Survivorship issues after stereotactic ablative RT for early-stage NSCLC

Predicting survival following SABR in early-stage NSCLC

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15-18 April 2015, Geneva, Switzerland

Organisers

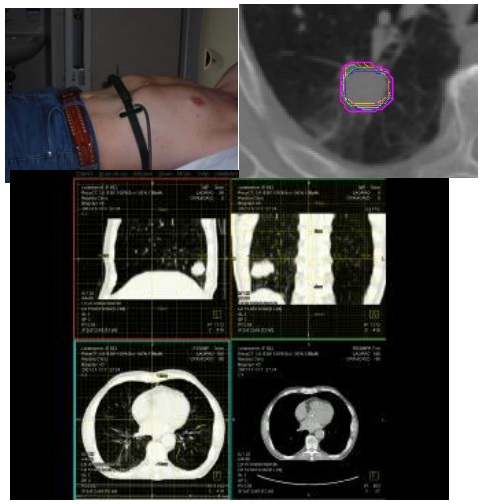
Partners

- I have no conflicts of interest to disclose

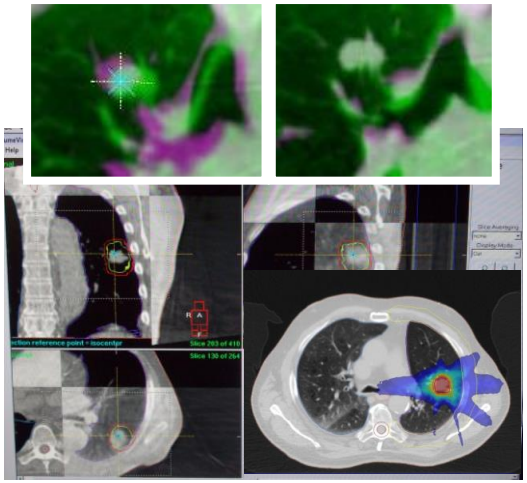
SBRT

A technique for delivering external beam radiotherapy

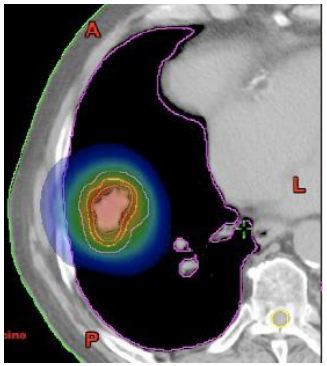
i. with a high degree of accuracy to an extra-cranial target,
ii. using high doses of irradiation,
iii. in 1-8 treatment fractions.

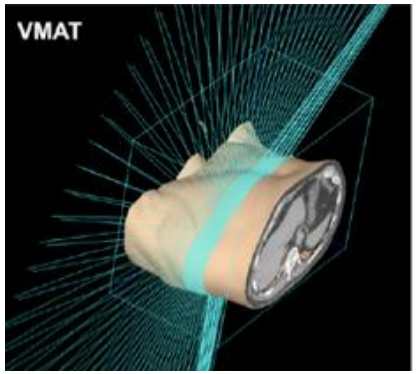


4-D imaging



Sophisticated plans
CT scan on treatment couch

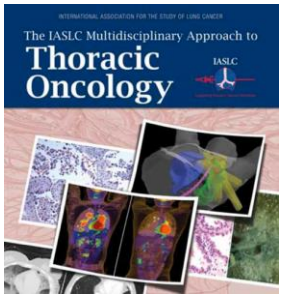




Delivery in <4 mins (FFF)

S. Senan, M. Guckemberger, U. Ricardi

IASLC Textbook Multidisciplinary approach to Thoracic Oncology, 2014



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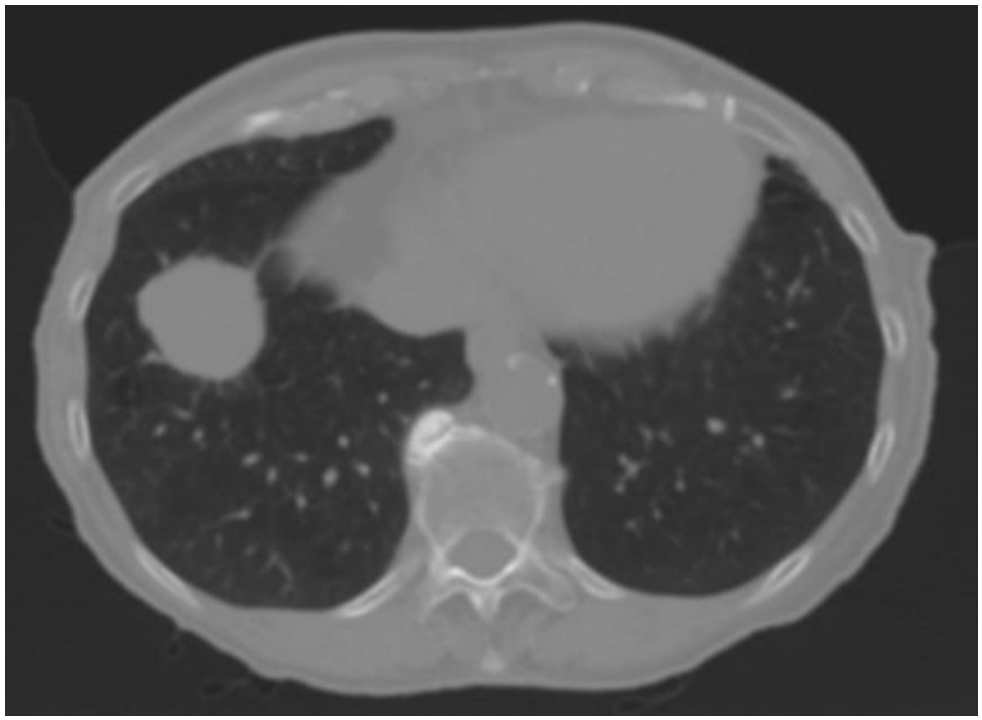
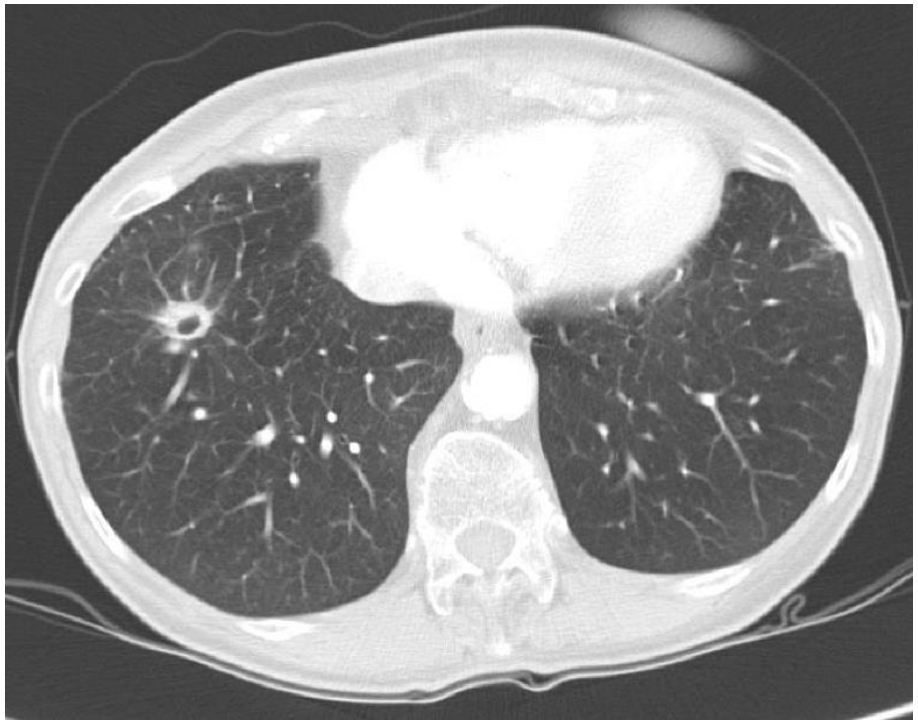
From SBRT to **SABR**
(Stereotactic ABlative Radiotherapy)





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SBRT in peripheral stage I a- I b NSCLC

Table 1. Summary of Results of Recently Reported Prospective Trials of SBRT for Stage I NSCLC

Author (Year)	Type/Stage	No. of Patients	Dose	Median Follow-up	Outcomes
Fakiris (Fakiris et al., 2009)	Phase II/Medically inoperable T1-2N0M0 NSCLC	70	T1: 20 Gy x 3 T2: 22 Gy x 3	50.2 months	3-year LC: 88.1% 3-year OS: 42.7% 3-year CaSS: 81.7%
Baumann (Baumann et al., 2009)	Phase II/Medically inoperable stage I NSCLC	57	15 Gy x 3 to 67%	35 months	3-year LC: 92% 1-, 2-, and 3-year OS: 86%, 65%, and 60% 1-, 2-, and 3-year CaSS: 93%, 88%, and 88% 3-year PFS: 52%
Koto (Koto et al., 2007)	Phase II/Stage I NSCLC	31	15 Gy x 3 (45 Gy) and 7.5 Gy x 8 (60 Gy)	32 months	3-year LC: 77.9% for T1 and 40% for T2 3-year OS: 71.7% 3-year CSS: 83.5%
Ricardi (Ricardi et al., 2010)	Phase II/Stage I NSCLC	62	15 Gy x 3	28 months	3-year LC: 87.8% 3-year CSS: 72.5% 3-year OS: 57.1%
Timmerman (Timmerman et al., 2010)	RTOG Phase II/ Medically inoperable T1-2N0M0 NSCLC (peripherally located)	55	18 Gy x 3	34.4 months	3-year LC: 97.6% 3-year DFS: 48.3% 3-year OS: 55.8%

Abbreviations: LC, local control; OS, overall survival; CSS, cause-specific survival; CaSS, cancer-specific survival; DFS, disease-free survival.

Loo et al, Discovery Medicine 2011

Need for pre-treatment pathology prior to SABR

- Models to predict the probability of malignancy using clinical, CT and FDG-PET features of a solitary pulmonary nodule (SPN) have been developed
- Caution should be employed however if such models have not been validated for specific geographic regions of practice
- A likelihood of malignancy threshold of 85% has been suggested prior to treatment of a SPN without pathologic confirmation of malignancy

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Studies demonstrating the variable rates of pathologic confirmation worldwide prior to SABR in ES-NSCLC

Reference	Study type	N° of patients	Region	% biopsy	Overall Survival
Haasbeek	Population registry	1570	Netherlands	72	50% (2 yrs)
Ricardi	Retrospective	196	Italy	100	68% (3 yrs)
Guckenberger	Retrospective	591	Central Europe	85	47% (3 yrs)
Grills	Retrospective	505	United States Canada Netherlands Germany	87-95 72 41 70	48% (3 yrs)
Onishi	Retrospective	2278	Japan	73	91% (2 yrs)
Senthi	Retrospective	676	Amsterdam	35	41 mo (md)
Baumann	Prospective	57	Sweden Denmark Norway	67	60% (3 yrs)
Timmerman	Prospective	55	North America	100	56% (3 yrs)

[Louie et al, R&O 2015]

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Post-SABR recurrences (676 patients)

	Local	Regional	Distant
Actuarial 2-year rates	4.9%	7.8%	14.7%
Actuarial 5-year rates	10.5%	12.7%	19.9%

	Median time to event
Local recurrence	14.9 months (95% CI 11.4-18.4)
Regional recurrence	13.1 months (95% CI 7.9-18.3)
Distant recurrence	9.6 months (95% CI 6.8-12.4)
2nd primary tumors	18 months (95% CI 12.5-23.5)

- Stage I-II NSCLC (2003-2011); median follow-up 32.9 months (IQR 14.9 - 50.9);
- 66% of recurrences were distant (DR); isolated DR made up 46% of recurrences

Senthi S, Lancet Oncol 2012

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Int. J. Radiation Oncology Biol. Phys., Vol. 77, No. 4, pp. 1146–1150, 2010

0360-3016/$–see front matter

doi:10.1016/j.ijrobp.2009.06.017

CLINICAL INVESTIGATION **Lung**

STEREOTACTIC BODY RADIATION THERAPY FOR EARLY-STAGE NON–SMALL-CELL LUNG CANCER: THE PATTERN OF FAILURE IS DISTANT

Jeffrey D. Bradley, M.D.,* Issam El Naqa, Ph.D.,* Robert E. Drzymala, Ph.D.,* Marco Trovo, M.D.,† Griffin Jones,* and Mary Dee Denning, R.N.*

