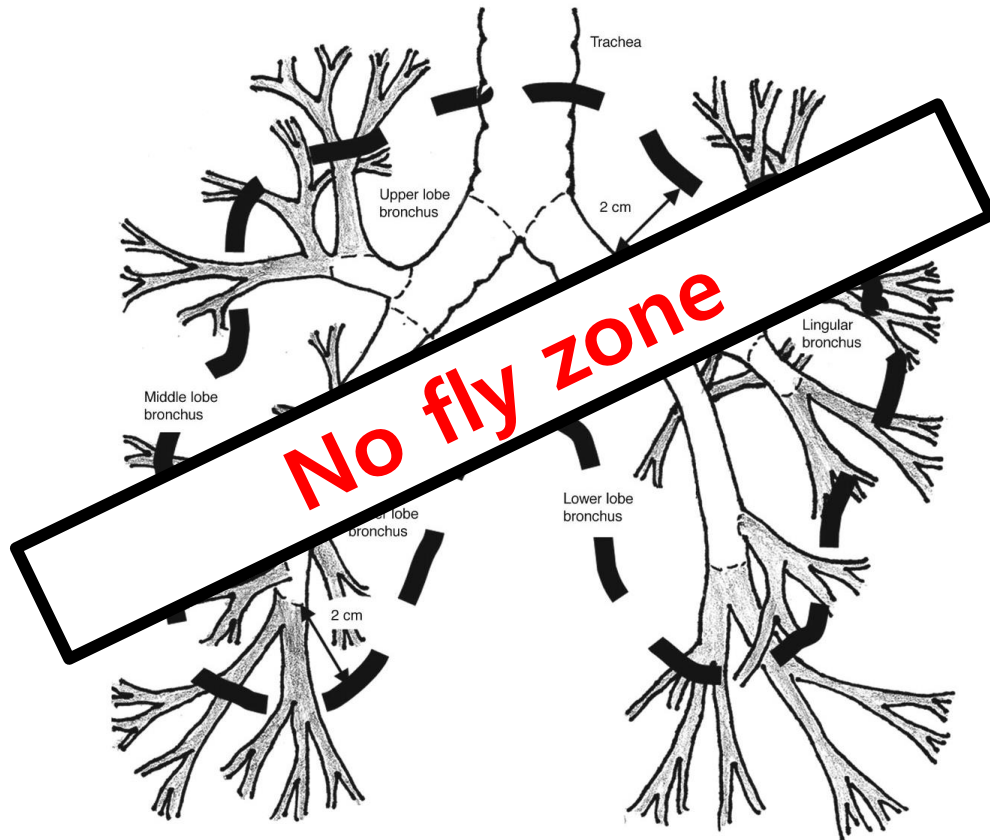


Central and Ultracentral



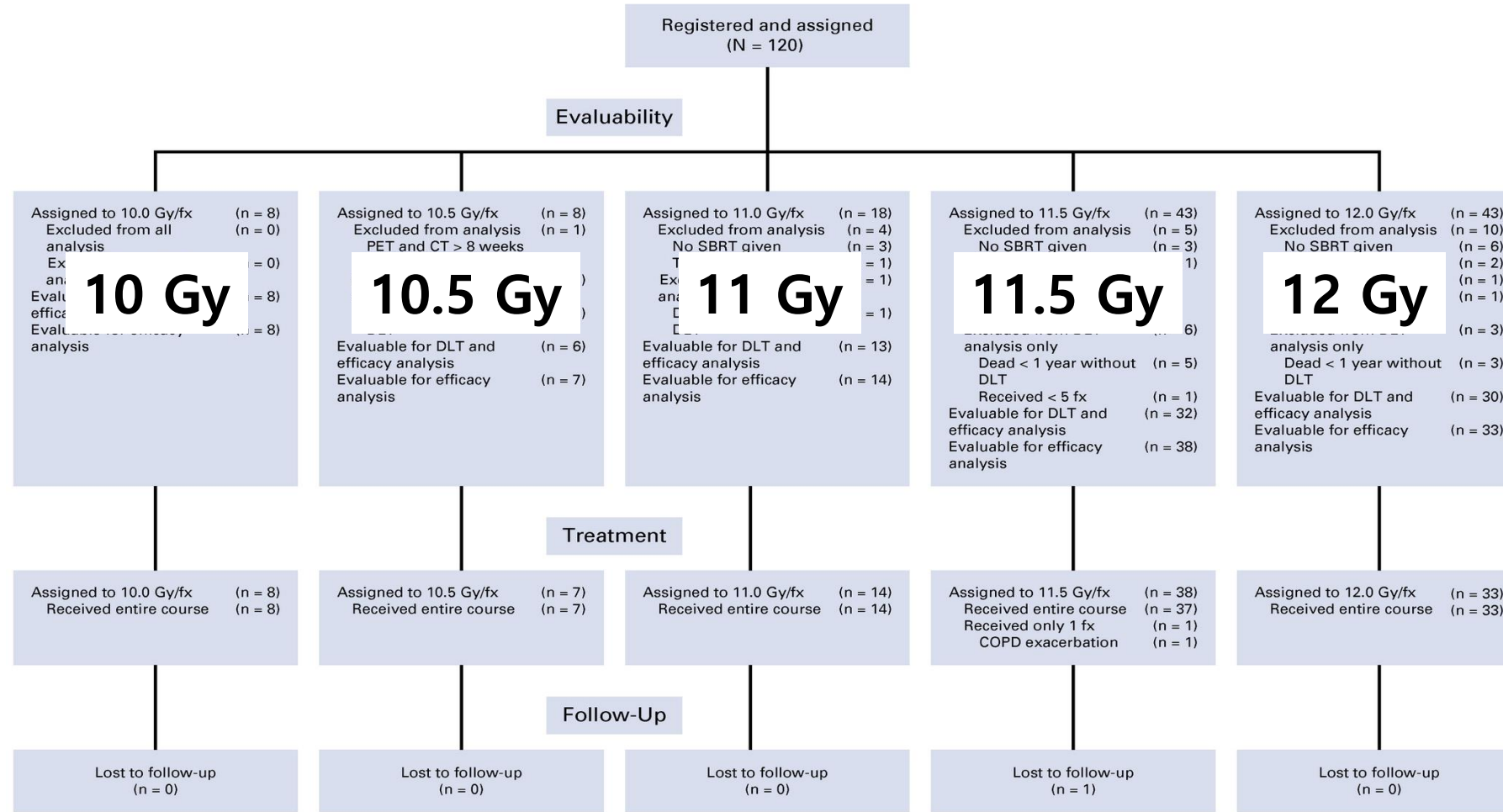
Central and Ultracentral

Tumor location is the primary determinant of toxicity.



- * **Central tumors:**
< 2 cm of trachea and proximal bronchial tree
- * **Ultracentral tumors:**
Directly abutting

RTOG 0813: 5 fraction schedule



RTOG 0813: 5 fraction schedule

- **Dose limiting toxicity (> 3 grade within 1yr)**
 - Radiation pneumonitis, bleeding, hypoxia, deaths

Treatment Arm	Evaluable Sample Size	No. of DLTs	Probability (95% CI)	DLTs	Grade	Days Since End of SBRT
Level 5: 10 Gy/fx	8	0	2.0 (0.6 to 5.1)			
Level 6: 10.5 Gy/fx	6	1	2.7 (0.8 to 6.5)	Death NOS	5	147
Level 7: 11 Gy/fx	13	1	4.3 (1.5 to 9.6)	Sinus bradycardia	5	130
Level 8: 11.5 Gy/fx	32	2	5.7 (2.1 to 12.0)	Hypoxia	3	88
				Hypoxia	3	166
Level 9: 12 Gy/fx	30	1	7.2 (2.8 to 14.5)	Pneumonitis	3	174
				Pleural effusion	3	264

RTOG 0813: 5 fraction schedule

TABLE 4. Relapse Pattern and Outcomes

Relapse Pattern	Outcomes, No. (%)				
	Level 5: 10.0 Gy/fx (n = 8)	Level 6: 10.5 Gy/fx (n = 7)	Level 7: 11.0 Gy/fx (n = 14)	Level 8: 11.5 Gy/fx (n = 38)	Level 9: 12.0 Gy/fx (n = 33)
Local control rate, % (90% CI)					
1 year	100 (NA)	100 (NA)	100 (NA)	92.1 (86.8 to 100)	97.0 (90.9 to 100)
2 year	87.5 (62.5 to 100)	100 (NA)	85.7 (64.3 to 100)	89.4 (81.6 to 97.4)	87.9 (78.8 to 97.0)
3 year	75.0 (37.5 to 100)	100 (NA)	85.7 (64.3 to 100)	86.7 (78.5 to 94.7)	84.7 (72.7 to 93.9)
OS rate, % (95% CI)					
No. of deaths	8	6	9	25	20
1 year	100 (NA)	71.4 (25.8 to 92.0)	85.7 (53.9 to 96.2)	84.2 (68.2 to 92.6)	93.9 (77.9 to 98.4)
2 year	75.0 (31.5 to 93.1)	57.1 (17.2 to 83.7)	71.4 (40.6 to 88.2)	67.9 (50.4 to 80.3)	72.7 (54.1 to 84.8)
3 year	75.0 (31.5 to 93.1)	42.9 (9.8 to 73.4)	64.3 (34.3 to 83.3)	51.6 (34.7 to 66.2)	54.0 (35.6 to 69.2)
Median, months (95% CI)	41.6 (21.3 to 67.9)	25.8 (1.7 to 61.1)	51.4 (16.5 to NR)	38.1 (24.8 to 65.0)	39.7 (28.4 to NR)

