happinnovation 20•20
SAMSUNG MEDICAL CENTER

Application of Stereotactic Radiotherapy

2018. 7. 21

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Contents

Fractionation

Conventional fractionation: 1.8-2.0 Gy/fx

- In the 1930's, splitting radiation dose into a number of small fractions yielded better outcomes than a single exposure

- **The Four Rs of radiobiology**
  - **Repair** of sublethal damage
  - **Repopulation**
  - **Reassortment** of cells within the cell cycle
  - **Reoxygenation**

FIGURE 23.1 Conventional multifraction radiotherapy was based on experiments performed in Paris in the 1920s and in the 1930s. Rams could not be sterilized with a single dose of x-rays without extensive skin damage, whereas if the radiation were delivered in daily fractions over a period of time, sterilization was possible without skin damage. The testes were regarded as a model of a growing tumor and skin as dose-limiting normal tissue.

Hypofractionation

Smaller number of larger dose fractions

- Shorten the overall treatment time to enhance local control
- Development of treatment delivery technique (3D-CRT, IMRT…) enables improved dose distributions with normal tissue sparing.

- **BED** (biologically effective dose, $\alpha/\beta=10$)
  - 60 Gy in 30 fractions: 72 Gy_{10}
  - 60 Gy in 20 fractions: 78 Gy_{10}
  - 60 Gy in 15 fractions: 84 Gy_{10}

  ➡ 60-75% local control
  - 60 Gy in 8 fractions: 105 Gy_{10} → 115.2 Gy_{10} for 64 Gy/8fx
  - 60 Gy in 4 fractions (SBRT): 150 Gy_{10}

SBRT for Early Stage NSCLC

Delivers very high, ablative dose (≥ 100 Gy_{10}) in 1-10 fractions

SBRT workflow or equipment items	Mandatory (minimum) requirements	Recommended for best practice
Equipment	C-arm linear accelerator with volumetric in-room image guidance	Dedicated C-arm stereotactic linear accelerator (more advanced IGRT, more precise accuracy) High-resolution MLC <10 mm
	Respiration correlated 4D-CT	
Staff teaching, training and credentialing	Written departmental protocols Multi-disciplinary project team for SBRT implementation and application Structured follow-up for clinical outcome assessment	Participation in dedicated SBRT teaching course (e.g. ESTRO) Participation in Vendor-organized dedicated SBRT training Hands-on training at SBRT-experienced center Supervision of first SBRT treatments by SBRT-experienced colleague
Patient selection for SBRT	Discussion in interdisciplinary tumor board Minimum ECOG 3	Biopsy confirmation of malignancy
	Minimum life expectancy of 1 year	
Treatment planning	3D conformal treatment planning Type B algorithms Respiration correlated 4D-CT imaging	D U
	ITV based motion management strategy	
Dose and fractionation	Risk adapted fractionation schemes for peripheral and central tumors, and for tumors with broad chest wall contact	
Inter- and intra-fraction image guidance	Daily pre-treatment volumetric image-guidance	D 4D

Radiotherapy and Oncology 2017;124:11-7

SBRT for Early Stage NSCLC

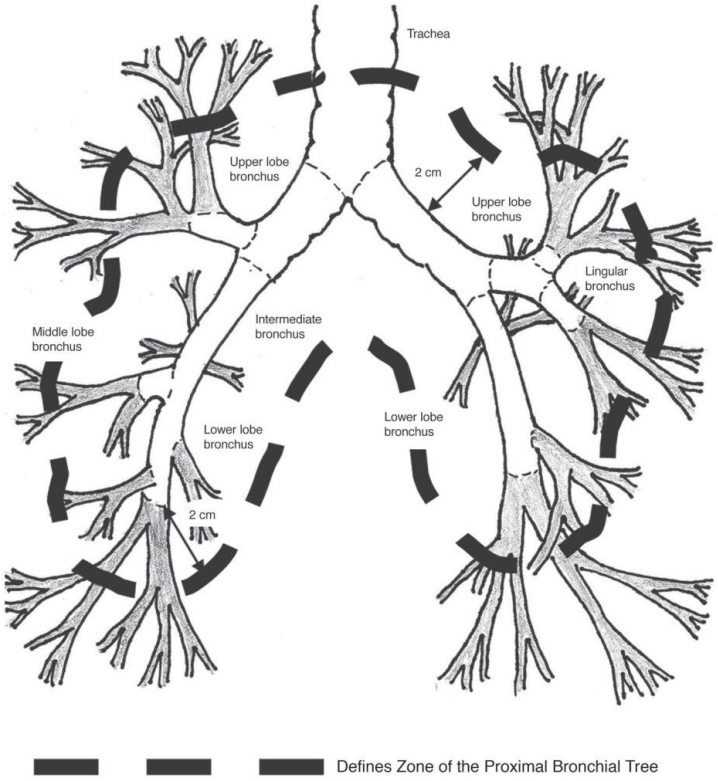
Prospective phase II study by Timmerman et al.

- 70 patients with cT1-2N0 NSCLC **(2002-**
- Radiation dose: 60-66 Gy in 3 fractions
- Median F/U: 17.5 (0.6-44.2) months
- **2Y LC 95%, Median OS 32.6 months**
- Tumor location (hilar/pericental vs. perip

predictor of gr≥3 toxicity (p = 0.004) → >

toxicity in patients with perihilar/central t

peripheral locations



J Clin Oncol 2006;24:4833-9

SBRT for Early Stage NSCLC

RTOG 0236 (Phase II multicenter study)

- 55 patients with peripheral cT1-2N0 NSCLC (<5 cm)
- Radiation dose: 54 Gy in 3 fractions
- Median F/U: 34.3 (4.8-49.9) months
- 3Y primary tumor control: 97.6%
  - 3Y primary tumor+involved lobe (local) control: 90.6%
  - 3Y OS: 55.8%
- Grade 3/4 adverse events: 7 (12.7%) / 2 (3.6%)

JAMA 2010;303:1070-6

SBRT for Centrally Located NSCLC

Prospective database at VU University Medical Center

- 63 patients with stage I NSCLC in high-risk locations
  - 37 central hilar location (proximal bronchial tree)
  - 26 abutting pericardium (11) or mediastinal structure
- Radiation dose: 60 Gy in 8 fractions
- Median F/U: 35 (1-55.7) months
- **2Y LC, OS: 92.6%, 69.0%**
- Grade 3 toxicity: 4 (6%)

J Thorac Oncol 2011;6:2036-43

SBRT for Centrally Located NSCLC

Systemic review for centrally located primary or metastatic lung tumors

- 563 tumors including 315 early stage NSCLC
- BED≥100 Gy_{10} is important for local control
- All treatment-related mortality: 2.8% (16/563)
  - 3.6% (BED>210 Gy_3) vs. 1.0% (BED≤210 Gy_3)
- Grade 3-4 toxicity: 8.6% of central tumors

Author (year)	BED_{10}	Overall survival	Cause-specific survival	Local control
Chang [26] (2008)	113	–		Crude rate 89%
Song [36] (2009)	106	50% at 2 years	–	89% at 2 years
Milano [27] (2009)	100	72% at 2 years	–	73% at 2 years
Fakiris [24] (2009)	180	Median 24 months	–	–
Unger [28] (2010)	72	–	–	63% at 1 year
Oshiro [29] (2010)	80	–	–	60% at 2 years
Baba [35] (2010)	90	72% at 3 years	82% at 3 years	66% at 3 years
Bradley [32] (2010)	86	75% at 2 years[a,b]	90% at 2 years[a,b]	86% at 2 years
Andratschke [34] (2011)	60	29% at 3 years	–	64% at 3 years
Haasbeek [32] (2011)	105	64% at 3 years	–	93% at 3 years
Bral [23] (2011)	150	–	–	Crude rate 94%
Olsen [38] (2011)	100	–	–	100% at 2 years
Rowe [37] (2012)	114	–	–	94% at 2 years
Nuyttens [30] (2012)	132	53% at 3 years[b]	3 years 80%	76% at 2 years
Janssen [31] (2012)	77	–	–	87% at 1 year[a]

Radiotherapy and Oncology 2013;106:276-82

SBRT for Early Stage NSCLC

Which is the optimal BED?

- Meta-analysis for 2587 patients (34 studies)
- 4 BED groups: <83.2 / 83.2-106 / 106-146 / >146 Gy_{10}
- 2Y OS: 62.3% / 76.1% / 68.3% / 55.9%

→ Higher OS for medium or medium-high BED ($p \leq 0.004$)

- BED 83.2-146 Gy_{10} for SBRT may currently more beneficial and reasonable in stage I NSCLC

	2-year LCR (18–20, 22, 23, 26, 35, 36, 38, 44, 46, 51)*	*p* value		
		Medium	Medium to High	High
Low	0.942 (0.871–1.000)	0.164	0.874	0.751
Medium	0.874 (0.818–0.930)		0.028	0.031
Medium to High	0.942 (0.901–0.982)			0.453
High	0.928 (0.908–0.947)			
Total	0.923 (0.907–0.940)			

IJROBP 2011;81:e305-16

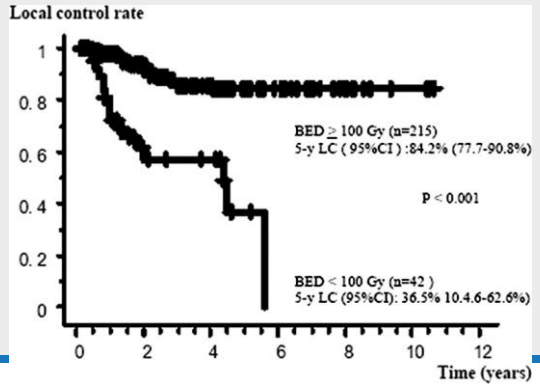
SBRT for Early Stage NSCLC

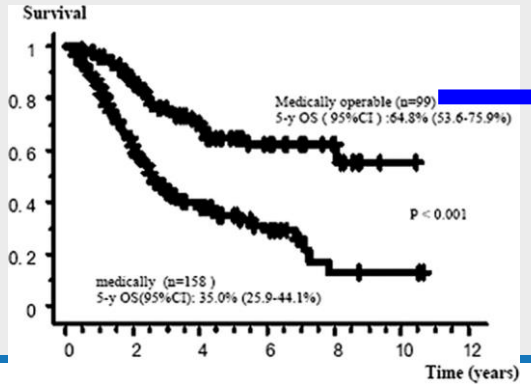
Japanese Multi-institutional retrospective study

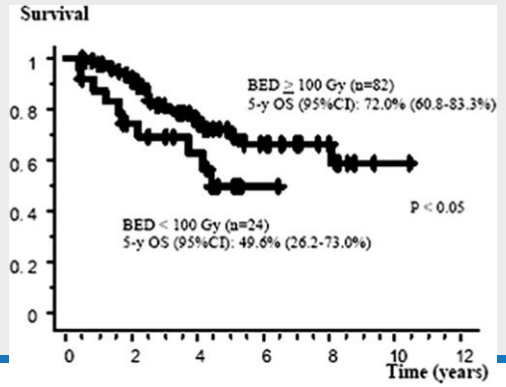
- 257 patients with cT1-2N0 NSCLC
- Median BED: 111 (57-180) Gy_{10}
- Median F/U: 38 (2-128) months
- Better local control and survival with BED ≥100 Gy_{10}

TABLE 2. Recurrence Rate According to the BED and Stage

	Total cases	BED <100 Gy	BED ≥100 Gy	*p*	Stage IA	Stage IB	*p*
Local tumor	36/257 (14.0%)	18/42 (42.9%)	18/215 (8.4%)	<0.01	20/164 (12.2%)	16/93 (17.2%)	0.21
Regional nodal metastasis	29/257 (11.3%)	9/42 (21.4%)	20/215 (9.3%)	<0.05	17/164 (10.4%)	12/93 (12.9%)	0.54
Distant metastasis	51/257 (19.8%)	11/42 (26.2%)	40/215 (18.6%)	0.3	32/164 (19.5%)	19/93 (20.4%)	0.87





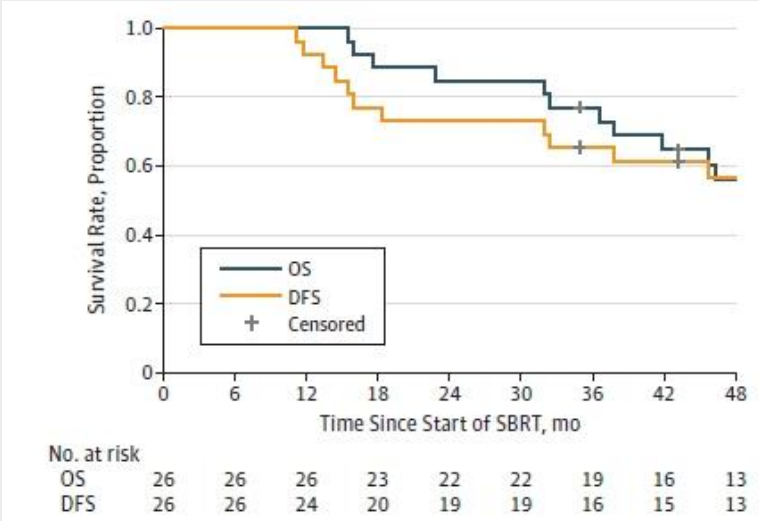


J Thorac Oncol 2007;2:s94-100

SBRT for Operable Stage I NSCLC

RTOG 0618 study

- Single-arm phase 2 study
- Operable biopsy-proven peripheral T1-2N0M0 NSCLC <5 cm
- SBRT: 54 Gy in 3 fractions
- Primary endpoint: Primary tumor control → 2Y 96%
- Secondary endpoint: Toxicity, DFS, OS
  - 4Y DFS: 57%
  - 4Y OS: 56%
  - Regional failures in 3 patients
  - Distant failures in 5 patients