Radiotherapy and Oncology 94 (2010) 1–11

ELSEVIER

Contents lists available at ScienceDirect

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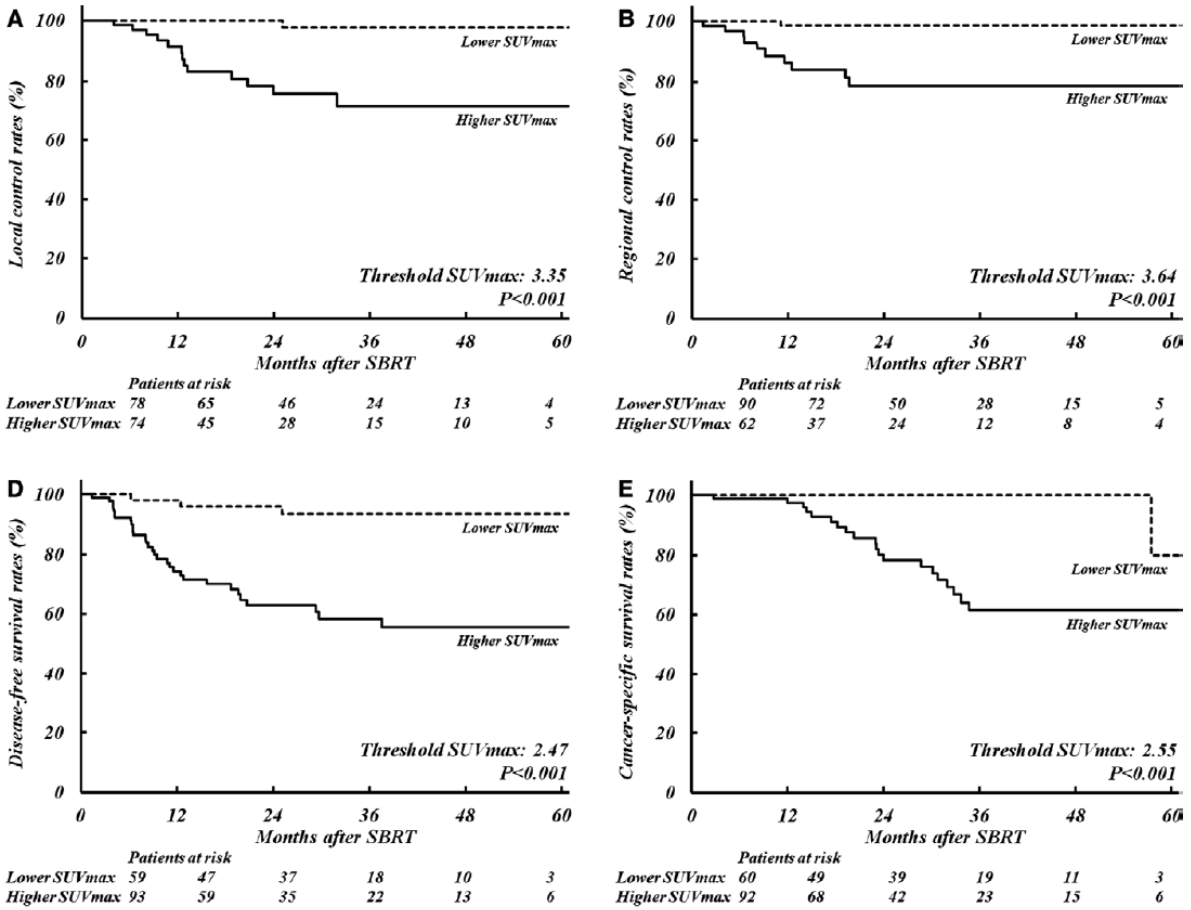
journal homepage: www.thegreenjournal.com

Systematic review

Systemic review of the patterns of failure following stereotactic body radiation therapy in early-stage non-small-cell lung cancer: Clinical implications

Alexander Chi [a,*], Zhongxing Liao [b], Nam P. Nguyen [a], Jiahong Xu [c], Baldassarre Stea [a], Ritsuko Komaki [b]

Maximum Standardized Uptake Value on FDG-PET Is a Strong Predictor of Overall and Disease-Free Survival for Non–Small-Cell Lung Cancer Patients after Stereotactic Body Radiotherapy

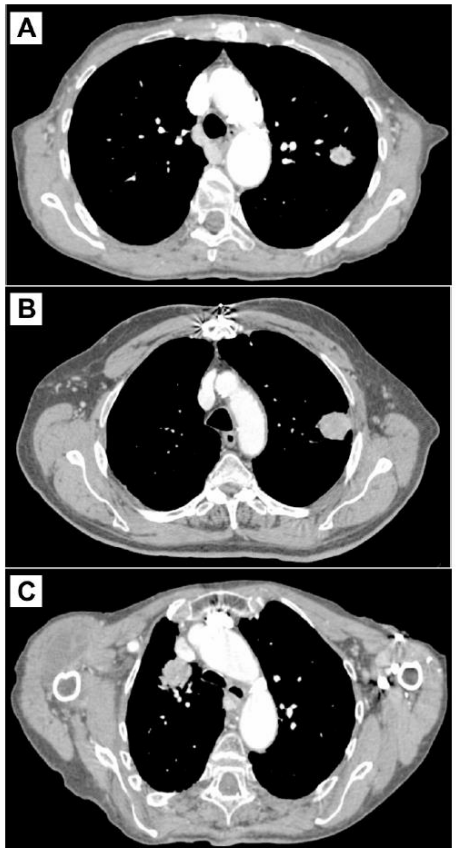


[Takeda et al, JTO 2014]

Imaging Features Associated With Disease Progression After Stereotactic Ablative Radiotherapy for Stage I Non–Small-Cell Lung Cancer

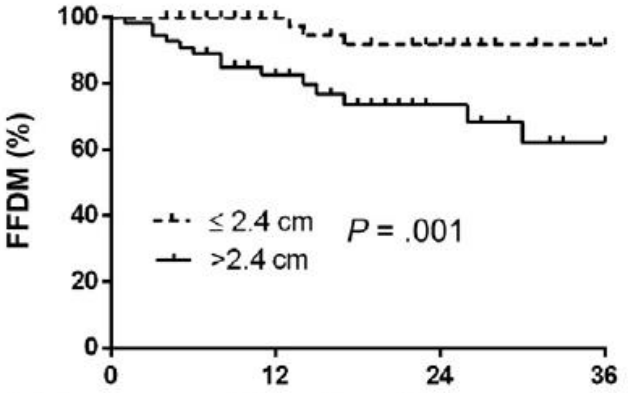
Clinical Lung Cancer July 2014

David B. Shultz,[1] Nicholas Trakul,[1] Jonathan A. Abelson,[1] James D. Murphy,[1] Peter G. Maxim,[1,2] Quynh-Thu Le,[1,2] Billy W. Loo, Jr,[1,2] Maximilian Diehn[1,2,3]



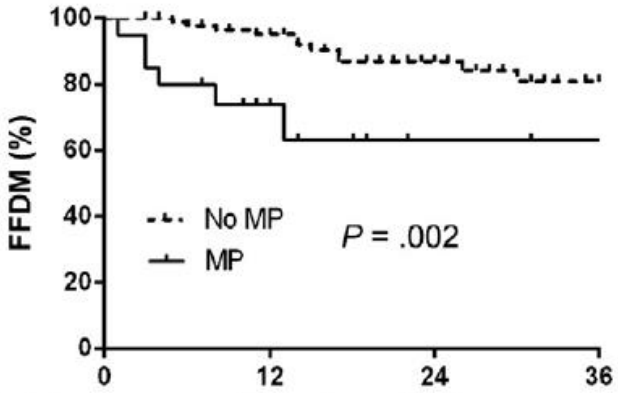
	Univariate				Multivariate[a]	
Tumor Variable	**FFLP**	**FFRP**	**FFDM**	**OS**	**FFDM**	**OS**
Maximum Tumor Dimension[b]						
	.374	.328	**.037** (HR, 5.33; 95% CI, 1.72-16.47)	.1085	**.014** (HR, 5.26; 95% CI, 1.41-19.70)	
BED_{10}-LQ, Gy						
	.452	.580	.182	**.0353** (HR, 0.99; 95% CI, 0.98-1.0)	—	.427
BED_{10}-LQ-L, Gy						
	.435	.331	.696	.14	—	—
Contact with CWP						
	.361	.676	.091	.804	—	—
Contact with MP						
	.478	.166	**.005** (HR, 4.24; 95% CI, 1.55-11.62)	**.005** (HR, 3.40; 95% CI, 1.70-6.77)	**.001** (HR, 7.51; 95% CI, 2.41-23.42)	**.002** (HR, 3.58; 95% CI, 1.63-7.87)
Central versus Peripheral[c]						
	.430	.302	**.013** (HR, 3.20; 95% CI, 1.27-8.01)	**.044** (HR, 1.89; 95% CI, 1.02-3.94)	—	—
SUVmax						
	.894	.413	**.018** (HR, 1.09; 95% CI, 1.01-1.17)	**.009** (HR, 1.07; 95% CI, 1.02-1.12)	**.053** (HR, 1.08; 95% CI, 1.00-1.16)	**.011** (HR, 1.07; 95% CI, 1.02-1.12)
Arc-Based versus CyberKnife Treatment						
	.038 (HR, 0.238; 95% CI, 0.06-0.92)	.416	.842	.740	—	—
Nonsquamous Histology						
	.866	.136	.435	.656	—	—

A Maximum tumor dimension



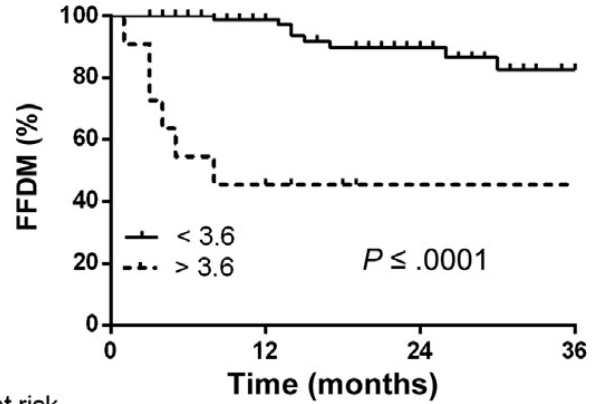
No. at risk				
≤ 2.4 cm	60	43	25	16
> 2.4 cm	57	35	15	10

B Contact with the pleura adjacent to the mediastinum



No. at risk				
No MP	97	69	37	19
MP	20	9	3	2

D Distant metastasis risk score



No. at risk				
≤ 3.6	91	65	32	15
>3.6	11	5	2	2

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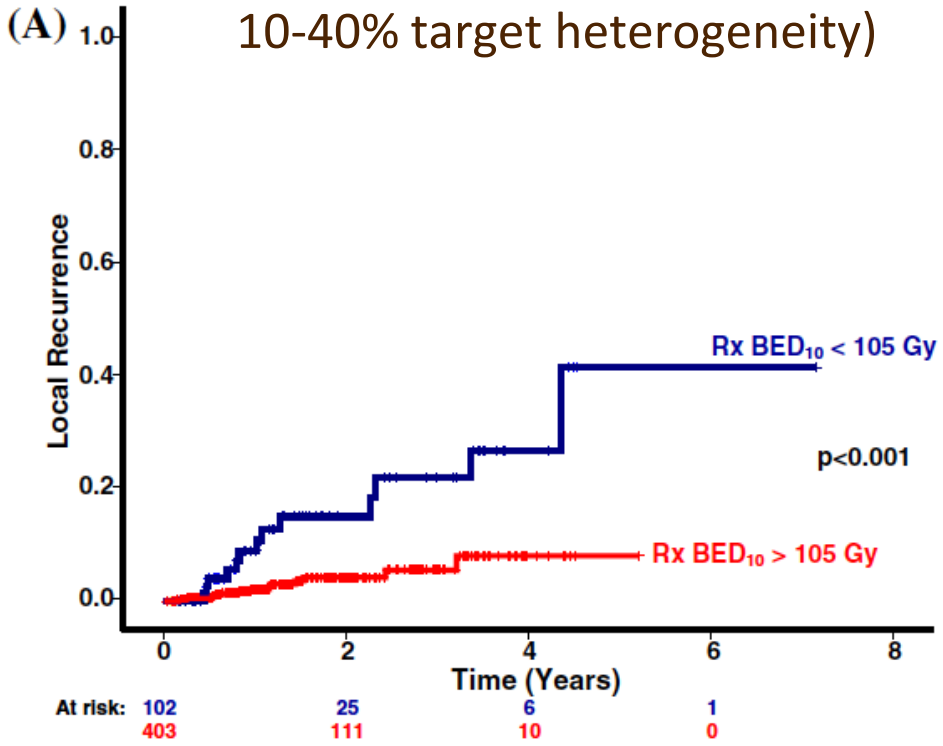
Dose-response in SBRT