1y local control 97-100%
3y local control 75-84.7%

Ultracentral tumors

Year	Reference	N	Dose fractionation	Local control (2yr)	Toxicity
2014	Li et al	82	70 Gy / 10fx	96.2%	Grade 3: 3.6% Grade 5: 1.2
2016	Tekatli et al	47	60 Gy / 12fx	78%	> Grade 3, 38% Grade 5: 13%
2018	Raman et al	26	60 Gy / 8fx (77%) 50 Gy / 10fx	100%	Grade 2-3: 7.9%
2021	Breen et al	110	50 Gy / 5fx 60 Gy / 8fx 48 Gy / 4fx	84%	Grade 5: 4%
2021	HILUS	65	56 Gy / 8fx	83%	> Grade 3: 34% Grade 5: 15%

SUNSET: ongoing trial

- **Ultracentral definition:** PTV touches or overlaps the central bronchial tree, esophagus, pulmonary vein, or pulmonary artery
- **Multicenter phase I dose-finding study**
- Dose fractionation: 60 Gy in 15fx, 10fx, 8fx

Case 2.

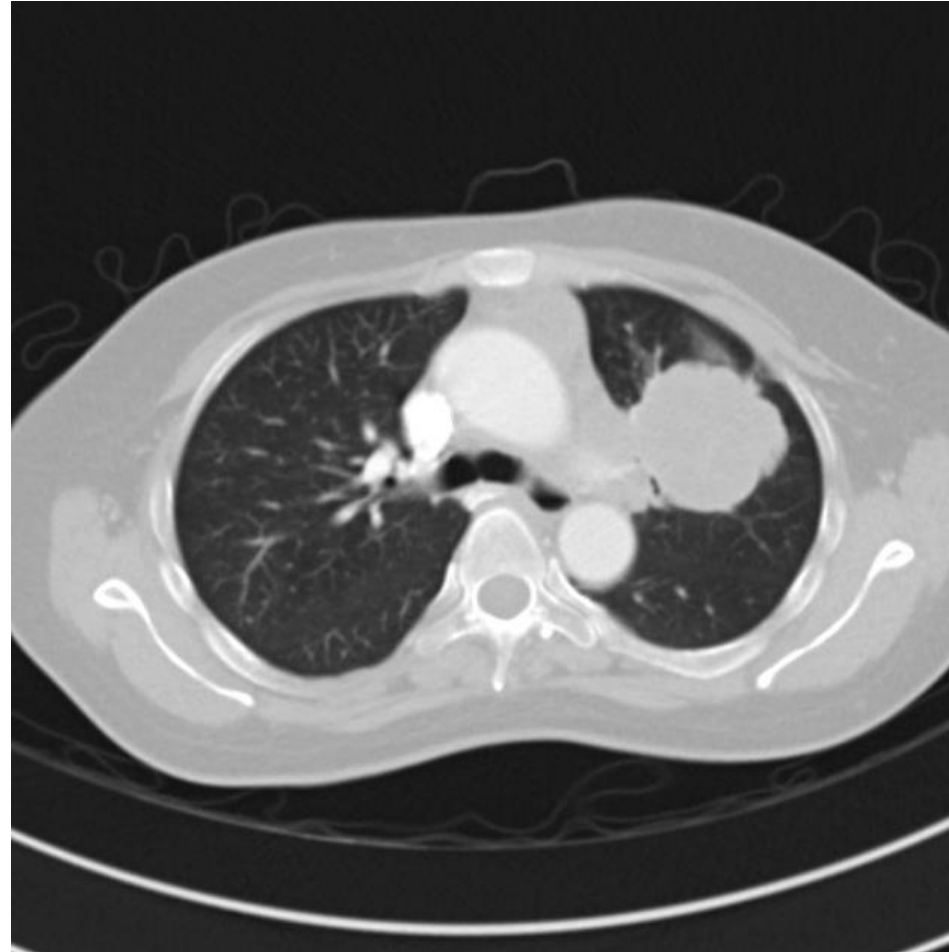
75/M

No lymphadenopathy
Medically inoperable

Organ at risk (OAR)

Lung

Proximal bronchial tree
Esophagus
Spinal cord



Large tumors (> 5cm)

- Historically, patients with medically inoperable lesions smaller than 5 cm have been eligible for SBRT clinical trials
- RTOG 0236, RTOG 0813, and RTOG 0915
- The main reason for excluding larger tumors is concern about **potential toxicity** in a somewhat frail patient population.

Clinical Management Considerations

A potentially confounding association between tumor size and SBRT dose regimen.

In which larger tumors tended to be located **closer to critical dose-limiting organs at risk** and were thus treated with less biologically potent SBRT dose regimens.

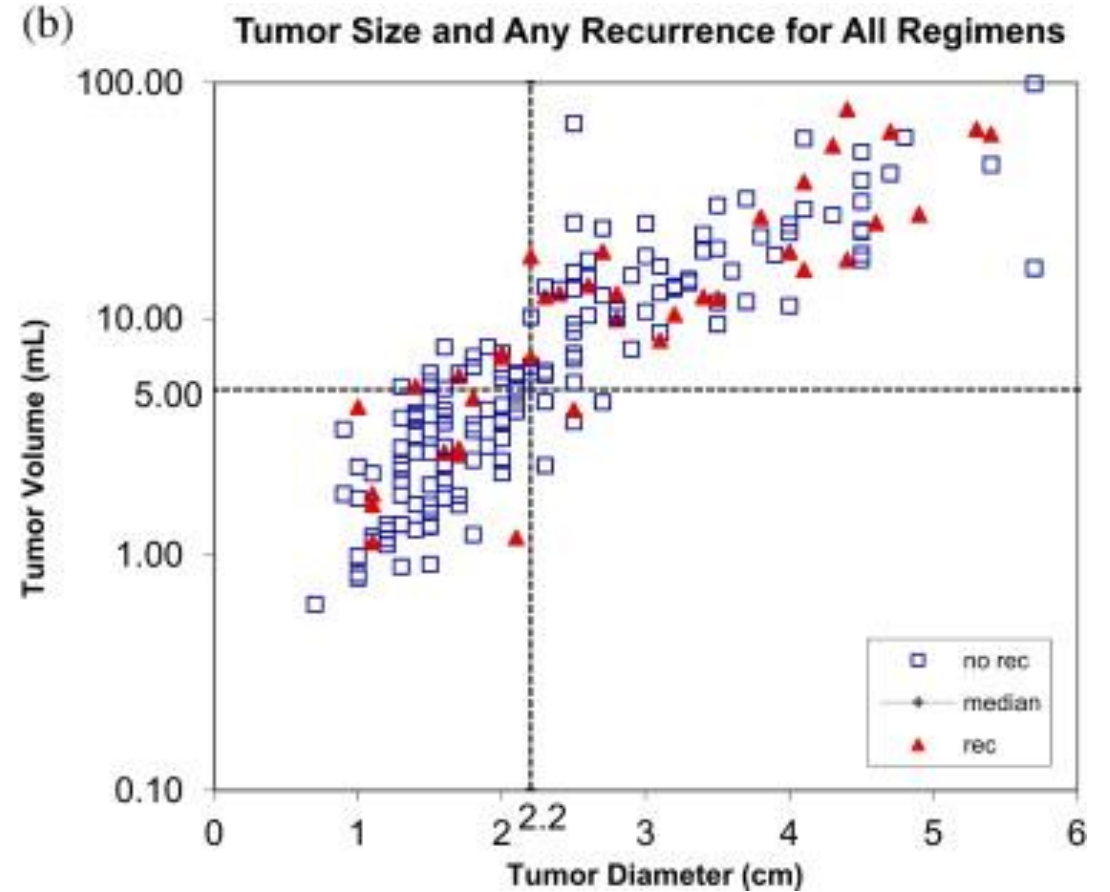
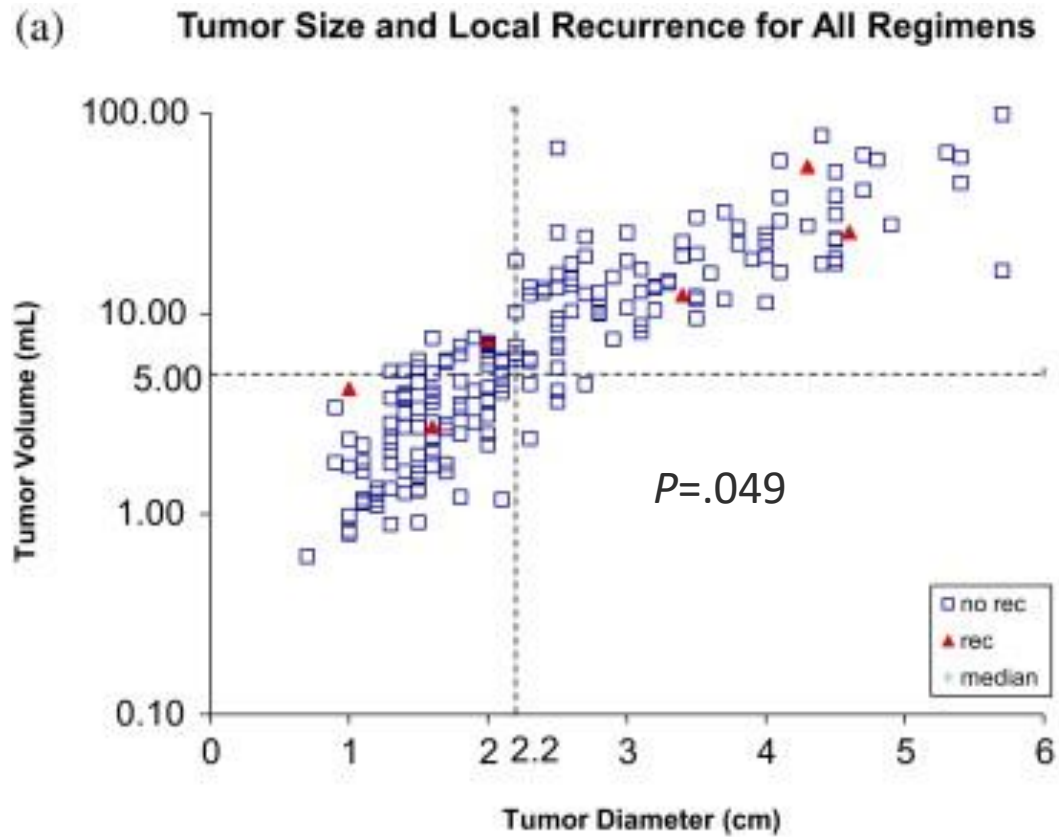
Treatment outcomes