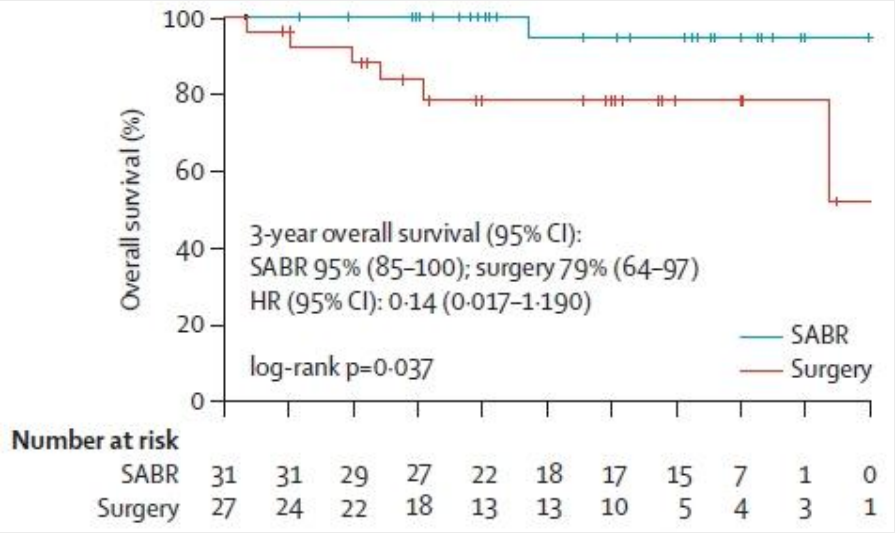
SBRT for Operable Stage I NSCLC

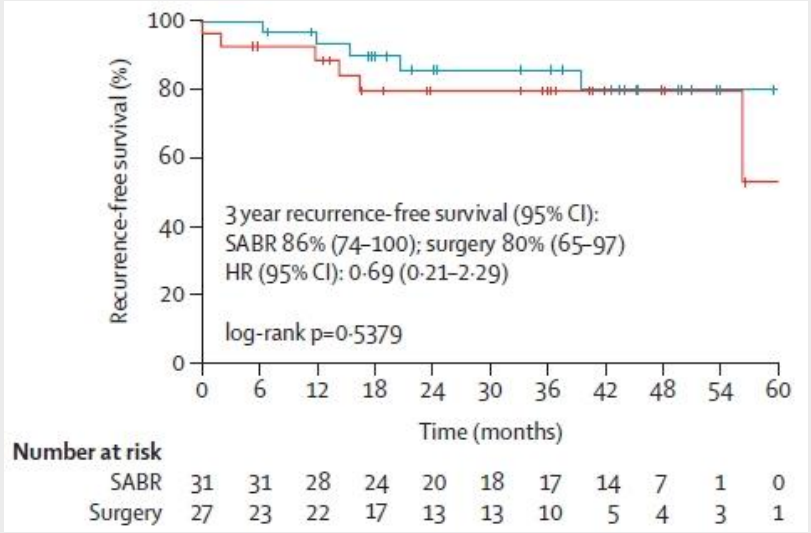
Pooled analysis of 2 randomized trials (STARS + ROSEL)

- Operable cT1-2a (<4 cm) NSCLC

→ Randomly assigned in 1:1 ratio to SABR or Lobectomy

- Pooled analysis in the ITT population using OS as primary endpoint
- Median F/U: 40.2 months

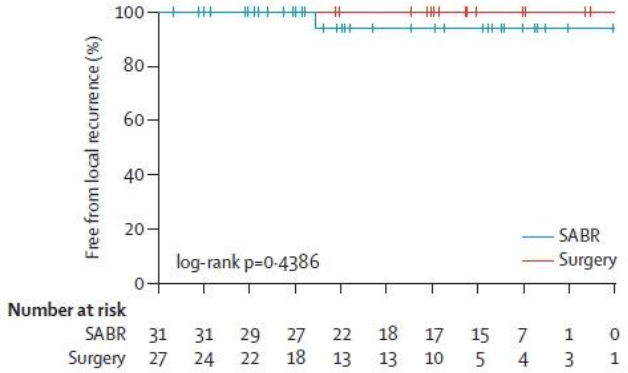


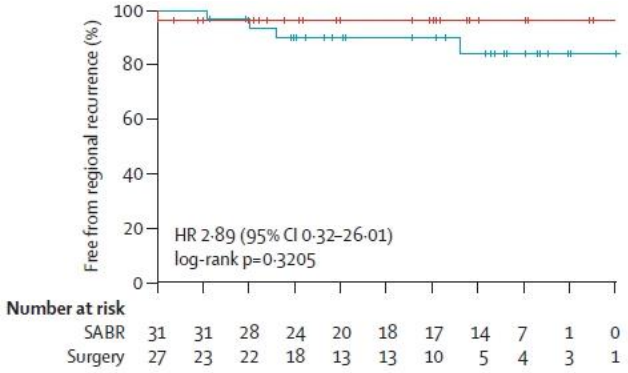


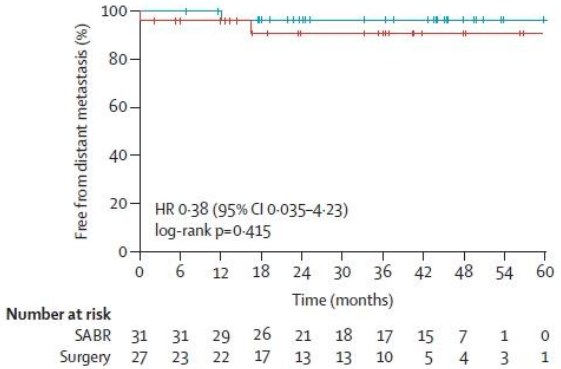
Lancet Oncol 2015;16:630-7

SBRT for Operable Stage I NSCLC

Pooled analysis of 2 randomized trials (STARS + ROSEL)







- Local/regional/distant failure: 1/4/1 (SBRT) vs. 0/1/2 (Surgery)
- Grade ≥3 adverse events: 10% vs. 44%

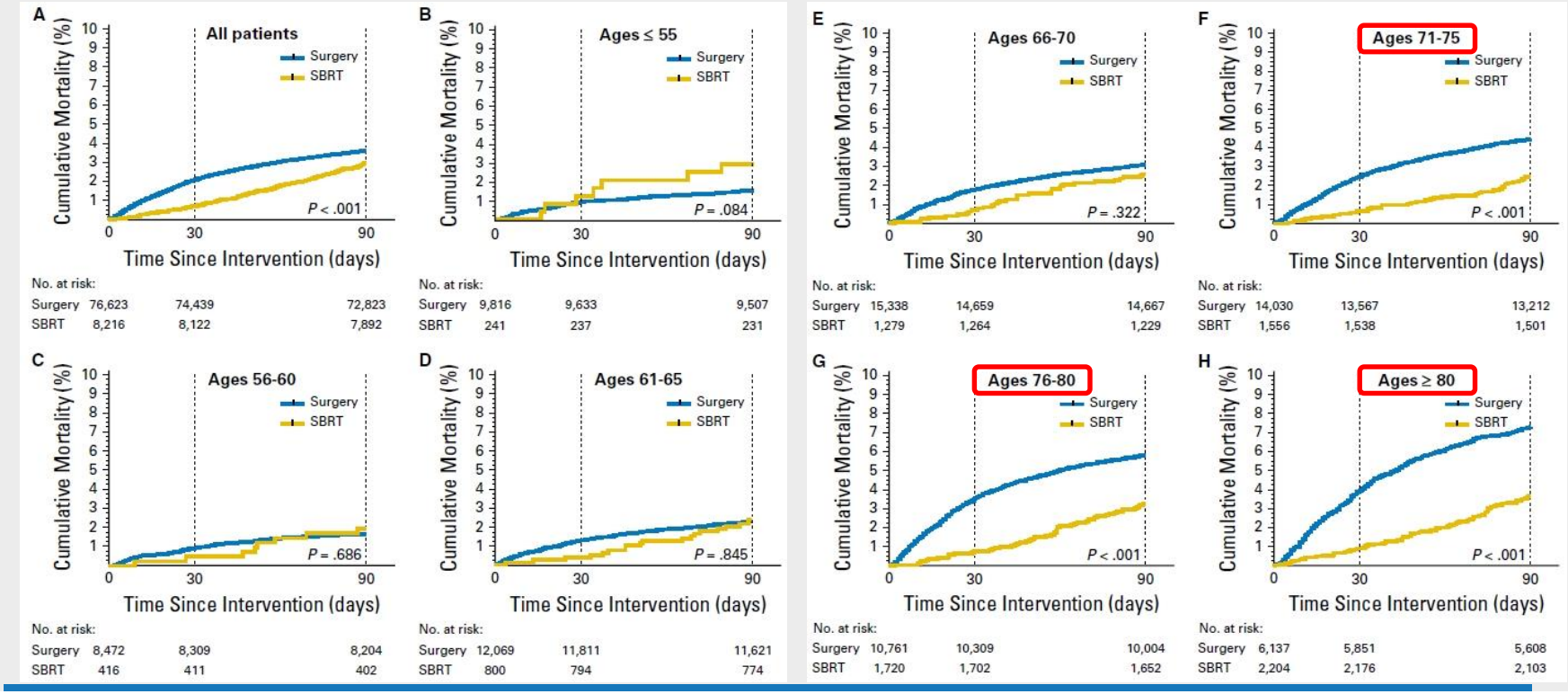
- SABR could be an option for treating operable stage I NSCLC.
- Small sample size and short F/U → Additional studies are warranted.

Lancet Oncol 2015;16:630-7

SBRT for Early Stage NSCLC

Post-treatment mortality after surgery and SBRT

- 76623 pts with surgery and 8216 pts with SABR for T1-2aN0 NSCLC between 2004-2013 → 30-day and 90-day mortality compared.



J Clin Oncol 2018;36:642-51

SBRT for Early Stage NSCLC

Post-treatment mortality after surgery and SBRT

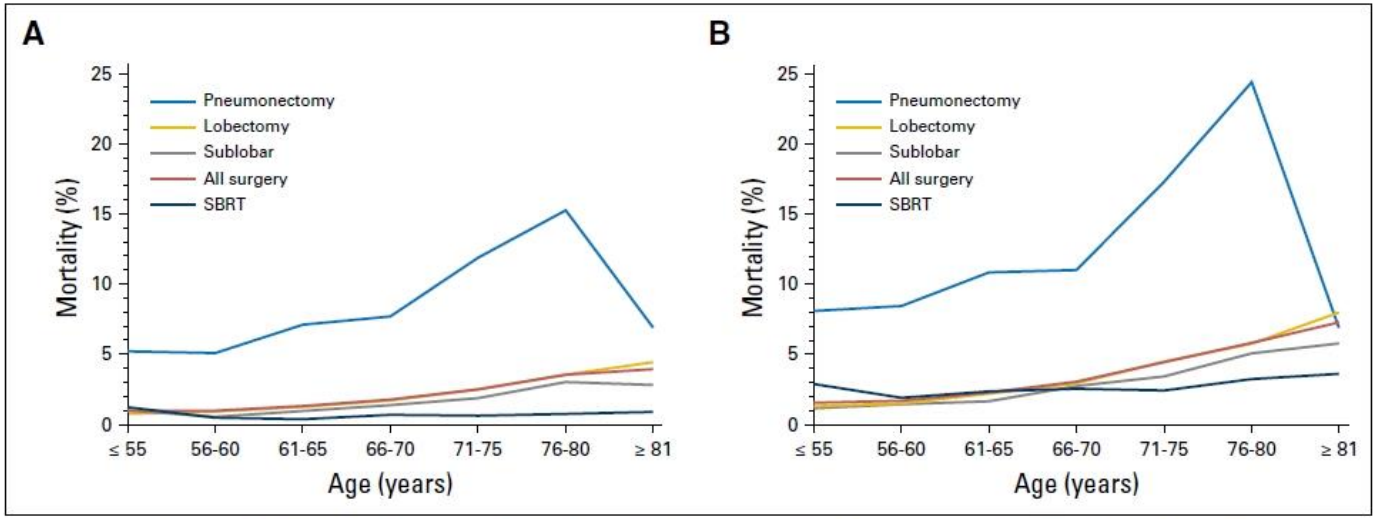


Fig 2. Unadjusted absolute mortality rates at (A) 30 days, and (B) 90 days by intervention type. SBRT, stereotactic body radiotherapy.

- Differences in 30- and 90-day post-treatment mortality between surgery and SBRT increased as a function of age, with the largest differences in favor of SBRT observed among patients >70 years

→ Informed shared decision-making in elderly or high-risk patients

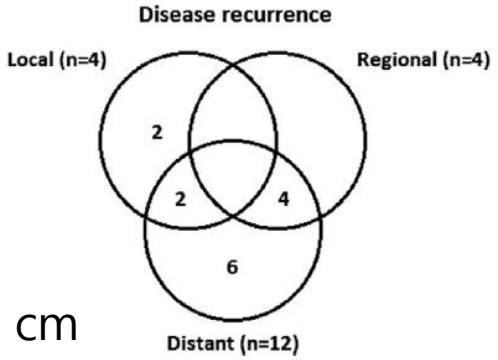
J Clin Oncol 2018;36:642-51

SBRT for Early Stage NSCLC

Patterns of failure after SBRT

Event[a]	Actual Incidence, %
Local disease recurrence	7.7
Regional disease recurrence	12.3
Locoregional disease recurrence	18.5
Distant metastases	12.3
Any disease recurrence	27.7

≤5 cm >5 cm



- Regional and distant failures were the dominant patterns of failure.