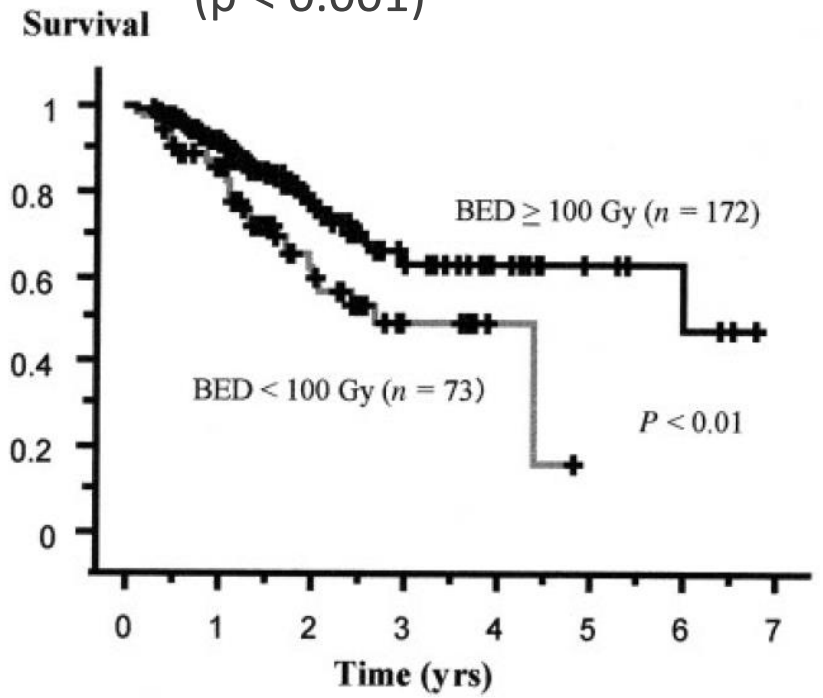
Prescription to the edge of the PTV (60-90% of the isocenter dose;
10-40% target heterogeneity)



Kestin et al, R&O, 2014

The BED_{10} was based on prescription dose at isocenter

5-year local control rate: 84% for BED_{10} > 100 Gy vs 37% for BED_{10} < 100 Gy
($p < 0.001$)



Onishi et al, Cancer 2004

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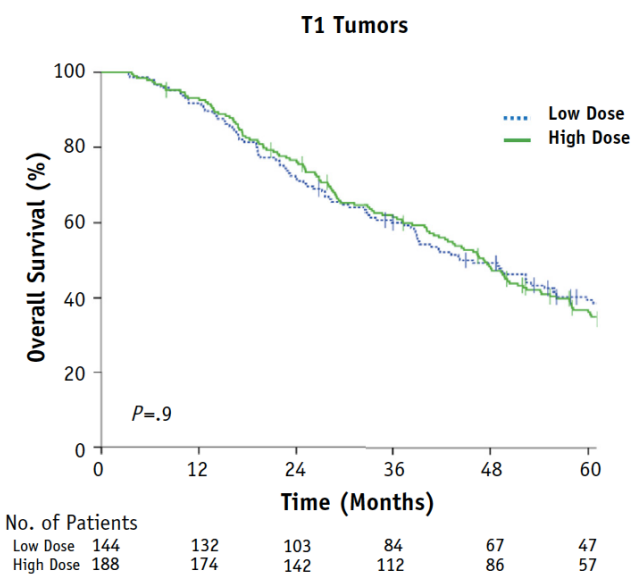
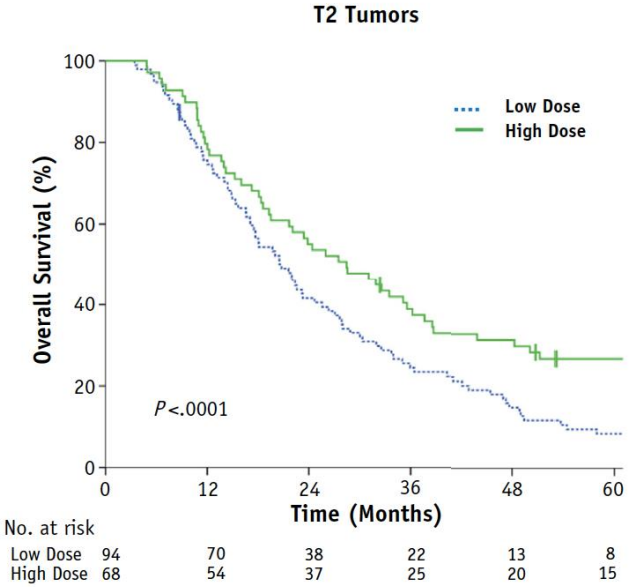
Increasing Radiation Therapy Dose Is Associated With Improved Survival in Patients Undergoing Stereotactic Body Radiation Therapy for Stage I Non–Small-Cell Lung Cancer

Matthew Koshy, MD,*,† Renuka Malik, MD,†
Ralph R. Weichselbaum, MD,*,† and David J. Sher, MD, MPH‡

Int J Radiation Oncol Biol Phys, Vol. 91, No. 2, pp. 344–350, 2015





Summary

We examined different stereotactic body radiation therapy dosing regimens using a large national database, focusing on the relative impact of dose as a function of tumor stage. This analysis found that patients with T2 tumors treated with a biologically effective dose >150 Gy had a significantly improved survival compared with patients treated with a biologically effective dose <150 Gy.

The median calculated BED of the cohort was 150 Gy, which is roughly equal to 54 Gy in 3 fractions

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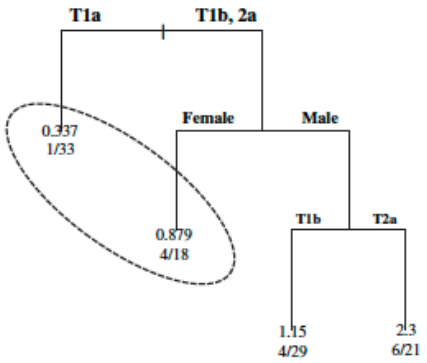
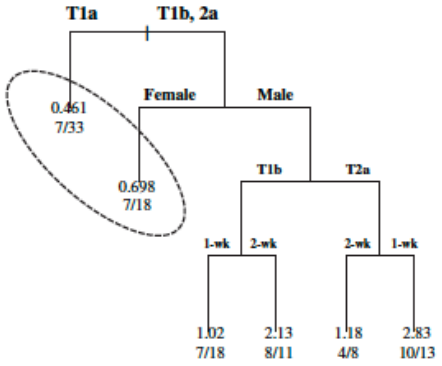
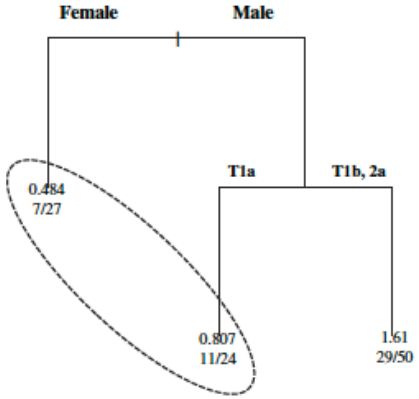
PROGNOSTIC FACTORS IN STEREOTACTIC BODY RADIOTHERAPY FOR NON–SMALL-CELL LUNG CANCER



a) Local progression



b) Disease progression



c) Overall survival

Conclusions: Tumor diameter and sex were the most significant factors in SBRT for NSCLC. T1a or female patients had good prognosis. © **2011 Elsevier Inc.**

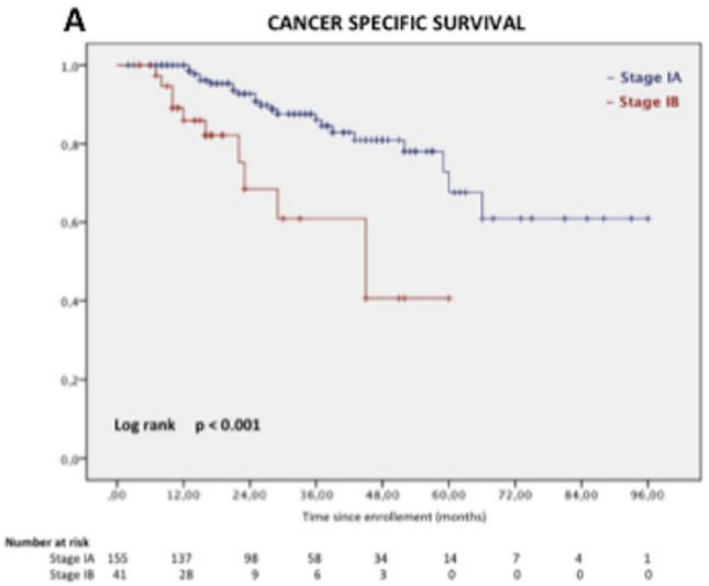
[Matsuo et al, IJROBP 2011]

Stereotactic Ablative Radiotherapy for stage I histologically proven non-small cell lung cancer: An Italian multicenter observational study

Table 3
Multivariate analysis.

Parameter	LR		DFS		OS		CSS	
	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*	HR (95% CI)	*p*
Stage								
IB vs IA	0.55 (0.03–10.3)	0.69	3.06 (1.62–5.77)	0.001*	2.46 (1.28–4.74)	0.007*	3.47 (1.50–7.98)	0.003*
GTV volume								
>13 cc vs ≤13 cc	4.4 (0.73–26.7)	0.1	1.04 (0.57–1.88)	0.89	1.04 (0.59–1.82)	0.89	1.37 (0.59–3.16)	0.45
Sex								
Male vs Female	0.5 (0.08–3.2)	0.47	1.05 (0.57–1.92)	0.87	0.94 (0.51–1.74)	0.86	0.79 (0.31–1.98)	0.61
Age								
>75 years vs ≤75 years	0.6 (0.15–2.57)	0.52	1.39 (0.83–2.36)	0.21	1.39 (0.83–2.32)	0.2	1.28 (0.63–2.61)	0.49
Histology								
Adenocarcinoma vs others	2.42 (0.39–14.84)	0.34	1.12 (0.64–1.97)	0.68	1.21 (0.68–2.16)	0.8	1.17 (0.52–2.61)	0.69

Abbreviations: LR, local recurrence; DFS, disease-free survival; OS, overall survival; CSS, cancer-specific survival; HR, hazard ratio; CI, confidence interval.
* Statistically significant.



Ricardi et al, Lung Cancer 2014

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Safety and Efficacy of Stereotactic Body Radiotherapy for Stage I Non–Small-Cell Lung Cancer in Routine Clinical Practice

A Patterns-of-Care and Outcome Analysis

TABLE 3. Multivariate Analysis of Factors Influencing OS and FFLP

		OS			FFLP		
Parameter		***p***	**HR**	**95% CI**	***p***	**HR**	**95% CI**
Performance status	<80	0.02	1.44	1.05 to 1.97			
Clinical stage	IB	0.007	1.52	1.12 to 2.07	0.08	1.66	0.95 to 2.92
Baseline FEV_1 (%)	Continuous variable	0.07	0.99	0.99 to 1.00			
Biopsy status	No biopsy	0.09	1.49	0.94 to 2.35	0.02	2.53	1.17 to 5.48
Staging FDG-PET	Yes				>0.1		
Histology	SCC				0.03	2.03	1.06 to 3.89
PTV-encompassing dose (Gy BED)	≥106	0.01	0.62	0.43 to 0.90	0.04	0.39	0.16 to 0.93
Dose inhomogeneity (PTV-encompassing dose / maximum dose) (%)	≥ 80				0.06	1.74	0.98 to 3.08
IGRT technology	In-room IGRT				>0.1		
SBRT procedures/institution and year	<9	>0.1			>0.1		

OS, overall survival; CI, confidence interval; FFLP, freedom from local progression; HR, hazard ratio; FEV_1, forced expiratory volume in 1 second; SCC, spindle cell carcinoma; SBRT, stereotactic body radiotherapy; BED, biological effective dose; FDG-PET, fluoro-deoxy-glucose positron emission tomography; IGRT, image-guided radiotherapy; PTV, planning target volume.