Table 1 Clinical studies of stereotactic body radiation therapy for large (≥ 5 cm) non-small cell lung tumors

Reference	Sample size	Dose (Gray)/ fractions (no.)	Median follow-up (months)	Local control	Crude grade ≥ 2 toxicities (%)	Crude grade ≥ 3 toxicities (%)	Instances of grade 5 events	Overall survival
Woody <i>et al.</i> (29)	40	50/5 (68%), 60/8 (20%)	11	64% (locoregional) at 18 months	13	8	0	20 months
Verma <i>et al.</i> (30)	92	50/5 (47%), 48/4 (23%)	12	96% at 1 year, 73% at 2 years	25	7	1	21 months
Peterson <i>et al.</i> (31)	41	50/5 (median)	15	95% (crude) at 15 months	17	10	0	65% at 1 year, 34% at 2 years
Tekatli <i>et al.</i> (32)	63	50/5 or 60/8	55	96% at 2 years	–	30	12	28 months
Verma <i>et al.</i> (33)	201	50/5 (30%), 48/4 (23%)	41	–	–	–	–	25 months

8 pts with ILD

Treatment outcomes



Case 3.

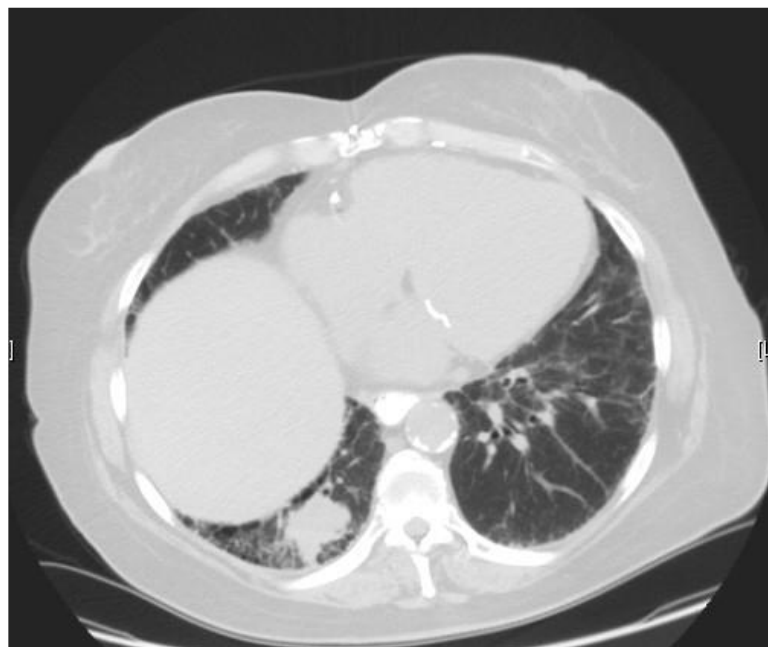
75/M

No lymphadenopathy
Medically inoperable
ILD

Organ at risk (OAR)

Lung

Proximal bronchial tree
Esophagus
Spinal cord

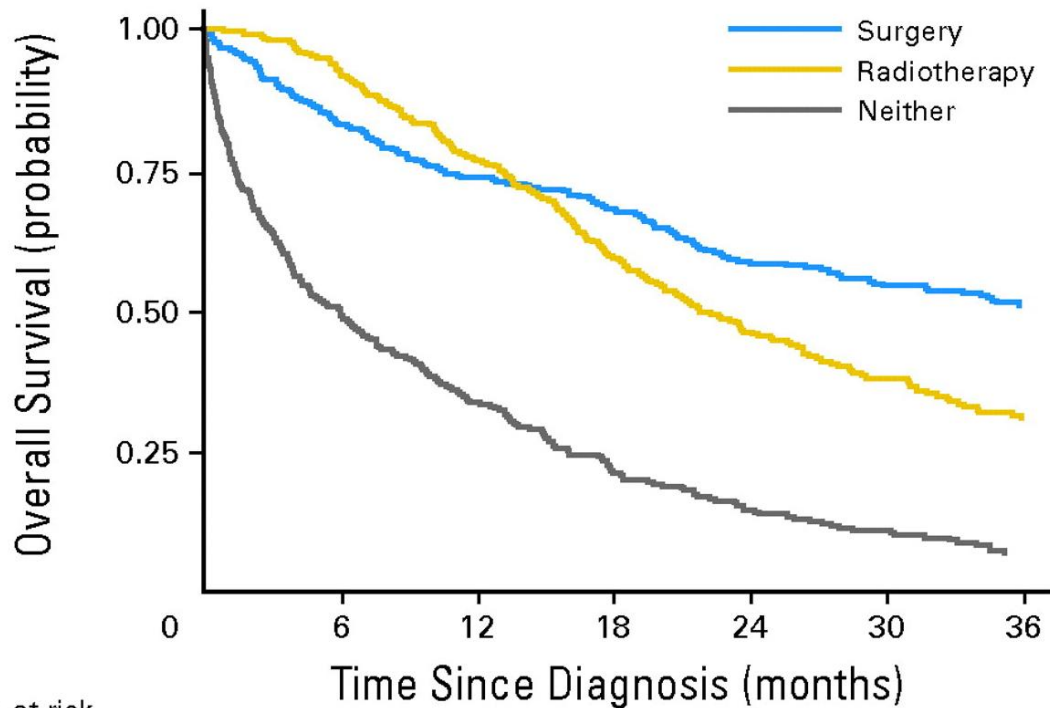


Clinical Management Considerations

- Many consider ILD and IPF a relative contraindication to SBRT, but alternative options may be limited.
- Options
 - Surgery
 - Systemic treatment
 - Observation
 - **SBRT**

Should We Treat or Not

Overall survival for elderly (≥ 75 years)



Stage I NSCLC, Amsterdam(1999 to 2007).

Patients undergoing no treatment with **21% dying within 30 days** of diagnosis a **median survival** of less than **6 months**.

Patients with untreated ES-NSCLC have a **60% to 70% risk of mortality at 1 year**.

Should We Treat or Not

Estimating ILD Severity and Clinical Course

ILD-GAP Index	Predicted Mortality		
	1 year	2 years	3 years
0-1	3.1	6.6	10.2
2-3	8.8	18.0	26.9
4-5	18.2	35.0	49.2
>5	33.5	58.4	74.8

ILD, interstitial lung disease; GAP, gender age physiology.

Table 2. ILD-GAP Index

	Predictor	Points
	ILD Subtype	
	IPF	0
ILD	Unclassifiable ILD	0
	CT-ILD or Idiopathic NSIP	-2
	Chronic HP	-2
	Sex	
G	Female	0
	Male	1
	Age	
A	≤60	0
	61-65	1
	>65	2
	Physiology	
	FVC, % predicted	
	>75%	0
	50%-75%	1
	<50%	2
P	DLCO, % Predicted	
	>55%	0
	36%-55%	1
	≤35%	2
	Cannot perform	3
	Total possible points	8

Should We Treat or Not

Year		N of pts (no ILD)		OS (no ILD)	Toxicity (vs. no ILD)
2018	Glick et al.	39 (537)	54-60 / 3fx 48 Gy / 4fx 60 Gy / 8fx	3yr 36.4% (48.4%)	G ≥2 pneumonitis: 20.5% (vs. 6.9%) G ≥3 pneumonitis: 10.3% (vs. 1.7%)
2015	Ueki et al	20 (117)	48 Gy / 4fx 60 Gy / 8fx	3yr 53.8% (70.8%)	G ≥2 pneumonitis: 55.0%; (vs. 12.4%) G ≥3 pneumonitis: 10.0% (vs. 1.4%)
2015	Yoshitake et al.	18 (260)	48 Gy/ 4fx	2yr 49.6% (86.7%)	G ≥2 pneumonitis: 50.0% (vs. 6.7%) G ≥3 pneumonitis: 39% (vs. 1.2%) G5 pneumonitis: 16.7% (vs. 0%)

ASPIRE-ILD (phase II): ongoing trial

- T1–2N0M0 non-small cell lung cancer with co-existing ILD
- The starting dose: **50 Gy /5fx**
- De-escalation dose: 50 Gy/10fx, 45 Gy/15fx
- Dose de-escalation will occur if 2 or more of the first 7 patients in a cohort experiences grade 5 toxicity within 6 months of treatment.