→ Can addition of IO improve outcomes after SABR in early NSCLC?

Cancer 2017;123:3031-9
J Thorac Oncol 2017;12:974-82

SBRT + Immunotherapy

iSABR

- Radiation is immunogenic

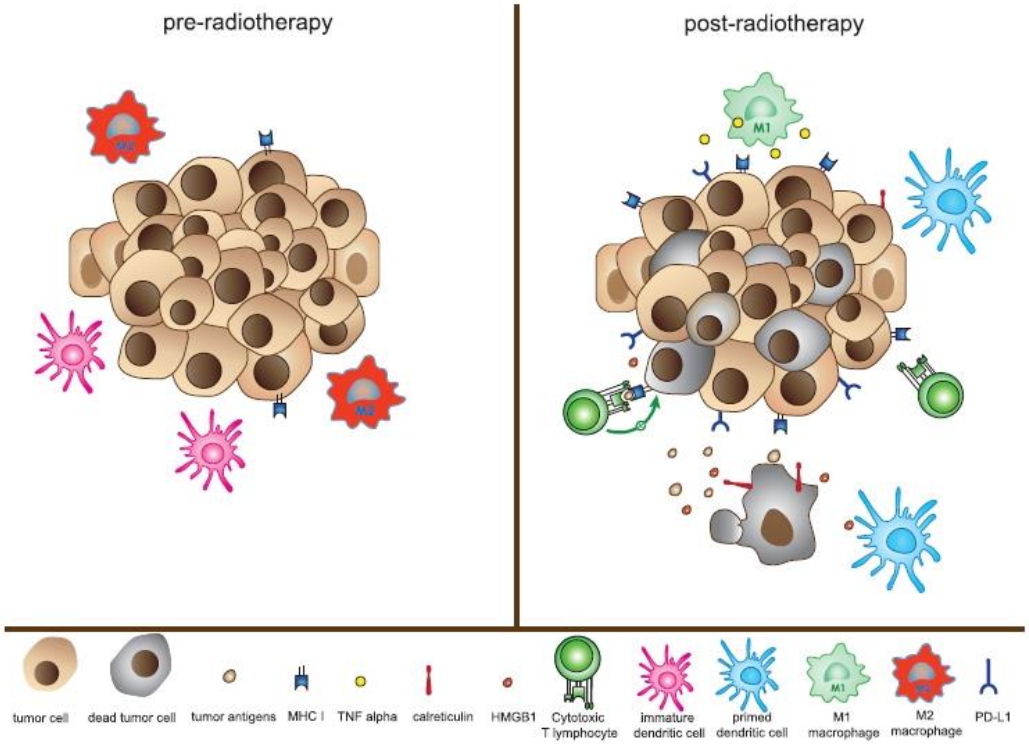
- SABR pin-point delivers ablative radiation dose to a tumor with minimal toxicity
  - Avoids damaging immune cells in nearby tissue and LNs
  - Expose tumor DNA for “sensing”
  - Sensing activates antigen presenting cells

→ Activated T-cells ready to fight cancer elsewhere

RT + Immunotherapy

Radiation-induced immune modulation

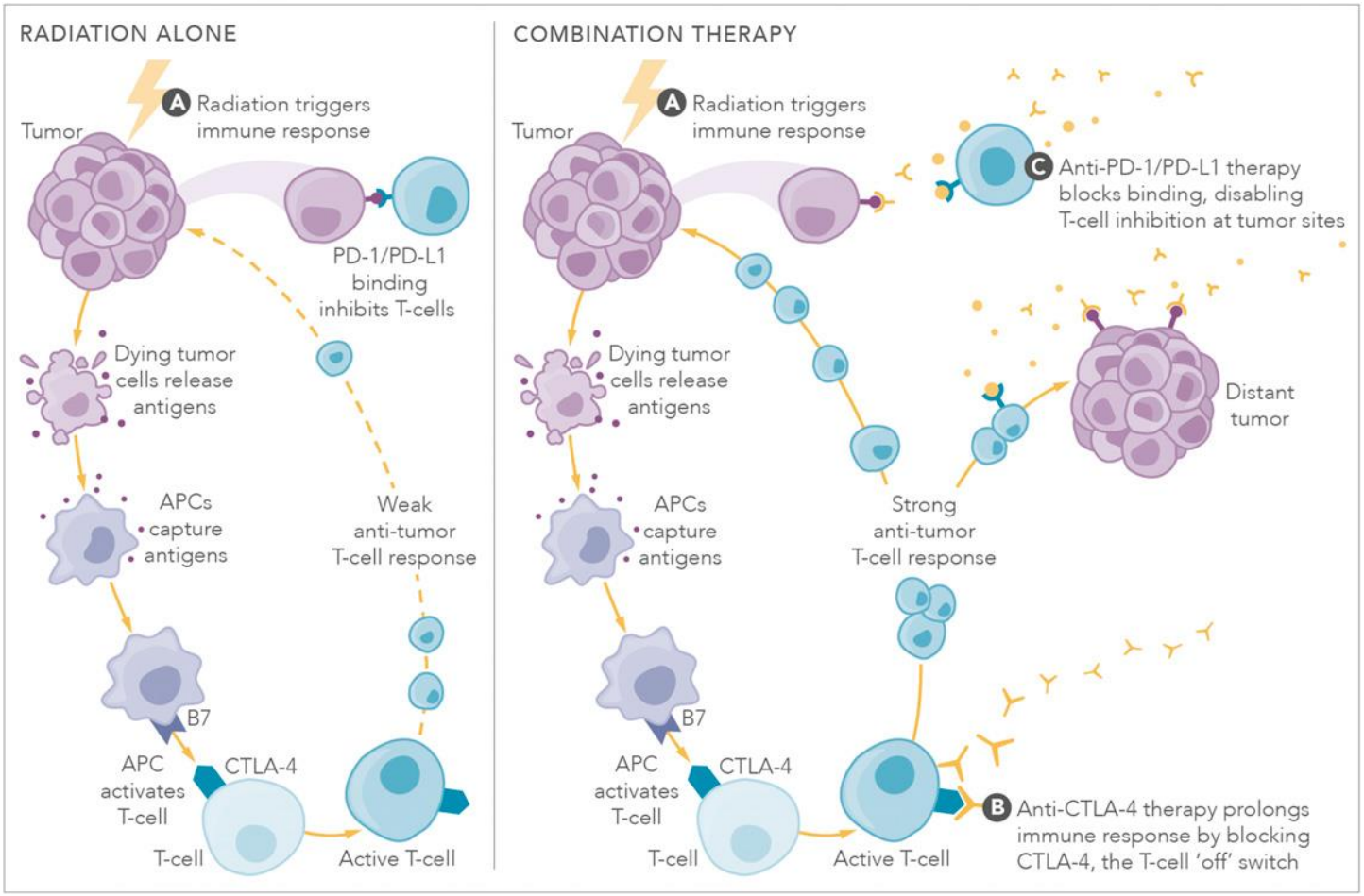
Tumor debulking and releasing tumor antigens	
Not systemically immunosuppressive	
Up-regulation of immunogenic cell surface markers	
ICAM-1	Chakraborty et al.[16]
MHC-1	Formenti et al.[17]
Fas	Chakraborty et al.[16]
Secretion of danger signals and cytokines	
IFN-g	Lugade et al.[18]
TNFa	Formenti et al.[17]
IL-1b	Formenti et al.[17]
Induction of immunogenic cell death	
Calreticulin	Obeid et al.[19]
HMGB1	Apetoh et al.[14]
Increased homing of immune cells to tumors	
Normalization of tumor vasculature	Ganss et al.[20]
Secretion of chemo-attractants (cxcl16)	Matsumura et al.[21]
Endothelial expression of VCAM-1	Lugade et al.[18]
Improved T-cell homing to tumors	Klug et al.[12]
Improved antigen presentation by APC's	
Irradiated tumors prime dendritic cells	Strome et al.[22]
Improved antigen presentation via TLR-4	Apetoh et al.[14]
Depletion of immunosuppressive cells	Wu et al.[13]
Shifting TAM polarization to M1	Klug et al.[12]
Up-regulation of cell surface PD-L1	Dovedi et al.[23]



J Thorac Oncol 2015;10:1685-93

RT + Immunotherapy

RT alone fails to elicit a strong systemic antitumor response



PNAS 2017;114:6416-20

SBRT + Immunotherapy

Ongoing studies

	NCT03446547	NCT03110978	NCT03446911
Site	ASTEROID (Sweden)	I-SABR (MDACC)	VUMC
N	216	140	20
Primary endpoint	Time to progression	Event-free survival	Toxicity
Arm A	SBRT	SBRT	SBRT prior to OP
Arm B	SBRT → Durvalumab Q4W for 12M	SBRT → Nivolumab Q2W for 7 doses	SBRT prior to OP + Pembrolizumab #2

SBRT for Clinically Diagnosed NSCLC

Japanese multi-institutional retrospective study

- 115 patients
  - Tumors were highly suggestive of primary lung cancer
  - Diagnosed as stage I lung cancer clinically
  - No pathologic diagnosis
- SBRT: 30-70 Gy in 2-10 fractions (Median BED 106 Gy_{10})

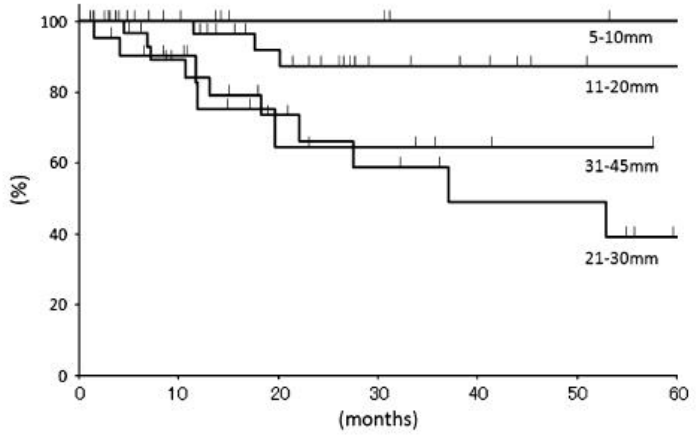


Fig. 1. Kaplan-Meier curve of overall survival rates for the patients with a tumor size (diameter) of 5 to 10 mm ($n = 11$), 11 to 20 mm ($n = 47$), 21 to 30 mm ($n = 35$), and 31 to 45 mm ($n = 22$).

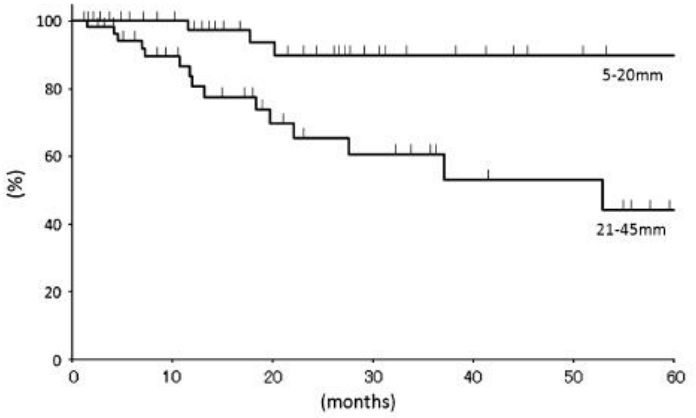


Fig. 2. Kaplan-Meier curve of overall survival rates for the patients with a tumor size (diameter) of 5 to 20 mm ($n = 58$) and 21 to 45 mm ($n = 57$). A statistically significant difference was found ($p < 0.0005$) between the two groups.

SBRT for Clinically Diagnosed NSCLC

Japanese multi-institutional retrospective study

- Tumor size ≤20 mm
  - Local progression: 2 (3.4%)
  - Grade 2 pulmonary complication: 2 (3.4%)
- Tumor size >20 mm
  - Local progression: 3 (5.3%)
  - Grade 2/3/5 toxicity: 5 (8.8%), 3 (5.3%), 1 (1.8%)

IJROBP 2009;75:683-7

SBRT for Clinically Diagnosed NSCLC

Comparison with histologically-proven NSCLC

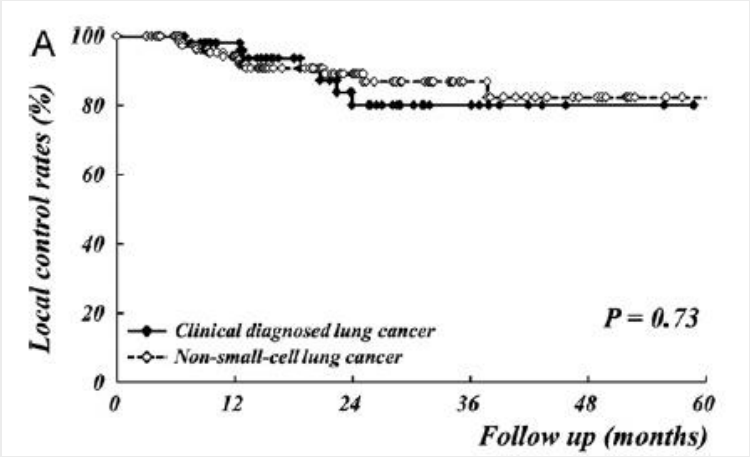
	Pathological NSCLC	Clinical NSCLC	*p*-Value
No. of patients	115	58	
Median follow up (month)	21.2 (6–63.7)	20.2 (6–58.8)	n.s.
Median age (range)	78 (55–89)	79 (65–91)	n.s.
Male/female	90 (78%)/25 (22%)	35 (60%)/23 (40%)	$p < 0.05$
Body mass index	21.13 (14.15–37.56)	22.18 (14.75–33.43)	n.s.
Operability: yes/no	31 (27%)/84 (73%)	7 (12%)/51 (88%)	$p < 0.01$
History of other cancers	25 (22%)	13 (22%)	n.s.
Median maximum diameter (cm)	2.8 (0.5–6.2)	2.65 (1–5.3)	n.s.
ITV (ml)	11.33 (0.47–77.24)	8.99 (1.74–79.42)	n.s.
PTV (ml)	41.32 (7.33–169.51)	38.11 (14.08–164.65)	n.s.
Location: central/peripheral	35 (30%)/80 (70%)	18 (31%)/40 (69%)	n.s.
T stage			n.s.
T1a	27 (23%)	20 (34%)	
T1b	38 (33%)	16 (28%)	
T2a	38 (33%)	20 (34%)	
T2b	5 (4%)	1 (2%)	
T3	2 (2%)	0 (0%)	
T4 (aorta; 5, PA; 1)	5 (4%)	1 (2%)	
Biopsy attempted	115 (100%)	30 (52%)	$p < 0.01$
Opacity: GGO (+solid)/solid	12 (10%)/103 (90%)	5 (9%)/53 (91%)	n.s.