[Guckenberger et al, JTO 2013]

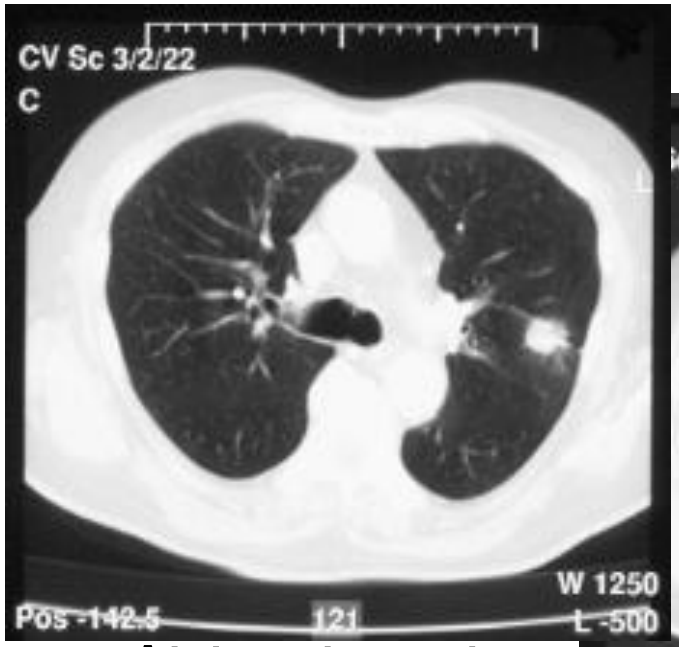
The effect of tumor size on curability of stage I NSCLC (7620 resected pts)

Survival rates @ 12 yrs

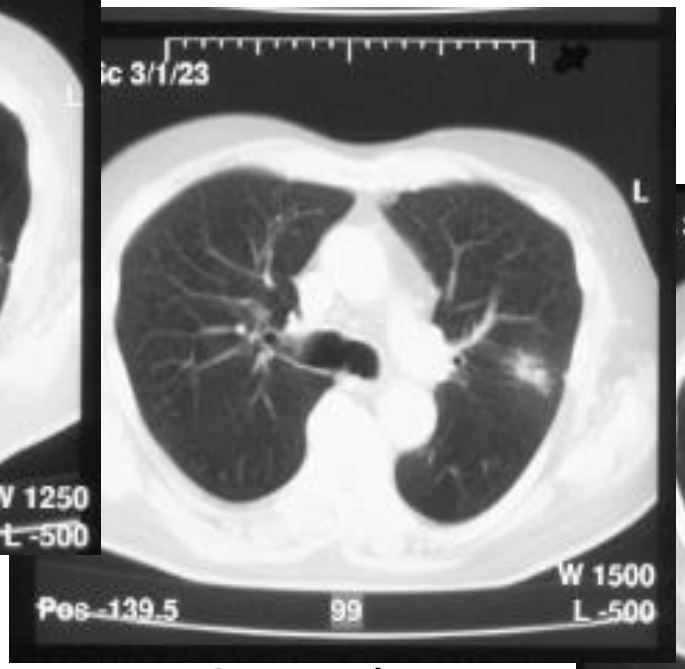
5-15 mm	69%
16-25 mm	63%
26-35 mm	58%
36-45 mm	53%
>45 mm	43%

Wisnivesky JP et al., Chest, 2005

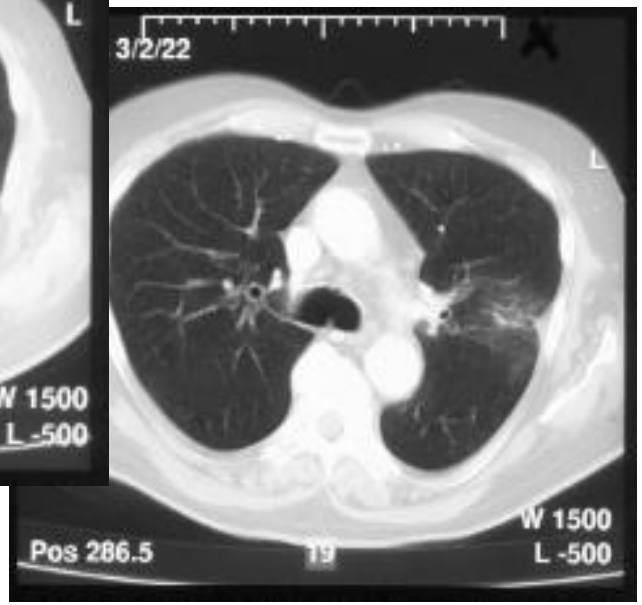
SBRT: treatment response



At treatment



At 3 months



At 130 months

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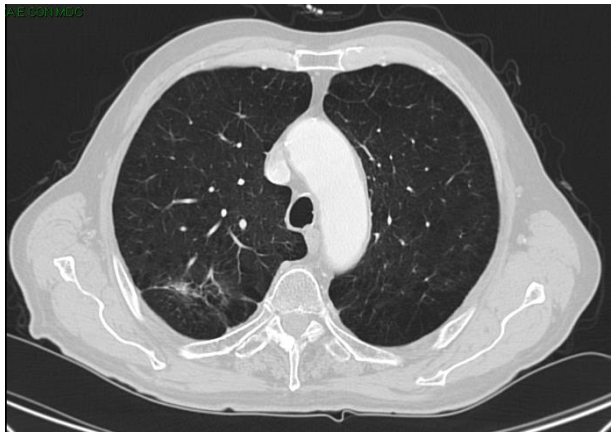
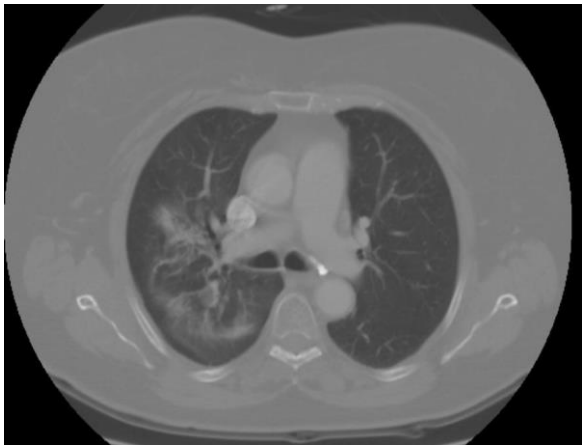
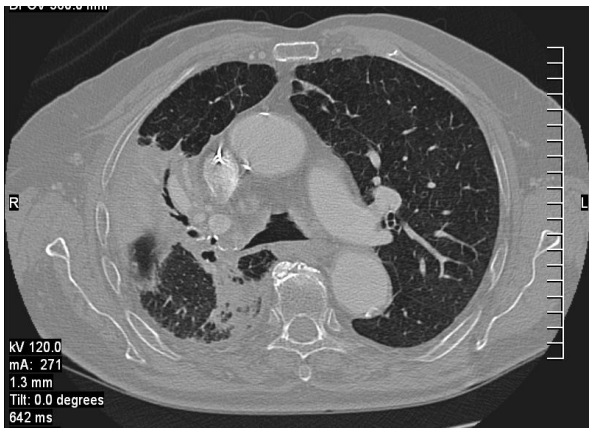
Acute radiological changes after SBRT

- Diffuse consolidation 20-30%
  (consolidation more than 5 cm in largest dimension)
- Patchy consolidation 8-22%
  (consolidation less than 5 cm in largest dimension)
- Diffuse ground glass opacities 4-8%
  (more than 5 cm of GGO)
- Patchy ground glass opacities 10-15%
  (less than 5 cm of GGO)
- No evidence of increased density 20-40%



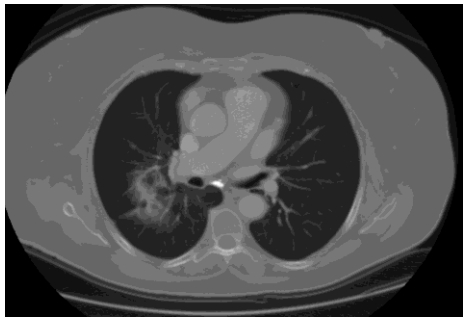




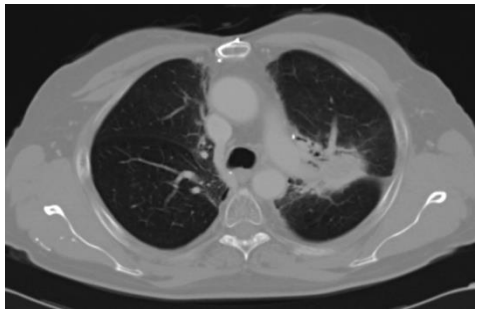
Late radiological changes after SBRT

Radiation fibrosis (later than 6 months)
(Koenig's classification, AJR 2002):

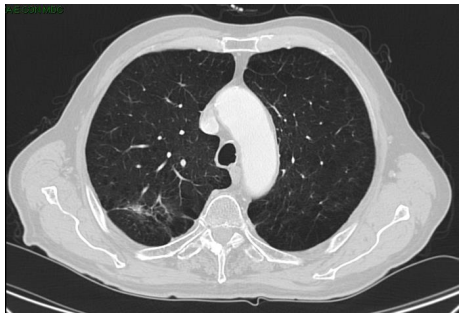
- Modified conventional pattern
- Mass-like pattern
- Scar-like pattern



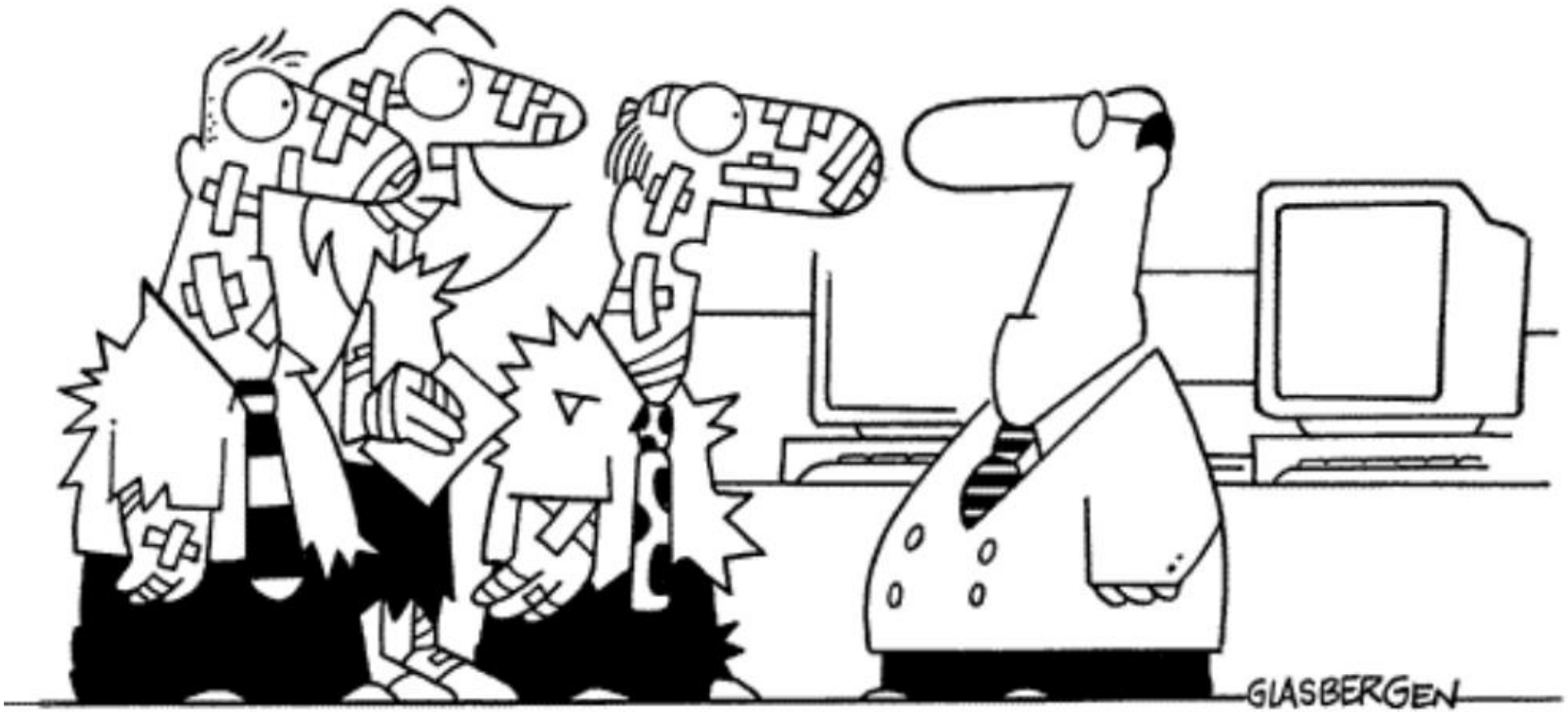
Modified conventional pattern



Mass-like pattern



Scar-like pattern



"Frankly sir, we're tired of being on the cutting edge of technology."