Early-stage lung cancer with ILD

- The management of lung cancer in the setting of ILD is challenging.
- If not surgery, then approach will depend on patient & tumor board consideration of relative risks of treatment vs. untreated lung cancer.
- **Using alternative dose.**

Case 4

65/M

3 yrs after prior SBRT

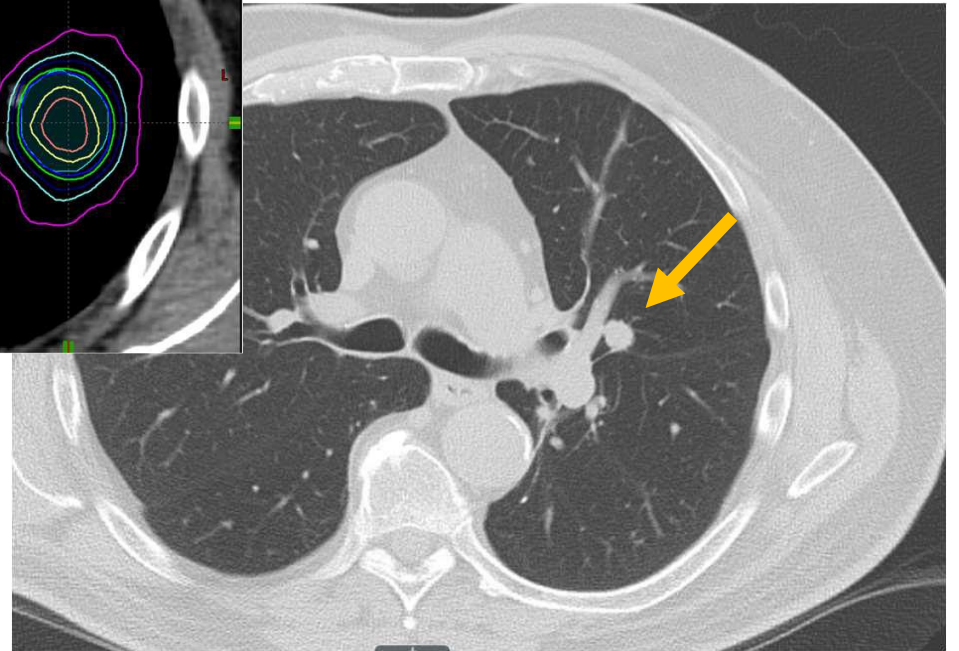
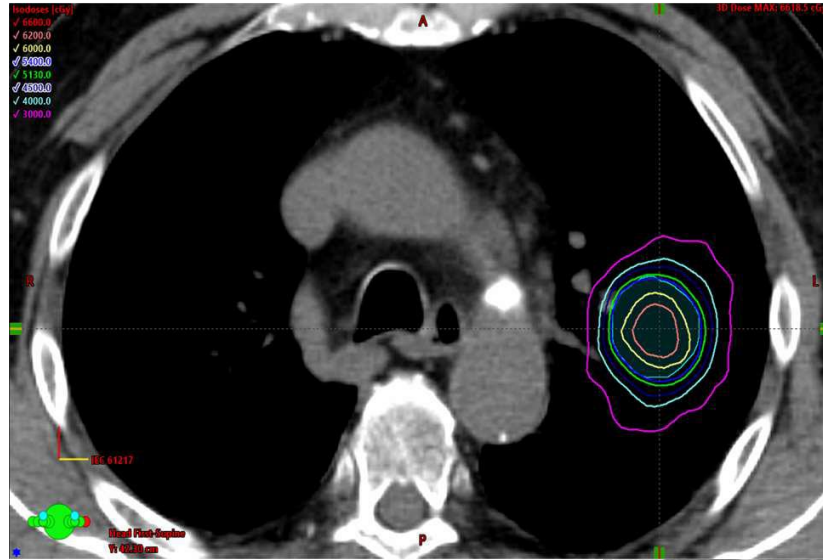
Organ at risk (OAR)

Lung

Proximal bronchial tree

Esophagus

Spinal cord



Salavage SBRT after lung SBRT

Year		N of pts	Initial SBRT	Re-SBRT	Local control	Toxicity (vs. no ILD)
2020	Kennedy et al.	21	50 Gy / 5fx 54 Gy / 3fx	50 GY /5fx 54 Gy /3fx	2-yr 81%	Gr 2 pneumonitis: 10% Gr 2 chest wall: 19% Gr 3 > 0%
2014	Hearn et al	10	50 Gy /5fx 30-34 Gy/1fx	50 Gy /5fx 60 Gy/3fx	60%	Gr 1-2 fatigue: 30% Gr 1-2 chest wall: 50% Gr 3+: 0%

Salvage of local recurrence after prior SBRT

- The controversy is less about "if" we should do it than "**how**" to do it safely, especially for lesions that **abut critical organs** such as the trachea, esophagus, and proximal bronchial tree.

Table 4 A comparison of putative cumulative dose constraints

OAR	α/β	This study (EQD2)	Paradis et al (EQD2) ^{*6}	Troost et al (EQD2, 9-mo interval) ²⁷	American Radium Society (EQD2) [†]
Spinal cord	2	D _{max} 60 Gy	D0.1cc <56.25 Gy	D _{max} <65 Gy	D _{max} <57 Gy
Esophagus	3	D _{max} 75-100 Gy	D0.1cc <90.6 Gy	D _{max} <100 Gy	V60 <40%, D _{max} <100-110 Gy
Brachial plexus	2	D _{max} 80-95 Gy	D0.1cc <85 Gy	D _{max} <85 Gy	D _{max} <85 Gy
Great vessels	3	D _{max} 110 – 115 Gy	D0.1cc <123 Gy	D _{max} <110 Gy	D _{max} <120 Gy
PBT	3	D _{max} <80-105 Gy [‡]	D0.1cc <90.6 Gy	D _{max} <110 Gy	D _{max} <110 Gy
Skin/Chest wall	2.5	ALARA	D0.1cc <105 Gy	n/a	n/a
Heart	2.5	ALARA	D0.1cc <85 Gy	D _{mean} <70 Gy	V40<50%
Lung	3	Individualized	Individualized	D _{mean} <22 Gy	V20<40%