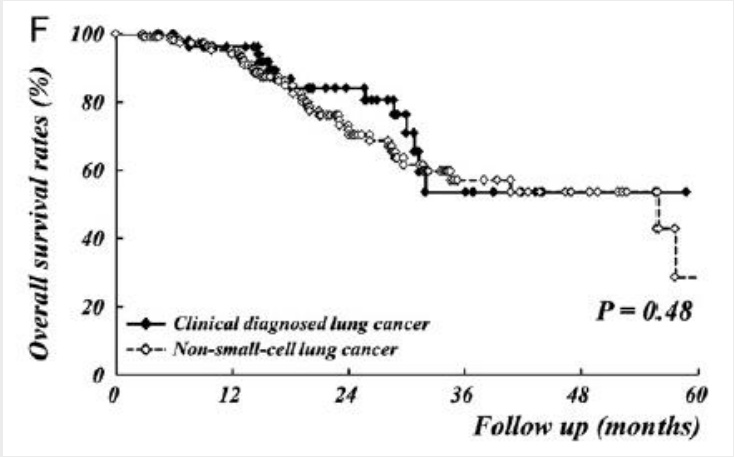
Lung Cancer 2012;77:77-82

SBRT for Clinically Diagnosed NSCLC

Comparison with histologically-proven NSCLC

- SBRT: 40-50 Gy in 5 fractions
- No significant differences in treatment outcomes



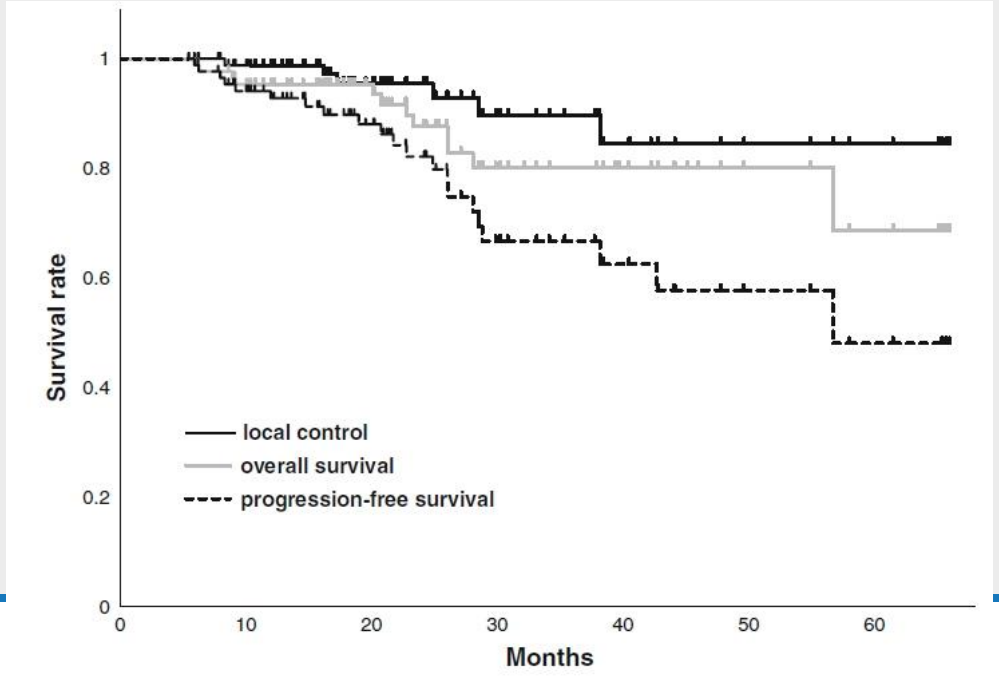


Lung Cancer 2012;77:77-82

SBRT for Clinically Diagnosed NSCLC

Single institution retrospective study

- 88 patients with small lung lesions (8-40 mm, median 19 mm)
- SBRT: 48 Gy in 4 fractions
- 3Y LC, PFS, OS: 90%, 67%, 80%
- Grade 2 toxicity: Pneumonitis 2 (2.3%), rib fracturs 6 (6.8%)

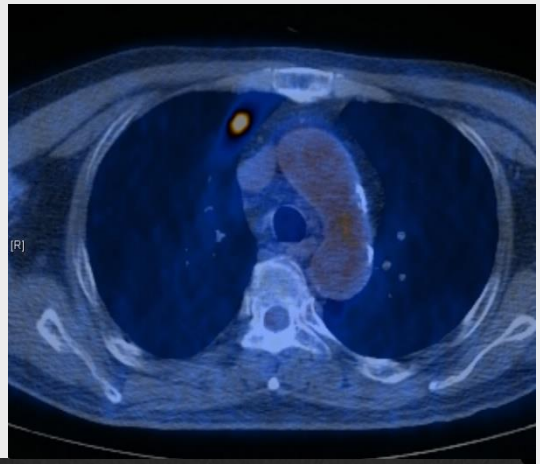


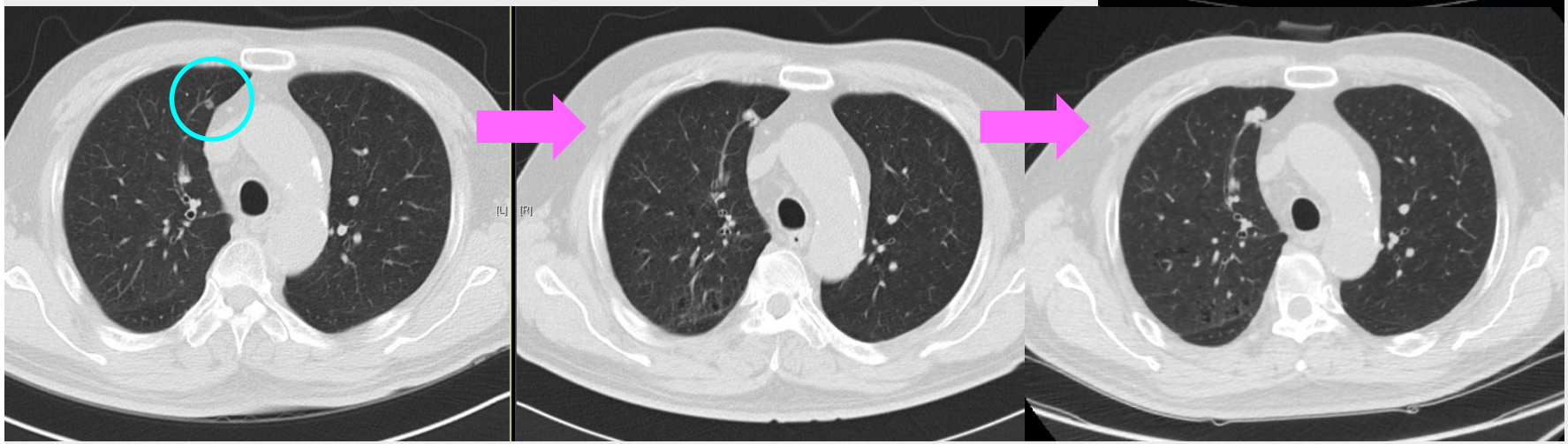
Int J Clin Oncol 2015;20:53-8

SBRT for Clinically Diagnosed NSCLC

M/73

- r/o Lung cancer (RUL, cT1N0)
  - 건강검진 detected RUL nodule (2015.11.20)
  - Increased size (2017.3.21)
  - DM CKD (stage 5), Chronic ischemic stroke
- PFT (2017/8/8): FEV1 2.40L (74%), DLCO 56%

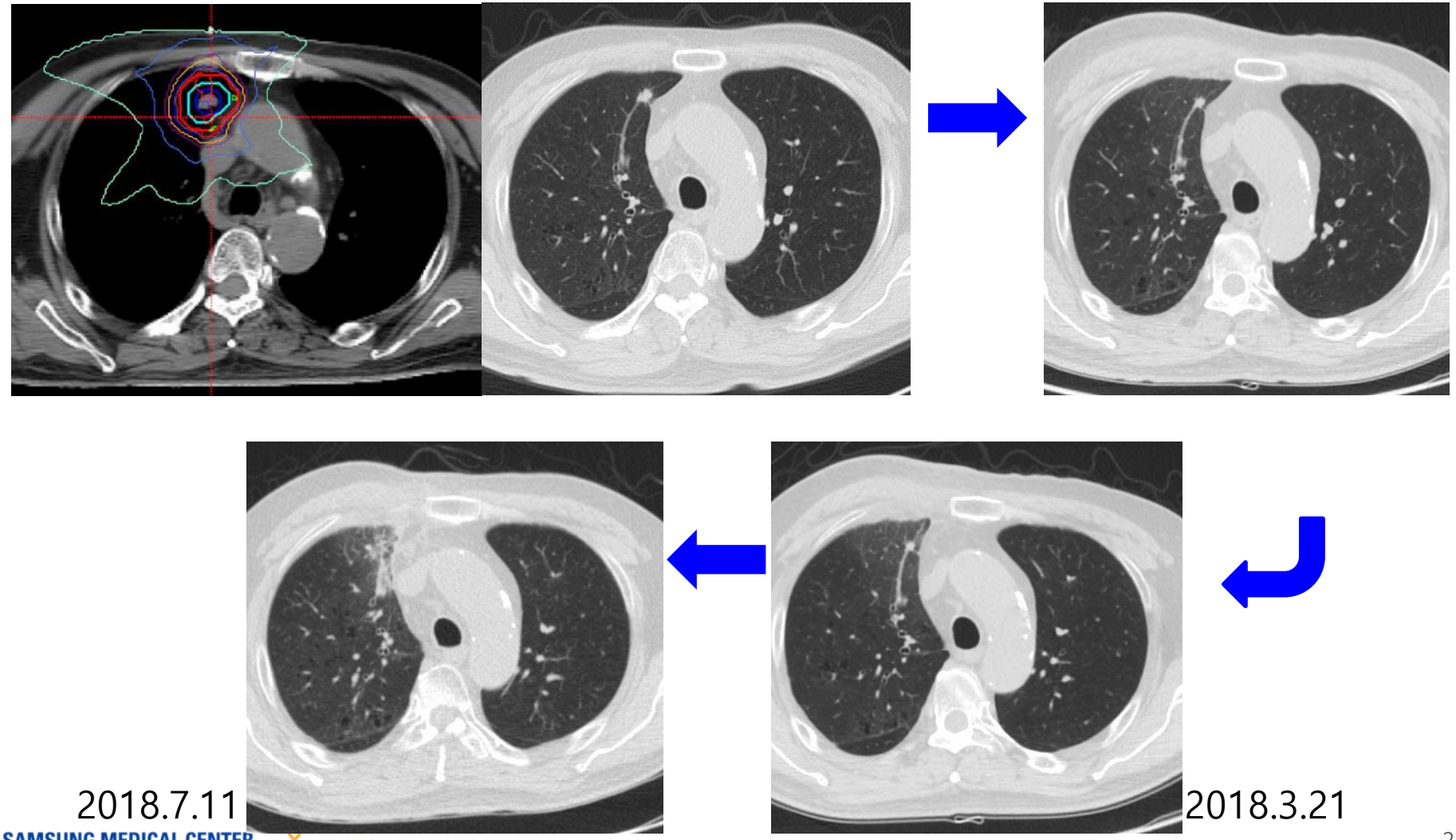




2015.11.20 → 2017.3.21 → 2017.7.24

SBRT for Clinically Diagnosed NSCLC

SBRT 60 Gy/4fx (2017.9.19-22)



SBRT for Clinically Diagnosed NSCLC

Summary

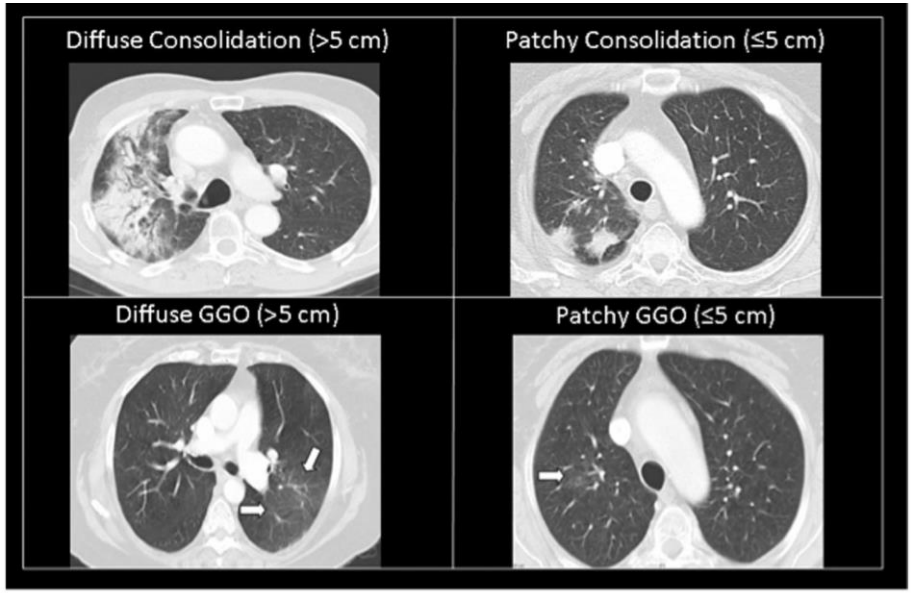
- Pathological diagnosis in necessary in principle.
- Invasive diagnostic procedures will be more frequently impossible because of patient's severe comorbidity.
- SBRT should be used with great caution.