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SABR is well tolerated: toxicity is uncommon

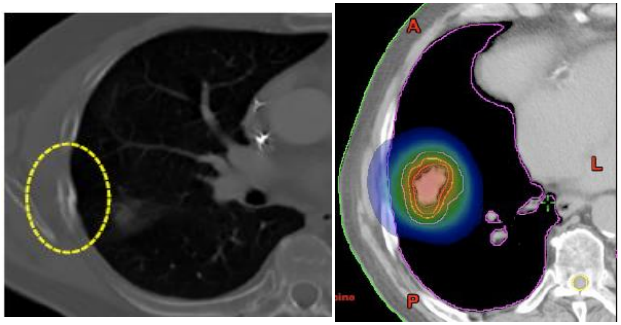
Grills IS, JTO 2012

- 505 lung tumors in 483 patients
- Median time to pneumonitis: 0.4 years

Pneumonitis grade	incidence
Grade 2 or higher	***7%***
Grade 3 or higher	2%
Grade 5	***0.2%***

Bongers E, 2011

- 500 pts with T1-2N0 tumors (2003-2009)
- Median follow-up 33 months (13-86 months)
- Severe chest wall toxicity uncommon
  - severe pain in 2.2%,
  - rib fractures in 2.7%



Japanese multi-institution analysis

Radiation pneumonitis ≥Grade 3 (CTCAE V3.0)

subgroup	Grade 3,4,5	Grade 5
All patients (n= 2278 pts)	***3.3%***	***0.6%***
Operable patients (n= 683 pts)	***1.9%***	***0.4%***
Pulmonary emphysema (+) (n= 449 pts)	***4.4%***	***1.1%***
Pulmonary fibrosis (+) (n= 243 pts)	***11.9%***	***5.9%***

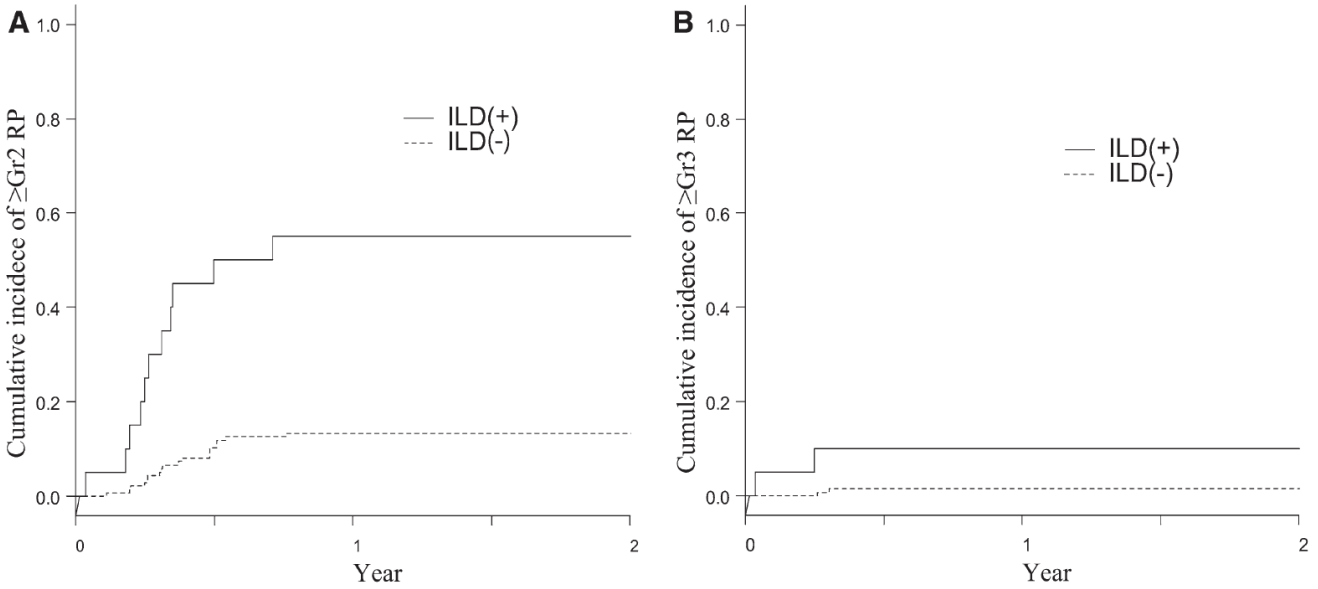
No pathological diagnosis: 606 pts

Onishi H, Proc ASTRO 2013

Impact of Pretreatment Interstitial Lung Disease on Radiation Pneumonitis and Survival after Stereotactic Body Radiation Therapy for Lung Cancer

Nami Ueki, MD, Yukinori Matsuo, MD, PhD,* Yosuke Togashi, MD,†‡ Takeshi Kubo, MD,§ Keiko Shibuya, MD, PhD,‖ Yusuke Iizuka, MD,* Takashi Mizowaki, MD, PhD,* Kaori Togashi, MD, PhD,§ Michiaki Mishima, MD, PhD,‡ and Masahiro Hiraoka, MD, PhD**

(*J Thorac Oncol.* 2015;10: 116–125)



Conclusions: Pre-existing ILD was a significant risk factor for symptomatic and severe RP. Prescreening for ILD findings is important for determining the radiation pneumonitis risk when planning SBRT.

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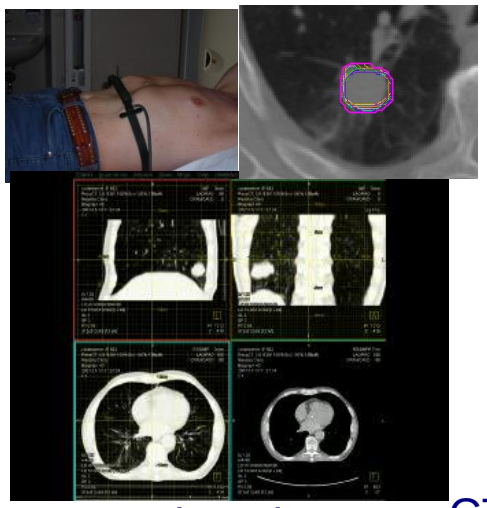
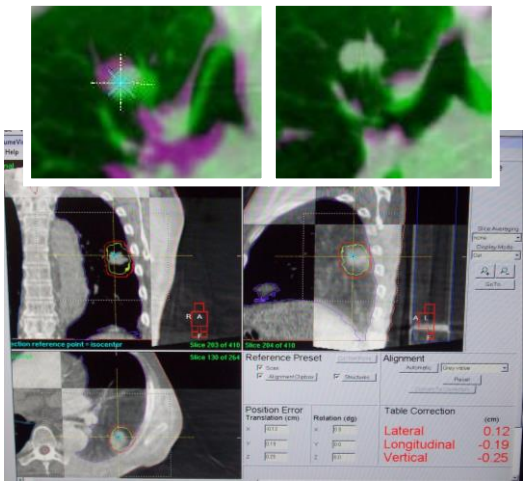
SBRT

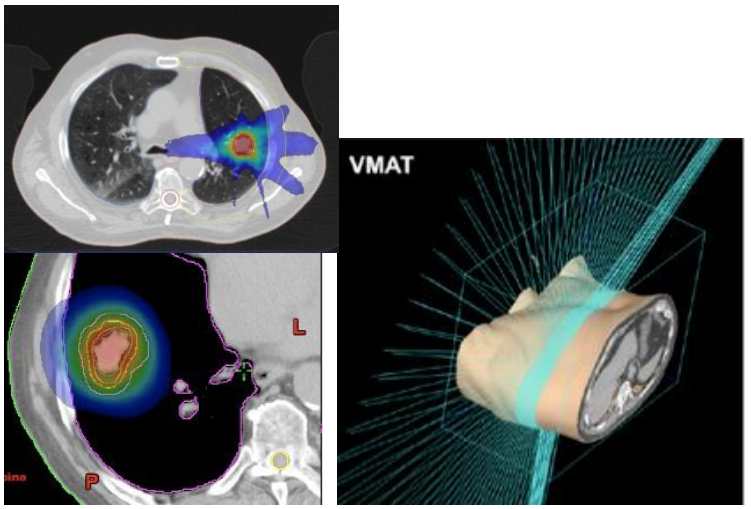
Efficacy and safety



4-D imaging



CT scan on treatment couch



Delivery in <4 mins (FFF)

SABR is the non-surgical treatment of choice in peripheral early stage NSCLC [NCCN guidelines 2014; ESMO Clinical Practice Guidelines 2013]

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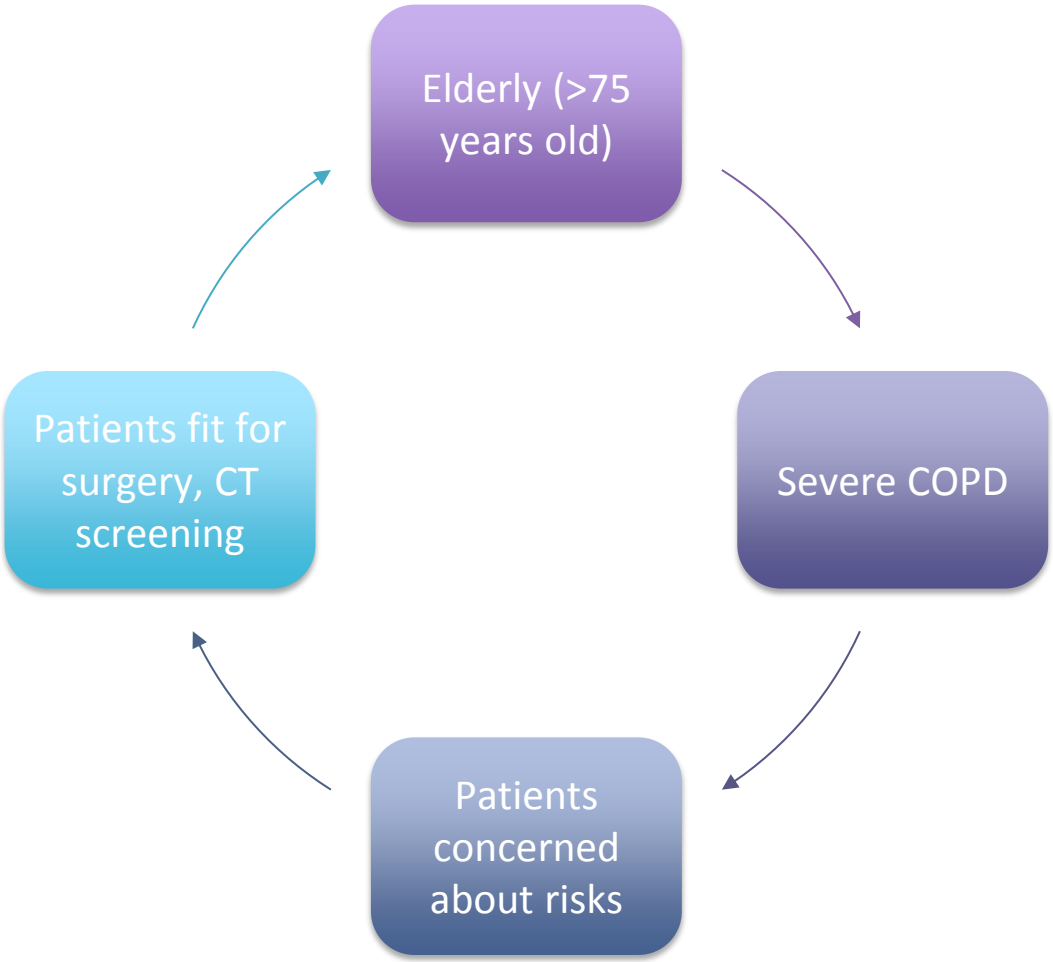
Treatment of early-stage lung cancer detected by screening: surgery or stereotactic ablative radiotherapy?