Case 5

62/F

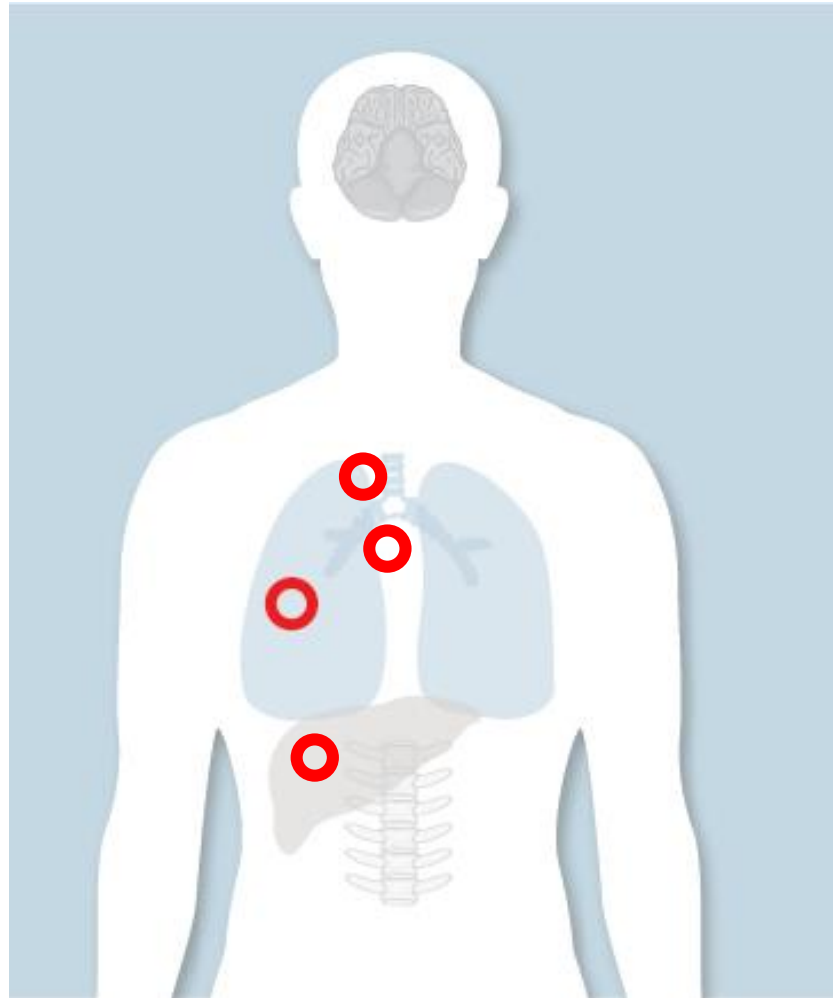
Oligometastatic NSCLC

cT2N2M1b

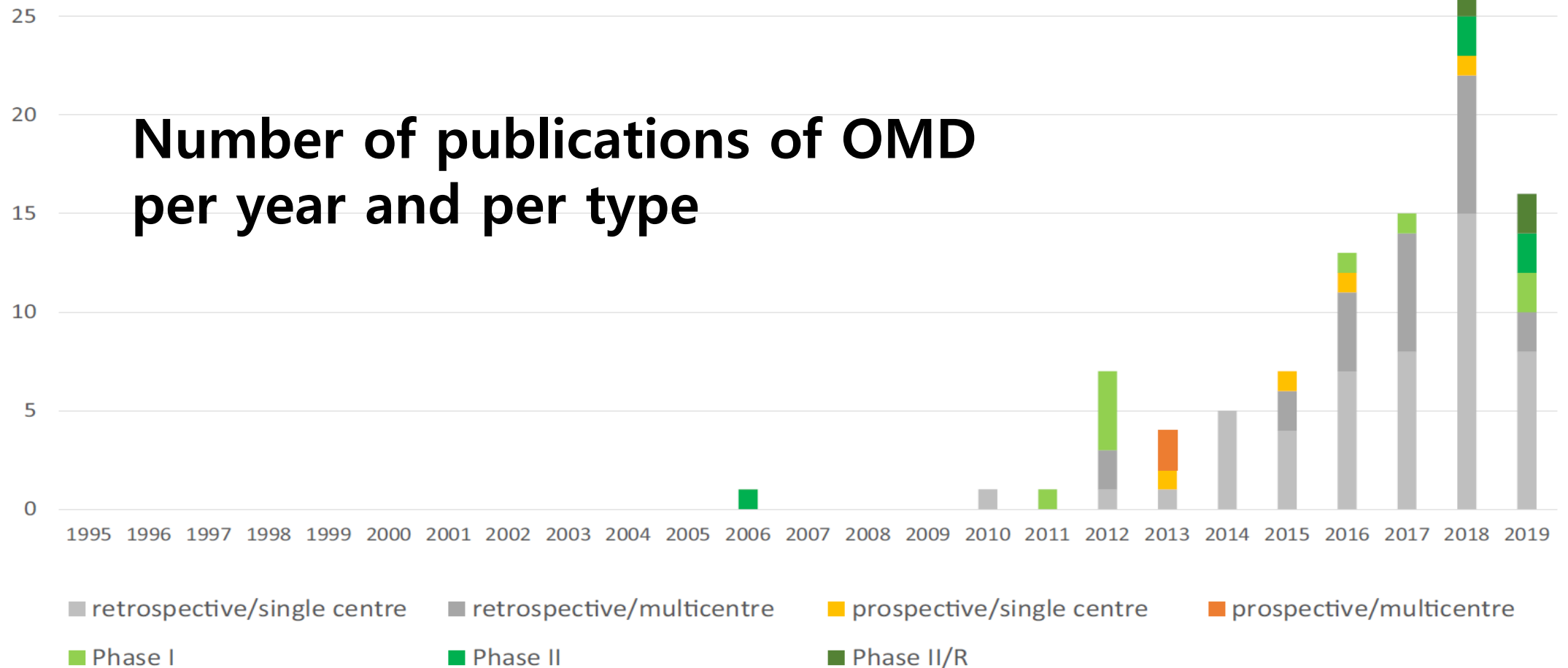
RML peripheral nodule
#4, 7

Single liver metastasis

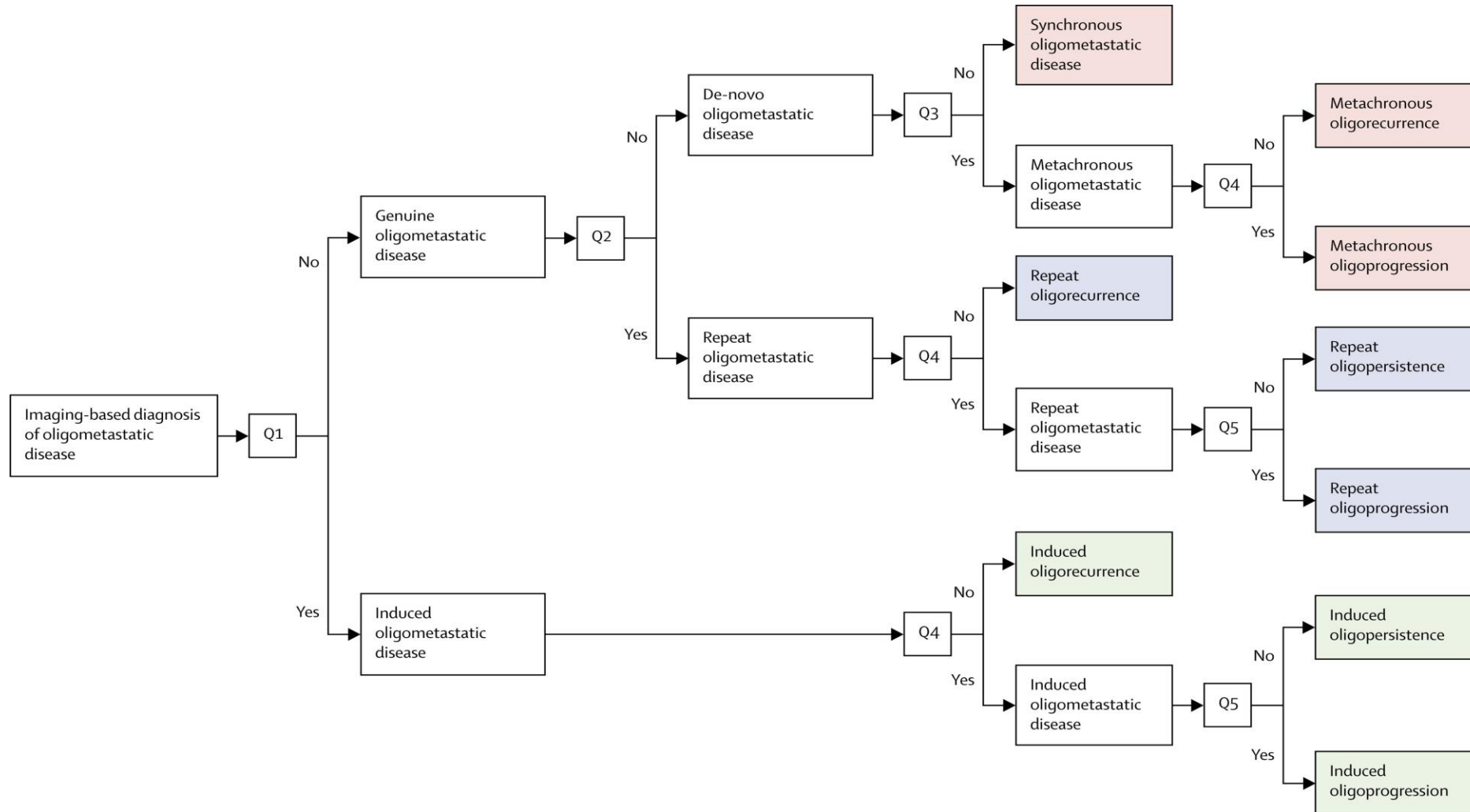
EGFR mutation+



Oligometastatic disease (OMD)



Characterisation and classification of OMD



Characterisation and classification of OMD

A De-novo oligometastatic disease

Synchronous oligometastatic disease



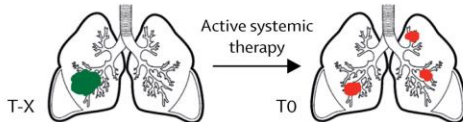
- T0: first time diagnosis of primary cancer (green) and oligometastases (red) within 6 months

Metachronous oligorecurrence



- T-X: diagnosis and treatment of primary cancer (green) in a non-metastatic state
- Systemic therapy-free interval
- T0: First time diagnosis of new oligometastases (red) >6 months after diagnosis of cancer

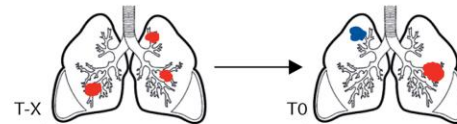
Metachronous oligopersistence



- T-X: diagnosis and treatment of primary cancer (green) in a non-metastatic state
- Under treatment with active systemic therapy
- T0: first time diagnosis of new oligometastases (red) >6 months after diagnosis of cancer