Int J Clin Oncol 2015;20:53-8

Radiologically Change

68 lesions from 61 patients

A



B

TABLE 2. Scoring System for Classifying Acute Radiological Changes After Stereotactic Body Radiotherapy (SBRT)[8]

Name	Description
Diffuse consolidation	Consolidation more than 5 cm in largest dimension. The involved region contains more consolidation than aerated lung
Patchy consolidation	Consolidation less than 5 cm in largest dimension and/or the involved region contains less consolidation than aerated lung
Diffuse GGO	More than 5 cm of GGO, (without consolidation). The involved region contains more GGO than normal lung
Patchy GGO	Less than 5 cm of GGO, (without consolidation), and/or the involved region contains less GGO than normal lung
No evidence of increased density	No new abnormalities. Includes patients with tumors that are stable, regressing or resolved, or fibrosis in the position of the original tumor that is not larger than the original tumor

GGO, ground glass opacity.

TABLE 3. Scoring System for Classifying Late Radiological Changes After Stereotactic Body Radiotherapy (SBRT)[10]

Name	Description
Modified conventional pattern	Consolidation, volume loss, and bronchiectasis similar to, but usually less extensive than, conventional radiation fibrosis. Larger than the original tumor size. Occasionally with associated GGO
Mass-like fibrosis	Well-circumscribed focal consolidation limited to area surrounding the tumor. The abnormality must be larger than the original tumor
Scar-like fibrosis	Linear opacity in the region of the tumor associated with volume loss
No evidence of increased density	No new abnormalities. Includes patients with tumors that are stable, regressing or resolved, or fibrosis in the position of the original tumor that is not larger than the original tumor

GGO, ground glass opacity.

J Thorac Oncol 2011;6:1221-8

Radiologically Changes after SBRT

Clinicians should be aware of these radiological findings

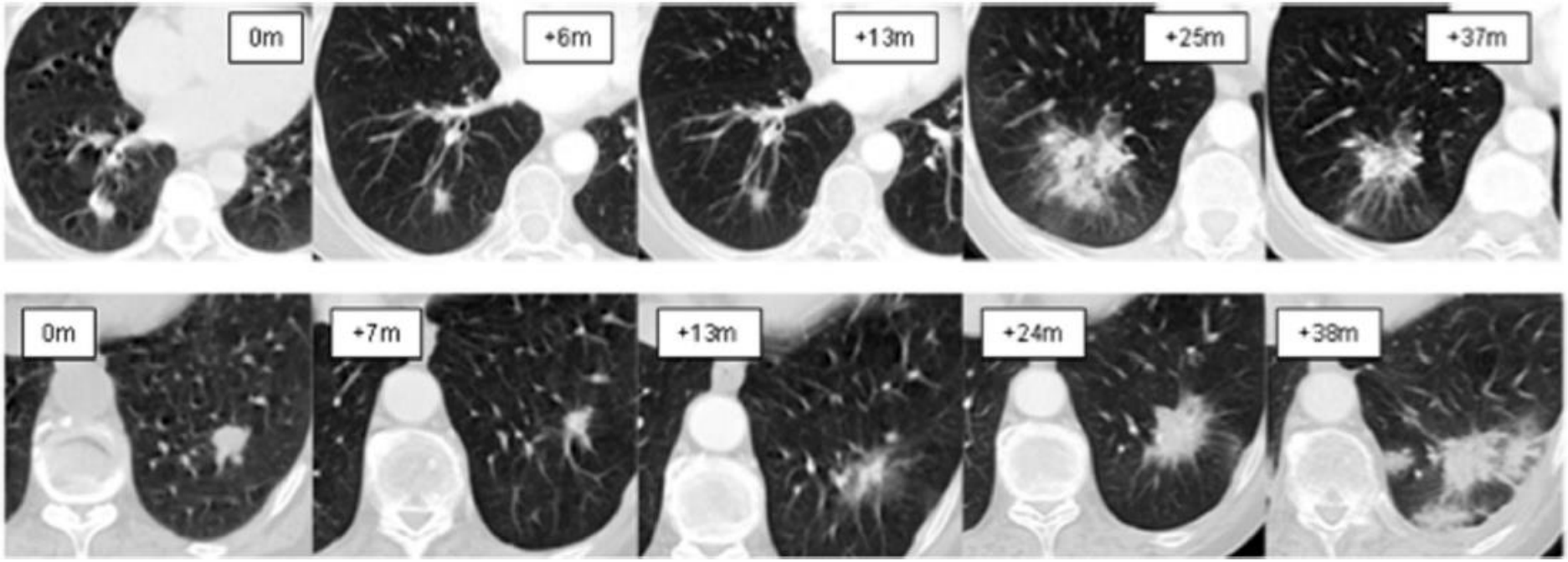


FIGURE 4. These two examples illustrate the dynamic nature of computed tomography (CT) changes after lung stereotactic body radiation therapy (SBRT) 3 × 20 Gy. In the top panel, the treatment CT is on the left. From left to right: "no increase in density" on CT at +6 and +13 months and then a "modified conventional" pattern first appears at +25 months and is still present at +37 months. In the case illustrated in the bottom panel, the treatment CT is again on the left. From left to right: no increase in density at +7 months changing to modified conventional pattern at +13 months, evolving to "mass-like" change on CT at +24 months post-SBRT and then reverting again to modified conventional at +38 months.

J Thorac Oncol 2011;6:1221-8

SBRT for Patients with ILD

Impact of pretreatment ILD on radiation pneumonitis

- 157 patients underwent SBRT for stage I NSCLC
- Pretreatment CT images were retrospectively evaluated.
- 20 patients with ILD findings: 11 UIP, 9 non-UIP patterns
- Cumulative incidence of Gr ≥2 RP: 18.7% → 55.0% vs. 13.3%
- 3Y OS: 53.8% vs. 70.8% (p=0.28)

TABLE 2. Numbers and Rates of Worst Radiation Pneumonitis Grade

RP Grade	All	ILD(+)	ILD(−)
No. of Patients (%)	*n* = 157	*n* = 20	*n* = 137
None	19 (12.1%)	1 (5.0%)	18 (13.1%)
Grade 1	109 (69.4%)	8 (40.0%)	101 (73.7%)
Grade 2	25 (15.9%)	9 (45.0%)	16 (11.7%)
Grade 3	1 (0.6%)	1 (5.0%)	0 (0%)
Grade 4	2 (1.3%)	1 (5.0%)	1 (0.7%)
Grade 5	1 (0.6%)	0 (0%)	1 (0.7%)

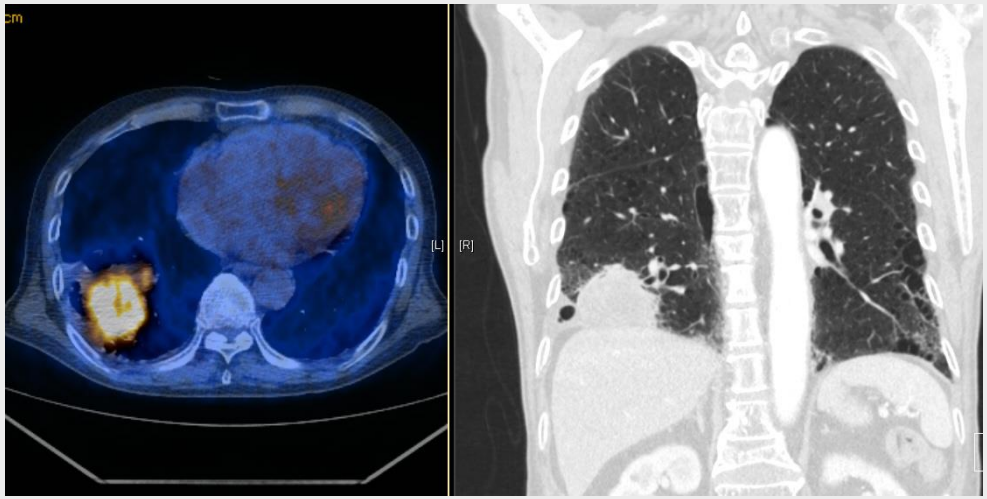
ILD, interstitial lung disease; RP, radiation pneumonitis.

J Thorac Oncol 2015;10:116-25

SBRT for Patients with ILD

M/75

- r/o Lung cancer (RLL, cT2bN0)
  - Primary pathology not proven, EBUS-TBNA #2R/4R/7/11R (-)
  - Underlying ILD (since 2014) with empysema
  - 건축현장 천장수리 40년
- PFT (2016/5/20): FEV1 2.63L (94%), DLCO 34%



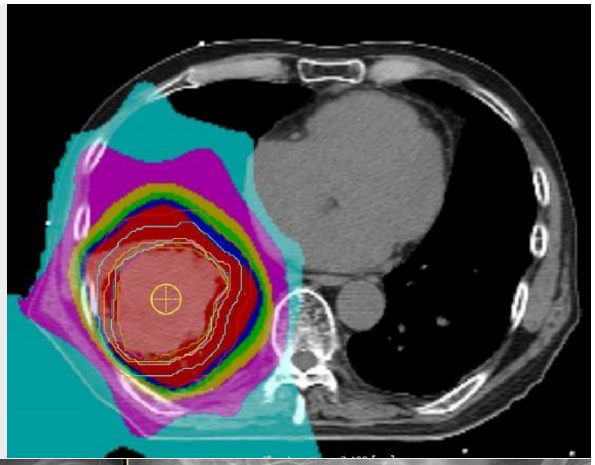
2016.5.26 2016.7.8

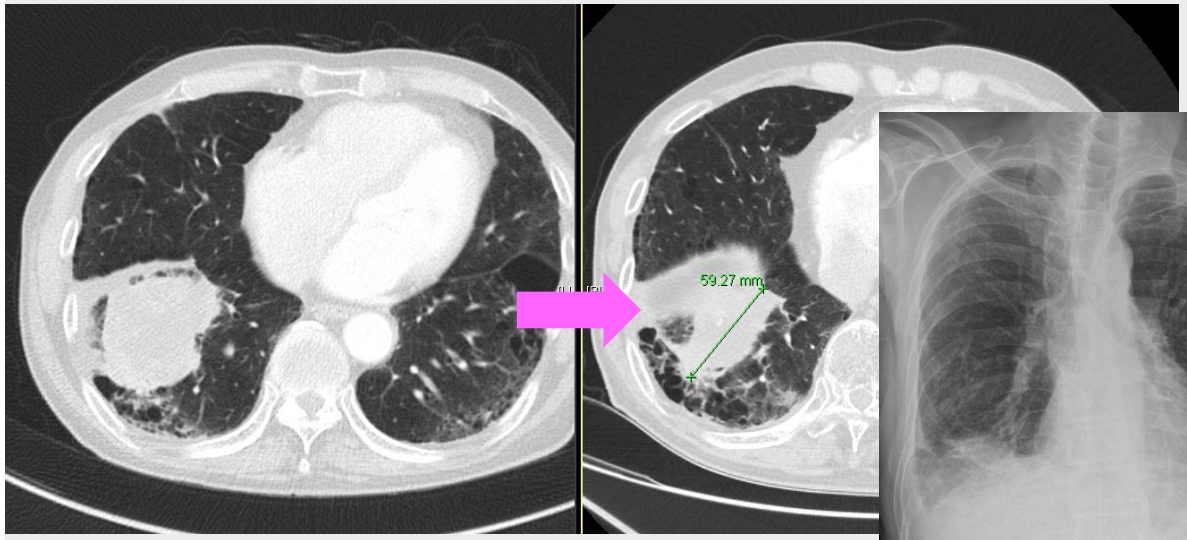
SBRT for Patients with ILD

M/75

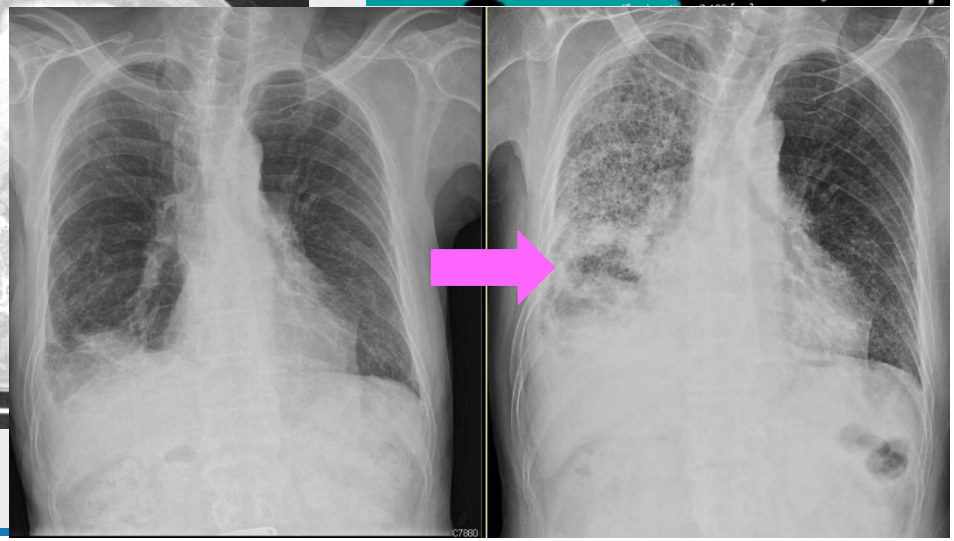
- Definitive PT 60 CGE/10fx (2016.8.10-25)
- Aggravated dyspnea (2016.11.9)