Suresh Senan, Marinus A Paul, Frank J Lagerwaard

Lancet Oncol 2013; 14: e270–74



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Clinical outcome after SBRT for early stage NSCLC

- SBRT in the elderly population, in patients with severe pulmonary comorbidities and in medically inoperable pts

  - ✓ SBRT is safely practiced in patients with severe pulmonary comorbidities and very poor pretreatment pulmonary function

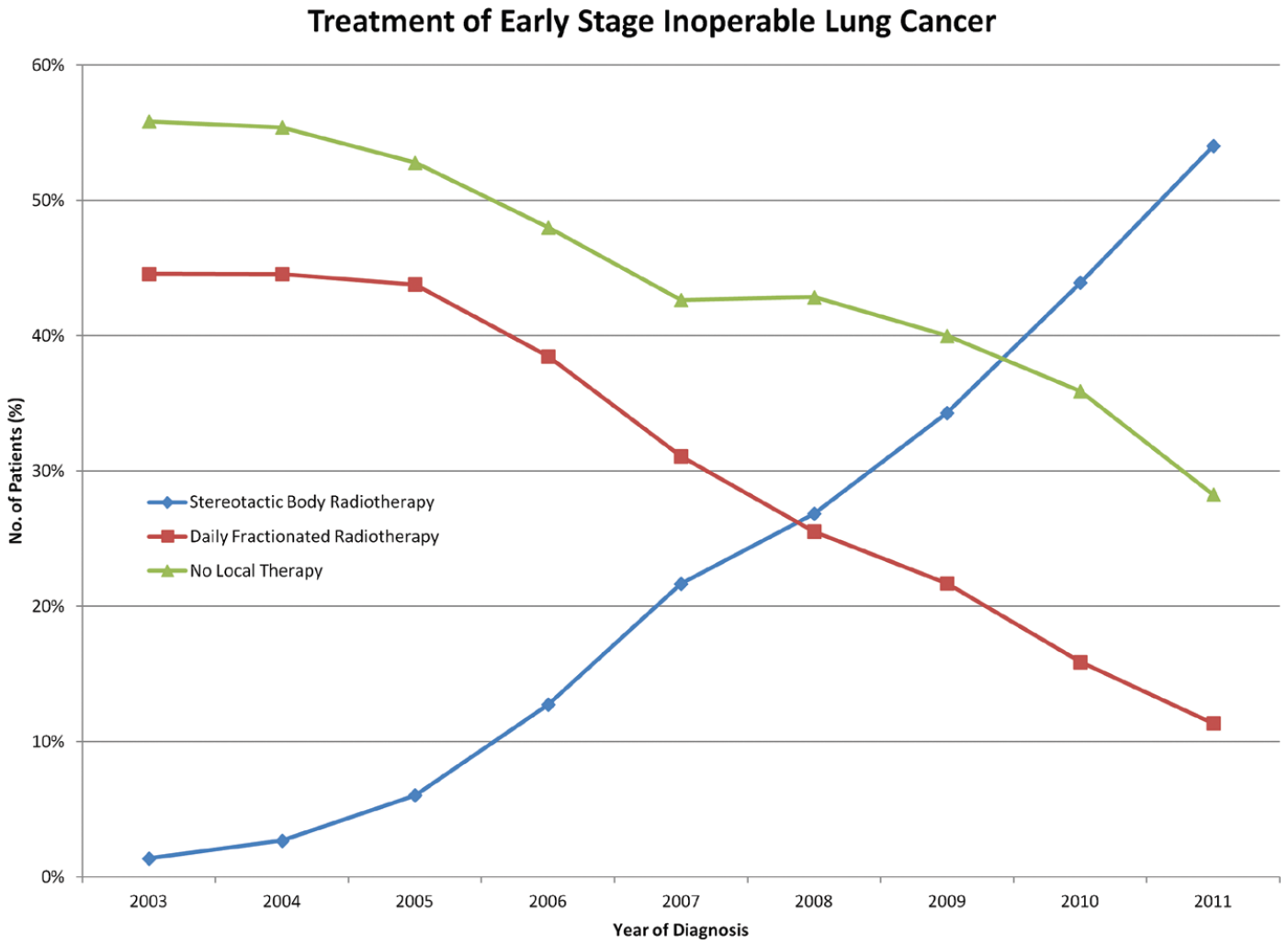
No Clinically Significant Changes in Pulmonary Function Following Stereotactic Body Radiation Therapy for Early-Stage Peripheral Non-Small Cell Lung Cancer: An Analysis of RTOG 0236

Sinisa Stanic

Int J Radiation Oncol Biol Phys, Vol. 88, No. 5, pp. 1092–1099, 2014

Conclusions: Poor baseline PFT did not appear to predict pulmonary toxicity or decreased overall survival after SBRT in this medically inoperable population. Poor baseline PFT alone should not be used to exclude patients with early stage lung cancer from treatment with SBRT.

Disparities in Treatment of Patients with Inoperable Stage I Non–Small Cell Lung Cancer: A Population-Based Analysis



[Koshy et al, JTO 2015]

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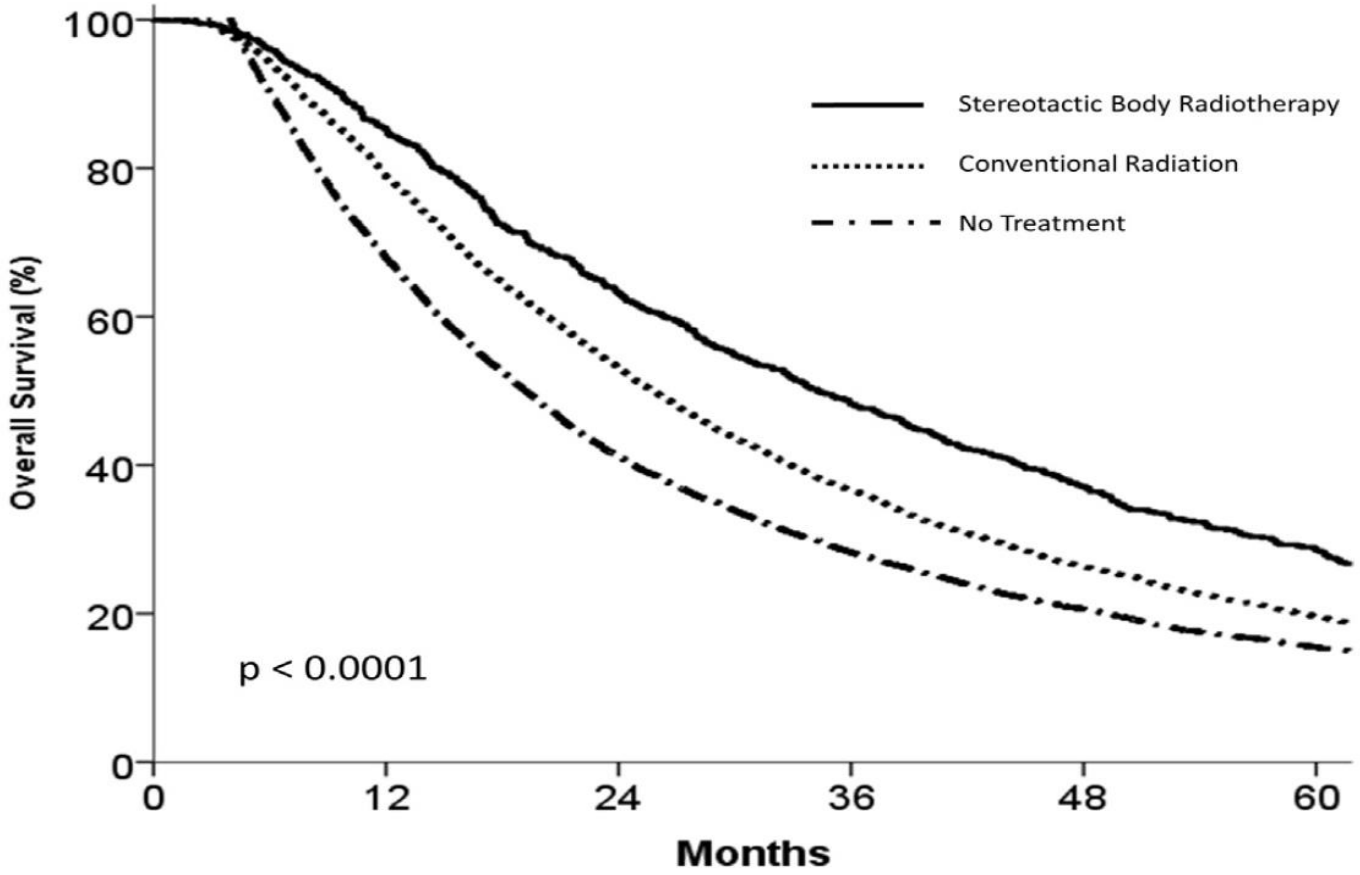
Overall survival among patients with inoperable stage I non-small cell lung cancer



No. of Patients

Stereotactic Body Radiotherapy	772	638	462	347	260	179
Conventional Radiation	5374	4146	2747	1887	1328	947
No Treatment	6887	4566	2698	1824	1284	897

[Koshy et al, R&O 2015]

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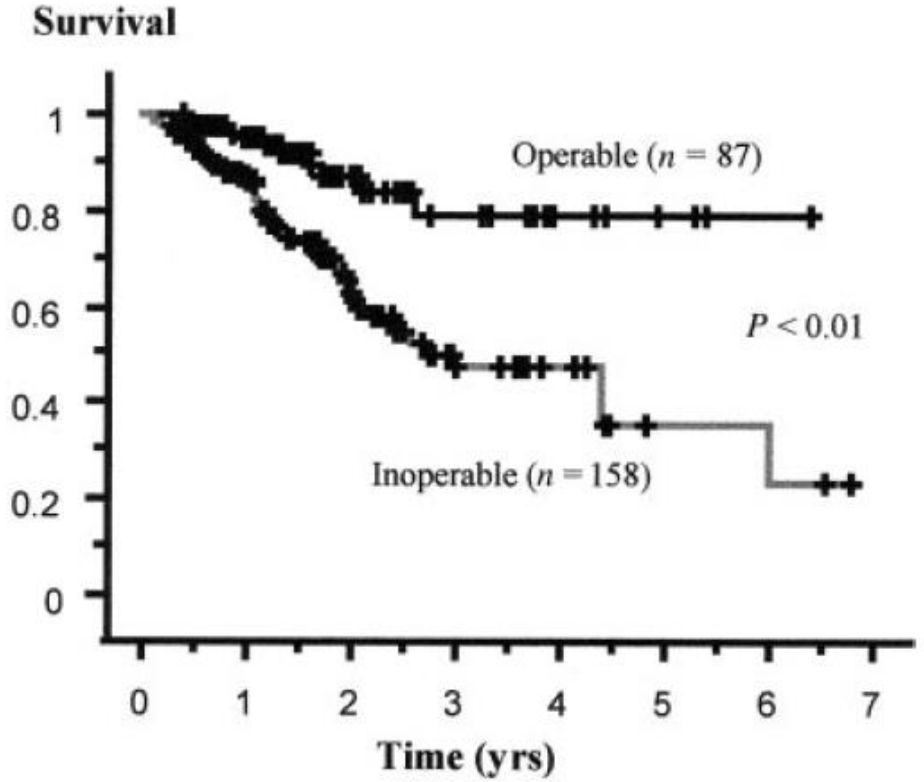
Clinical outcome after SBRT for early stage NSCLC and implications for patient selection

- SBRT vs. lobectomy for medically operable patients refusing surgical resection
  - Few studies (limited numbers of patients) after SBRT where surgical resection was refused by the patients

Hypofractionated Stereotactic Radiotherapy (HypoFXSRT) for Stage I Non-small Cell Lung Cancer: Updated Results of 257 Patients in a Japanese Multi-institutional Study

Hiroshi Onishi, MD, Hiroki Shirato, MD,† Yasushi Nagata, MD,† Masahiro Hiraoka, MD,‡ Masaharu Fujino, MD,† Kotaro Gomi, MD,§ Yuzuru Niibe, MD,|| Katsuyuki Karasawa, MD,|| Kazushige Hayakawa, MD,¶ Yoshihiro Takai, MD,# Tomoki Kimura, MD,** Atsuya Takeda, MD,†† Atsushi Ouchi, MD,‡‡ Masato Hareyama, MD,‡‡ Masaki Kokubo, MD,§§ Ryusuke Hara, MD,|||| Jun Itami, MD,|||| Kazunari Yamada, MD,¶¶ and Tsutomu Araki, MD**



CANCER October 1, 2004 / Volume 101 / Number 7

J Thorac Oncol. 2007 Jul;2(7 Suppl 3):S94-100

Phase III RCT of Surgery versus SABR

Table 1 – Approved Phase III Randomized Trials of Operable Stage I NSCLC Patients (all prematurely terminated due to poor accrual)

Dutch ROSEL trial, NCT00687986, "Randomized Clinical Trial of Stereotactic Radiotherapy or Surgery in Patients with Stage IA Non-Small Cell Lung Cancer who are fit to undergo Primary Resection".