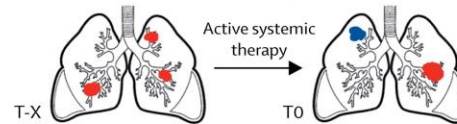
B Repeat oligometastatic disease

Repeat oligorecurrence



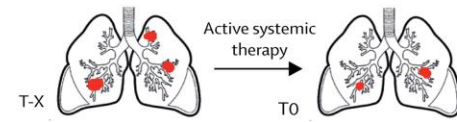
- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Systemic therapy-free interval
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases

Repeat oligopersistence



- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Under treatment with active systemic therapy
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases

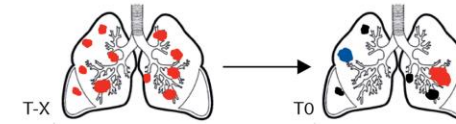
Repeat oligopersistence



- T-X: diagnosis of oligometastases followed by local treatment or systemic treatment or both
- Under treatment with active systemic therapy
- T0: diagnosis of persistent non-progressive (red) oligometastases

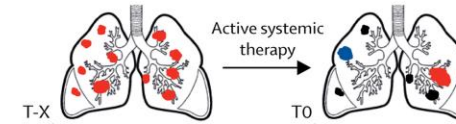
C Induced oligometastatic disease

Induced oligorecurrence



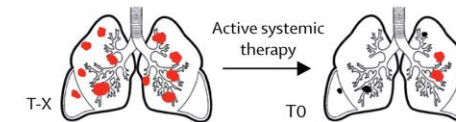
- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Systemic therapy-free interval
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases, possible residual non-progressive metastases (black)

Induced oligopersistence

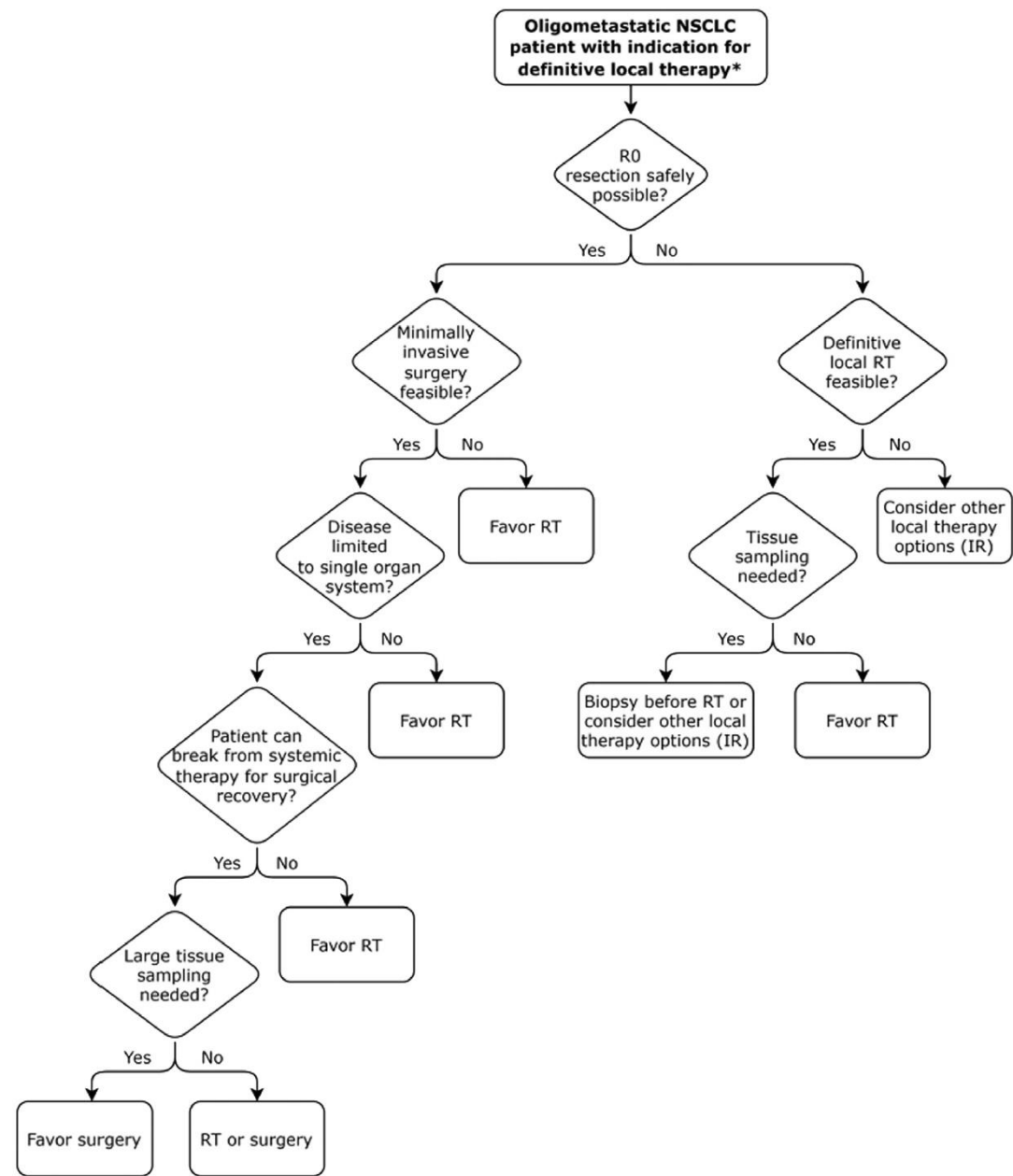
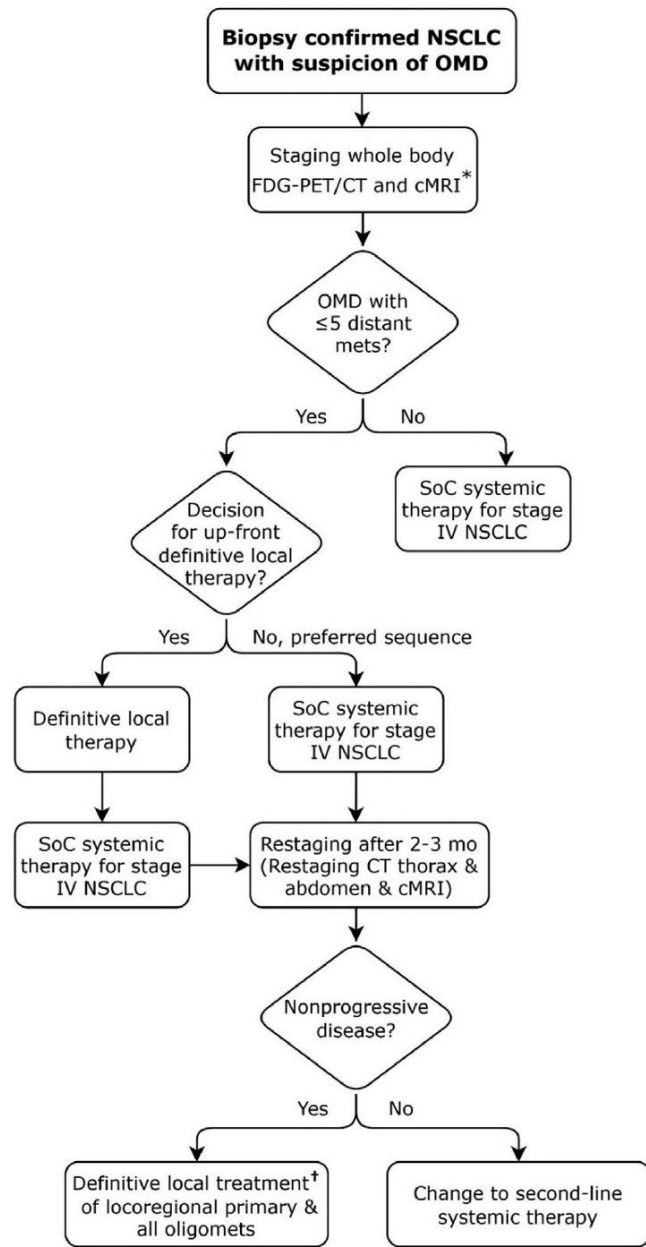


- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Under treatment with active systemic therapy
- T0: diagnosis of new (blue) and growing or regrowing (red) oligometastases, possible residual non-progressive metastases (black)

Induced oligopersistence



- T-X: diagnosis of polymetastatic metastatic disease followed by systemic treatment with or without local treatment
- Under treatment with active systemic therapy
- T0: diagnosis of persistent non-progressive oligometastases (red), where response is worse compared with other residual metastases (black)



EGFR-TKIs + SBRT

2 RCTs, Denovo, synchronous oligometastatic NSCLC



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Article

Randomized Trial of First-Line Tyrosine Kinase Inhibitor With or Without Radiotherapy for Synchronous Oligometastatic EGFR-Mutated Non-Small Cell Lung Cancer

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Original Article

EGFR-TKIs plus stereotactic body radiation therapy (SBRT) for stage IV Non-small cell lung cancer (NSCLC): A prospective, multicenter, randomized, controlled phase II study