→ Expired (2016.11.11)





2016.7.8 → 9.28



2016.11.9

SBRT for Patients with IPF

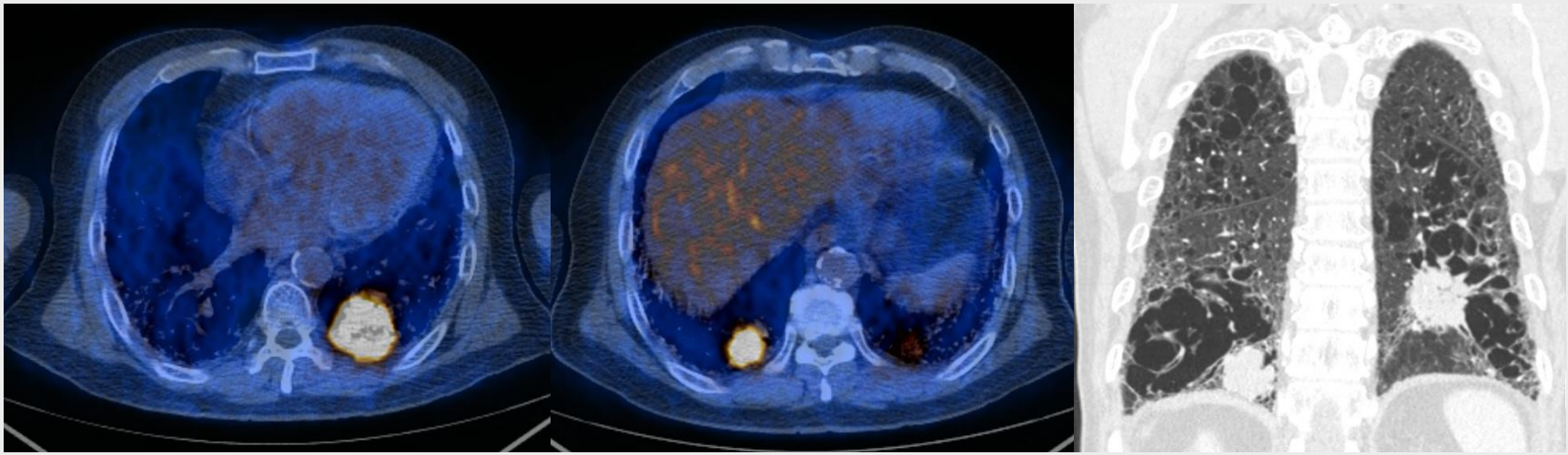
M/69

- Bilateral lung cancer (LLL AD, RLL carcinoma)
  - Underlying IPF combined emphysema
  - Angina, s/p PCI (2011), s/p CAG (2006)
  - CKD
- PFT (2017/4/13): FEV1 1.99L (78%), DLCO 31%

Lung Perfusion Result

(Counts)	Left	Right
Upper	084K	043K
Middle	125K	199K
Lower	029K	063K
Total	238K	304K

(% Ratios)	Left	Right
Upper	15.48	7.87
Middle	23.12	36.69
Lower	5.28	11.56
Total	43.88	56.12

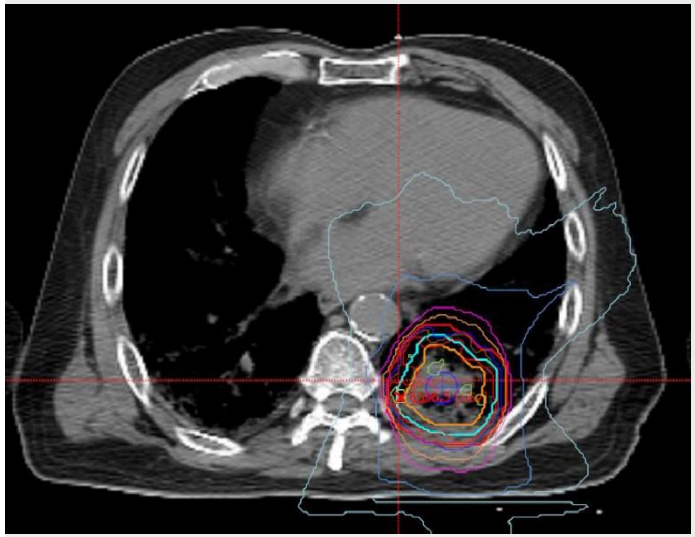


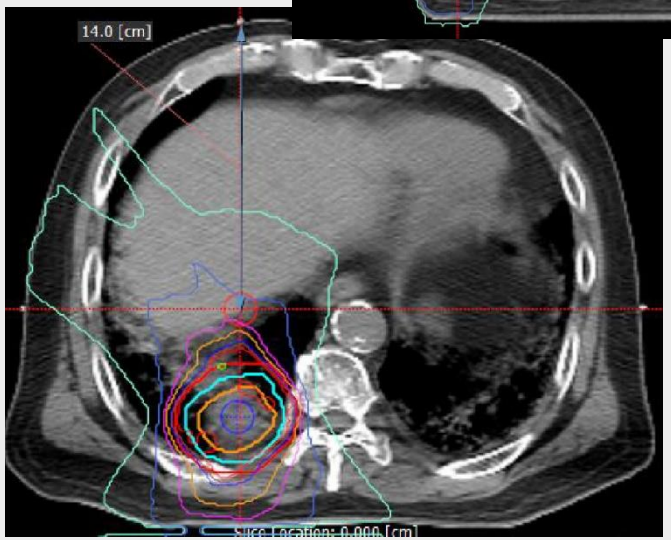
2017.4.13

SBRT for Patients with IPF

M/69

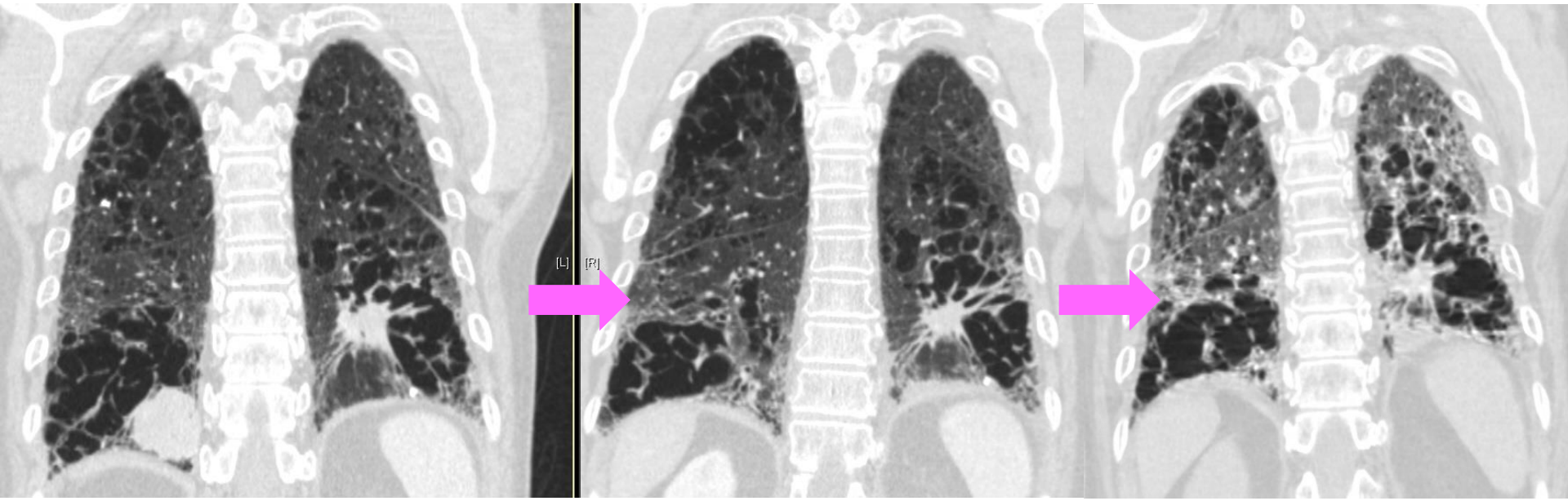
- SBRT to LLL 60 Gy/4fx (2017.4.25-28)
- SBRT to RLL 60 Gy/4fx (2017.6.5-9)
- Palliative RTx to Rt rib 8 Gy/1fx (2017.9.6)





SBRT for Patients with IPF

2017.10.7 expired d/t IPF AE

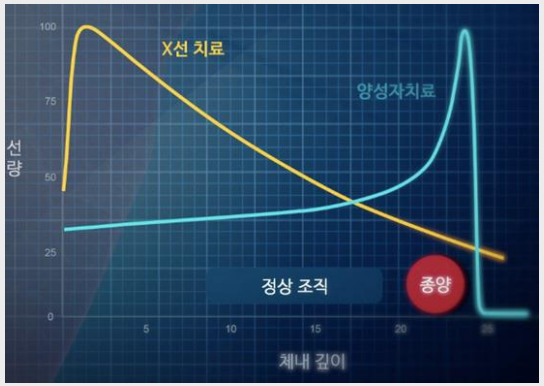


2017.6.1 → 2017.7.10 → 2017.9.3

Proton Therapy

양성자를 높은 에너지로 가속하여 암 조직을 파괴하는 치료

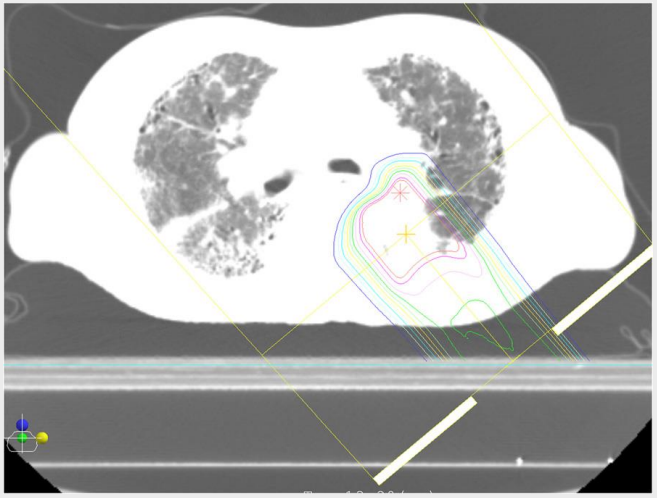
- **Bragg peak**: 일정한 깊이에서 최대의 에너지를 집중
  - Bragg peak 이후에는 전혀 방사선이 남지 않음 (**멈춘다**)
  - X-선에 비해 정상 조직에 조사되는 방사선이 적음
- Potential indication in early stage NSCLC
  - Larger tumors
  - Central tumors
  - Tumors near the brachial plexus
  - Multiple tumors

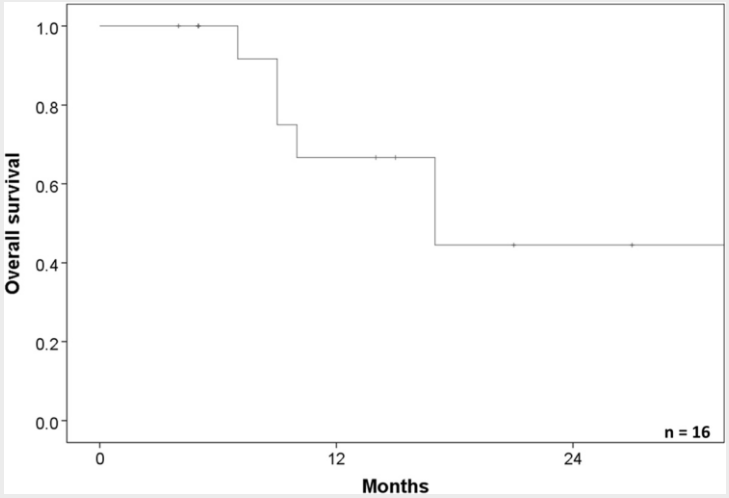


- Small peripheral lesions: Rarely improves dosimetry in a clinically meaningful way

Proton Therapy for Patients with IPF

- 16 IPF patients received PBT for lung tumors (15 primary)
- Median dose: 80.0 Gy RBE (range, 66.0-86.4 Gy RBE)
- Cumulative incidence of RP: 19.8% (Gr 5 in 1 case)
- 1Y/2Y OS: 69.6%, 44.4%





Proton Therapy for Patients with IPF

M/78

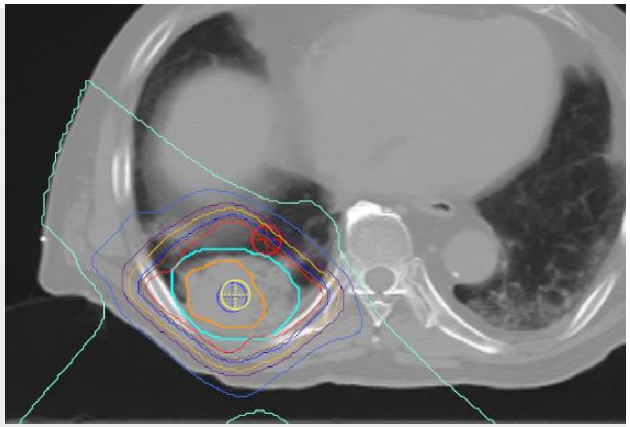
- NSCLC (AD,RLL,cT2aN0)
  - Inoperable d/t IPF, old age (outside hospital)
  - HTN, BPH on medication
- PFT (2017/7/28): FEV1 1.93L (65%), DLCO 89%