- Sponsored by the The Netherlands Organisation for Health Research and Development.
- Opened at 9 centers
- Opened 2008, Closed 2010
- Enrolled 22 of 960

STARS Trial, NCT00840749, "Randomized Study to Compare CyberKnife to Surgical Resection in Stage I Non-small Cell Lung Cancer"

- Sponsored by Accuray©
- Opened at 15 centers
- Opened 2009, Closed 2013
- Enrolled 36 of 1,030 patients

ACOSOG-Z4099/RTOG-1021, NCT01336894, "A Randomized Phase III Study of Sublobar Resection (+/- Brachytherapy) versus Stereotactic Body Radiation Therapy in High Risk Patients with Stage I Non-Small Cell Lung Cancer (NSCLC)"

- Sponsored by American College of Surgeons
- Opened at 53 centers
- Opened 2011, Closed 2013
- Enrolled 10 of 420 patients

Absence of **randomized data** does not imply the **absence of evidence**, and we must rely on other forms of **comparative effectiveness research** to inform clinical practice [Louie AV, Lancet Oncol 2013]

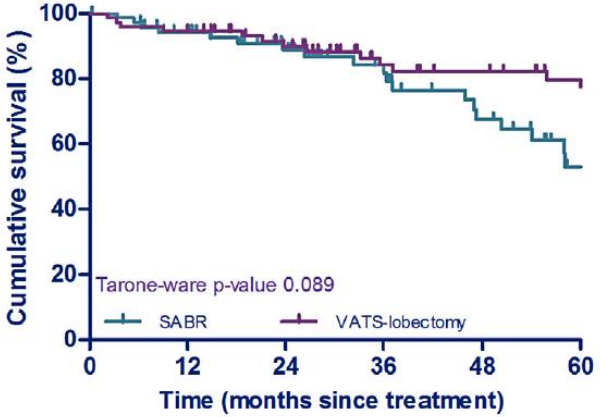
Comparison of clinical outcome of stage I non-small cell lung cancer treated surgically or with stereotactic radiotherapy: Results from propensity score analysis

Sahar Mokhles[a,*], Naomi Verstegen[b], Alex P.W.M. Maat[a], Özcan Birim[a], Ad J.J.C. Bogers[a], M. Mostafa Mokhles[a], Frank J. Lagerwaard[b], Suresh Senan[b], Johanna J.M. Takkenberg[a]

Lung Cancer 87 (2015) 283–289

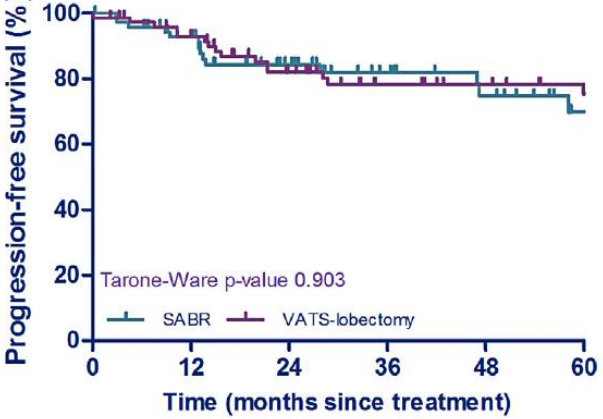
Methods: We selected 577 patients, 96 VATS or open lobectomy were treated at Erasmus University Medical Center Rotterdam and 481 SABR patients were treated at VU University Medical Center Amsterdam with clinical stage I NSCLC.
Results: Matching of patients according to propensity score resulted in a cohort that consisted of 73 patients in the surgery group and of 73 patients in the SABR group. Median follow-up in the surgery and SABR group was 49 months and 28 months, respectively. Overall survival of patients who underwent surgery was 95% and 80% at 12 and 60 months, respectively. For the SABR group this was 94% at 12 months and 53% at 60 months. No statistical significant difference ($p = 0.089$) in survival was found between these groups.
Conclusions: In this study we found no significant differences in overall survival in propensity matched patients diagnosed with stage I NSCLC treated either surgically or with SABR. After 3 years there seems to be a trend toward improved survival in patients who were treated surgically.

a



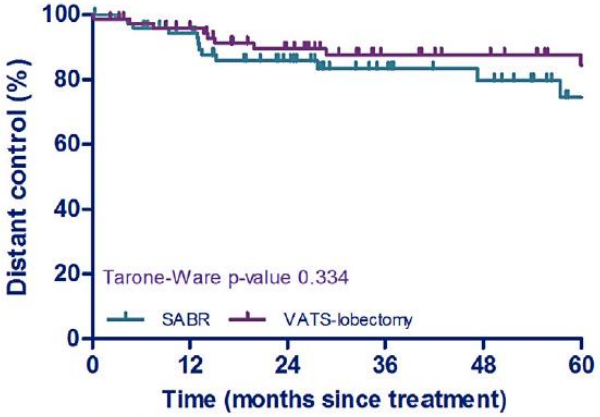
#Patients at risk					
SABR	62	46	34	24	13
VATS-lobectomy	70	58	42	38	32

b



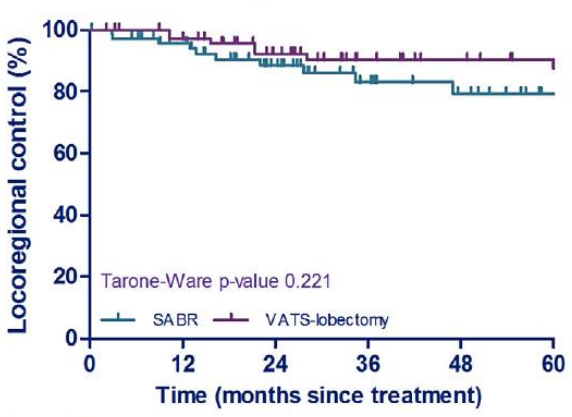
#Patients at risk					
SABR	61	42	29	22	13
VATS-lobectomy	67	50	38	34	29

c



#Patients at risk					
SABR	61	42	29	23	13
VATS-lobectomy	66	54	40	36	29

d



#Patients at risk					
SABR	61	43	28	21	13
VATS-lobectomy	69	54	41	36	32

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Better outcome for surgery after 3 years:

- optimal lymph node staging: adjuvant therapy
- still some differences between the two groups:
  matching was done with only a limited number of variables
  (i.e., staging procedure not included as covariate)
- respiratory failure over time (RILI)
- unable to provide CSS rates

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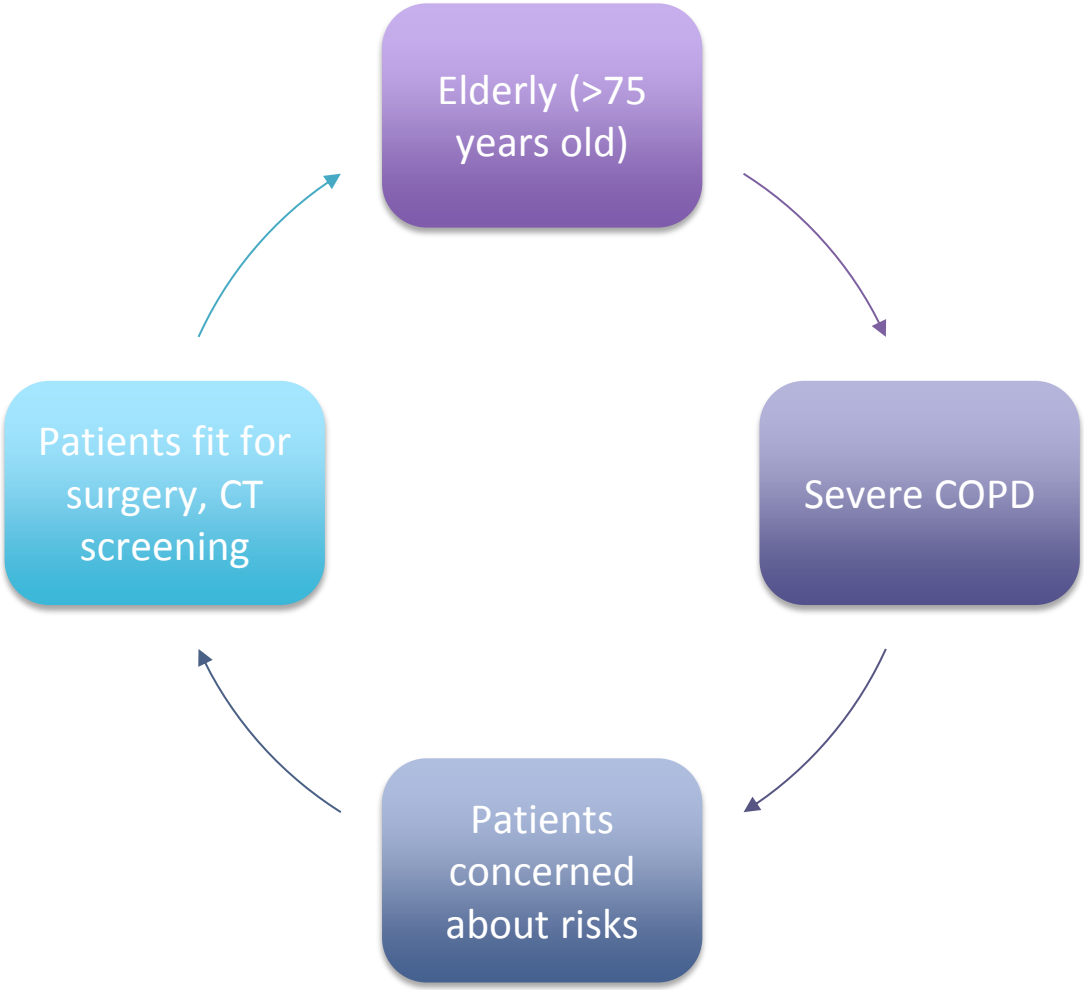
Treatment of early-stage lung cancer detected by screening: surgery or stereotactic ablative radiotherapy?