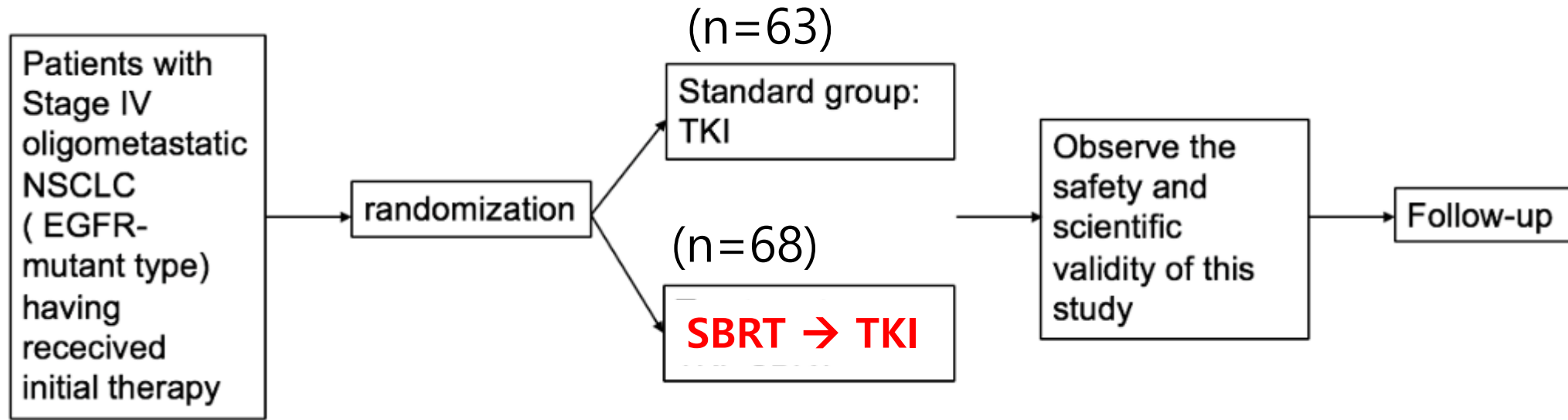
Ping Peng^{a,1}, Juejun Gong^{a,b,1}, Yujie Zhang^{a,1}, Shuchang Zhou^c, Yichen Li^a, Guang Han^d, Rui Meng^e, Yongshun Chen^f, Ming Yang^g, Qian Shen^a, Qian Chu^a, Shu Xia^a, Peng Zhang^a, Lu Zhang^a, Yuan Chen^{a,*}, Li Zhang^{a,*}

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Wang et al. J Natl Cancer Inst . 2023 Jun 8;115(6):742-748.

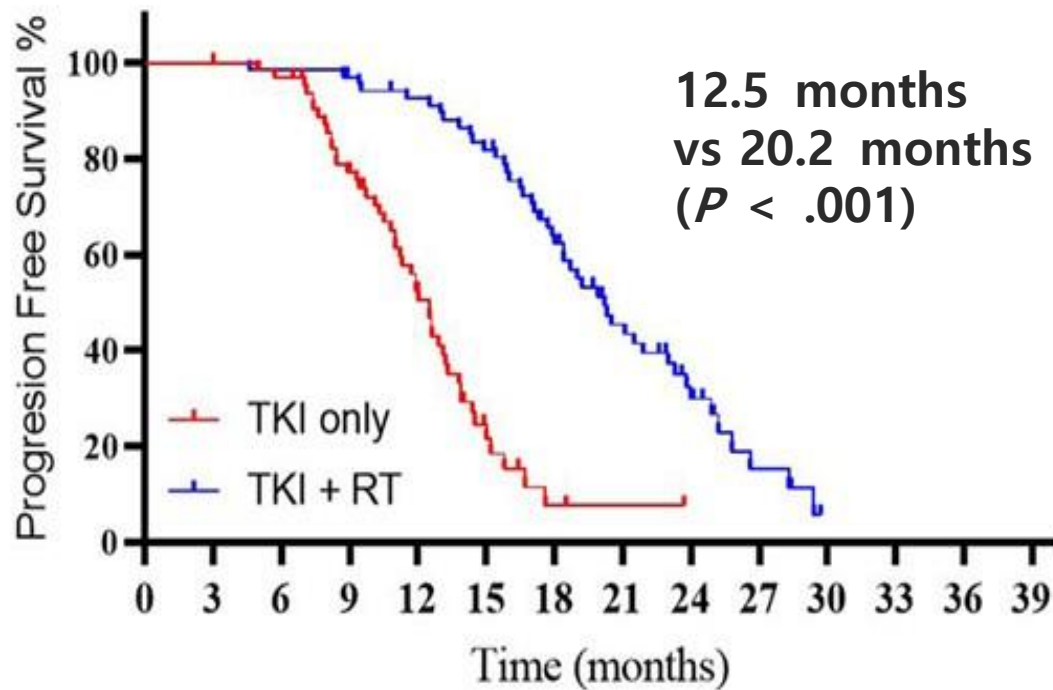
Peng et al. Radiother Oncol . 2023 Jul;184:109681.

SINDAS trial (phase III)

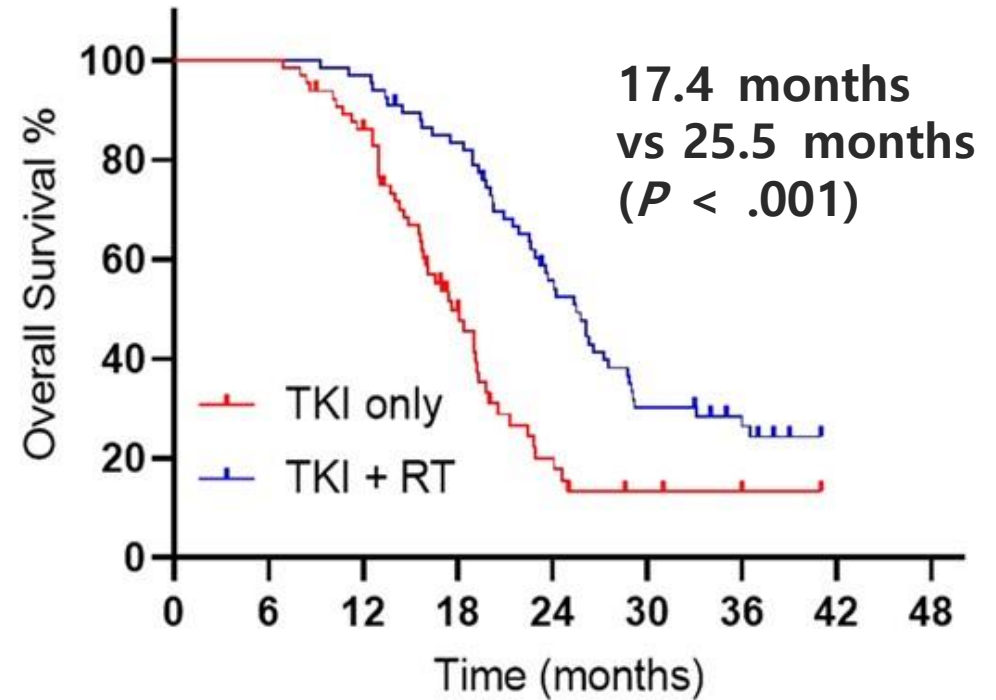


- (≤ 5 metastases; ≤ 2 lesions in any one organ)
- RT (25-40 Gy /5fx): all metastases, primary tumor, involved LNs

SINDAS trial (phase III)



TKI only	65	65	62	48	28	8	3	2	1	0	0
TKI + RT	68	67	67	65	60	51	37	22	12	5	1



TKI only	65	65	55	26	9	5	3	2
TKI + RT	68	68	66	56	36	20	14	9

SINDAS trial

Toxicity	TKI only, No. (%)			TKI + RT, No. (%)		
	Grade 1/2	Grade 3	Grade 4	Grade 1/2	Grade 3	Grade 4
Skin rash	47 (72.3)	5 (7.7)	4 (6.2)	46 (67.6)	8 (11.8)	2 (2.9)
Pruritus	20 (30.8)	7 (10.8)	1 (1.5)	22 (32.4)	5 (7.4)	0 (0.0)
Fatigue	47 (72.3)	0 (0.0)	1 (1.5)	46 (67.6)	0 (0.0)	0 (0.0)
Neutropenia	20 (30.8)	0 (0.0)	0 (0.0)	16 (23.5)	0 (0.0)	0 (0.0)
Anemia	18 (27.7)	0 (0.0)	0 (0.0)	22 (32.4)	0 (0.0)	0 (0.0)
Thrombocytopenia	3 (4.6)	0 (0.0)	0 (0.0)	3 (4.4)	0 (0.0)	0 (0.0)
Transaminitis	11 (16.9)	0 (0.0)	1 (1.5)	8 (11.8)	0 (0.0)	1 (1.5)
Diarrhea/nausea	43 (66.2)	0 (0.0)	0 (0.0)	38 (55.9)	0 (0.0)	0 (0.0)
Esophagitis	18 (27.7)	2 (3.1)	0 (0.0)	24 (35.3)	2 (2.9)	1 (1.5)
Pericarditis	0 (0.0)	1 (1.5)	1 (1.5)	0 (0.0)	0 (0.0)	0 (0.0)
Pleural effusion	0 (0.0)	0 (0.0)	2 (3.1)	2 (2.9)	0 (0.0)	0 (0.0)
Pneumonitis (symptomatic)	1 (1.5)	1 (1.5)	0 (0.0)	3 (4.4)	3 (4.4)	1 (1.5)
Pneumonitis (asymptomatic)	14 (21.5)	1 (1.5)	0 (0.0)	19 (27.9)	1 (1.5)	0 (0.0)