2017.7.28

Proton Therapy for Patients with IPF

M/78

- Definitive PT 64 CGE/8fx (2017.8.31-9.11)
- PFT (2017/10/30): FEV1 2.30L (82%)
- PFT (2018/2/8): FEV1 1.81L (65%)
- PFT (2018/6/4): FEV1 1.99L (68%) DLCO 77%

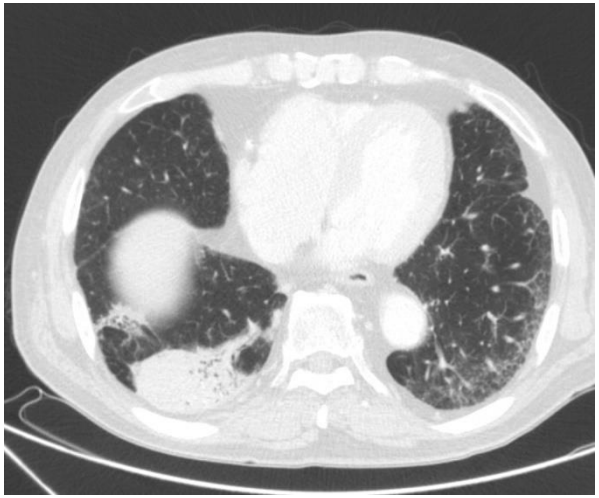


2017.7.6 → 2018.1.29

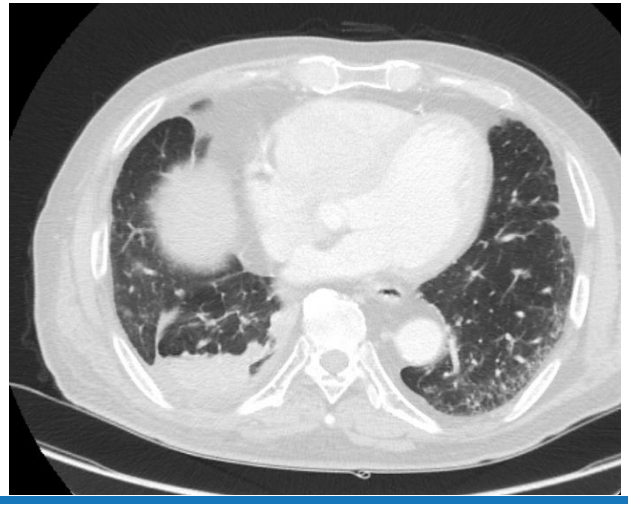
Proton Therapy for Patients with IPF

M/78

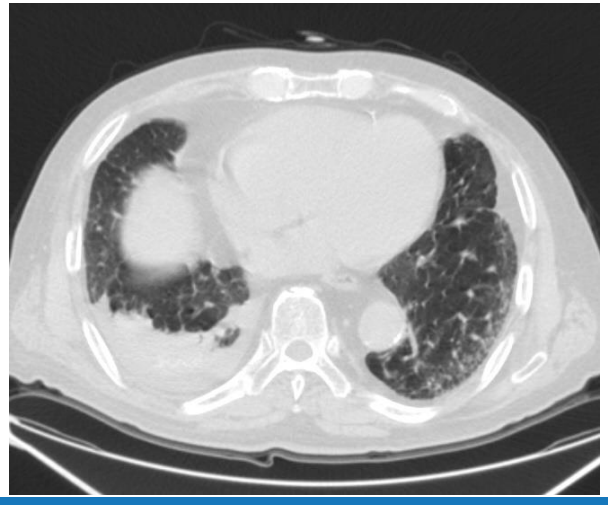
2017.7.28



2017.10.21



2018.5.4

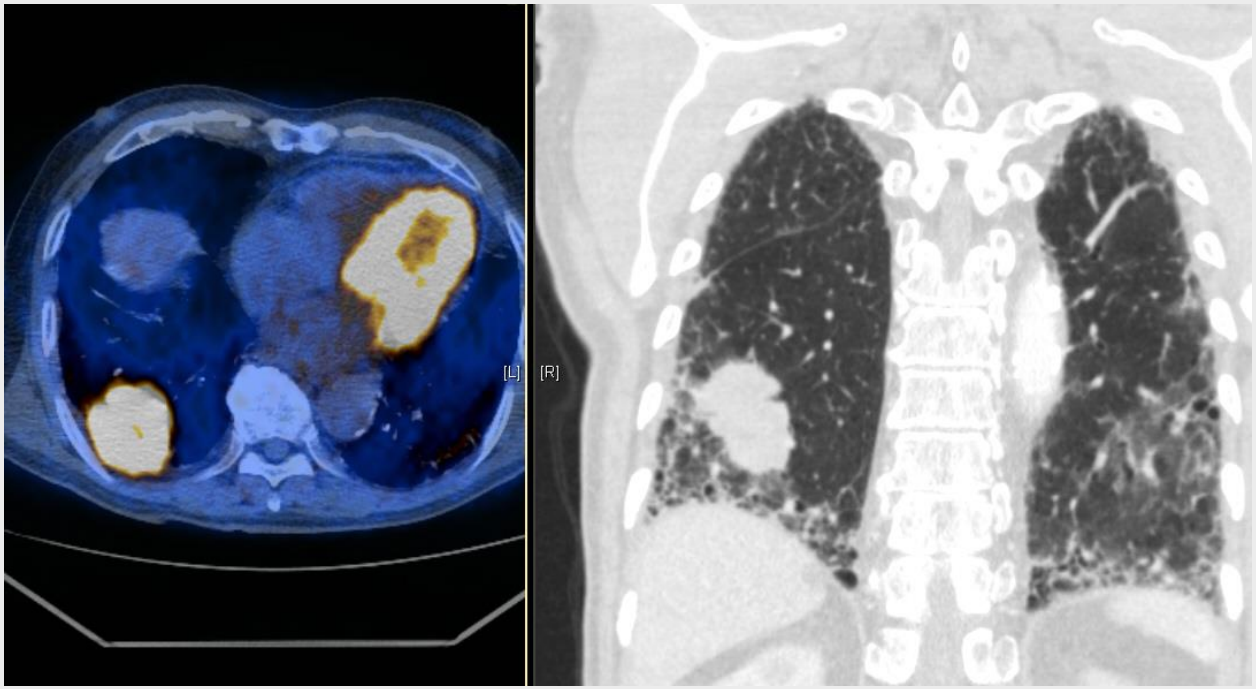


2018.1.29

Proton Therapy for Patients with IPF

M/86

- NSCLC (SQ,RLL,cT3N0)
  - IPF since 2009
  - CKD
- PFT failed

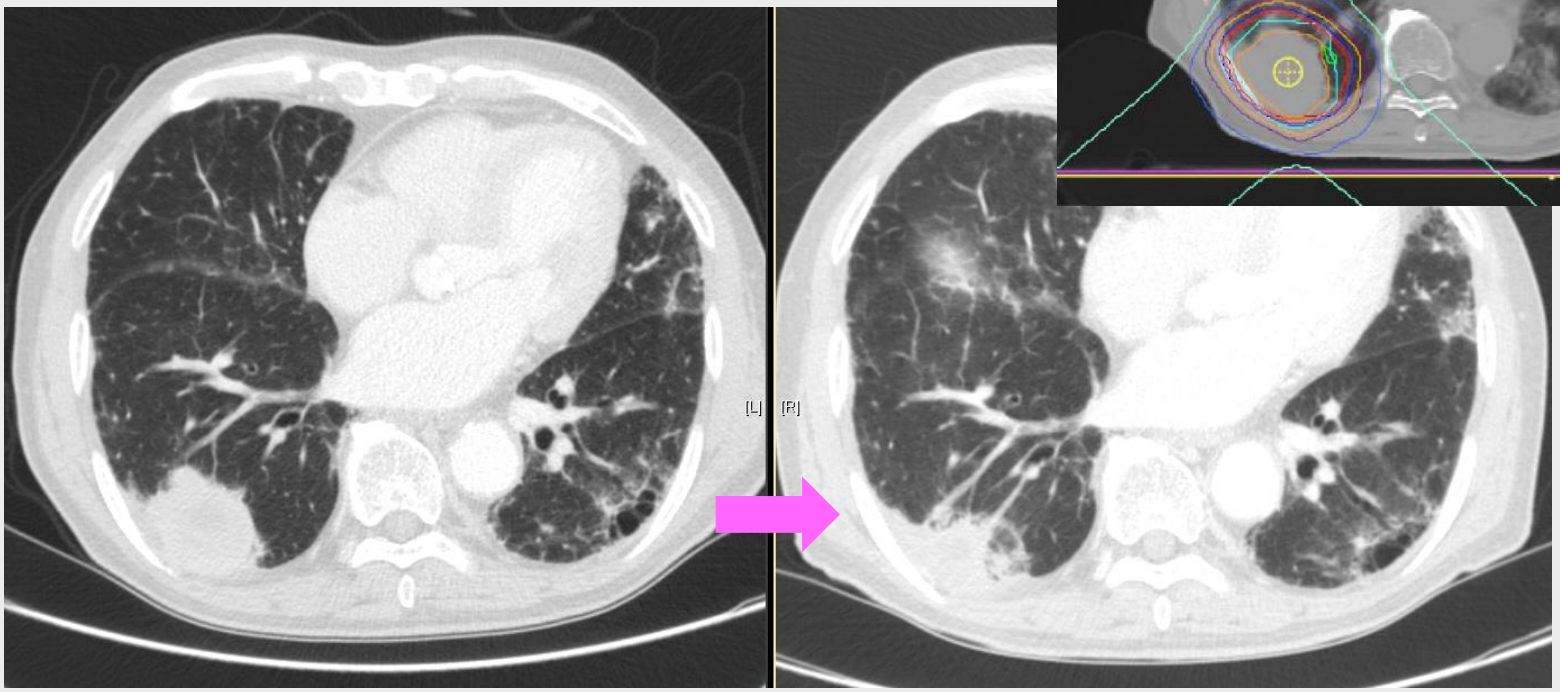


2018.3.8

Proton Therapy for Patients with IPF

M/86

- Definitive PT 64 CGE/8fx (2018.4.4-4.16)



2018.3.8 → 5.11

Proton Therapy for Patients with IPF

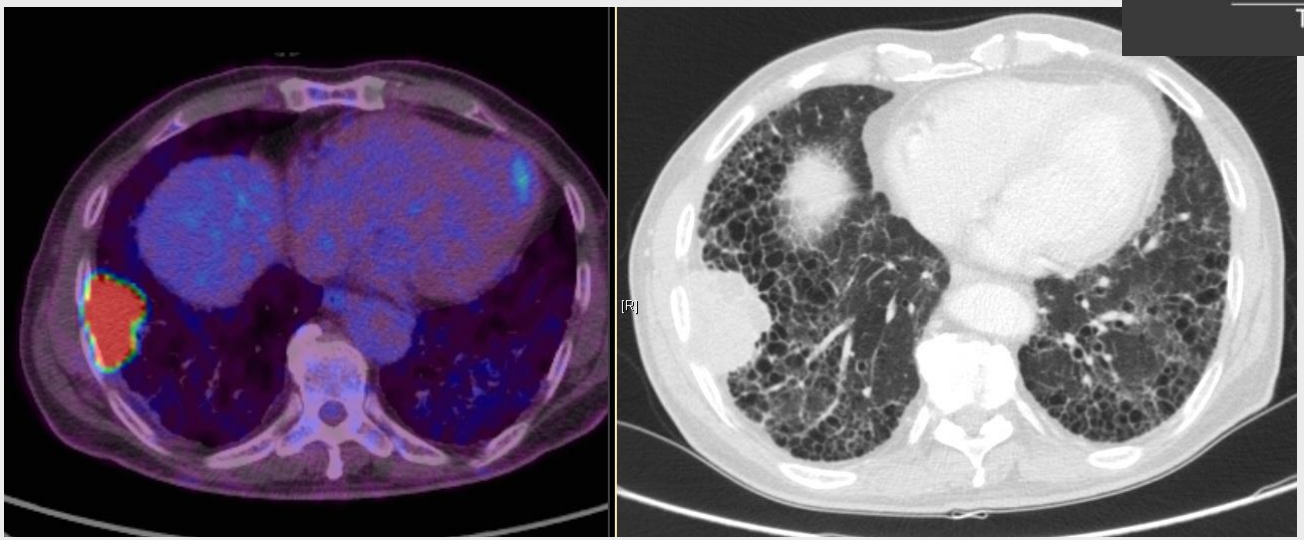
M/78

- NSCLC (SQ,RLL,cT3N0)
  - Underlying IPF
  - Cerebral infarction (2016.8.15)
- PFT (2017/3/31): FEV1 2.31L (104%) DLCO 56

Lung Perfusion Result

(Counts)	Left	Right
Upper	055K	076K
Middle	108K	213K
Lower	034K	065K
Total	197K	354K

(% Ratios)	Left	Right
Upper	9.96	13.74
Middle	19.59	38.73
Lower	6.20	11.78
Total	35.75	64.25