Suresh Senan, Marinus A Paul, Frank J Lagerwaard

Lancet Oncol 2013; 14: e270–74



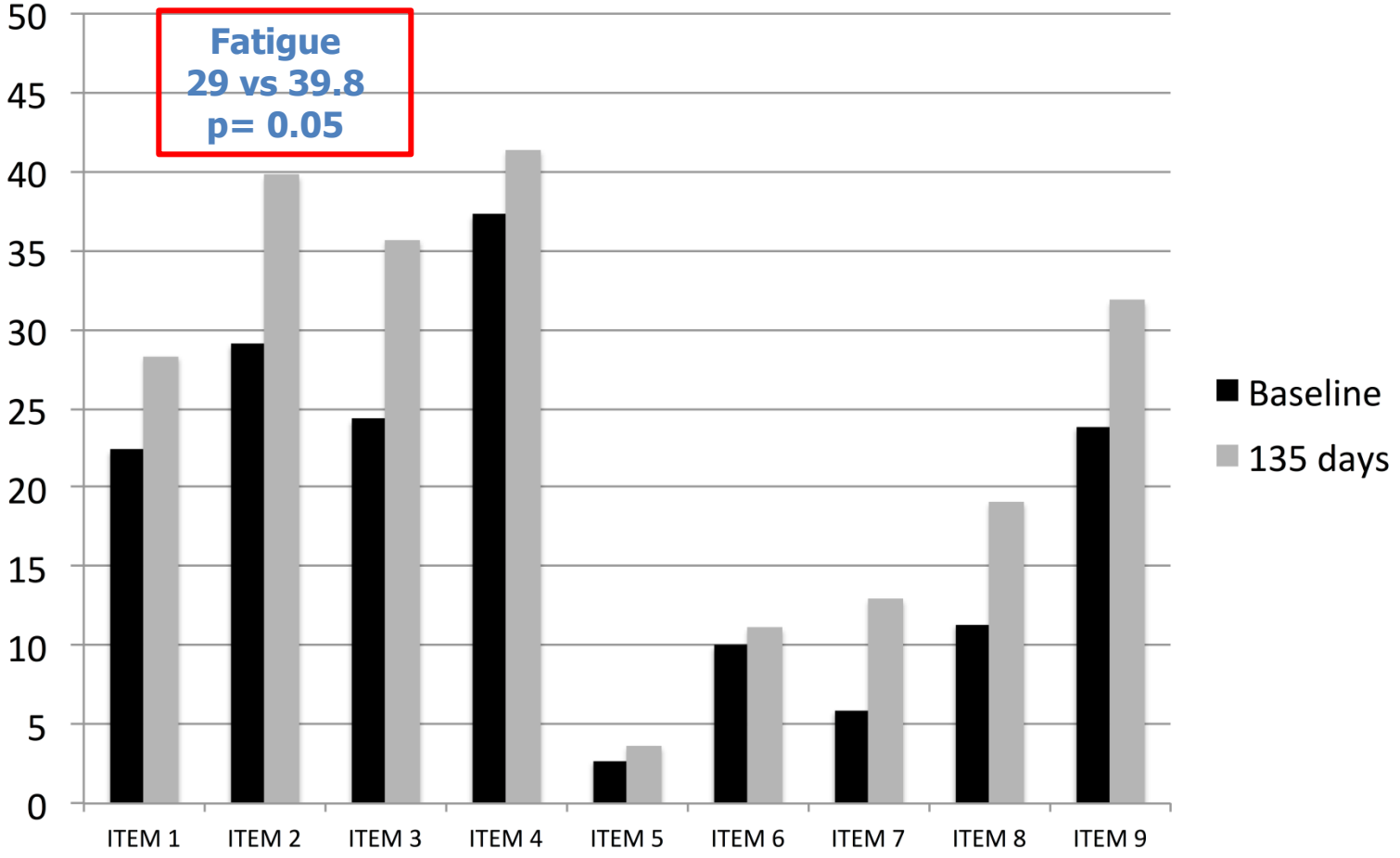
Surgery or SABR: weighing the arguments

Surgery or SABR: role of the patient in decision making

Survivorship following SABR

- QoL:
  - minimal clinically meaningful changes in pulmonary function and QoL

Quality of life



- Lung Cancer Symptom Scale (LCSS)
- Worsening of the item 2 "Fatigue" (mean basal value=29, mean value at T_{135}=39.8, p = 0.05)
- Non-significant changes for other items

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Survivorship following SABR

- Second primary lung cancer (SPLC):
  - risk of developing a SPLC at a rate of approximately 3% per year (smoking cessation!)

A Brief Report on Outcomes of Stereotactic Ablative Radiotherapy for a Second Primary Lung Cancer: Evidence in Support of Routine CT Surveillance

Gwendolyn H.M.J. Griffioen, MD, Frank J. Lagerwaard, MD, PhD, Cornelis J.A. Haasbeek, MD, PhD, Ben J. Slotman, MD, PhD, and Suresh Senan MRCP, FRCR, PhD

(*J Thorac Oncol.* 2014;9: 1222–1225)

TABLE 1. Patient, Tumor, and Treatment Characteristics (n = 107)

Characteristics	n (%) or Median (Range)
Male gender	73 (68%)
Age at SPLC (years)	72 (50–90)
Treatment interval (months)	48 (6–349)
COPD	85 (79.4%)
Charlson Comorbidity Index	3 (0–10)
WHO Performance Score (PS)	1 (0–3)
Stage initial lung cancer (7th TNM)	
Stage I	67 (62.6%)
Stage II	18 (16.8%)
Stage III	17 (15.9%)
Stage IV	3 (2.8%)
Unknown	2 (1.9%)
Treatment initial lung cancer	
Lobectomy/bilobectomy/trimodality	78 (72.9%)
Pneumonectomy	17 (15.9%)
Wedge/segmentectomy	3 (2.8%)
CRT	7 (6.5%)
Palliative (chemo or RT)	2 (1.9%)

Metachronous second primary lung cancer (SPLC)

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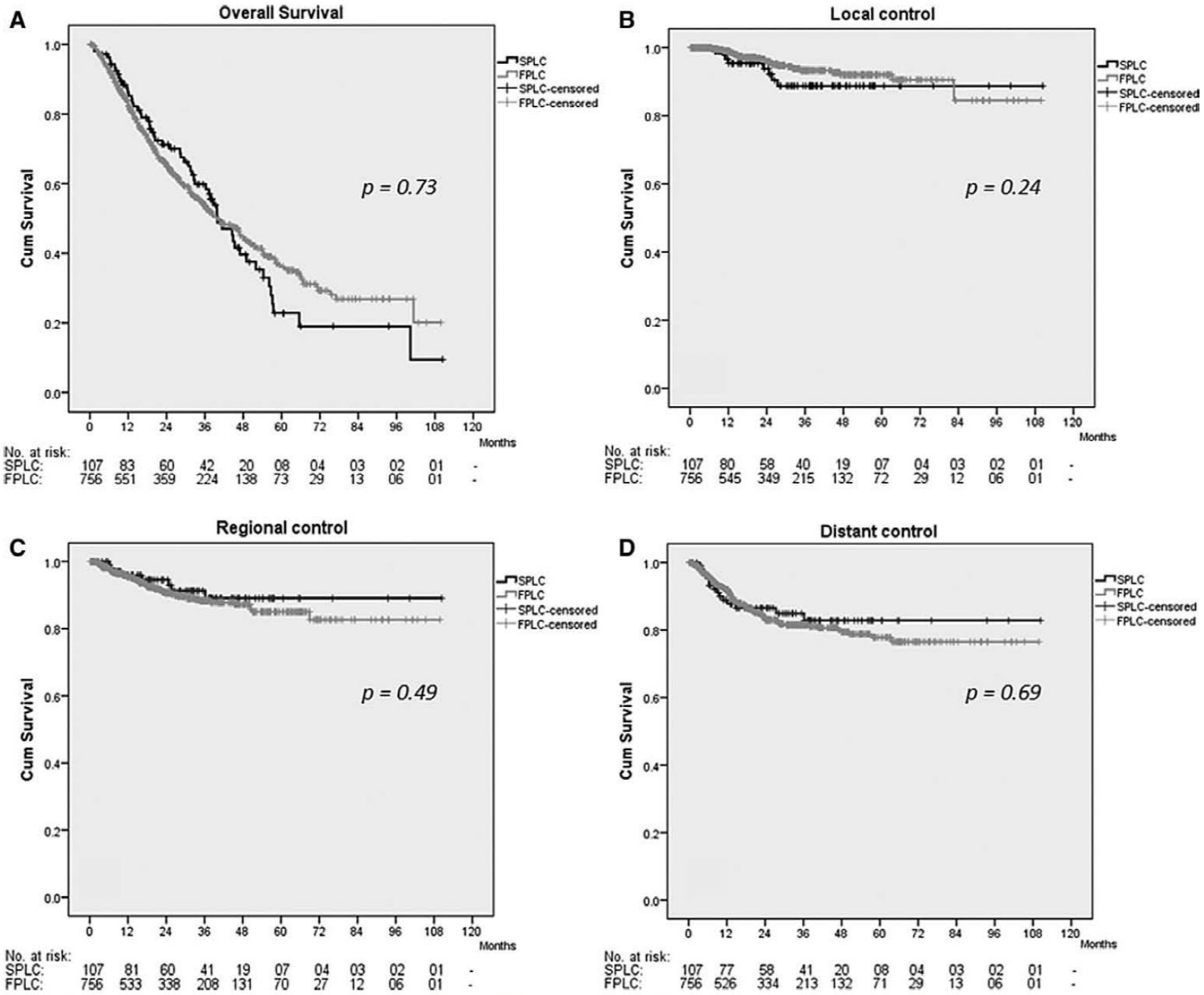


FIGURE 2. Kaplan-Meier curves comparing (*A*) overall survival and (*B*) local, (*C*) regional, and (*D*) distant control rates between patients treated with stereotactic ablative radiotherapy for a "first" primary lung cancer (FPLC; gray line, $n = 756$) and a metachronous second primary lung cancer (SPLC; black line, $n = 107$)

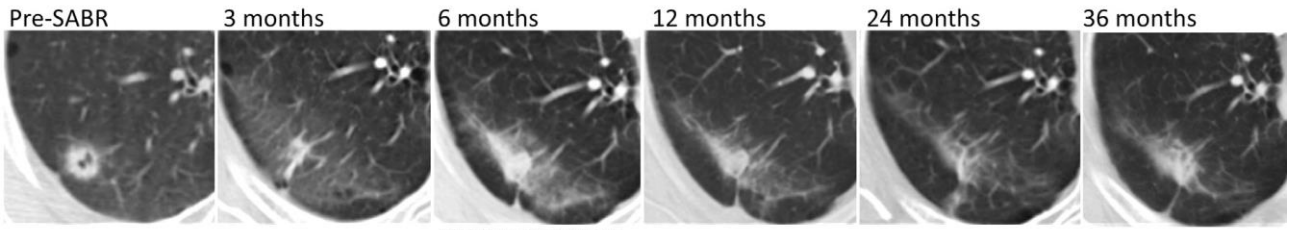
Survivorship following SABR

- Distinguishing fibrosis versus recurrence:
  - benign CT changes that mimic recurrence
  - high-risk radiological features on serial CT scan
  - SUV_{max} value above 5 highly suggestive of relapse

Fibrosis or recurrence after SABR?

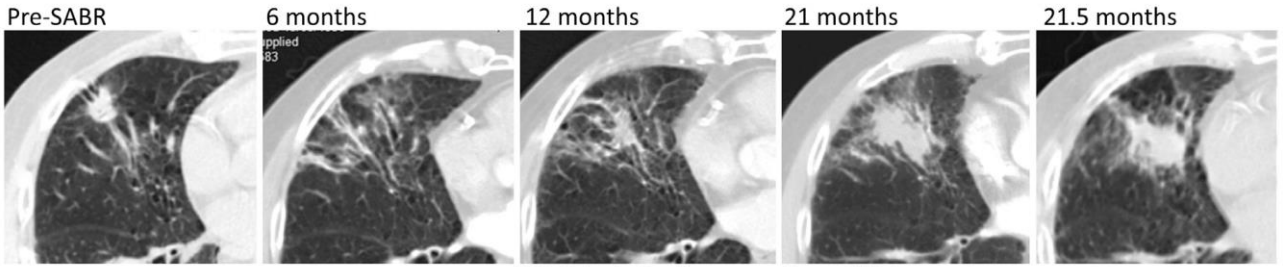
High-risk feature	Sensitivity (%)	Specificity (%)
Enlarging opacity	92	67
Sequential enlargement	67	100
Enlargement after 12 months	100	83
Bulging margin	83	83
Linear margin disappearance	42	100
Loss air bronchogram	67	96
Cranio-caudal growth of ≥5 mm and ≥20%	92	83

A. No Recurrence



HRF: Enlarging Opacity

B. Recurrence



HRFs: Enlarging Opacity
Craniocaudal Growth

Sequential Enlargement
Enlargement after 12 months
Linear Margin Disappearance
Bulging Margin

Loss of Air Bronchogram

Huang K al, Radiother Oncol 2014

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Predicting survival after SABR in ES-NSCLC

- Patient factors:
  - Clinical (age, comorbidities, ILD, Charlson Index)
  - Risk of SPLC (smoking)

- Tumor factors:
  - Tumor size
  - Imaging-based biomarkers (SUV_{max})
  - Mediastinal node staging (CT, CT-PET, EBUS-EUS)

- Radiation factors:
  - Dose
  - Planning issues

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