EGFR-TKIs + SBRT, randomized, phase II

- TKI only (n=32) vs, TKI → SBRT (n=30)

Radiotherapy site classification, n (%)

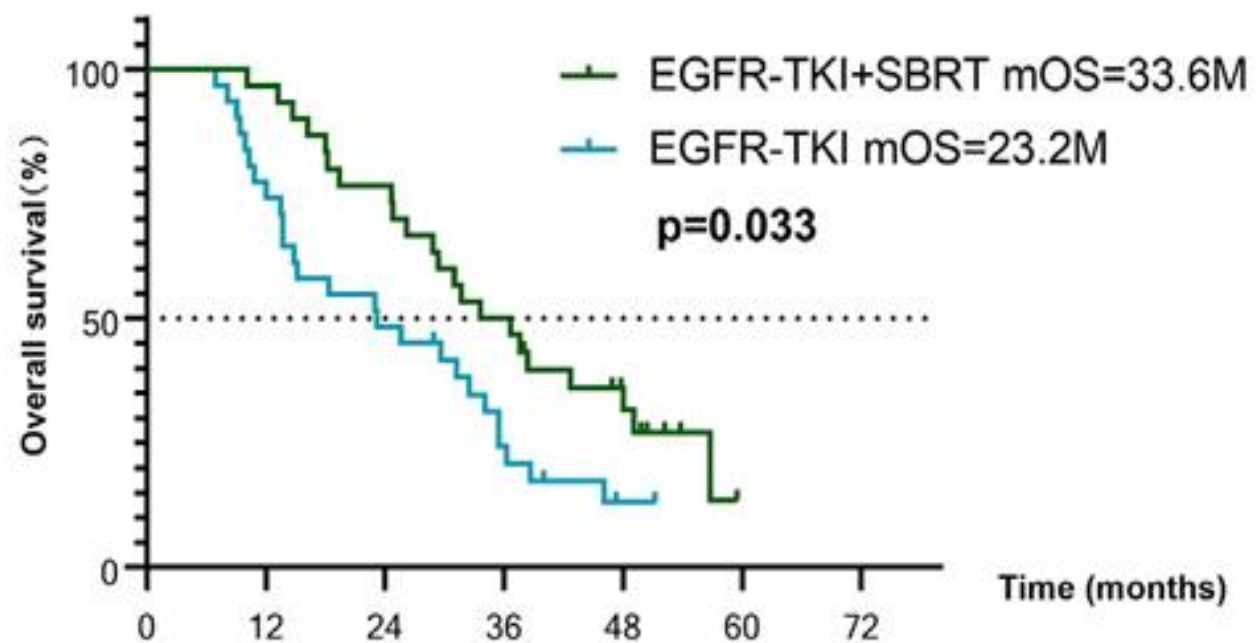
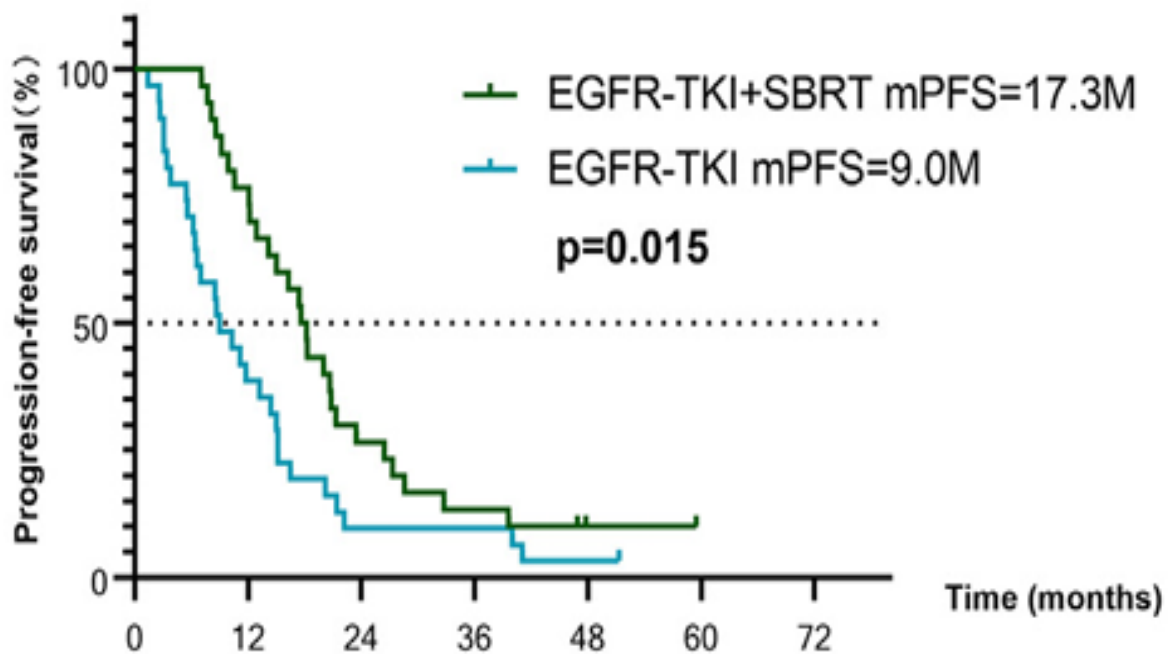
Primary	13(43.33)
Metastasis	5(16.67)
Primary + Metastasis	12(40.00)

Radiation Site

Dose (Gy/fractions) , n (%)

Lung	40 Gy/5F, 10(33.33)
	50 Gy/5F, 14(46.67)
mediastinum	30 Gy/5F, 7(23.33)
Adrenal gland	30 Gy/5F, 2(6.67)
liver	40 Gy/5F, 3(10.00)
Bone	30 Gy/5F, 5(16.67)
Brain	30 Gy/5F, 7(23.33)

EGFR-TKIs + SBRT, randomized, phase II



Supplementary 4: Common toxicity data

Characteristic	EGFR-TKI group (n=31)	EGFR-TKI+ SBRT group (n=30)	Total (n=61)	P value
Leukopenia				
No	24(77.42)	19(63.33)	43(70.49)	0.4246
Grade 1	5(16.13)	9(30.00)	14(22.95)	
Grade 2	2(6.45)	2(6.67)	4(6.56)	
Diarrhea				
No	23(74.19)	13(43.33)	36(59.02)	0.0058
Grade 1	4(12.9)	15(50.00)	19(31.15)	
Grade 2	4(12.9)	2(6.67)	6(9.84)	
Esophagitis				
No	30(96.77)	25(83.33)	55(90.16)	0.1188
Grade 1	1(3.23)	4(13.33)	5(8.2)	
Grade 2	0(0.00)	1(3.33)	1(1.64)	
Pneumonia				
No	26(83.87)	21(70.00)	47(77.05)	0.4288
Grade 1	4(12.9)	7(23.33)	11(18.03)	
Grade 2	1(3.23)	2(6.67)	3(4.92)	
Rash				
No	19(61.29)	8(26.67)	27(44.26)	0.0058
Grade 1	5(16.13)	16(53.33)	21(34.43)	
Grade 2	7(22.58)	6(20.00)	13(21.31)	
Abnormal liver function				
No	25(80.65)	25(83.33)	50(81.97)	0.7869
Grade 1	4(12.9)	2(6.67)	6(9.84)	
Grade 2	2(6.45)	3(10.00)	5(8.2)	
Anemia				
No	22(70.97)	16(53.33)	38(62.3)	0.3125
Grade 1	7(22.58)	12(40.00)	19(31.15)	
Grade 2	2(6.45)	2(6.67)	4(6.56)	
Weakness				
No	22(70.97)	18(60.00)	40(65.57)	0.6286
Grade 1	6(19.35)	9(30.00)	15(24.59)	
Grade 2	3(9.68)	3(10.00)	6(9.84)	
Gastritis				
No	27(87.1)	22(73.33)	49(80.33)	0.0351
Grade 1	2(6.45)	8(26.67)	10(16.39)	
Grade 2	2(6.45)	0(0.00)	2(3.28)	

Gr 2: 50% in the EGFR-TKIs + SBRT group
vs. 45.2% in the EGFR-TKIs group.

no Gr 3 or greater toxicity

TKIs with SBRT

- As compared with a first-line TKI alone, **addition of SBRT** statistically significantly improved PFS and OS for EGFR-mutated NSCLC.
- Optimal timing, dose and target of RT are unknown.
- Further randomized data are required to confirm these results.

Conclusoins

Take home message

- Further **randomized data are required to confirm** in these challenging situations.
- **SBRT is an effective treatment modality** for patients with ES-NSCLC and OM NSCLC.
- It is often the only locoregional treatment option for patients with severe comorbidities.

Take home message

- Although the benefits of giving SBRT treatment often outweigh the risks in most clinical scenarios, **SBRT can be associated with serious toxicities** and the risk should be informed consent to patients.
- **Multidisciplinary tumor board** should be considered to provide a consensus recommendation regarding the choice of SBRT versus other modalities.