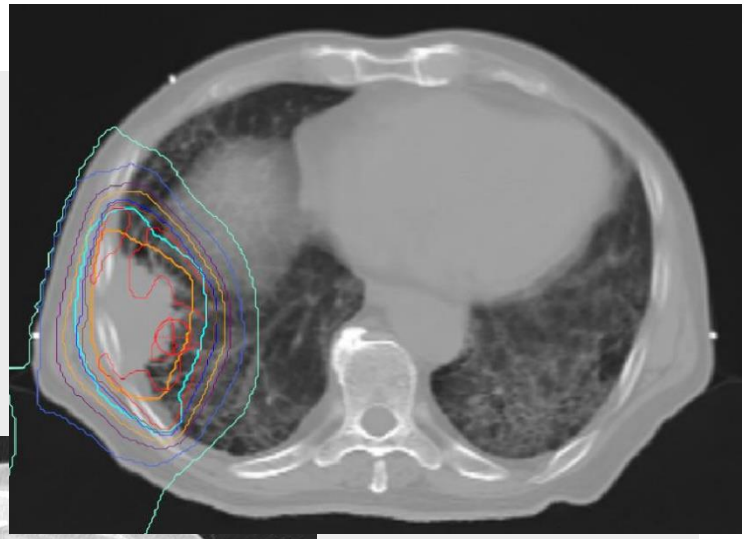


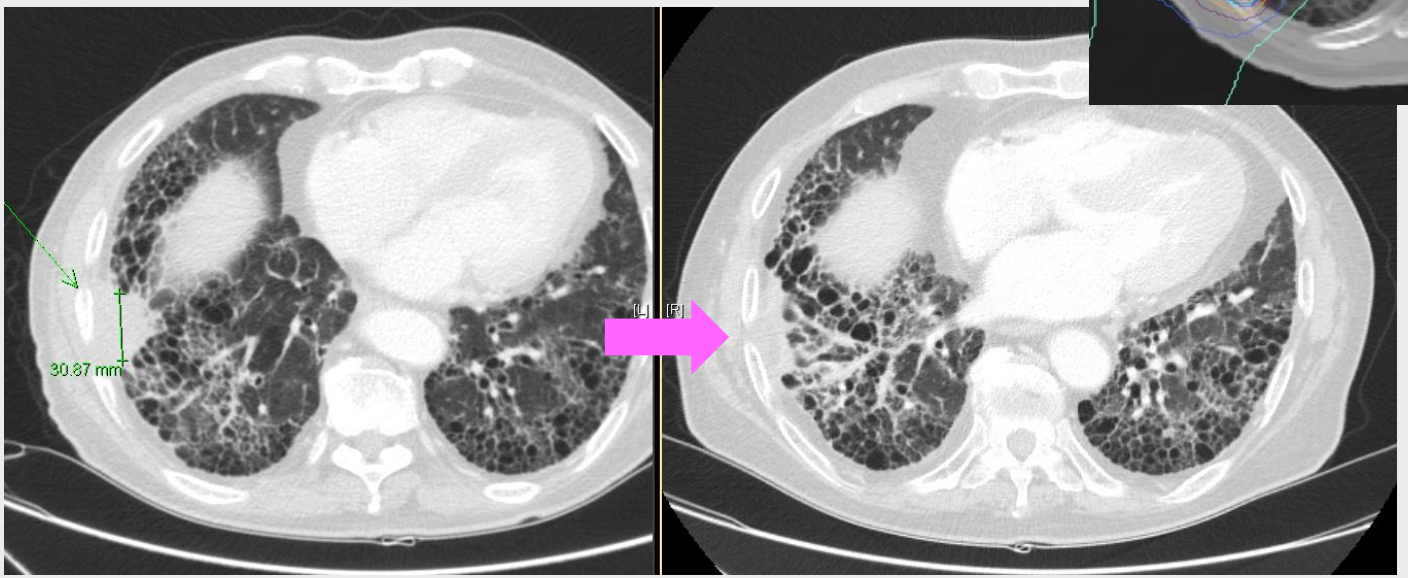
2017.3.17 2017.3.31

Proton Therapy for Patients with IPF

M/78

- Definitive PT 60 CGE/10fx (2017.4.19-5.4)
- Admission d/t radiation pneumonitis
  vs. IPF AE (2017.6.7-22)



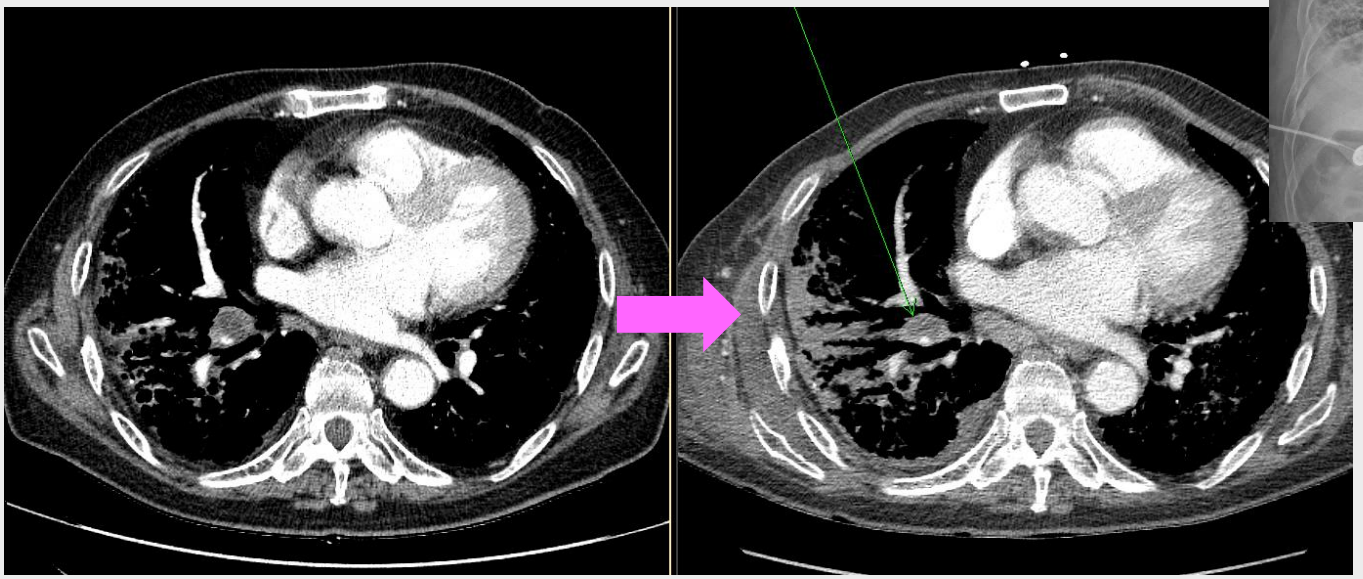


2017.5.31 2017.11.1

Proton Therapy for Patients with IPF

M/78

- PD with 10R LN with bronchopneumonia in both LL
  - GC #2 (2018.1.3-30)
  - Pembrolizumab #2 (2018.2.8-3.20)
- Expired d/t pneumonia (2018.4.21)

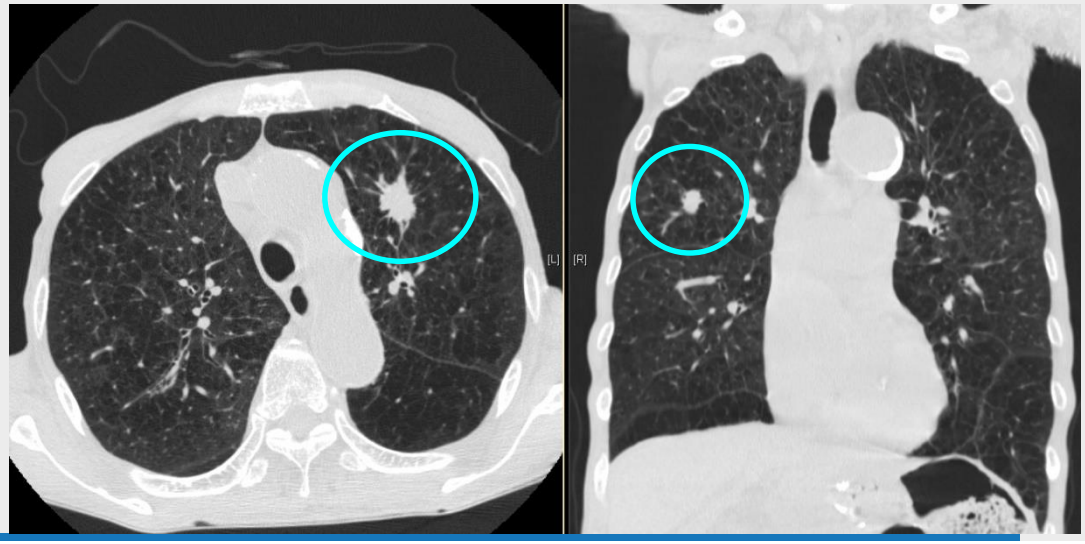


2017.11.1 2018.4.11

Patients with IPF

M/81

- r/o Lung cancer (RUL,LUL)
  - Underlying COPD
  - Both EIA, CFA stenosis
  - Stomach cancer, s/p STG B-I (2005.2.7)
- PFT (2018/1/22): FEV1 0.75L (36%)
- 체중 32 kg



2018.2.1

SBRT for Patients with ILD (IPF)

Summary

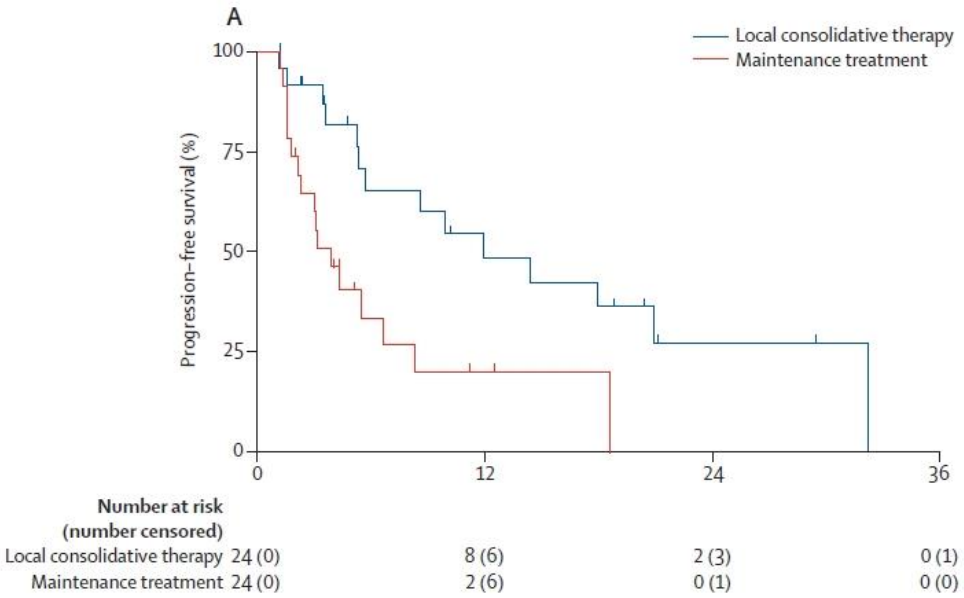
- SBRT for patients with ILD (IPF) should be used with great caution.
  - Patient selection is very important.
  - **Life expectancy** should be considered.
  - Proton therapy (SBPT) could be an useful option.

- 심한 폐기능 저하, 만성폐쇄성 질환 혹은 폐섬유화증을 가진 폐암 환자에서의 양성자치료 – 전향적 임상 연구
  - 병리학적으로 진단된 원발성 비소세포폐암 환자
  - 폐기능이 FEV1 ≤1.0 L or DLCO ≤50% or PF 진단 (폐섬유화증 여부는 호흡기내과 진료 확인 필요)

SBRT for Oligo-metastatic NSCLC

Multicentre, randomized, controlled, phase 2 study

- Stage IV NSCLC (≤3 metastatic lesions)
- No progression after 1st-line systemic therapy
- Local consolidative therapy vs. Maintenance treatment alone
- Primary endpoint: PFS → Median 11.9 vs. 3.9 months (p=0.0054)
- Adverse events: Similar



Lancet Oncol 2016;17:1672-82

SBRT for Oligo-metastatic NSCLC

Single center phase 2 randomized study

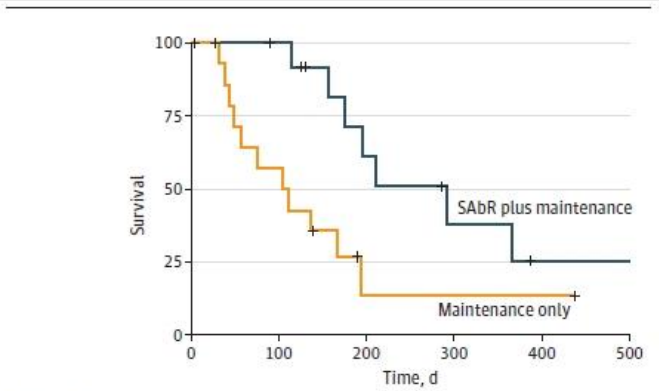
- Stage IV NSCLC (≤5 metastatic lesions) without driver mutation
- SD or PR after 4-6 cycles platinum chemotherapy
- SBRT before maintenance treatment
- Primary endpoint: PFS → Median 9.7 vs. 3.5 months (p=0.01)
- No difference in toxic effect

Table 3. Patterns of Failure by Treatment Assignment[a]

Site of Progression	SAbR Plus Maintenance, No.	Maintenance, No.
Brain	1	4
Liver	2	0
Lung	0	8
Bone	1	1
Pancreas	1	0
In-field	0	7

Abbreviation: SAbR, stereotactic ablative radiotherapy.

[a] Patients treated with SAbR had no failure within the treated field.



Log-rank testing reveals a statistically significant benefit in progression-free survival for SAbR-plus-maintenance chemotherapy (hazard ratio, 0.304; 95% CI, 0.113-0.815; *P* = .01). SAbR indicates stereotactic ablative radiotherapy.

JAMA Oncol 2018;4:1e173501